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# Impact of physical exercise on memory and learning in healthy older women: a quasi-experimental study

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## Abstract

**Purpose** The population of people over the age of 65 is currently growing thanks to social and health policies. It presents an increase in age-related diseases due to a series of morphological and physiological changes in these population groups. We aimed to study the effect of a physical exercise program on memory and learning.

**Methods** A quasi-experimental pilot study carried out with a sample of 73 healthy female subjects who were divided into two groups: an intervention group and a control group. Both groups underwent a neuropsychological evaluation before and after the intervention.

**Results** Subjects in the intervention group performed physical exercise 3 times a week, 50 min each session. The subjects in the control group did not perform any type of physical exercise and completed their daily life activities. The intervention group improvement in cognitive functions after the intervention and obtained higher scores against the control group.

**Conclusion** Regular physical exercise improves global cognitive function, visuoconstructive capacity, and memory functions.

**Keywords** Aged, Aging, Exercise, Cognition, Elderly

## Introduction

The current global demographic trends reveal a noteworthy shift in age distribution, with 1 in 11 individuals worldwide now surpassing the age of 65. Projections for the year 2050 anticipate a substantial increase, indicating that 1 in 6 people will fall into this age bracket, constituting 16% of the world's population. This aging demographic is accompanied by morphological and physiological transformations. Notably, an estimated 47 million people worldwide are currently living with dementia, with projections soaring to 74.7 million in 2030 and a staggering 131.5 million by 2050 [1].

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The impact of age-related cognitive changes is profound due to its prevalence and consequential functional implications. Among older adults, a common concern is the alteration in cognitive functions. Researchers such as Clemente and Nilson [2–4] have identified a significant decline in episodic memory coupled with a gradual loss of visual working memory [5, 6]. The age-related deterioration in cognitive function is characterized by compromised neuronal plasticity, reduced neurogenesis, and neuronal death [7]. Moreover, substances like tobacco and alcohol may exert a detrimental influence on neurogenesis decline [8, 9].

A recent survey, EDADES [10] highlights that women over 65 years old exhibit lower tobacco and alcohol consumption compared to men. This observation may offer insight into why women tend to demonstrate better cognitive function than men in advanced age. Beyond cognitive decline, aging is intricately linked to a progressive reduction in physical capacity [11]. The physical state of the elderly is commonly categorized as vulnerable, with associated poor health outcomes. Consequently, frailty emerges as a well-defined state of heightened physical vulnerability [12]. Frailty is described as an age-associated biological syndrome marked by a decline in biological functional reserve and physical fitness resistance to stressors. This results in a cumulative decline in multiple physiological functions and an increased susceptibility to adverse health outcomes such as falls, hospitalizations, disabilities, and even mortality [13, 14]. Significantly, there exists a close interconnection between cognitive impairment and physical frailty, both being complex aging syndromes often involving more than one physiological system [15].

Based on the results of multiple studies, we can affirm that physical exercise is essential to prevent of chronic diseases, frailty and cognitive impairment [16–21], therefore, it should be an essential tool in public health [22]. There are two main types of exercise: Aerobic exercise (fast walking), to improve cardiovascular health; and resistance training (weight training), which increases muscle mass and strength. Each type of training has its distinct physiology and benefits [23] such as benefits in neurogenesis, neuronal survival and synaptic plasticity mediated through brain-derived neurotrophic factor (BDNF) and other neurotrophins [24, 25].

Regarding aerobic exercise, several meta-analyses in adults above 55 years old have found aerobic effects in the areas of attention, processing speed, executive function (EF), memory, and working memory [26–28], with some suggesting strongest effects for EF [28] but there have also been negative conclusions [29, 30]. On the other hand, increasing evidence indicates that resistance training may also improve cognitive function [31–34]. Nevertheless, these findings were not confirmed in other

studies [35, 36], suggesting that more evidence is still needed. This controversy regarding the impact of aerobic and resistance training could be due to the great heterogeneity of the times used, the weekly sessions, the type of exercise or the sample used. None of the above studies have assessed cognitive domains specifically. In addition, the interventions performed were either aerobic exercise programs or strength exercise programs, none of them proposed a mixed exercise program.

