Effect of multicomponent exercise in cognitive impairment: A systematic review and meta-analysis

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Abstract

Background: Multicomponent physical exercise is the most recommended type of physical intervention in older adults, however, this effect on cognition is unclear. This study assesses the effect of multicomponent physical exercise on global cognition in people with mild cognitive impairment or dementia.

Methods: Randomized controlled trials published until January 2021 were searched across three electronic databases (PubMed, Scopus, and Cochrane Database). Data about exercises included in the multicomponent intervention (endurance, strength, balance, or flexibility), the inclusion of aerobic exercise, and the change in global cognition were extracted. The effect size was represented as a standardized mean difference. Risk of bias was assessed by the RoB2 tool.

Results: A total of 8 studies were included. The overall effect size suggested an effect of multicomponent exercise on global cognition. However, the subgroup analysis showed an effect only when aerobic exercise was included in the intervention. No effect when mild cognitive impairment and dementia were assessed separately was found.

Conclusion: This study suggests that multicomponent physical exercise could have an effect on global cognition in people with mild cognitive impairment or dementia only when aerobic exercise is included in the intervention. Our results support the inclusion of structured physical exercise programs in the management of people with cognitive impairment.

Background:

In recent decades we are living a paradox, while we have experienced a steady increase in life expectancy, which has been accompanied by an increase in chronic conditions and associated with a high functional cost¹. This functional cost not only brings health consequences, but also a huge socioeconomic impact. Few conditions exemplify this picture as cognitive impairment, a condition that affects almost fifty million people worldwide according to the latest World Health Organization (WHO) report². This report highlights the high importance of implementing an international plan for risk factors education, assessment and management early diagnosis, targeted treatment, caregiver assistance, and dementia-related research. However, although most developed countries have designed and implemented national strategies to reduce the burden of dementia, their impact has been slightly modified^{3,4}.

Currently, there is not enough evidence available for disease-modifying pharmacological treatments⁵, and the benefits of these treatments on cognition are limited^{6,7}. For this reason, non-pharmacological treatments to manage dementia and mild cognitive impairment (MCI) are currently a relevant research topic⁸. Research on physical activity and physical exercise, as part of non-pharmacological interventions, have been of interest not only for their effects on physical performance but also for their effects on cognitive function. Actually, it has been suggested that physical exercise significantly improves cognition in people with MCI or dementia, compared to other non-pharmacological interventions^{9–12}.

Among the effect of different types of physical exercise on the cognition of people with cognitive impairment, some questions remain unanswered, such as the effect of multicomponent physical exercises. This type of exercise includes endurance, strength, balance, and flexibility training¹³, and is the most recommended exercise for older people showing positive effects on functional decline during hospitalization¹⁴, frailty¹⁵, and sarcopenia¹⁶. However, the effects of multicomponent physical exercise on cognitive function are still unclear. Therefore, the aim of this systematic review and meta-analysis is to estimate the effect of multicomponent physical exercise on global cognition in people with MCI or dementia.

Methods:

Protocol and registration:

The protocol of this systematic review was registered at the International Prospective Register of Systematic Reviews (PROSPERO), with the register identification CRD42020184660. In addition, the protocol was approved by the Ethics Committee of the Pontificia Universidad Javeriana and the Hospital Universitario San Ignacio.

Search strategy:

A search was performed on MEDLINE (via PubMed), Scopus, and Cochrane Database up to January 2021. The search was aimed to identify published randomized controlled trials assessing the effect of multicomponent physical exercise on global cognition in people with dementia and MCI. We examined the reference list of eligible studies to expand the search. The complete MEDLINE search strategy is displayed in Supplementary material (Supplementary Table S1).

Inclusion criteria:

The studies included in this systematic review met the following inclusion criteria: (i) Participants: adult participants with dementia or MCI secondary to either. (ii) Intervention: multicomponent physical exercise defined as an exercise program including endurance, strength, balance, or flexibility¹³. We included studies developing any intervention program that included at least two of the above-mentioned exercises. We included studies with and without aerobic exercise as part of the intervention. Studies that included cognitive activities in addition to intervention were excluded. (iii) Outcome: global cognition measured by any validated neuropsychological test. (iv) Control: any kind of control was included except for physical activity programs. (v) Type of study: randomized controlled trials. We included in this review only studies in English and Spanish.

Study identification and data extraction:

After defining the search strategy, all records were imported into the reference management system (Mendely, desktop version 1.19.4) to exclude duplicate records. Two authors (LVS and CAB) independently performed the search literature and data extraction, with the intervention of a third author in case of disagreement (ICR). The following data were extracted from the selected studies using an ad-hoc form: author, publication year, country, sample size, female proportion, mean age in control and intervention group, type of cognitive impairment, types of physical exercises included in the intervention, length of the intervention (weeks), number of sessions per week, duration per session (minutes), type of control group, cognitive assessment tool and effect on global cognition.

