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TREATMENT OF COGNITIVE IMPAIRMENT IN THE ELDERLY: MILD COGNITIVE IMPAIRMENT AND DEMENTIA. A SYSTEMATIC REVIEW

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Abstract
The best socio-sanitary conditions of the 21st century lead to an aging of society. In advanced age, the appearance of cognitive deterioration is more frequent, which raises the need to design therapeutic strategies to mitigate it. In addition to drug treatment, there are other interventions such as the type of diet, cognitive training, music therapy, acupuncture, physical exercise, etc. Due to the scientific evidence and the ease of practicing physical exercise as a therapeutic intervention, we propose to carry out a systematic bibliographic review on this treatment.
Therefore, our objective is to study the efficacy of physical exercise in mild cognitive impairment and dementia.
To this end, a systematic literature search was carried out in PubMed database using the MeSH terms: „Cognitive Dysfunction”, „Dementia”, „Alzheimer Disease”, „Therapeutics”, „Exercise”, „Exercise Therapy” and „Aged”.
We define efficacy in terms of improvement in global cognitive status or by cognitive domains after the application of the intervention with physical activity and by applying different scales to assess cognition.
It is concluded that aerobic physical activity is the most effective treatment for both mild cognitive impairment and dementia, the most favored cognitive domains being memory, global cognition and executive function. This therapy involves few adverse effects. More randomized controlled studies are needed in order to provide more scientific evidence for these results.

Keywords: mild cognitive impairment, dementia, elderly, physical activity.

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Resumé
Les meilleures conditions socio-sanitaires du 21ème siècle conduisent à un vieillissement de la société. À un âge avancé, l'apparition d'une détérioration cognitive est plus fréquente, ce qui soulève la nécessité de concevoir des stratégies thérapeutiques pour l'atténuer. En plus du traitement médicamenteux, il existe d'autres interventions telles que le type de régime, l'entraînement cognitif, la musicothérapie, l'acupuncture, l'exercice physique, etc. En raison des preuves scientifiques et de la facilité de pratiquer l'exercice physique comme intervention thérapeutique, nous proposons de réaliser une revue bibliographique systématique sur ce traitement. Par conséquent, notre objectif est d'étudier l'efficacité de l'exercice physique dans les troubles cognitifs légers et la démence. A cet effet, une recherche documentaire systématique a été réalisée dans la base de données PubMed en utilisant les termes MeSH : « Cognitive Dysfunction », « Dementia", « Alzheimer Disease", « Therapeutics », « Exercise", « Exercise Therapy » et « Aged ». Nous définissons l'efficacité en termes d'amélioration de l'état cognitif global ou par domaines cognitifs après l'application de l'intervention avec une activité physique et en appliquant différentes échelles pour évaluer la cognition.
Il est conclu que l'activité physique aérobie est le traitement le plus efficace pour les troubles cognitifs légers et la démence, les domaines cognitifs les plus favorisés étant la mémoire, la cognition globale et la fonction exécutive. Cette thérapie entraîne peu d'effets indésirables. D'autres études contrôlées randomisées sont nécessaires afin de fournir davantage de preuves scientifiques de ces résultats.

Mots clés : troubles cognitifs légers, démence, personnes âgées, activité physique.

Rezumat
Cele mai bune condiții socio-sanitare ale secolului XXI duc la o îmbătrânire a societății. La vârstă înaintată, apariția deteriorării cognitive este mai frecventă, ceea ce amplifică necesitatea de a concepe strategii terapeutice pentru a o atenua. Pe lângă tratament medicamentos, există și alte intervenții precum dietă, antrenament cognitiv, terapie prin muzică, acupunctură, exercițiu fizic etc. Datorită dovezilor științifice și a ușurinței de a practica exercițiul fizic ca intervenție terapeutică, ne propunem să efectuăm o revizuire bibliografică sistematică asupra acestui tratament.
Prin urmare, obiectivul nostru este de a studia eficacitatea exercițiului fizic în tulburări cognitive ușoare și demență. În acest scop, a fost efectuată o căutare sistematică a literaturii în baza de date PubMed folosind termenii MeSH: „Cognitive Dysfunction", „Dementia", „Alzheimer Disease", „Therapeutics", „Exercise", „Exercise Therapy" și „Aged". Definim eficacitatea în termeni de îmbunătățire a statusului cognitiv global sau pe domenii cognitive după aplicarea intervenției prin activitate fizică și prin aplicarea diferitelor scale de evaluare a cogniției.
S-a ajuns la concluzia că activitatea fizică aerobică este un tratament eficient atât pentru deficiența cognitivă ușoară, cât și pentru demență, domeniile cognitive cele mai favorizate fiind memoria, cogniția globală și funcția executivă. Această terapie implică puține efecte adverse. Sunt necesare mai multe studii randomizate controlate pentru a oferi mai multe dovezi științifice pentru aceste rezultate.

Cuvinte cheie: deficit cognitiv minor, demență, vârstnici, activitate fizică.