Therefore, the novelty of our study lies in the implementation of a mixed physical exercise program (aerobic exercise + strength training), based on the recommendations of the World Health Organization [37] regarding the type of physical exercise and the duration of sessions for adults over 65 years old. Thus, our study aimed was to examine the effect of a physical exercise program (Geriatric Revitalization Program) on memory and learning in a sample of subjects over 65 years old.

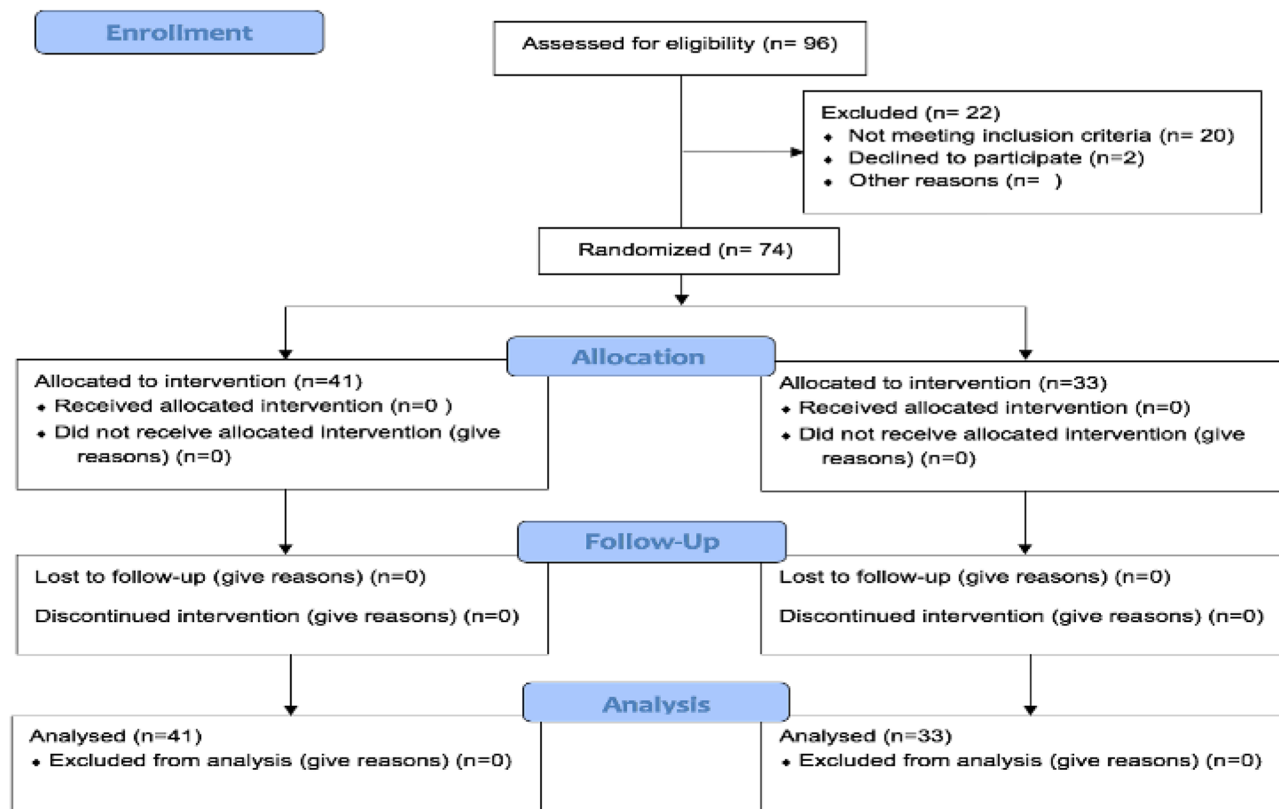
## Methods

We present a quasi-interventional pilot study with 73 participants. The sample was selected from the Geriatric Revitalization Program. A random cluster sampling has been used to select eight neighborhood associations out of the twenty that participate in the Geriatric Revitalization Program (GRP), achieving a total of 96 participants who met the requirements to participate in the study. Randomization was performed employing a computer software (xMaR, open-source free software for online minimization and randomization for clinical trials).

