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Review article

Effectiveness of intervention based on physical exercise in patients with Alzheimer's disease

Efectividad de la intervención basada en el ejercicio físico en pacientes con enfermedad de Alzheimer

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Citation

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Abstract

Introduction: Alzheimer's disease (AD) is a pathology characterized by slow and progressive neuronal degeneration, which leads to loss of memory, language, orientation and behavior. Multidisciplinary teams must address AD through pharmacological and non-pharmacological interventions, among the latter is the performance of physical exercise as it has been proven that it delays its appearance and slows its progression. Objective: To know the validity of physical exercise as a non-pharmacological treatment for patients with Alzheimer's disease. Methodology: A systematic descriptive and explanatory literature review was carried out by searching for articles in scientific databases, following the methodology of the PRISMA statement. Results: Physical exercise has an effect that despite being minimal is of great importance, among these are: the decrease in the abnormal production of β-amyloid protein, increased blood flow, capillary angiogenesis in the brain, the increase in the production of endorphins that reduce depression, brain neuroplasticity, improvement in the physical state and body composition of patients, thus improving their quality of life.

Keywords: Alzheimer's disease, Dementia, Physical Exercise.

Resumen

Introducción: la enfermedad de Alzheimer (EA) es una patología caracterizada por la degeneración neuronal lenta y progresiva, que conduce a la pérdida de memoria, lenguaje, orientación y conducta, los equipos multidisciplinarios deben abordar la EA mediante intervenciones farmacológicas y no farmacológicas, entre los últimos se encuentra la realización de ejercicio físico, pues se ha comprobado que retrasa su aparición y retarda su progresión. Objetivo: conocer la validez del ejercicio físico como tratamiento no farmacológico para los pacientes con enfermedad de Alzheimer. Metodología: se realizó una revisión sistemática de la literatura de carácter descriptivo y explicativo, mediante la búsqueda de artículos en bases de datos científicas, siguiendo la metodología de la declaración de PRISMA. Resultados: el ejercicio físico posee un efecto que, a pesar de ser mínimo, es de gran importancia, entre estos se encuentran: la disminución en la producción anómala de la proteína β-amiloide, el incremento del riego sanguíneo, la angiogénesis capilar en el cerebro, el incremento en la producción de endorfinas que reducen la depresión, la neuroplasticidad cerebral, la mejora en el estado físico y composición corporal de los pacientes, de esta forma mejora su calidad de vida.

Palabras clave: Enfermedad de Alzheimer, Demencia, Ejercicio Físico.

Introduction

Alzheimer's disease (AD) is a pathology characterized by neuronal degeneration with its own cytological, histological, and immunohistochemically changes, with a topographical distribution that can differentiate it from standard patterns of senescence. Diagnostic certainty requires histopathological confirmation, which shows the presence of neurofibrillary tangles inside neurons formed by tau protein with defects in its phosphorylation and abnormal amyloid extracellular plaques, loss of synapses, neuronal deterioration, and vascular deposition of amyloid [1].

Currently, epidemiological studies reveal that about 50 million people have dementia, 60-70 % represent AD and that its incidence will increase to 10 million every year. The prevalence of AD in Latin America is 6.7% in Peru, 8% in Venezuela, 11.5% in Argentina, and 5.3% in Brazil. In Ecuador, there is no concrete epidemiological data about AD. However, it is estimated that one out of three older Ecuadorian adults suffers from some dementia [1].

Pathophysiologically, the genesis of the disease is thought to begin with the formation of an amyloid β-protein that accumulates, forming neurotoxic polymers, resulting in a reduction of synapses leading to glial cell activation triggering a microglial inflammatory reaction, driving the release of cytokines from the apoptosis cascade and oxidative stress [2].

Multidisciplinary teams should address AD through pharmacological and non-pharmacological interventions designed to delay cognitive decline, minimize brain dysfunction, and manage the performance of other functions. Among the non-pharmacological treatments, physiotherapy plays a vital role in reducing the complications of this disease since exercise aims to improve functional capacity, reduce the use of drugs, reduce the risk of falls, and minimize functional defects during the disease [2,3].

Physical activity has multiple beneficial effects on AD by delaying its onset and slowing its development for several reasons. First, physical exercise generates specific metabolic and neuropathological changes that target the root cause of the disease. Secondly, aerobic exercise or flexibility training, mainly yoga, is helpful to improve the clinical manifestations, both psychological and neurological, typical of the progression of the pathology [1,2].

Rolland et al. conducted a study in which 23 individuals with moderate and severe AD underwent aerobic exercise for about seven weeks. Cognitive-behavioral improvements and decreased risk of falls were observed. However, no significant changes in patients' functional autonomy were evidenced in this study. It is concluded that allowing patients with AD to participate in daily activities, combined with physical exercise, can improve balance, flexibility, cardiorespiratory endurance, muscular strength, bone density, sleep quality, and social activity. It also reduces emotional and behavioral changes [4,5].