1. Introduction

According to the World Health Organisation (WHO), the universal population is increasing its life expectancy and the number of people over 60 years of age is estimated to increase from 900 million in 2015 to two billion in 2050. Consequently, the prevalence and incidence of neurodegenerative diseases, such as Alzheimer's disease (AD) or mild cognitive impairment (MCI) has increased compared to previous years (Lin *et al.* 2020) neurodegenerative diseases cause progressive neuronal deterioration, leading to a reduction in both the independence and functionality of the person suffering from the disease and, in the more advanced stages of the disease, to the point of compromising their autonomy. Finally, the patient may require a caregiver, who will generally be acquired by a family member (Abril Carreres *et al.*2004). MCI can be defined as a decline in attention, memory, and cognitive function beyond what is expected for a person's educational level and age, without this being a handicap in performing activities of daily living (ADLs). It can be considered an intermediate stage between the normal state of the brain and dementia, which involves impairment of functional abilities. The incidence rate of MCI is estimated to range from 21.6 to 71.3 per 1000 people/year in older adults. The conversion rate from MCI to dementia is ten percent per year, increasing to 80 percent-90 percent after six years (Eshkoor *et al.* 2015). There are several additional risk factors for developing MCI, such as low educational level, apolipoprotein E genotype, sleep disordered breathing, vitamin D deficiency, previous illnesses, and cardiovascular disease, among others (Langa & Levine, 2014).

As mentioned above, dementia is the loss of cognitive functions such as the ability to think, remember and reason, as well as behavioural changes that interfere with ADLs. Functional impairments include disturbances in memory, language, visual perception, problem solving, self-care and concentration. In some cases, it sometimes includes disorders of emotion and personality. While dementia is more common with advancing age, it is not a normal part of ageing (Garre-Olmo, 2018).

There are different types of dementia, depending on their etiology, clinical symptoms, and other associated diseases. According to this they can be classified into vascular dementia, front-temporal dementia, Parkinson's disease dementia, Lewy body dementia and Alzheimer's disease, the latter being the most prevalent (60-80 percent). AD is characterised by neuronal deterioration and has a progressive course (Garre-Olmo, 2018).

The Diagnostic and Statistical Manual of Mental Disorders (DSM) of the American Psychiatric Association (APA), fifth edition (DSM-V), examines the symptom domains for the diagnosis of neurocognitive disorder. This includes the section designated neurocognitive disorders, which replaces the category of delirium, dementia, amnesic disorders, and other cognitive disorders, established in the previous edition (DSM-IV-TR) (Distancia, n.d.; Palau., 2015).

Thus, DSM-V encompasses the term Minor and Major Neurocognitive Disorder. The term MCI is replaced by the term Minor Neurocognitive Disorder and the term dementia by Major Neurocognitive Disorder. The difference between

the two is manifested in terms of the patient's ability to perform ADLs and the magnitude of symptoms. In addition, a third category of neurocognitive disorders, delirium, is included (Palau *et al.*, 2015).

The diagnostic criteria set out in the DSM-V for both major neurocognitive disorder and minor neurocognitive disorder are given by Diagn *et al.* (Diagn, 1923). Also, in other instances, different scales are used for the assessment of cognitive disorders such as the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975), the Montreal Cognitive Assessment (MoCA) (Nasreddine *et al.*, 2005) or the Alzheimer disease assessment scale-cognitive (ADAS-Cog) (Rosen *et al.*, 1984), among others.

Treatment for neurocognitive disorders can be divided into two main areas, pharmacological and non-pharmacological. Regarding pharmacological treatment, it should be noted that no drug has been shown to be effective in reducing the risk of progression of MCI to dementia. Among the drugs studied are cholinesterase inhibitors and memantine, but their use is not recommended due to their limited effect and possible adverse effects. Other therapies such as testosterone supplementation or herbal supplements such as Ginkgo Bilboa have been ruled out (Langa & Levine, 2014). Similarly, the efficacy of drug treatment for dementia is controversial (Schwarz *et al.*, 2012).

On the other hand, non-pharmacological treatment includes interventions such as diet, music therapy, aromatherapy, cognitive training, computerised games, acupuncture, and physical activity, among many others (Ramos Cordero & Yubero, 2016).

The focus of this paper is the study of physical interventions and their efficacy in the treatment of neurocognitive disorders. Numerous scientific evidence has shown that physical exercise affects brain plasticity, influencing cognition and psychological well-being. According to the WHO, physical exercise is defined as planned, structured, repetitive physical activity with the ultimate or intermediate goal of improving or maintaining one or more components of physical fitness. Examples are aerobic and anaerobic activity, with a specified frequency, duration, and intensity. Neuroplasticity is the ability of the nervous system to change in response to experience. In this context, physical exercise would be the modifying environmental factor. Structural changes observed in humans following physical therapy include increased grey matter volume in the frontal and hippocampal regions, elevated levels of neurotrophic factors (peripheral BDNF) and increased blood flow. All these changes correlate with increased cognitive performance, corresponding to increased functional neuronal efficiency. The biological and psychological effects of physical therapy could be explained in part through epigenetic mechanisms. The term „epigenetics" is based on a model that explains how genes can interact with their environment to produce the phenotype. This involves various biochemical modifications of DNA (methylation), histones (methylation or acetylation) and the expression of non-coding RNA (miRNA). All of these contribute to the expression and/or repression of genes involved in memory or neurogenesis (BDNF) (Mandolesi *et al.*, 2018).

Due to the scientific evidence and the ease of physical exercise as a therapeutic intervention, we propose to carry out a systematic literature review on this treatment.

2. Materials and Methods

This systematic review (SR) was developed considering the principles of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement (Mandolesi *et al.* 2018).

2.1. Search strategy

A systematic search of the NCBI (National Center for Biotechnology Information) PubMed database was performed. Full articles were accessed through the University of Salamanca.

