### Review

# The effect of physical activity interventions on cognitive function of older adults: A systematic review of clinical trials

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ARTICLE HISTORY: Received 2 August 2021/Revised 19 October 2021/Published Online 21 February 2022

#### **ABSTRACT**

Prevalence of dementia or of milder form of cognitive impairment is increasing and a pharmaceutical treatment remains pending. These facts underline the need of identifying modifiable factors and targeted interventions that could reduce the incidence of the disease or control its progression. Physical activity (PA) has been shown to have a beneficial effect on cognitive function, however findings to date remain controversial. The aim of this systematic review is to summarize the most recent data from clinical studies investigating the relationship between cognitive impairment and PA in adults older than 60 years of age. For this purpose, PubMed, Scopus and Google Scholar searches were conducted, and a total of thirty-five studies were selected and reviewed. Eleven studies investigated the effect of PA on individuals without cognitive impairment and seven of them presented some significant improvement, mostly on specific cognitive domains and only one in global cognition. Fourteen studies included populations with mild cognitive impairment (MCI) and twelve of them reported significant improvements in cognitive function. The majority of them presented a beneficial effect on global cognition and executive function. Finally, nine studies investigated interventions on populations with a diagnosis of dementia and only four of them showed any cognitive benefit following their interventions. There was no consistently observed association of a specific type of exercise and greater improvement or improvement in certain domains of cognition nor was there a minimum duration of intervention required for the improvements to take effect. In conclusion, the majority of the latest published literature suggests a protective role of PA on cognitive function. People with MCI seem to benefit the most from PA interventions, benefits in people with normal cognition are more subtle and harder to detect, while findings from studies in people with dementia remain contradictory. As findings are not currently in total agreement, further long-term prospective intervention studies are required in order to elucidate the reasons of this heterogeneity.

KEYWORDS: Cognitive function, cognitive decline, aging, healthy aging, physical activity, clinical studies, review.

#### Introduction

The number of people living with dementia was estimated at 50 million in 2019 by World Health Organization (WHO) and has been forecasted to affect 135 million by 2050. Mild cognitive impairment (MCI) is a condition between dementia and the expected cognitive decline of normal aging. Many population studies have been

conducted in the recent years aiming to document the frequency of MCI, and estimates ranged between 15–20% in the population over 60 years of age.<sup>2</sup> It has been hypothesized that compared to the general population people suffering from MCI are at increased risk to develop dementia in the following years, with a great number of these people progressing annually from one stage to the next.<sup>3</sup> Cognitive frailty is another term used

to describe MCI accompanied with mild physical frailty in geriatric populations.<sup>4</sup> MCI and dementia can be considered as a continuum with the risk of progressing with aging. Given that currently there is no pharmacological cure for dementia, there is an imperative need for the identification of modifiable risk factors and targeted interventions that could reduce the burden of the disease by delaying or even reversing the progression of MCI to dementia and preventing further cognitive deterioration in people already diagnosed.

Physical activity (PA) is considered a promising intervention for the prevention of cognitive impairment in older adults. The meta-analyses of prospective, observational studies by Santos-Lozano et al,<sup>5</sup> and Guure et al,6 reported an association of physical activity with lower probability of development of Alzheimer's Disease (AD) and a protective effect in the rate of cognitive decline in patients with AD and other forms of dementia, respectively. In addition, a meta-analysis of randomized controlled trials (RCTs) of Northey et al,7 reported that PA interventions improved cognitive function of older adults regardless of their cognitive status, while the meta-analysis of Falck et al, presented a beneficial impact of PA on cognitive function of healthy older adults.8 Similar results have been reported regarding PA interventions on patients with AD or other forms of dementia. 9,10 On the other hand, in a meta-analysis of twelve clinical trials, Young et al reported no evidence that physical activity interventions have any cognitive benefit for healthy older adults.<sup>11</sup> Conclusively, the published literature is not in total agreement over the effects of PA on cognitive function, as some findings remain conflicting for reasons that are still elusive. Additionally, to our knowledge, there is no published work assessing the effect of PA comparatively among populations of different cognitive status (normal cognition, MCI and dementia) and little is known about the characteristics of PA interventions that seem to be associated with the most beneficial effects for cognition.