Physical exercise has a positive impact on patients with AD; for this reason, it is advisable to incorporate structured and planned exercise programs with aerobic exercise, strength training, coordination, and balance within the non-pharmacological scheme and combine this plan with psychological, social, and cognitive therapy, this therapy has been widely applied in recent years due to its low cost and simplicity.

Methodology

A systematic review of the descriptive and explanatory literature on the effectiveness of physical exercise-based intervention in patients with Alzheimer's disease was carried out, following the indications of the PRISMA Report flowcharts.

A bibliographic study through a systematic review was carried out considering scientific publications whose content is related to this topic. For this review, the research was performed in the following electronic databases that deal with health sciences: Google Scholar, Ovid, Taylor, and Francis, Scielo, Elsevier, Dialnet, Web of Science, and Research Gate. The search for information was agreed to be from 2016 to 2021. All studies used in this review were published in English and Spanish and conducted worldwide. Keywords used: "Alzheimer's disease", "Dementia", "Exercise Therapy", "Physical Exercise", "Physical Activity", "Physical Therapy", "Exercise Training".

As inclusion criteria, open access scientific productions available in the previously mentioned digital databases, corresponding from 2016 to 2021, both in English and Spanish, were considered, which evidenced the effects of physical exercise in patients with Alzheimer's disease.

The exclusion criteria were all those scientific articles that do not correspond to the time frame established between 2016 - 2021, studies or publications that do not appear in the scientific databases described above, that have no relation to the objective of the review, and finally, those duplicated or repeated publications. The search strategies in each digital database are described in Table 1.

Table 1: Search strategies in the digital database.

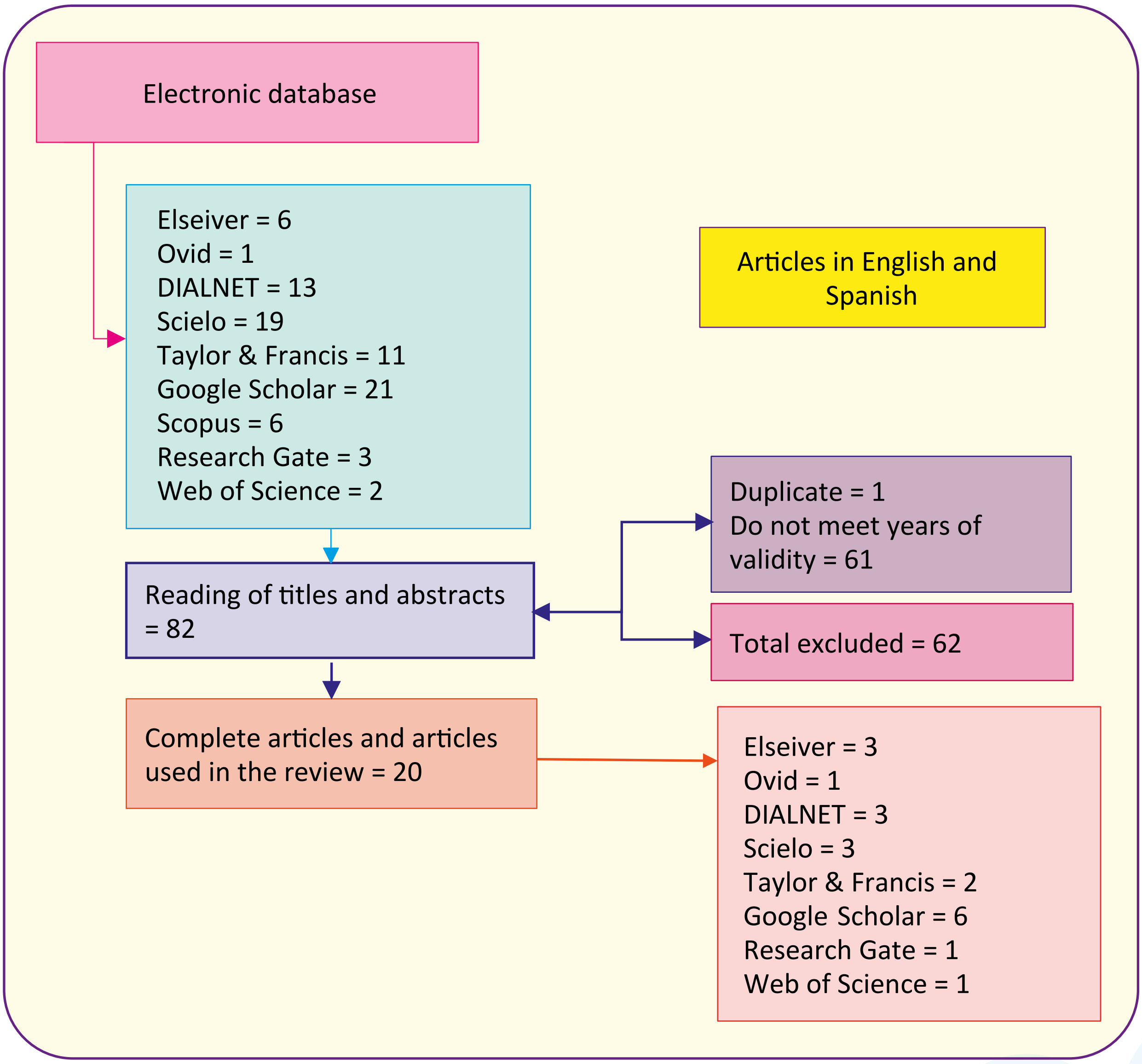
No.	Bibliographical source	Search method	Number	Language	Type of document
1	ELSEVIER	Effects of physical exercises and basic guidelines for its prescription in patients with Alzheimer	4	Spanish	Article
		Physical exercise in the prevention and treatment of Alzheimer's disease	2	English	Article
2	OVID	Effect of interventions based on physical exercise and diet on the evolution of mild cognitive impairment to dementia in people over 45 years. Systematic review	1	English	Systematic review
3	DIALNET	Physical exercise in patients diagnosed with Alzheimer's disease.	4	Spanish	Article
		Effects of physical exercise in the prevention of falls in the patient with Alzheimer's disease.	3	Spanish	Article
		Regular practice of physical exercise as a way to stop the Alzheimer's disease progression.	6	Spanish	Article
4	SCIELO	Alzheimer's disease Exercise Therapy	1	Spanish	Article
		Physical exercise in the Alzheimer's disease.	6	Spanish	Article
		Physical therapy in patients with Alzheimer's disease.	12	English	Article
5	TAYLOR AND FRANCIS	Physical therapy in Alzheimer's disease.	5	English	Article
		Physical exercises in Alzheimer's.	6	English	Article
6	GOOGLE SCHOLAR	Effectiveness of physical rehabilitation in patients diagnosed with Alzheimer's dementia, vascular dementia, dementia with Lewy bodies, or mixed dementia. Bibliographical review	5	Spanish	Thesis
		Physic al activity effect on cognitive impairment and dementia.	6	Spanish	Article
		Effect of a hatha yoga program in patients with Alzheimer's Disease (AD).	2	Spanish	Article
		Physical exercise and senescence: influence of physical activity in Alzheimer.	3	Spanish	Thesis
		Strategies of physiotherapeutic intervention applied in patients with Alzheimer's disease.	5	Spanish	Article
7	SCOPUS	Aerobic and strength training exercise programmed forcognitive impairment in people with mild to moderate dementia: The DAPA RCT.	6	English	Article