The following ¨MeSH¨ (Medical Subject Headings) were used for the search: „Cognitive Dysfunction", „Dementia", „Alzheimer Disease", „Therapeutics", „Exercise", „Exercise Therapy" and „Aged". In addition, „treatment" and „physical training" were used as „text words", „therapy" as a „subtitle" and „Cognition Disorders" as a „major topic". These terms were combined with the Boolean operators OR and AND. We used as search filters the date of publication (from 2015 until July 2021), language (English or Spanish) and study type (randomised controlled trial). The search strategy was: (((("Cognitive Dysfunction"[MeSH]) OR ("Cognition Disorders"[MeSH])) OR (("Dementia"[MeSH]) OR „Alzheimer Disease"[MeSH])) AND ((((("Therapeutics"[MeSH]) OR „therapy"[Subheading]) OR (treatment)) AND ((("Exercise"[MeSH]) OR „Exercise Therapy"[MeSH]) OR (physical training)))) AND ("Aged"[MeSH]).

2.2. Inclusion and exclusion criteria

After the initial search, articles that met the established inclusion criteria were selected, discarding those articles that met one or more exclusion criteria, and then proceeded to their study (Table 1).

Table 1. Inclusion and exclusion criteria

INCLUSION CRITERIA	EXCLUSION CRITERIA
Clinical trials: controlled randomised.	Longitudinal studies.
Articles in English or Spanish.	Grey literature, case reports, letters to the editor, protocols, narrative reviews.
Patients diagnosed with MCI or dementia (including AD).	Patients with other types of cognitive disorders (secondary to toxics, stroke, or post-surgical intervention).
Patients with advanced age (>50 years).	Young patients with cognitive disorders. cognitive disorders.
Diagnosis and efficacy determined with neuropsychological or cognitive tests (MMSE, Adas Cog, MoCA scale etc.).	Articles that do not include efficacy variables.

INCLUSION CRITERIA	EXCLUSION CRITERIA
	Preclinical experimental studies.
Intervention: (a) Aerobic physical exercise (two-fifteen months). b) Aerobic physical exercise + other activities (four-twelve months). c) Resistance physical exercise (Three-seven months).	Interventions with other types of therapy.
Publication date from 2015 until July 2021.	

2.3. Data extraction and analysis

Data from the articles were extracted systematically in a table following the PICO format (Patients, Intervention, Comparison, Outcomes), i.e., patients, intervention, comparison, and outcomes (Table 2) (Mandolesi *et al.* 2018). All data obtained from the articles are presented in annex A.

Efficacy is defined in terms of improvement of the overall cognitive state or by cognitive domains after the application of the intervention with physical activity and through the application of the different scales to assess cognition (MMSE, MoCA, Adas-Cog etc.).

Table 2. PICO Format

Patient: Number of patients and type of cognitive impairment.
Intervention: a) Aerobic physical activity. b) Aerobic physical activity combined with other activities. c) Resistance physical activity.
Comparison: control group and treatment group.
Results: - Global cognitive status. - Cognitive status by domains.

2.4. Assessment of study quality

To assess the methodological quality of the clinical trials included in this SR, the Jadad Scale was applied (Cascaes da Silva *et al.* 2013). The score on this scale ranges from 0 to five points, the higher the score, the better the methodological quality of the clinical trial assessed. Thus, a score of five points is considered „rigorous" and a score of less than three points is considered „poor". The criteria analysed by this scale are:

- Whether the study was randomised.
- Whether the method of randomisation was explained.
- Whether the study was double-blind.
- Whether the conditions of blinding were explained and whether they were adequate.
- Whether population losses were described.

The scoring of each of the studies assessed according to this scale is set out in the tables for each article (Annex A).

3. Results

3.1. Selection of studies

306 articles were found after searching the PubMed database. After eliminating duplicate citations, 220 studies were finally obtained. After reviewing the abstracts and/or titles, 34 were considered for full text review. Finally, 18 randomised controlled trials were included in this systematic review (Figure 1).

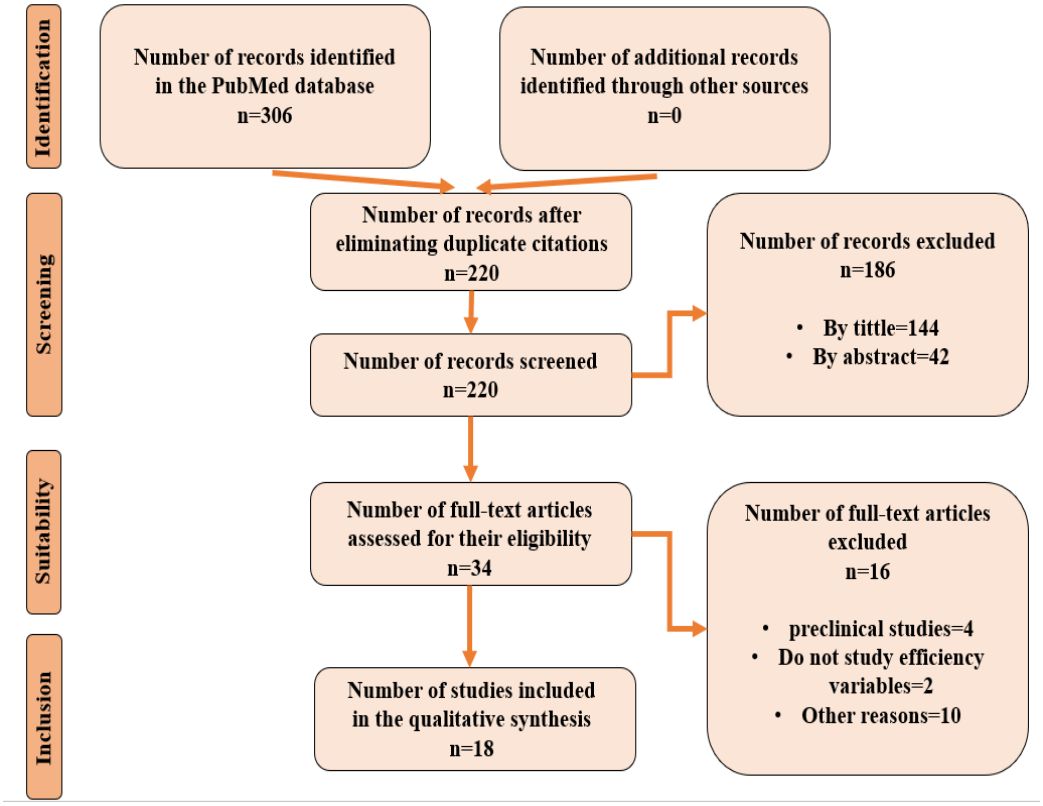

Figure 1. PRISMA flow chart.