The aim of this systematic review was to report recent results from clinical trials assessing the effect of PA interventions (including type, duration, etc.) on cognition of non-institutionalized older people, compare the effects among populations of different cognitive status and discuss the potential mechanisms that link PA and cognition.

#### **Material and Method**

#### Search strategy

For the purpose of this review, a literature search on PubMed, Scopus and Google Scholar, was conducted. The search query included the following terms: "aging", "older", "physical activity", "exercise", "cognition", cognitive performance", "cognitive function", "cognitive functioning", "cognitive impairment". Reference list from the studies obtained were used for additional content.

#### Inclusion criteria

Methodological filters used in the present review included: (i) studies in humans only, (ii) randomized clinical trial design (defined by WHO as a type of research that studies new tests and treatments and evaluates their effects in human health outcomes), (iii) older people (>60 years of age) of both sexes; (iv) non-institutionalized, (v) who had not known major health conditions (aside from cognitive impairment or dementia). Tai-Chi and yoga-type interventions were excluded, since they cannot be entirely considered as PA. The search in the literature was restricted to studies that have been published over the past 10 years (from May 2010 to May 2020) and were written in English language.

#### Study selection

The retrieved papers were firstly screened by Title and then by Abstract by 2 authors (VG and EM). The papers that passed this process underwent full text screening by the same 2 authors; in the case of opposing opinions, the third author (DP) had the role of a judge. Main results, and potential mediating factors reported by studies included were extracted, in order to summarize findings and compare studies. No data analysis was performed, since this is a narrative review.

#### **Results**

Search query provided 1535 results. Fifty-five remained after Title and Abstract screening, upon completing full text screening a total of 35 studies met the inclusion criteria and were included in the review. The quality of the selected studies was assessed using the RoB 2 Cochrane tool for the estimation of risk of bias (table 1). All included studies fulfilled the basic principles of randomized clinical (intervention) trials.

## Effect of PA on participants without Cognitive Impairment

A summary of characteristics of the studies included in this section is presented in table 2. Eleven studies investigated the effect of various forms of PA on older adults without any form of cognitive impairment or dementia. Table 2 summarizes the characteristics of these studies.

Table 1. Estimated risk of bias.

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Authors	Year	Estimated Risk		
Song D et al	2019	Low Risk		
De Oliveira Silva F et al	2019	Some Concerns		
Marston KJ et al	2019	Low Risk		
Lamb et al	2018	Some Concerns		
Langoni CS et al	2018	Some Concerns		
Bademli K et al	2018	High Risk		
Shimada H	2018	Some Concerns		
Amjad I.et al	2018	Some Concerns		
Choi W et al	2018	Low Risk		
Yoon DH et al	2018	High Risk		
Zhu Y et al	2018	Low Risk		
Iuliano E et al	2017	Low Risk		
Hong SG et al	2017	Low Risk		
Liu Ambrose et al	2016	Low Risk		
Mavros Y et al	2016	Some Concerns		
Ohman H et al	2016	Some Concerns		
Hoffman K et al	2016	Low Risk		
Tarazona-Santabalbina FJ.	2016	Low Risk		
Alghadir AH et al	2016	Low Risk		
Sink MK et al	2015	Low Risk		
Yang SY et al	2015	Low Risk		
Holthoff VA et all	2015	Low Risk		
Iuliano E et al	2015	High Risk		
Lu J et al	2015	Low Risk		
Fiatarone Singh MA et al	2014	Low Risk		
Linde K et al	2014	Some Concerns		
Ruiz JR et al	2014	Low Risk		
Nouchi R et al	2013	Low Risk		
Vreugdenhill A et al	2012	Some Concerns		
Venturelli M et al	2011	Some Concerns		
Maki Y et al	2011	Some Concerns		
Yaguez LK et al	2010	Some Concerns		
Muscari A et al	2009	Low Risk		

#### Effect on Global Cognition

Regarding global cognition, the study by Muscari et al<sup>12</sup> presented stabilization of MMSE scores of the trained group, while the control group showed a significant decrease of 1.21 points after twelve months of intervention (endurance exercise), indicating a small to moderate effect size (Cohen's alpha=0.48). However, the studies by Shimada et al and Ruiz et al,<sup>13,14</sup> studies that set the MMSE as their primary cognitive outcome, did not show any significant difference compared to their controls after the intervention period.