A total of 22 subjects dropped out of the study for different reasons (Two people finally declined to participate, 20 did not meet the inclusion criteria once reviewed), and the remaining 74 participants were divided into two groups: the intervention group and the control group. The flow chart is detailed in Fig. 1. The intervention group followed the regular physical exercise program of six months duration, three days a week for a maximum of 50 min in each session, adding a total of 150 min of physical exercise a week as indicated by the guidelines of the World Health Organization [37]. None of the subjects in this group had previously performed physical exercise programs. The control group was not part of the Program and carried out their activities of daily living as usual and none of them practiced physical exercise. Once month participants were contacted via telephone to make sure they did not engage in physical activity. In these phone calls, they were asked if they had recently had any health problems, if they had exercised on their own, or if they had joined a physical exercise program.

## Participation criteria

The inclusion criteria for the intervention group were the following: Female sex, aged between 65 and 80 years



**Fig. 1** Flow Chart

old, being a participant in the GRP and knowing how to read and write. The exclusion criteria were refusal to sign the informed consent form and failure to meet any of the inclusion criteria mentioned above. In addition, the presence of diabetes, neurodegenerative disorders, cardiovascular diseases (hypertension), psychiatric disorders, sensory defects in the visual field, and the taking of drugs for the pathologies referred to above and the presence of a family history of cognitive impairment would be relevant to exclude a person from the study. The inclusion criteria for the participants assigned to the control group were the same as those above, except the individuals did not take part in the Geriatric Revitalization Program or any other type of physical exercise program or activity. Therefore, the sample consisted of healthy women, with the concept of healthy being understood as “not suffering from any manifest diagnosed medical condition that requires medication prescribed continuously”.

#### Main variables

1. Global Cognition (orientation to time and place, attention/concentration, short-term memory, language skills, visuospatial abilities — visual and spatial relationships between objects and ability

to understand and follow instructions) measured by tests Mini Cognitive Exam (MCE): This is the most widely used brief cognitive test and with the most studies carried out. The author of this test is Folstein, who developed this screening test in 1975. There are multiple versions in Spanish. It is a screening test commonly used to check for cognitive impairment (problems with thinking, communication, understanding, and memory) The maximum score is 30 points, one point is given each time the subject answers correctly, and 0 points when he does it incorrectly. The cut-off point is 24 points for people with schooling < 21 for people with low education and < 18 points for illiterates. The test takes approximately 10 min [38].

2. Short- term memory measured by Benton’s Visual Retention Test (BVRT): Assesses visuospatial processing, visual memory, and visuoconstructive skills, and visual and verbal conceptualization. It is also sensitive to cognitive alterations associated with normal aging. The test consists of ten sheets that contain a set of visual stimuli of increasing difficulty that the subject must reproduce, either from memory or by copying them. There are three parallel forms (C, D, and E) and four possible application modes. The interpretation of the test is based on an

evaluation of the number of correct reproductions and the number of errors made, thus allowing both a quantitative and qualitative analysis of the results [39].

3. Verbal memory measured by Rey’s Audio Verbal Learning Test (RAVLT): Allows to assess the extent of immediate memory, provides a learning curve, reveals biases towards retroactive and proactive interference patterns, assesses existing confabulation in memory tasks, and measures retention after a mediating activity. The list consists of 15 unrelated words. A first reading of the list is made at the rate of one word per second and the subject is asked to try to remember as many as possible. When the examinee begins to say the words he remembers, the order in which he says them is noted to identify the memory pattern. Then a second reading of the list is made and the subject is reminded to say as many as they remember, including those said the first time, also recording their responses. The same procedure is then carried out for the third, fourth, and fifth time. The score awarded for each trial is the total number of words remembered. The total score is the sum of the hits of the 5 trials. Thus, we can obtain the so-called Learning Curve, which is the difference between the successes of the fifth and the first trial. After 30 min, the Delayed Recall test is carried out, in which they were asked to say the words that they still remember, and also proceeding to write down their answers [40].