3.2. Characteristics of the studies

The included studies were published between 4 June 2015 and 14 February 2020. The total number of patients included in this SR is 2043, of which 1212 belong to the treatment groups and 831 to the control groups. The sample size of the treatment groups, in the included clinical trials, varies between 17 and 329. All participants are elderly (>50 years). Patients had a cognitive disorder, either MCI or dementia. Of the total patients included in the statistically significant results, 45.75 percent (n=259) had dementia, 9.71 percent (n=55) had MCI/dementia (mixed) and 44.52 percent (n=252) had MCI. The clinical studies were randomised controlled clinical trials.

3.3. Results of the studies

The data obtained from each article are presented in Annex A. For didactic purposes we only include the results in graphical form for those articles that present statistically significant results between the study group and the control group. It is worth mentioning that the control groups received the usual care, consisting of performing ADLs (basic activities of daily living), IADLs (instrumental activities of daily living), recreational activities, physiotherapy sessions and occasionally low-intensity exercise sessions.

Regarding the description „other activities" in the therapy section, the following are included: warm-up, stretching, strength exercises, balance exercises, functional and cognitive task exercises. In the following, we show the results of the articles classified according to the assessment of cognitive impairment globally or by domains.

3.4. Assessment of global cognitive impairment

Percentage of articles analysing global cognitive impairment

Of the eighteen articles studied, fifteen presented results with statistically significant differences (83.33 percent). Of these fifteen, three papers analysed global cognitive impairment (Figure 2).

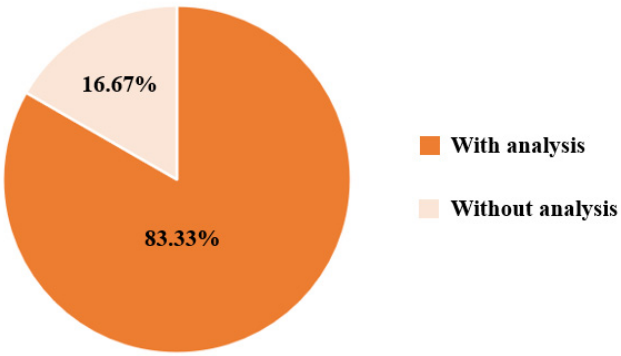

Figure 2. Percentage of articles with analysis of global cognitive impairment.

Percentage of patients with analysis of global cognitive impairment

Thus, the patients whose results show statistically significant global cognitive differences are 54.12 percent (n=656) of the total number of patients (n=1212) (Figure 3).

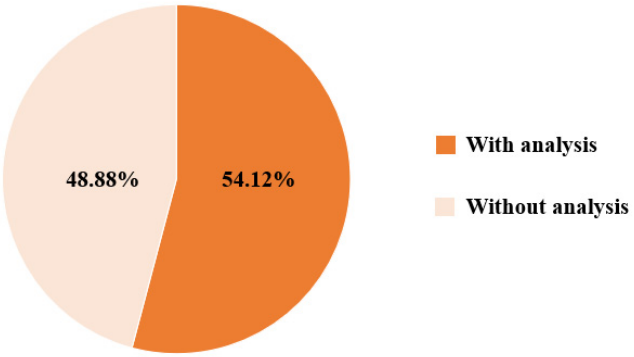

Figure 3. Percentage of patients with analysis of global cognitive impairment.

3.5. Assessment of cognitive impairment by domains

We present the results of the articles classified according to the type of disorder (MCI and dementia, including Alzheimer's disease) and the type of therapy (aerobic physical activity, aerobic physical activity plus other activities and endurance physical activity).

MCI articles with analysis of cognitive impairment by domains

We collected twelve articles whose results showed statistically significant differences in the study of cognitive impairment by domains. Of these twelve articles, seven pertain to patients with MCI. Figure 4 shows on the x-axis the article reference number of each paper and on the y-axis the sum of the positive cognitive domains. The „positive" („yes") rating of each cognitive domain is represented by an area with a specific colour (Figure 4).

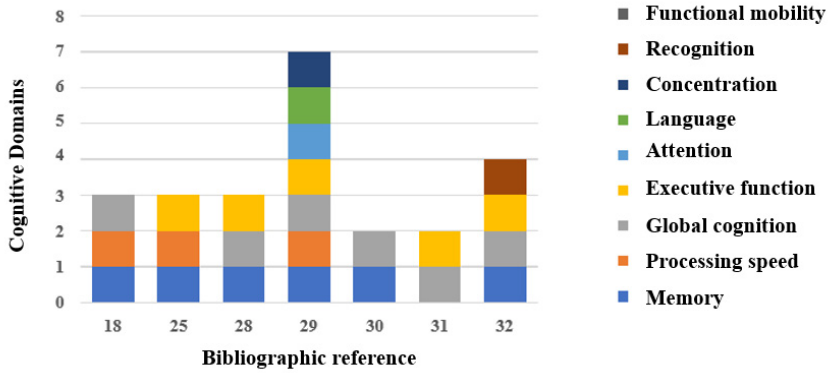

Figure 4. Articles on MCI with domain analysis of cognitive impairment.