#### Effect on Specific Domains of Cognition

The study by Marston et al15 revealed that their trained groups presented a statistically significant improvement in delayed verbal memory following their twelve-week intervention of resistance training. In the study of Linde et al,16 the trained group, with a sixteen-week combined aerobic and strengthening intervention, presented significant improvements in cognitive speed. Furthermore, the study by Maki et al<sup>17</sup> presented significant improvement in word fluency, following a twelve-week intervention of walking. The study by Nouchi et al<sup>18</sup> investigating the effect of combined aerobic, strength and stretching exercise showed significant improvements in executive functions, episodic memory and processing speed of their trained group, but not in working memory, reading ability and attention which were also tested. Alghadir et al in their study<sup>19</sup> used a set of tests evaluating orientation, visual perception, spatial perception, motor praxis, vasomotor organization, thinking operations and attention-concentration to assess the effect of a 24-week aerobic intervention. This study showed significant improvements for their trained group in each subcategory of the test. Finally, in the clinical study by Iuliano et al, (2015)<sup>20</sup> that compared different types of exercise interventions (aerobic, resistance, postural) and a control group, it was shown that the aerobic group presented improvements in the Attentive Matrices Test, as well as Raven's Progressive Matrices Test that evaluate attention and abstract reasoning, respectively, the resistance group improved in Drawing Copy Test, which assesses praxis abilities, whereas postural and control group did not show any improvements. However, the studies by Iuliano et al (2017) and Hong et al<sup>21,22</sup> that investigated the effect of different physical activity interventions on various domains of cognition and specifically memory performance did not present any benefits in their trained groups.

#### **MCI and Cognitive Frailty**

Fourteen studies investigated the effects of physical activity interventions on the cognitive function of people with MCI or at cognitive frailty. A summary of characteristics of the studies included in this section is presented in table 3.

#### Effect on Global Cognition

Ten studies<sup>23–32</sup> assessed the effect of their interventions on global cognition setting having as primary outcomes MMSE, Clinical Dementia Rating (CDR), Alzheimer's Disease Assessment Score ADAS-cog, or Montreal Cognitive Assessment (MoCA) scores. In their

Table 2. Study's characteristics in people with no cognitive impairment.

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
Marston KJ et al	2019	N=45 Age 41–69	High Load Resistance vs Moderate Load vs Controls	Twice a week/ 12 weeks	CogState computerized battery	Improved in Some Domains Cognition Delayed verbal memory
Shimada H.	2018	N=100 Age over 65	Golf training vs Controls	Once a week/ 24 weeks	MMSE	No Difference in Cognition
Iuliano E et al	2017	N=80 Mean Age=67	Resistance training vs Cardio Training vs Postural Training vs Control	12 weeks	Various cogni- tive tests	No Difference in Cognition
Hong SG et al	2017	N=47 Age over 65	Resistance training vs Controls	12 weeks	Various cogni- tive tests	No Difference in Cognition
Alghadir AH et al	2016	N=100 Ager 65–95	Moderate Aerobic Training vs Control	24 weeks	LOTCA battery	Improved Cognition
Iuliano E et al	2015	N=80 Age over 55	Aerobic vs Resistance vs Postural vs Controls	12 weeks	Various cogni- tive tests	Improved Different domains of Cognition based on intervention
Linde K et al	2014	N=70 Age 60–75 years	Physical training vs Cognitive training vs Combined vs controls	16 weeks	Various cogni- tive tests	Improved Cognition for all interventions vs con- trols Cognitive Speed
Ruiz JR et al	2014	N=20 Age over 90	Aerobic and Resistance vs Control	8 weeks	MMSE, GDS	No difference in Cognition
Nouchi R	2013	N=64 Age over 60	Combined Exercise vs Controls	4 weeks	Various Cognitive tests	Improved Cognition
Maki Y et al	2011	N=150 Age Over 65	Walking vs Controls	12 weeks	5–Cog Test	Improvement in Word Fluency
Muscari A et al	2009	N=120 Age 65–74	Endurance Exercise Training vs Controls	12 months	MMSE	Stabilized Cognition