Risk of bias:

The risk of bias was assessed independently by two authors using the revised Cochrane risk-of-bias tool for randomized trials (RoB2)¹⁷. The RoB2 included assessment of six domains: randomization process, derivation for intended interventions, missing outcome data, measurement of the outcome, selection of the reported results, and overall results. Each domain was rated as low, moderate, and high risk of bias. To report on the risk of bias, a graphical representation was used.

Data analysis:

The effect size (ES) and 95% confidence intervals (CIs) for the effect of physical exercise programs on global cognition were calculated using the Cohen's d index. A pooled ES was estimated using a random-effects model based on the Der Simonian and Laird method¹⁸. We consider the ES classified as proposed by Cohen et al¹⁹; small effect (0.2), moderate effect (0.5), and large effect (0.8). Inconsistence across studies was assessed using the I^2 statistic²⁰, whose values were considered as follows: not important (0–40%), moderate (30–60%), substantial (50–90%), and considerable (75–100%). Moreover, the corresponding p value were also considered. To determine the size and clinical relevance of heterogeneity, τ^2 statistic was calculated and interpreted as low when τ^2 was lower than 0.04, moderate when was from 0.04 to 0.14 and as substantial when it was from 0.14 to 0.40²¹.

For global cognition measured by using more than one scale, a pooled ES was calculated. Subgroup analyses were conducted considering: i) the inclusion of aerobic exercise in the exercise protocol and ii) the type of cognitive impairment distinguishing between patients with MCI and dementia.

The small study effect was graphically assessed using a funnel plot, additionally, the Egger test was estimated. Finally, the trim-and-fill analysis was used to estimate the number of studies needed to remove publication bias, and to estimate the ES without publication bias. Stata/IC software, version 16.1 for Windows was used for statistical analysis.

Results:

Study identification:

A total of 2789 records were found following the search strategy. After removing duplicates, and reviewing the title and abstract, 31 relevant papers were chosen for full reading. Finally, only 8 articles met the inclusion criteria (Figure 1). The excluded articles and the reason to exclusion are reported in the Supplementary Table S2.

Characteristics of included studies:

Eight studies assessing the effect of multicomponent physical exercise on global cognition in people with dementia and MCI^{22–29} were included in the review. The studies included 367 participants from seven countries: France^{24,26}, Spain²², Brazil²³, Croatia²⁵, Korea²⁷, United States²⁸, and Japan²⁹. The mean age was between 77.7 and 77.9 years in the intervention and control group, respectively, and women accounted for 70.3%. Five studies^{23,24,26–28} included only participants with dementia and three with MCI^{22,25,29}.

Regarding multicomponent physical exercise interventions, all studies included at least two types of exercise considered in the definition of multicomponent physical exercise¹³. All studies included balance exercises, four included flexibility exercises^{22,26–28} and one did not include strength training²⁶. Aerobic exercise was part of the intervention in six studies^{22,24,26–29}. The intensity of physical activity was considered low to moderate in three papers^{22,26,29}, moderate in two^{24,28}, and low in one²⁷, additionally, two studies did not report on exercise intensity^{23,25}. The length of the intervention programs was 8 to 52 weeks, including 1 to 7 sessions per week, and 30 to 90 minutes per session.

The Mini-Mental State Examination^{22–24,27,29} was the most widely used cognitive measurement tool, other tools included were Montreal Cognitive Assessment (MoCA)²⁵, Brief Cognitive Screening Battery (BCSB)²³, Rapid Evaluation of Cognitive Function (ERFC)²⁶, Boston Naming Test (BNT)²⁸, Hopkins Verbal Learning Test (HVLT)²⁸, and Alzheimer's Disease Assessment Scale-Cognitive (ADAS-Cog)²⁹. Table 1 summarizes the studies included in the review.