3.6. Percentage of MCI patients with analysis of cognitive impairment by domains

The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with MCI (n=252) were 67 percent in memory, 32 percent in processing speed, 91.26 percent in global cognition, 77.77 percent in executive function, 12 percent in attention, 12 percent in language, 12 percent in concentration and seven percent in recognition (Figure 5).

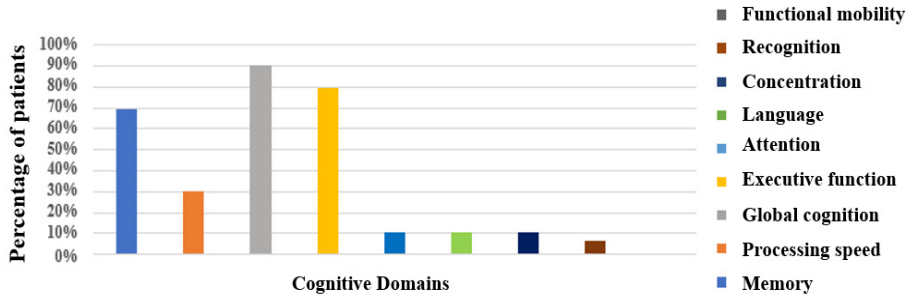

Figure 5. Percentage of MCI patients with cognitive impairment analysis by domains.

3.7. Percentage of MCI patients with analysis of cognitive impairment by domains according to type of therapy

Aerobic Exercise

The time of therapy application was between six and 12 weeks. The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total of patients with MCI in the aerobic exercise intervention were 100 percent in memory, 48.70 percent in processing speed, 100 percent in global cognition, 76.03 percent in executive function, 24.79 percent in attention, 24.79 percent in language, 24.79 percent in concentration and 14.04 percent in recognition (Figure 6).

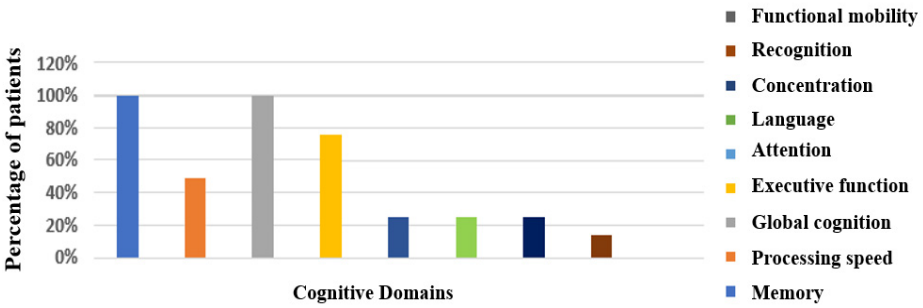

Figure 6. Percentage of MCI patients in the analysis of the different cognitive domains in the aerobic exercise intervention.

Aerobic exercise and other activities

No articles studied these variables.

Resistance Exercise

The time of application of the therapy was between three and fifteen months. The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with MCI in the resistance exercise intervention were 34.40 percent in memory, 16.79 percent in processing speed, 83.20 percent in global cognition and 79.38 percent in executive function (Figure 7).

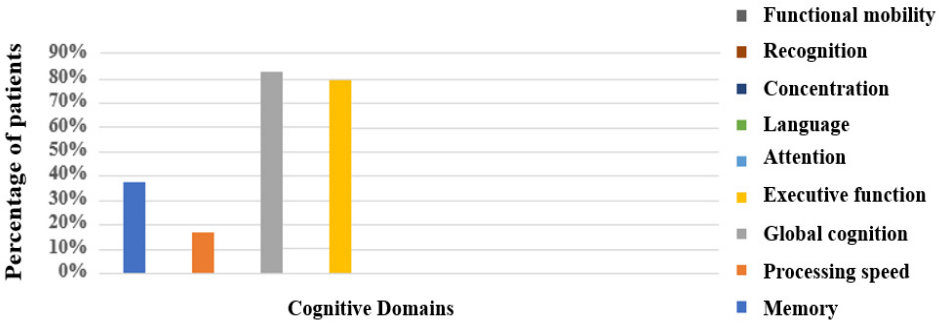

Figure 7. Percentage of patients with MCI in the analysis of the different cognitive domains in the resistance exercise intervention.

3.8. MCI/dementia (mixed) articles with analysis of cognitive impairment by domains

Of the twelve articles whose results showed statistically significant differences in the study of cognitive impairment by domains, two pertain to patients with MCI/dementia (Figure 8).

Figure 8. Articles on MCI/dementia (mixed) with analysis of cognitive impairment by domains.

Percentage of patients with MCI/dementia (mixed) with analysis of cognitive impairment by domains

The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with MCI/dementia (n=55). with respect to the total number of patients with MCI/dementia (n=55) was 49.09 percent in global cognition and 50.09 percent in executive function (Figure 9).

3.9. Percentage of MCI/dementia (mixed) patients with cognitive impairment analysis by domains according to type of therapy

Aerobic Exercise

No articles studied these variables.

Aerobic exercise and other activities

The time of application of the therapy was between three and six months. The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total of patients with MCI/dementia in the aerobic exercise intervention and other activities was 40.09 percent in global cognition and 50.90 percent in executive function (Figure 9).