ADAS cog: Alzheimer's Disease Assessment Scale-cognition, ADL: Activities of Daily Living, GDS: Geriatric Depression Scale, LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment

studies Song et al,<sup>24</sup> Bademli et al<sup>25</sup> and Amjad et al<sup>26</sup> included aerobic exercise interventions; Lu et al,<sup>27</sup> Mavros et al<sup>28</sup> and Fiatarone Singh et al<sup>29</sup> included resistance training; Tarazona-Santabalbina et al,<sup>30</sup> de Oliveira Silva et al,<sup>31</sup> Langoni et al<sup>32</sup> and Choi et al<sup>33</sup> included multimodal programs that combined different types of exercise (aerobic, strength, flexibility, endurance etc.). All of the studies mentioned above presented significant improvements in global cognition of their trained groups compared to controls, except for the study of de Oliveira Silva et al.<sup>31</sup>

#### Effect on Specific Domains of Cognition

Seven studies used tests that assessed the effect of their interventions on different domains of cognitive function and five of them presented improvements for their trained groups. Specifically, the study by de Oliveira Silva et al<sup>31</sup> showed significant improvement in Clock Drawing Test (associated with executive function) and Verbal Fluency (associated with semantic memo-

ry) following a 12-week multimodal training program. Four more studies presented significant improvements in Trail Making Tests (which are associated with processing speed and executive function) following a sixweek aerobic, <sup>26</sup> a twelve-week resistance (dumbbell), <sup>27</sup> a sixteen-week resistance <sup>34</sup> and a twelve-week aerobic (dancing) <sup>35</sup> training intervention. The dancing intervention was also associated with improvements in Logical Memory, as depicted be the Wechsler Memory Scale.

#### **Dementia**

Nine studies investigated the effect of various forms of physical activity on the cognitive function of people with Alzheimer's disease (AD) or other forms of dementia. A summary of characteristics of the studies included in this section is presented in table 4.

#### Effect on AD patients

Seven of the reviewed studies included populations with a confirmed diagnosis of Alzheimer's Disease. 31,36-41

Table 3. Study's characteristics in people with mild cognitive impairment (MCI).

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
Song D et al	2019	N=120 Age over 60	Moderate Intensity Aerobic	16 weeks	MoCA	Improved Cognition
De Oliveira Silva F et al	2019	N=56 Age over 65	Multimodal Training vs Controls	12 weeks	CDR, MMSE, CDT, VF	Improved Cognition
Langoni CS et al	2018	N=52 Age over 60	Multicomponent exercise vs Controls	24 weeks	MMSE	Improved Cognition
Bademli K et al	2018	N=60 Age over 65	Physical Activity Program vs Controls	20 weeks	MMSE	Improved Cognition
Amjad I.et al	2018	N=40 Mean Age=59	Aerobic vs Controls	6 weeks	MMSE, MoCA, TMT A and B	Improved Cognition
Choi W et al	2018	n=60 Mean age=74 years	GKP vs Controls	6 weeks	MoCA score	Improved Cognition for both, more for trained
Yoon DH et al	2018	N=45 Age over 65	Resistance Training vs Controls	16 weeks	Various Cognitive Tests	Improved Cognition
Zhu Y et al	2018	N=60 Age 50-85	ADR vs Controls	12 weeks	Various cogni- tive tests	Improved Cognition
Hong SG et al	2017	N=47 Age over 65	Resistance training vs Controls	12 weeks	Various cogni- tive tests	No Difference in Cognition
Mavros Y et al	2016	N=100 Age over 55	Progressive Resistance Training vs Controls	6 months	ADAS-cog,	Improvements in Cognition
Tarazona- Santabalbina FJ	2016	N=100 Age over 70	Multimodal Exercise vs Controls	24 weeks	MMSE	Improved Cognition
Sink MK et al	2015	N=1635 Age over 70	Multimodal Exercise vs Controls	24 months	DSC, HVLT-R	No difference in cognition
Lu J et al	2015	N=45 Age over 65	Dumbbell training vs Controls	12 weeks	ADAS-cog, TMT B, DST,	Improved Cognition
Fiatarone Singh MA et al	2014	N=100 Mean Age=70	PRT vs Cogntitive Training vs Combined vs Controls	6 months	ADAS-cog	Improved Cognition for PRT only