The three tests used to assess the neuropsychological capacity of patients have been converted and validated in the Spanish population [38, 41, 42].

In this study, the requirements of the Ethics Committee of the University of Salamanca and the International Code of Medical Ethics of the World Medical Association for experimentation in humans (Declaration of Helsinki) were met. Protocol nº 381.

**Procedures, measures, and statistical analysis**

The sociodemographic variables measured were: age, years of schooling, marital status, and education level

(Table 1) Procedures, Measures, and Statistical Analysis. All the participants were informed in advance about the purposes of the research, and all gave their written informed consent. The intervention group followed the regular physical exercise program of six months’ duration, three days a week for a maximum of 50 min in each session, adding an overall 150 min of physical exercise a week as indicated by the guidelines of the World Health Organization [37]. None of the subjects in this group had previously performed physical exercise programs.

The control group was not part of the Program and carried out their activities of daily living as usual and none of them practiced physical exercise. Once a month participants were contacted via telephone to make sure they did not engage in physical activity. All neuropsychological tests were performed individually in October (time 1) and May (time 2).

The neuropsychological evaluations and the correction of said tests were carried out by people outside the research to avoid any type of bias. Furthermore, they were blinded as they did not know to which group each person in the sample belonged to dynamic mobility warm-up for 4–5 min, with dynamic and static stretching exercises; Stretching of the main muscle groups after exercise: chest, dorsum, biceps, triceps, deltoid, shoulders, quadriceps, gluteus, biceps femoral, rectus femoris, gastrocnemius, abdominal. Aerobic exercises with the available materials (sticks, balls, weights, rings). Muscle strength and endurance training; Hydration and close monitoring of the participants; Stretching of the main muscle groups. Exercise intensity was measured via the Borg scale [43] by indicating to subjects that they should be in a score between 3 and 6 of perceived exertion. All sessions were directed and supervised by qualified physiotherapists. A typical session of the GRP is shown in the supplementary material. Once the physical exercise program was completed, a second neuropsychological evaluation was carried out in both groups. The data of the quantitative variables were analyzed using means, standard deviations, medians, and interquartile ranges. Qualitative variables were described by counts and percentages were analyzed. The Kolmogorov-Smirnov test with the Lilliefors correction and the boxplot test were used to evaluate the assumption of normality. Levene’s test was used

**Table 1** Descriptive statistics by age group, years of schooling, marital status and educational level

Sociodemographic Variables	Control Group Mean (SD)/Counts			Intervention Group Mean (SD)/Counts			p-value		
Age	71,21 (±4,32)			72,70 (±4,13)			0,138		
Years of schooling	8,42 (±2,56)			8,18 (±1,55)			0,576		
Marital Status	Single	Married	Widower	Single	Married	Widower	0,238		
	9 (27,3%)	19 (57,6%)	5 (15,2%)	6 (14,6%)	30 (73,2%)	5 (12,25%)			
Educational level	Primary	G.B.E	Mid-level	Higher	Primary	G.B.E	Mid-level	Higher	0,201
	20 (61%)	1 (3%)	8 (24,2%)	4 (12,1%)	16 (39%)	4 (9,8%)	20 (48,8%)	1 (2,4%)	

SD Standard Deviation, G.B.E General Basic Education

to evaluate the equality of variances of the populations. The t-test was used to analyze differences between intervention groups on quantitative socio-demographic variables when these variables follow normal distributions. The nonparametric Mann-Whitney U test was used in the case of non-normal distribution. Chi-square test was used to analyze the association between intervention groups and qualitative socio-demographic variables.