Table 1
Characteristics of the included studies

Author, year and country	Sample size (women %)	Age (mean±SD)	Cognitive impairment type	Physical activity included	Physical activity intensity	Program duration (weeks)	Sessions per week	Session duration (minutes)	Control type	Results (SMD)
Bisbe et al, 2020 Spain	I: 14 (50) C: 17(47.1)	I: 77.2(5.1) C: 72.8(5.6)	aMCI	Aerobic Strength Balance Flexibility	Low to moderate	12	2	60	Choreographed dances	MMSE: 0.23(-0.39, 0.84)
Christofolletti et al, 2008 Brazil	I: 17(70.5) C: 20(70)	I: 72.9(2.3) C: 79.4(2.0)	Dementia	Strength Balance	NR	26	3	60	Not motor intervention	MMSE: 0.05(-0.59, 0.703) BCSB test <i>Nominatio</i> 0.265(-0.3, 0.915) <i>Incidental memory:</i> 0.133(-0.5, 0.781) <i>Immediate memory:</i> -1.288(-1.2, -0.578) <i>Learning memory:</i> -0.926(-1.6, -0.246) <i>Delayed memory:</i> -0.133(-0.7, 0.513) <i>CDT:</i> 0.286(-0.3, 0.936) <i>Verbal fluency:</i> -0.872(-1.5, -0.195) <i>Recognitic</i> -0.090(-0.0, 0.556)
de Souto Barreto et al, 2017 France	I: 44 (93.2) C: 47 (76.6)	I: 88.3(5.1) C: 86.9(5.8)	Dementia	Aerobic Strength Balance Coordination	Moderate	24	2	60	Social intervention	MMSE: 0.038(-0.3, 0.450)
Greblo et al, 2017 Croatia	I: 14(100) C: 14(100)	70.4(3.9)	MCI	Strength Balance	NR	8	3	30	Pilates	MoCA: 0.88(0.077, 1.687)
Kemoun et al, 2010 France	I: 15(75) C: 16(73.3)	I: 82(5.8) C: 81.7(5.1)	Alzheimer-type dementia	Aerobic Balance Flexibility	Low to moderate	15	1	60	Usual care	ERFC: 0.889(0.15, 1.628)
Kwak et al, 2008 Korea	I: 15(100) C: 15(100)	I: 79.6(6.6) C: 82.2(7.0)	Dementia	Aerobic Strength Balance Flexibility	Low	52	1	40	NR	MMSE: 1.02(0.267, 1.791)

MMSE = Mini-Mental State Examination; BCSB = Brief Cognitive Screening Battery; MoCA = Montreal Cognitive Assessment; ERFC = Rapid Evaluation of Cognitive Function; BNT = Boston Naming Test; HVLT = Hopkins Verbal Learning Test; ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive; NR = not reported; MCI = mild cognitive impairment; aMCI = amnesic mild cognitive impairment

Author, year and country	Sample size (women %)	Age (mean±SD)	Cognitive impairment type	Physical activity included	Physical activity intensity	Program duration (weeks)	Sessions per week	Session duration (minutes)	Control type	Results (SMD)
Steinberg et al, 2009 US	I: 14 (71.4) C: 13 (69.2)	I: 76.5(3.9) C: 74(8.1)	Alzheimer-type dementia	Aerobic Strength Balance Flexibility	Moderate	12	7	NR	Home safety assessment	BMT: 0.087(-0.64, 0.842) HVL: 0.013(-0.74, 0.768)
Suzuki et al, 2013 Japan	I: 47 (50) C: 45 (48)	I: 74.8 (7.4) C: 75.8 (6.1)	MCI	Aerobic Strength Balance	Low to moderate	26	2	90	Education about health promotion	MMSE: 0.221(-0.11, 0.631) ADAS-Cog: -0.303(-0.71, 0.108)
MMSE = Mini-Mental State Examination; BCSB = Brief Cognitive Screening Battery; MoCA = Montreal Cognitive Assessment; ERFC = Rapid Evaluation of Cognitive Function; BNT = Boston Naming Test; HVL = Hopkins Verbal Learning Test; ADAS-Cog = Alzheimer's Disease Assessment Scale-Cognitive; NR = not reported; MCI = mild cognitive impairment; aMCI = amnesic mild cognitive impairment										

Risk of bias:

The risk of bias was assessed using the revised Cochrane risk-of-bias tool for randomized trials (RoB2)¹⁷. Depending on the intervention effect of interest, the studies were divided into intention-to-treat effect^{24,25,27–29} or per-protocol effect^{22,23,26}. Overall bias was reported as low risk in 20% of studies with an intention-to-treat analysis and 33.3% in those with a per-protocol approach. Supplementary Figure S1.

Effect of physical activity on global cognition and Subgroup analysis:

The ES of multicomponent physical exercise on global cognition in MCI and dementia was 0.34 (95% IC: 0.08, 0.60). We found a moderate inconsistency ($I^2 = 41.21\%$). Between-trials heterogeneity was considered moderate ($\tau^2 = 0.06$).

For the subgroup analysis considering the type of cognitive impairment, the pooled ES was 0.34 (95% CI: -0.05, 0.74; $I^2 = 57.59\%$) for dementia and 0.34 (95% CI: 0.00, 0.69; $I^2 = 15.52\%$) for MCI. For the subgroup analysis by the inclusion of aerobic exercises in the exercises protocol, the ES was 0.32 (95% CI: 0.03, 0.61; $I^2 = 44.78\%$) for those multicomponent physical exercise including aerobic exercise and 0.44 (95% CI: -0.38, 1.25; $I^2 = 62.39\%$) for those not including aerobic exercise, respectively (Figures 2 and 3).