ADAS cog: Alzheimer's Disease Assessment Scale-cognition, ADL: Activities of Daily Living, CANTAB: Cambridge Neuropsychological Test Automated Battery, CDR: Clinical Dementia Rating, CDT: Clock Drawing Test, DSC: Digit Symbol Coding, DST: Digit Span Test, HIFE: High Intensity Functional Exercise

HVLT-R: Hopkins Verbal Learning Test revised, GDS: Geriatric Depression Scale, GKP: Ground Kayak Paddling

LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MCI: Mild Cognitive Impairment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, SDMT: Symbol Digit Modalities Test, SIB-s: Severe Impairment Battery- short form, TMT: Trail Making Test, VF: Verbal Fluency, WMS-R LM: Wechsler Memory Scale-Revised Logical Memory

All these studies used a validated tool to assess global cognition. Six of these used MMSE and/or ADAScog, while the remaining one<sup>36</sup> used The Cambridge Neuropsychological Test Automated Battery (CANTAB), which is a computerized neuropsychological test that can detect early stages of dementia and distinguish them from depression. Three of the studies mentioned above, those conducted by Yaguez et al,<sup>36</sup> Vreugdenhil et al<sup>37</sup> and Yang et al,<sup>38</sup> presented significant improvements following six weeks of movement training (a multimodal program that consists of fifteen exercises), sixteen weeks of walking and twelve weeks of aerobic

interventions, respectively. The studies by Vreugdenhil et al and Yang et al presented improvements in global cognition (Cohen's d= 0.32 and 6.1, respectively), while the study by Yaguez et al presented improvements in the domains of attention, visual memory and working memory. On the contrary, the remaining four studies conducted by de Oliveira et al,<sup>31</sup> Ohman et al,<sup>39</sup> Hoffman et al<sup>40</sup> and Holthoff et al<sup>41</sup> did not report any improvement in global cognition for individuals with Alzheimer's disease following aerobic or multimodal exercise interventions. Regarding specific domains of cognition, like executive function, assessed with Clock

**Table 4.** Study's characteristics in people with dementia.

Authors	Year	Sample	Intervention	Duration	Cognitive Outcome	Results
De Oliveira Silva F et al	2019	N=56 Age over 65	Multimodal Training vs Controls	12 weeks	CDR, MMSE, CDT, VF	Improved Cognition for MCI not AD
Lamb SE et al	2018	N=494 Age 78	Aerobic and Strength Exercise vs Controls	16 weeks	ADAS-cog	No difference in Cognition
Liu Ambrose T et al	2016	N=70 Mean Age=74	Aerobic Training vs Controls	6 months	ADAS-cog	Improvements in Cognition
Ohman H et al	2016	N=210 Age over 65	Home Exercise vs Group Exercise vs Control	12 months	MMSE, VF, CDT, CDR	No Difference in Cognition
Hoffman K et al	2016	N=200 Age 50–90	Moderate to High Intensity Aerobic vs Controls	16 weeks	SDMT, MMSE, ADAS–cog	No Difference in Cognition
Yang SY et al	2015	N=50 Age 50–80	Aerobic Exercise	12 weeks	MMSE, ADAS–cog	Improved Cognition
Holthoff VA et al	2015	N=30 Age 50–90	Multimodal Exercise vs Controls	12 weeks	MMSE	No Difference in Cognition
Vreugdenhill A et al	2012	n=40 Mean Age=74	Home Based Exercise and walking vs Controls	16 weeks	MMSE, ADAS–cog	Improved Cognition
Yaguez L K et al	2010	N=27 Mean Age=72.5 Years	Movement Training vs Controls	6 weeks	CANTAB	Improved Cognition