The two-factor ANOVA was used to analyze the change over time (within-subjects factor: pre-post time) between the intervention groups (between-subjects factor: intervention-control) in each test. When the tests were defined by subscales, the three-way ANOVA was used: two within-subject's factors (pre-post time and subscales) and between-subjects factors (intervention and control groups). The Bonferroni correction was used for post hoc analysis in ANOVA. The magnitude of the change over time between groups for each dimension was measured by Cohen's standardized mean difference ( $d$ ) and its standard error (SE). Cohen provides rough guidelines to evaluate this effect size:  $d = 0,2$  (small effect),  $d = 0,5$  (medium effect), and  $d = 0,8$  (large effect). Statistical significance is declared when the  $p$ -value is less than 0,05. The data were analyzed with the IBM-SPSS version 26 (Armonk, New York, USA).

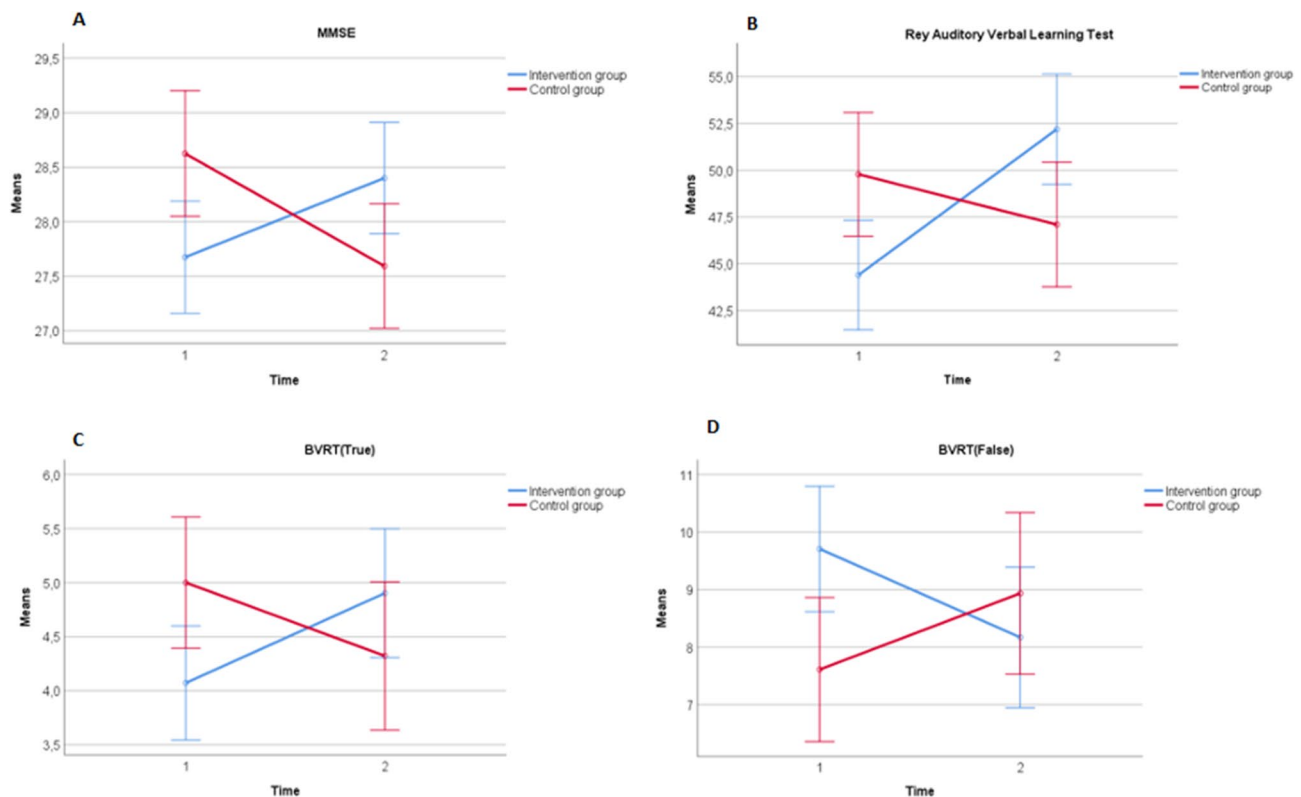
## Results

Age shows symmetric distribution in both groups. No significant differences were found between the intervention group regarding age, year of schooling and marital status, and educational level (Table 1). Regarding the Mini Cognitive Exam, the intervention period interaction was statistically significant ( $F = 17,68$ ;  $df_1 = 1$ ,  $df_2 = 71$ ;  $p$  value  $< 0,001$ ), that is, the change that occurs in period 2 regarding period 1 in the intervention group is different from the control group, as described in Fig. 2A.