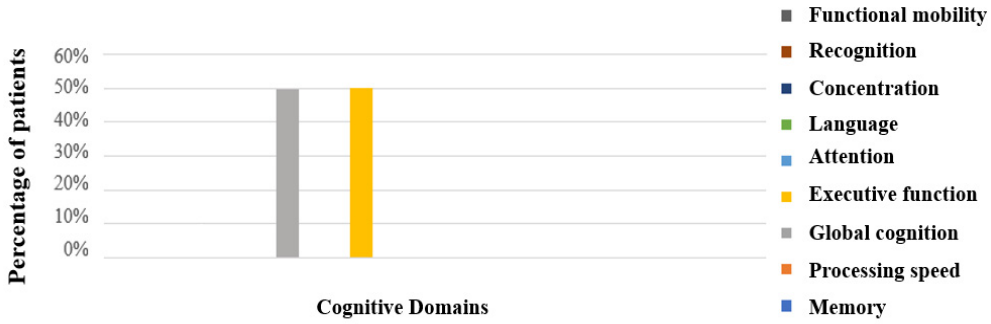

Figure 9. Percentage of patients with MCI/dementia (mixed) with analysis of cognitive impairment by domains.

Endurance exercise

No articles studied these variables.

3.10. Articles on dementia with analysis of cognitive impairment cognitive domains

Of the twelve articles whose results showed statistically significant differences in the study of cognitive impairment by domains, three pertain to patients with dementia (Figure 10).

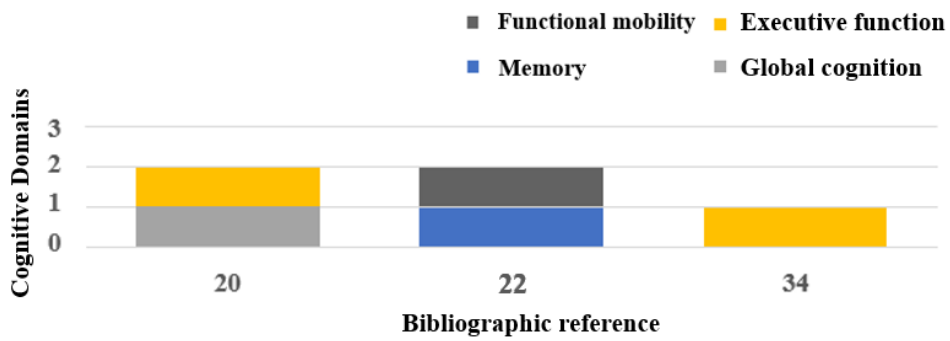

Figure 10. Articles on dementia with analysis of cognitive impairment by domains.

Percentage of patients with dementia with analysis of cognitive impairment by domains

The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with dementia (n=259) were 19.69 percent in memory, 54.05 percent in global cognition, 80.30 percent in executive function and 19.69 percent in functional mobility (Figure 11).

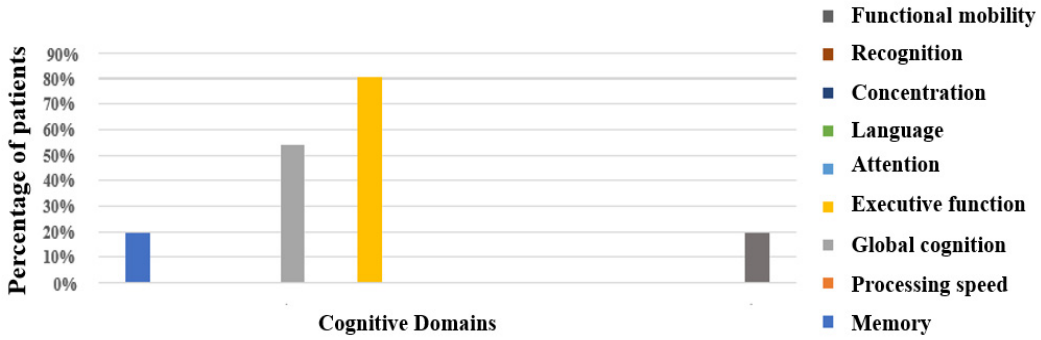

Figure 11. Percentage of dementia patients with cognitive impairment analysis by domains.

3.11. Percentage of dementia patients with analysis of cognitive impairment by domains according to type of therapy

Aerobic Exercise

The time of application of the therapy was between three and fifteen months. The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with dementia in the aerobic exercise intervention was 42.85 percent in cognitive domains and 42.85 percent in cognitive domains with respect to the total number of patients with dementia where: 42.85

percent in memory, 57.14 percent in executive function and 42.85 percent in functional mobility (Figure 12).

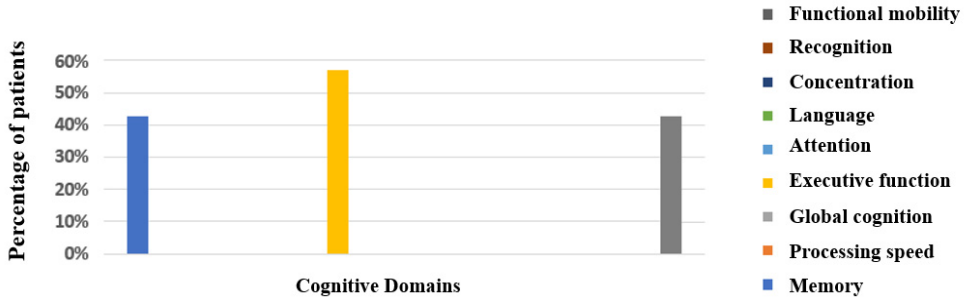

Figure 12. Percentage of dementia patients in the analysis of the different cognitive domains in the aerobic exercise intervention.