AD: Alzheimer's Disease, ADAS cog: Alzheimer's Disease Assessment Scale – cognition, ADL: Activities of Daily Living, CANTAB: Cambridge Neuropsychological Test Automated Battery, CDR: Clinical Dementia Rating, CDT: Clock Drawing Test, DSC: Digit Symbol Coding, DST: Digit Span Test, GDS: Geriatric Depression Scale, HIFE: High Intensity Functional Exercise, HVLT–R: Hopkins Verbal Learning Test revised LOTCA: Lowenstein Occupational Therapy Cognitive Assessment, MCI: Mild Cognitive Impairment, MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, SDMT: Symbol Digit Modalities Test SIB–s: Severe Impairment Battery– short form, TMT: Trail Making Test, VF: Verbal Fluency

Drawing Test, and Semantic Memory, evaluated with Verbal Fluency test that were examined in the studies of Ohmann et al and de Oliveira Silva et al<sup>39,31</sup> the trained groups did not show any benefit compared to the controls.

#### Other Forms of Dementia

The study by Lamb et al<sup>42</sup> investigated the effect of a twenty-four-week combined aerobic and strength program on the cognitive function of people with clinically diagnosed dementia, without further specifying its form. This study reported that there was no improvement or stabilization of the cognitive function of their trained group compared to the control group. Finally, Liu-Ambrose et al<sup>43</sup> in their study investigated the effect of a six-month aerobic training intervention on the cognitive function of individuals with ischemic vascular cognitive impairment. This study showed a significant improvement in global cognition of the trained group relatively to the controls as depicted by the ADAS-cog test score that was, however, diminished in the 6-month follow-up assessment.

#### Discussion

This review of clinical studies confirmed that there is evidence linking physical activity interventions to improvements of cognitive function, with the majority of the studies reporting significant benefits for their trained groups in global cognition or at least in some cognitive domains, regardless of their cognitive status. Regarding specific aspects of cognitive function, executive function was the one that was most consistently reported to improve after the physical activity interventions, which is in accordance with previous published literature.<sup>7,8</sup>

Regarding the effects of PA on specific populations, seven out of the eleven studies on healthy older adults reported some cognitive benefits for their intervention groups. Additionally, people without cognitive impairment seemed to benefit more in specific cognitive domains and not in global cognition. However, due to the multitude of cognitive tests that were used, no consistent link could be identified between interventions and a specific cognitive domain. This heterogeneity is also reflected in the latest meta-analyses and systematic reviews, as some report mild to moderate benefits in

specific cognitive domains,<sup>44–46</sup> while others do not.<sup>11–47</sup> This can be partly attributed to the fact that cognitive deterioration in healthy older adults is slow and subtle, making differences between intervention and control groups hard to detect, especially with crude tests that are designed to diagnose dementia, such as MMSE.

On the other hand, people with MCI were consistently presented to benefit in global cognition in the present review. In a meta-analysis by Sanders et al,48 there was a similar trend with healthy older adults to benefit more in specific domains of cognition, while those with MCI benefit more in global cognition after PA interventions. Recently published literature seems to be in agreement with the findings of the present review, as PA interventions are consistently reported to have a beneficial effect on the cognitive function of people with MCI.<sup>49,50</sup> This might be attributed to the fact that cognitive impairment is progressing faster in people with MCI compared to healthy older adults, but it could also indicate that it can be reversed, making people with MCI potentially the ones that might benefit the most out of targeted PA interventions.