The size of the effect of change between intervention group in this instrument is  $d = -1,00$  ( $SE = 0,25$ ) (Table 2).

The two-way interaction was relevant for the overall RAVLT scale as expected ( $F = 17,68$ ;  $df_1 = 1$ ,  $df_2 = 71$ ;  $p$ -value  $< 0.0001$ ) (Table 3). Figure 2B shows the control group mean is higher in time 1 than in time 2 while this change is opposite in the intervention group where the mean is lower in time 1 than in time 2. Therefore, the changes are different in the control group than in the intervention group. The effect size is  $d = -1.547$  ( $ES = 0.268$ ).

The three-way analysis of variance shows a statistically significant interaction between pre-post time, BVRT scale, and intervention group measurements ( $F = 16,499$ ;  $df_1 = 1, df_2 = 71$ ;  $p$  value  $< 0.001$ ). This means that the



**Fig. 2** Shows the interactions of both groups in each of the cognitive tests used. **A:** Interaction of both groups in the MCE; **B:** Interaction between both groups and times on the global scale of the Rey Auditory Verbal Learning Test; **C:** Interaction of both groups in the BVRT (True); **D:** Interaction of both groups in the BVRT (False). Note the time factor is a repeated measure factor (within-subjects factor)

**Table 2** Descriptive statistics for the control group and intervention in two experimental times for neuropsychologic evaluation

Variables	Time 1		Time 2	
	Control	Intervention	Control	Intervention
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
Global Cognition				
MCE	28,64 (± 1,50)	27,67 (± 1,72)	27,64 (± 1,75)	28,40 (± 1,50)
Short- term memory				
Rey Auditory Verbal Learning Test				
RAVLT 1	4,58 (± 1,70)	4,90 (± 1,59)	5,03 (± 2,023)	5,80 (± 1,60)
RAVLT 2	7,39 (± 1,66)	6,46 (± 1,60)	6,91 (± 2,376)	8,12 (± 1,79)
RAVLT 3	9,15 (± 1,92)	8,00 (± 2,17)	8,88 (± 1,949)	9,20 (± 20,15)
RAVLT 4	10,15 (± 1,96)	8,71 (± 1,94)	9,36 (± 1,817)	9,93 (± 1,94)
RAVLT 5	10,45 (± 1,79)	9,12 (± 2,22)	10,00 (± 1,969)	10,41 (± 1,94)
RAVLT 6	8,39 (± 2,36)	7,27 (± 2,53)	7,91 (± 2,532)	8,63 (± 2,78)
RAVLT total	50,18 (± 9,09)	44,39 (± 9,76)	47,76 (± 9,04)	52,20 (± 10,25)
Visual Memory				
Benton Visual Retention Test				
BVRT True	4,97 (± 1,82)	4,07 (± 1,57)	4,34 (± 1,96)	4,90 (± 1,86)
BVRT False	7,72 (± 3,42)	9,71 (± 3,55)	8,97 (± 3,91)	8,17 (± 3,89)

SD Standard Deviation. MCE Mini Cognitive Exam, RAVLT Rey Auditory Verbal Learning Test, BVRT Benton Visual Retention Test

\*Bonferroni correction

**Table 3** Change in contrast for each variable

	Mean Difference	SE	CI95%		p-value*
			Lower limit	Upper limit	
RAVLT 1	-0,45	0,45	-1,34	0,44	1
RAVLT 2	-2,14	0,45	-3,04	-1,25	<0,001
RAVLT 3	-1,47	0,39	-2,24	-0,69	0,002
RAVLT 4	-2,01	0,43	-2,87	-1,14	<0,001
RAVLT 5	-1,75	0,42	-2,60	-0,90	<0,001
RAVLT 6	-1,85	0,49	-2,83	-0,87	0,002

RAVLT Rey Auditory Verbal Learning Test, SE Standard error of mean differences

\*Bonferroni correction

change over time for the intervention group is not the same for each subscale.