Aerobic exercise and other activities

The time of application of the therapy was one year. The percentage of patients who obtained results with statistically significant differences in the analysis of the different cognitive domains with respect to the total number of patients with dementia in the aerobic exercise and other activities intervention was 100 percent in global cognition and 100 percent in executive function (Figure 13).

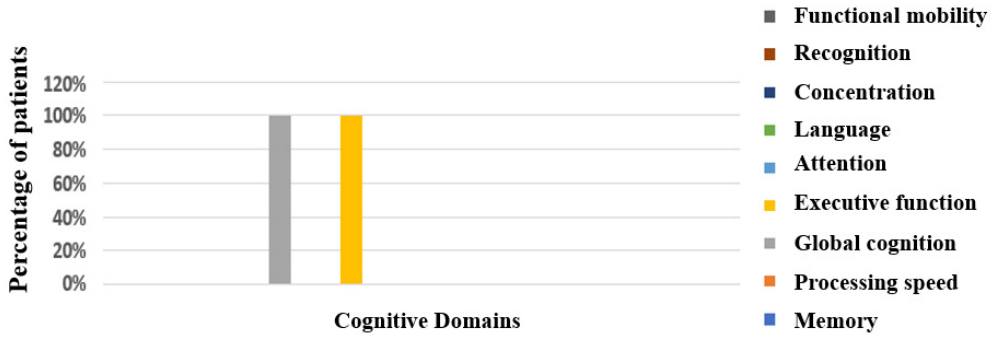

Figure 13. Percentage of dementia patients in the analysis of different cognitive domains in the aerobic exercise intervention and other activities.

Endurance exercise

No articles studied these variables.

4. Discussions

The improved socio-health conditions of the 21st century population lead to an increase in life expectancy and consequent ageing. However, this leads to an increase in neurodegenerative diseases, including cognitive disorders (Brodziak *et al.* 2015). Different therapeutic strategies have been designed to complement the efficacy of pharmacological treatment, including physical exercise, cognitive

training, music therapy, diet, acupuncture, etc (Ramos Cordero & Yubero, 2016). The aim of this SR is to analyse the efficacy of physical exercise on different cognitive domains in older people with MCI or dementia.

Numerous neurocognitive tests were used both to diagnose patients and to measure the efficacy of physical exercise on cognition, with scales measuring global cognition, such as the MMSE, being more commonly used (Folstein *et al.* 1975). Heterogeneity was observed among the different tests. Heterogeneity was observed between the different physical exercise interventions in the studies. The most common exercises were cycling (Cancela *et al.* 2016; Fonte *et al.* 2019), balance (de Oliveira Silva *et al.* 2019; Öhman *et al.*, 2016), walking (Bademli *et al.*, 2019), dancing (Rainbow T H Ho *et al.*, 2020; Rainbow Tin Hung Ho *et al.*, 2015; Zhu *et al.*, 2018), elastic band (Hong *et al.*, 2018; Yoon *et al.*, 2017), kayaking (Choi & Lee, 2019) and strength training combined with aerobics (Öhman *et al.*, 2016). In this study, physical exercise is found to significantly benefit memory, global cognitive ability and executive function in both MCI and dementia patients. Likewise, the population suffering from MCI showed improvement compared to the control group in a greater number of cognitive domains, in contrast to dementia, in which positive effects were observed only in four of the nine cognitive domains studied (Figure 11). The most effective type of intervention is aerobic physical exercise in MCI, as shown in Figure 6. This may be since half of the trials studied this type of cognitive impairment. The time of application of the therapy in the different intervention groups ranged from two to fifteen months, which may influence the interpretation of the results and their short- and long-term effects. It should be mentioned that physical activity does not only improve cognition, it has effects on quality of life, decreased risk of falls, cardiovascular function, etc (Warburton *et al.*, 2006). In all cases, training should be individualised and adapted to the situation of each patient.

Physical exercise is a type of non-invasive intervention, which may explain why most of the articles included in the SR do not specify adverse effects following the application of these therapies, and, in those that do mention them, do not describe the type of adverse events or in which group they occur. This contrasts with other types of treatment, such as pharmacological treatments (anticholinesterase inhibitors and glutamatergic transmission modulators), which are not free of adverse events such as vomiting, loss of appetite, insomnia, abdominal pain, bradycardia, etc (López Locanto, 2015). It should be noted that, being an elderly population, they have comorbidities, which may be associated with dropouts, deaths, and lack of adherence to the intervention. When giving advice, medical professionals should bear in mind that older people are better able to cope with the challenges of everyday life than is reflected in neuropsychological tests (Brodziak *et al.*, 2015).

As mentioned in the introduction, there are several mechanisms that may explain the beneficial effect of exercise on cognitive function. These include improved cerebral oxygenation, lower blood pressure, lower lipid levels, increased synthesis of growth factors that act on hippocampal neurons, etc. However, more

research is needed to deepen this knowledge (Mandolesi *et al.*, 2018). Although this SR reflects the success of physical exercise on cognitive function in elderly individuals, more studies are needed with larger sample sizes and stratifying patients according to the stage of cognitive impairment.

Conclusions

Among the different physical therapies, aerobic activity is the most effective treatment for both mild cognitive impairment and dementia. The cognitive domains that are most enhanced after aerobic exercise in both mild cognitive impairment and dementia are: memory, global cognition, and executive function. Physical activity as a therapy for cognitive impairment has few adverse effects. More randomised controlled studies are needed to provide further scientific evidence for these results.