Finally, regarding studies in populations with dementia, five out of nine studies (n=244) presented significant benefits for their trained groups, while the remaining four (n=934) did not present any. Recently published literature is also contradictory as PA interventions are reported to either provide some cognitive benefits<sup>51</sup> or not.<sup>52</sup> This can be attributed to many reasons that may have to do with the quality of the studies (small samples, insensitive cognitive tests, etc.). However, it may also reflect the fact that as cognitive deterioration progresses passed a certain point it may be more challenging to be reversed or slowed down.

Concerning the duration of the intervention, its intensity and the types of exercise, a minimal duration threshold was not found nor a consistent link between cognitive benefits and a specific type of physical activity or intensity level. Only one study<sup>20</sup> presented association of different types of exercise with specific domains of cognition, however, given its small sample and the number of the comparisons that were conducted its findings should be interpreted with great caution.

The observed heterogeneity regarding studies in populations with dementia can be attributed to several reasons. Dementia is a clinical diagnosis based on the deterioration of cognitive function experienced by the patients, that may result from various causes. Distinguishing between different causes of dementia can be challenging, even for specialists, as characteristic findings of different pathological entities frequently co-exist. In addition, the exact pathophysiological mechanisms for specific types

of dementia are not yet fully clarified, even for Alzheimer's Disease, which is the most common etiology of dementia contributing to the 60–70% of total cases according to WHO. Taking all these into account, it is clear that individuals with a clinical diagnosis of Dementia may vary greatly even when stratified for gender, age and cognitive performance and thus respond differently to interventions, causing studies to produce these conflicting results.

The effects of PA on cognitive function can be categorized as direct and indirect. Cerebral blood flow progressively declines with aging.53 This deterioration of cerebral perfusion has been linked with poorer cognitive performance.<sup>54</sup> Physical exercise has been shown to directly impact cerebral circuitry, by increasing its flow<sup>55</sup> and promoting vascular growth factors.<sup>56</sup> Aside from benefiting brain blood circulation, PA may also have a direct effect on brain neuronal function by the stimulation of Brain Derived Neurotrophic Factor (BDNF),57 which is considered to play a key role in neurogenesis and neuronal function.58 Finally, oxidative stress is currently believed to play some role in the pathophysiology of neurodegenerative diseases and Alzheimer's Disease in particular,<sup>59-61</sup> contributing to the cascade of events that lead to accumulation of amyloid-β, neuronal apoptosis and eventually dementia. Current knowledge suggests that physical activity can reduce oxidative stress and thus have a protective role in the development of these conditions. The indirect links of PA with cognitive function could be explained by the interplay with sleep quality and depressive mood.<sup>24</sup>

Physical exercise might seem a promising intervention for the prevention of cognitive impairment, however, there are some limitations that cannot be depicted by the studies mentioned above. Firstly, aging is often associated with health problems that limit mobility and may make individuals less willing and able to engage in physical activity. Another important issue is that the interventions of randomized trials are usually supervised by exercise experts, which is not possible in everyday life. Unless they are easily structured in a way that they can be incorporated in the every-day life of the individuals it is unlikely that they will adhere to them and benefit in the long term.

#### Conclusion

The comparative analysis of the effects of PA on cognitive function of populations with different cognitive status suggested that PA may have a protective role against cognitive impairment at the stages preceding dementia, while its effect on demented people is controversial. However, its value should be highlighted as an essential part of a healthy lifestyle.