Fig. 2C and D analyze the change over time for the intervention group in each variable. In period 1, the control group gets more hits, but after the time of intervention, the situation is reversed. The same crossover is reproduced with the errors, the control group obtains fewer errors than the intervention group in period 1, and this situation is reversed in period 2. If we compare

the change over time between the interventions group, we can observe statistically significant differences in both comparisons: BVRT correct answers ( $F = 13,15$ ;  $df1 = 1, df2 = 71$ ;  $p$  value = 0.001;  $d = -0.88$  ( $SE = 0.25$ )) and BVRT errors answers ( $F = 15,24$ ;  $df1 = 1, df2 = 71$ ;  $p$  value < 0.001;  $d = 0.94$  ( $SE = 0.25$ )).

### Discussion

In this research, we try to show the effects of a physical exercise program on aging, specifically on cognitive functions such as visuospatial processing, visual memory, immediate verbal memory, and visuoconstructive capacities, in healthy subjects over 65. The scores obtained by the subjects (of both groups) in the Mini Cognitive Exam in the first measurement show the absence of cognitive impairment. The fact that our subjects did not show cognitive impairment [38] indicates that the results obtained are highly consistent and reliable. The MCE results show a positive interaction in the scores obtained by both groups in both measurements, that is, the subjects in the intervention group obtained a significant improvement in test scores after the PRG. Best and his colleagues [44] obtained identical results in a sample of 199 subjects after a 12-month program. Lin [45] obtained similar results with a sample of 2,074 subjects divided into an intervention group (1,372) who performed physical exercise and a control group (702) who did not exercise. The intervention group obtained better cognitive performance in the MCE compared to the control group. Furthermore, the intervention group showed an improvement in test scores after the intervention. This was also the case for the subjects in our study.

However, a recent randomized clinical trial studying the defects of mindfulness training and exercise on cognitive function in older adults found no significant difference in improving episodic memory or executive function after 6 months. Unlike our work, they did it in older adults with subjective cognitive concerns, perhaps for this reason, their findings do not support the use of these interventions and in our healthy population it is effective [46].

On the other hand, the effect of GRP on visual memory and viscoconstructive skills provides an improvement in these variables. The intervention group showed a greater number of errors and a lower number of correct answers at the beginning of the Program concerning the control group. However, after the intervention, the trend of these scores is reversed, that is, these subjects obtained a higher number of correct answers and a lower number of errors. These results are in line with those obtained in previous studies [21] in a sample made up of healthy men and women over 65. Likewise, a recent meta-analysis [26] supports our results. This meta-analysis includes 36 randomized clinical trials in which it is concluded that

physical exercise can play an essential role in cognition, specifically in the variables that were studied through the BVRT. Also, these authors [47] reported that older adults who showed a higher level of physical fitness out of a total of 877 subjects, showed better scores in visual memory and visuoconstructive skills. Vidoni and colleagues [48] studied the relationship between the amount of aerobic exercise training and cognitive performance, particularly visuospatial processing. A longitudinal study [49] with a follow-up of 8 years indicates that cognitive functions such as visuoconstructive abilities measured through the BVRT are better preserved in those who perform moderate physical activity regularly in their daily lives. However, cognitive functions deteriorate more rapidly in those who do not engage in exercise. Nielson et al. [50] state that the improvement in visual memory is produced by an increase in muscle tension achieved through physical exercise.