Abbreviations
ABVD: Basic Activities of Daily Living.
ADAS: Alzheimer's Disease Assessment Scale (Alzheimer's Disease Assessment Scale).
ADAS-Cog: Alzheimer's Disease Assessment Scale Cognitive (Alzheimer's Disease Cognitive Assessment Scale).
IADL: Instrumental Activities of Daily Living.
APA: American Psychological Association.
ADL: Activities of Daily Living. BDNF: Brain-Derived Neurotrophic Factor.
MCI: Mild Cognitive Impairment.
DSM: Diagnostic and Statistical Manual of Mental Disorders.
AD: Alzheimer's disease.
EEG: Electroencephalogram.
EJ: Jadad Scale.
PD: Parkinson's disease.
MeSH: Medical Subject Headings.
MMSE: Mini Mental State Examination.
MoCA: Montreal Cognitive Assessment.
NCBI: National Centre for Biotechnology Information.
WHO: World Health Organization.
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses.
SR: Systematic Review.

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Annex A. Summary table of the articles analysed

REFERENCE	EJ	YEAR	DIAGNOSTIC	METHOD	TOTAL POPULATION (n)	INTERVENTION	DURATION	RESULTS
(Amjad *et al.*, 2019)	5	2018	MCI	Randomised controlled trial	40	Treadmill and stationary bike exercise in sessions of 20 to 40 minutes	3 times a week for 6 weeks	Significant improvement in Trial Marketing Test A and B and MoCa results (p=0.005 and p=0.036, respectively)
(Zhu *et al.*, 2018)	>3	2018	Amnesic MCI	Randomised controlled trial	60	35 minutes of dance session	3 times a week for 3 months	Improved memory and processing speed (p<0.001 and p<0.05, respectively)
(Lamb *et al.*, 2018)	>3	2018	Dementia	Randomised controlled trial	494	60-90 minutes of supervised physical exercise	2 times a week for 4 months	Non-significant improvement
(Öhman *et al.*, 2016)	>3	2016	AD	Randomised controlled trial	210	60 minutes of physical exercise	2 times a week for 12 months	Improved executive function (p=0.03)
(Yoon *et al.*, 2017)	5	2017	MCI	Randomised controlled trial	70	60 minutes of physical exercise	2 times a week for 12 weeks	Major improvements in MMSE and MoCA (p<0.001)
(Cancela *et al.*, 2016)	>3	2015	Dementia	Randomised controlled trial	114	15 minutes of aerobic exercise	15 minutes daily for 15 months	Significant improvement in memory and functional mobility (p=0.028 and p=0.043, respectively)
(Toots *et al.*, 2017)	5	2017	Dementia with MCI to moderate	Randomised controlled trial	186	39 high-intensity functional exercises	45 minutes daily for 4 weeks	Non-significant differences(p=0.644)

REFERENCE	EJ	YEAR	DIAGNOSTIC	METHOD	TOTAL POPULATION (n)	INTERVENTION	DURATION	RESULTS
(Fonte *et al.*, 2019)	5	2019	MCI/AD	Randomised controlled trial	87	90 minutes of cognitive rehabilitation techniques or physical resistance exercises	3 times a week for 6 months	Statistically significant benefit of these interventions in AD and MCI patients (p<0.001)
(Yoon *et al.*, 2017)	3	2018	MCI	Randomised controlled trial	45	60 minutes of physical exercise	3 times a week for 16 weeks	Significant improvement in executive function and processing speed (p<0.05)
(Bademli *et al.*, 2019)	3	2019	MCI	Randomised controlled trial	60	70 minutes of physical exercise	Daily for 20 weeks	Significant improvement (p<0.05)
(Rainbow Tin Hung Ho *et al.*, 2015)	>3	2015	Mild dementia	Randomised controlled trial	201	60 minutes of physical exercise of dance session	2 times a week for 12 weeks	Non-significant improvement
(Law *et al.*, 2019)	4	2019	MCI	Randomised controlled trial	59	30-40 minutes of physical exercise or cognitive training programme	12 sessions over 8 weeks	Significant improvement in memory (p=0.009)
(Choi & Lee, 2019)	5	2019	MCI	Randomised controlled trial	60	60 minutes of kayak	2 times a week for 6 weeks	Significant improvement in the MoCA test and significant correlation between muscle performance and cognitive function (p<0.05)
(Hong *et al.*, 2018)	>3	2017	MCI	Randomised controlled trial	56	60 minutes of resistance exercise	2 times a week for 12 weeks	Significant improvement in memory (p<0.05)

REFERENCE	EJ	YEAR	DIAGNOSTIC	METHOD	TOTAL POPULATION (n)	INTERVENTION	DURATION	RESULTS
(Broadhouse *et al.*, 2020)	>3	2020	MCI	Randomised controlled trial	82	90 minutes of resistance exercise and/or cognitive training programme	2-3 times a week for 26 weeks	Significant improvement in cognitive function (p<0.05)
(Bisbe *et al.*, 2020)	5	2020	MCI	Randomised controlled trial	31	60 minutes of choreographed exercise	2 times a week for 12 weeks	Significant improvement in global cognition, memory, and executive function (p<0.05)
(de Oliveira Silva *et al.*, 2019)	>3	2019	MCI/AD	Randomised controlled trial	56	60 minutes of aerobic exercise	2 times a week for 12 weeks	Significant improvement in executive function and functional mobility (p=0.03 and p=0.05, respectively)
(Rainbow T H Ho *et al.*, 2020)	4	2020	Dementia	Randomised controlled trial	204	60 minutes of dance movement and/or physical exercise	12 weeks	Significant improvement in executive function (p<0.01)