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### Ανασκόπηση

# Η επίδραση της φυσικής άσκησης στη νοητική λειτουργία του πληθυσμού μεγαλύτερης ηλικίας: Μια συστηματική ανασκόπηση κλινικών δοκιμών

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ΙΣΤΟΡΙΚΟ ΑΡΘΡΟΥ: Παραλήφθηκε 2 Αυγούστου 2021/Αναθεωρήθηκε 19 Οκτωβρίου 2021/Δημοσιεύθηκε Διαδικτυακά 21 Φεβρουαρίου 2022

#### ΠΕΡΙΛΗΨΗ

Ο επιπολασμός άνοιας ή ηπιότερων μορφών νοητικής έκπτωσης αυξάνεται και προς το παρόν δεν είναι διαθέσιμη κάποια αποτελεσματική φαρμακευτική θεραπεία. Αυτά τα γεγονότα υπογραμμίζουν την ανάγκη εντοπισμού τροποποιήσιμων παραγόντων και στοχευμένων παρεμβάσεων που θα μπορούσαν να μειώσουν τη συχνότητα εμφάνισης ή να ελέγξουν την εξέλιξη της νόσου. Η σωματική άσκηση (ΣΑ) έχει φανεί να έχει ευεργετική επίδραση στη νοητική λειτουργία, ωστόσο τα ευρήματα μέχρι σήμερα παραμένουν αμφιλεγόμενα. Ο σκοπός αυτής της συστηματικής ανασκόπησης είναι να συνοψίσει τα πιο πρόσφατα δεδομένα από κλινικές μελέτες που διερευνούν τη σχέση μεταξύ νοητικής έκπτωσης και ΣΑ σε ενηλίκους άνω των 60 ετών. Για τον σκοπό αυτόν, πραγματοποιήθηκε αναζήτηση στο PubMed, το Scopus και το Google Scholar και επιλέχθηκαν συνολικά τριάντα πέντε μελέτες για ανασκόπηση. Έντεκα μελέτες διερεύνησαν την επίδραση της ΣΑ σε άτομα χωρίς νοητική έκπτωση και επτά από αυτά παρουσίασαν κάποια σημαντική βελτίωση, κυρίως σε συγκεκριμένους γνωστικούς τομείς και μόνο μία στη συνολική νοητική λειτουργία. Δεκατέσσερεις μελέτες περιλάμβαναν πληθυσμούς με ήπια νοητική έκπτωση και δώδεκα από αυτές ανέφεραν σημαντικές βελτιώσεις στη νοητική λειτουργία. Η πλειοψηφία τους παρουσίασε ευεργετική επίδραση στη συνολική νοητική λειτουργία και εκτελεστική λειτουργία. Τέλος, εννέα μελέτες διερεύνησαν παρεμβάσεις σε πληθυσμούς με διάγνωση άνοιας και μόνο τέσσερεις από αυτές έδειξαν οποιοδήποτε νοητικό όφελος μετά τις παρεμβάσεις τους. Δεν παρατηρήθηκε συνεπής συσχέτιση συγκεκριμένου τύπου άσκησης και μεγαλύτερη βελτίωση ή βελτίωση σε ορισμένους τομείς της νόησης ούτε υπήρχε ελάχιστη διάρκεια παρέμβασης για να τεθούν σε ισχύ οι βελτιώσεις. Συμπερασματικά, η πλειοψηφία της πιο πρόσφατης δημοσιευμένης βιβλιογραφίας προτείνει έναν προστατευτικό ρόλο του ΣΑ στη νοητική λειτουργία. Τα άτομα με ήπια νοητική έκπτωση φαίνεται να επωφελούνται περισσότερο από τις παρεμβάσεις ΣΑ, τα οφέλη σε άτομα με φυσιολογική νόηση είναι πιο περιορισμένα και πιο δύσκολο να εντοπιστούν, ενώ τα ευρήματα από μελέτες σε άτομα με άνοια παραμένουν αντιφατικά. Καθώς τα ευρήματα δεν είναι σε απόλυτη συμφωνία προς το παρόν, απαιτούνται περαιτέρω μακροπρόθεσμες μελέτες μελλοντικής παρέμβασης προκειμένου να διευκρινιστούν οι λόγοι αυτής της ετερογένειας.

**ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ:** Νοητική λειτουργία, νοητική έκπτωση, γήρανση, υγιής γήρανση, σωματική άσκηση, κλινικές μελέτες, ανασκόπηση.

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