Regarding short-term memory, we again observed a significant interaction between the scores obtained by both groups. Therefore, the practice of regular physical exercise has a positive effect on short-term memory after the intervention and provides a parabolic shape of the learning curve, showing significant retention even after mediating activity. These results are consistent with the conclusions of the authors of the aforementioned meta-analysis [26] suggesting that regular exercise significantly improves short-term memory in healthy older adults [51, 52]. Furthermore, a recent meta-analysis [53] including 12 randomized controlled trials concluded that exercise leads to an improvement in short term memory in healthy older people. Another meta-analysis [54] that only studied the effect of resistance training concluded again that this type of physical exercise leads to improvements in short-term memory and immediate memory in healthy older adults. A recent randomized controlled trial involving 31 participants aged 61 to 78 years [53] demonstrated that a physical conditioning program can enhance immediate memory, with participants showing improved short-term memory performance. This aligns with the findings of our study, though it's noteworthy that the referenced trial was conducted over a period of 3 months, whereas our research extended to 6 months, as reported by Tran T et al. [54].

The relationship between physical frailty in the elderly and cognitive impairment is complex and bidirectional. Physical frailty is recognized as a precursor to mild cognitive impairment, which in turn can exacerbate physical frailty. Despite this recognized interconnection, the precise nature of the relationship between frailty and cognitive deficits remains somewhat elusive, with studies [55–57] yet to fully elucidate this association. In fact, frailty in the elderly is composed of physical, cognitive, and social aspects that interact and influence each other.

Not all studies show a benefit of physical exercise on cognitive processing. Lenze et al. in studying elderly with subjective cognitive concerns subjective cognitive concerns but no demonstrated cognitive impairment found no improvement in their episodic memory and executive function after 6 months of physical exercise. months of physical exercise [46].

#### **Contribute to the state of the art of the topic**

The results obtained from our study reveal a significant impact of the physical exercise program, combining aerobic and strength training, on memory improvement in healthy individuals aged 65 and above. This evidence underscores the crucial relevance of physical exercise as a preventive tool against age-related diseases, which are often associated with memory impairments. The observed enhancements in mnemonic function through the implementation of this program offer a promising outlook for promoting cognitive health in the elderly population. Beyond the direct benefits to memory, these findings support the notion that physical exercise is not only beneficial for physical health but also plays a fundamental role in preserving and strengthening cognitive functions in the aging process. These results reinforce the importance of incorporating comprehensive physical exercise programs as an integral part of public health strategies aimed at enhancing the quality of life and preventing conditions associated with aging.

#### **Limitation**

One of the main limitations of this work could be that the changes induced by exercise could have been influenced by psychosocial factors associated with the social interactions experienced by the participants when exercising in a group since there are studies that claim that people with depression and/or anxiety present lower cognitive performance [50]. Changes in these psychosocial factors could influence scores on cognitive variables. In addition, it was a quasi-experimental pilot study, with intervention sites selected based on their interest in participating in the research. The effects reported here are probably greater than what might be achieved since the training needs to be tested, nevertheless, in a randomized trial with a wider range of sites not involved in its development.

On the other hand, the sample of our study was composed only of women, so the results found should not be generalized to the general population. Finally, the level of education could be a confusing factor and it was impossible to explore its effect on results in this study due to low sample sizes in some categories.

Therefore, further studies with larger and more heterogeneous samples and considering social factors and interactions are needed.

## Conclusion

We can conclude that the subjects who participated in the GRP improved cognitive function after the intervention compared to the control group in visuospatial processing, visual memory, visuoconstructive skills, short-term memory, and a significant increase in short-term retention.

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12877-025-06614-0>.

Supplementary Material 1.

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Not applicable.

## Authors' contributions

Conceptualization JLSG and JLSR.; methodology JMV and RRRHV.; formal analysis, JMV.; investigation, JLSG. and JLSR.; data curation, JMV.; writing—original draft preparation, JLSG.; writing—review and editing, ACR, JMV and PMRM.; supervision, JMV and RJV. All authors have read and agreed to the published version of the manuscript.

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## Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

All methods were carried out in accordance with relevant guidelines and regulations. All experimental protocols were approved by ethics committee of the University of Salamanca/Protocol nº 381. All of the participants were informed in advance about the purposes of the research, and all gave their written informed consent.

### Consent for publication

Not applicable.

### Competing interests

The authors declare no competing interests.

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