Small study effects:

After visual inspection of the funnel plot and considering the Eger test, we found small study effects for the effect of multicomponent physical exercise on global cognition in MCI and dementia ($p = 0.009$). The trim-and-fill analysis showed that only one study was needed to remove the small study effects and that the ES of observed and imputed studies would be 0.274 (95% IC: -0.01, 0.56) (Supplementary Figure S2).

Discussion:

This systematic review and meta-analysis provide evidence supporting the effectiveness of multicomponent physical exercise associated with aerobic exercise on global cognition in people with MCI or dementia. Furthermore, this meta-analysis shows that when exercises protocol did not include aerobic exercise this effect disappeared. Also, we did not find an effect when MCI and dementia were analyzed separately.

Our data suggest that multicomponent physical activity plus aerobic exercise produces positive effects on global cognition in patients with MCI and dementia. Currently, multicomponent physical exercise is the one most frequently recommended for high-prevalent conditions in older adults such as frailty³⁰. Although the relationship between this type of exercise and cognitive functions is unclear, the effectiveness of physical exercise in reducing frailty and improving cognition, emotions, and social networks has been reported among frail older adults¹⁵, using multicomponent exercise but including aerobic exercise. This fact makes difficult to isolate the effect of the multicomponent exercise intervention approach, whose evidence on cognition remains inconclusive³¹, as well as the most suitable combination of components, duration and dose³².

The inclusion of aerobic exercise within the multicomponent physical exercise program seems to be of importance in positively impacting cognitive function. The positive effect of aerobic exercise has been reported among cognitively healthy individuals³³, and appears to be stronger as age increases, suggesting a protective effect against age-related cognitive decline. Additionally, aerobic exercise has demonstrated to positively impact on the cognitive function, behavior, and mobility³⁴ of patients with dementia and the global cognitive ability of older adults with MCI¹⁰, although some individual domains are not significantly improved (i.e. attention, verbal fluency, and visuospatial domains).

Some mechanisms have been proposed to explain the effects of multicomponent physical exercise on cognitive function. The association between multicomponent physical exercise (a composite strength and balance training program associated with a walking recommendation) and brain-derived neurotrophic factor (BDNF), a factor that promotes the growth and differentiation of neurons and supports the survival of existing neurons, was previously

explored. It seems that blood levels of BDNF are not affected by the multicomponent physical exercise intervention³⁵. This result is consistent with animal models in which strength exercise reduces aerobic exercise-induced adult hippocampal neurogenesis due to reduced BDNF and β -hydroxybutyrate³⁶, and with a study in young male participants that showed no effect of acute strength exercise on plasma levels of BDNF³⁷. Similarly, a meta-analysis that assessed the effect of physical activity on BDNF did not find the effect of strength exercises on BDNF levels³⁸. These results suggest that the multicomponent physical exercise, or at least the strength exercises, could have no effect on the neurogenesis processes.

As far as we know, this is the first systematic review and meta-analysis that explores the effect of multicomponent physical exercise intervention on cognition in patients with MCI and dementia, using the accepted definition of multicomponent physical exercise in the inclusion criteria. However, our study has some limitations. First, no information on independent cognitive domains was found, so only data on global cognition was reported. Second, few primary studies were found with a small sample size and therefore small study effects was found in the analysis. Finally, only published papers in English and Spanish were included, so no information on other languages was included.

Conclusion:

This systematic review and meta-analysis suggest a positive effect of the multicomponent physical exercises on global cognition in people with MCI or dementia only when aerobic exercise was included in the exercise protocol. However, due to the limitations of the included studies, these findings should be cautiously interpreted. Well-designed clinical trials comparing aerobic exercise to multicomponent exercise should be conducted to clarify the true effect on cognition. However, our results support the needed to include physical exercise in the cognitive rehabilitation protocols and cognitive impairment therapies.

Declarations

Ethics approval and consent to participate

This systematic review was approved by the Ethics and Research Comite at Pontificia Universidad Javeriana.

Consent for publication

Not applicable

Availability of data and materials

The datasets generated and/or analysed during the current study are available in file *data_set_srma.dta* of the repository *bmc_g-data-set* (https://github.com/lcvenegas/bmc_g-data-set)

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LCV, CAB, and ICR designed the protocol, defined the search terms, extracted data, and assessed the risk of bias. LCV and CAB analyzed the data extracted. LCV, CAB, and ICR wrote the manuscript. CCG revised the manuscript. VMV revised and approved the final version.

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Not applicable

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Figures

Figure 1

Flow diagram for searching and selection of the included studies.

Figure 2

Subgroup analysis by the type of cognitive impairment

Figure 3

Subgroup analysis of the inclusion or not of aerobic exercise

Supplementary Files

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