Bibliographic search procedure *The database of the virtual library of the Catholic University of Cuenca, whose platform is explicitly related to the health sciences field, was used. The information search period lasted one week, from April 5 to April 11, 2021. After considering the aforementioned inclusion and exclusion criteria, the research selection process is carried out according to the four stages of the PRISMA report flowchart.*

Results

At the end of the search for articles in general, 82 articles were obtained from the database. After reading and analyzing the titles and abstracts related to our study objective, the inclusion and exclusion methods were applied: 62 articles were excluded, 61 of them did not meet the validity period, and 1 article was excluded due to repetition in the database; and, finally, 20 articles were used in our study since they meet the criteria already described. This representation is detailed in Figure 1

Figure 1: Flowchart of article selection



Regarding the articles selected for our study, a statistical analysis was carried out, in which a percentage of 33% of the papers belonged to the GOOGLE ACADEMIC database, followed by DIALNET and SCIELO with a 20%, ELSEVIER with 14%, and finally, OVID and TAYLOR AND FRANCIS with 7% of the articles investigated. About the years of publication of the articles, we have that 27% corresponds to the year 2017, followed by 20% in the years 2019 and 2021, 13% for the years 2016 and 2020, and only 7% for the year 2018, as shown in Table 2.

Table 2: Detail of the articles with their respective database, year of publication, author, journal, and language.

Database	Published in	Publication authors	Year of publication	Language	Title	Objectives	Results
ELSEVIER	Revista Andaluzade Medicina del Deporte	Nascimento CMC, Varela S, Ayan C, Cancela JM.	2016	Spanish	Effects of physical exercises and basic guidelines for its prescription in Alzheimer's Disease.	To present the reasons why exercise could be beneficial through the description of the effects on metabolic and neuropathological aspects.	The reasons why exercise could be beneficial are presented by describing its effects on metabolic and neuropathological aspects related to this disease. The different organic responses that could be modulated through exercise on AD biomarkers are analyzed.
ELSEVIER	Spanish Journal of Geriatrics and Gerontology	Loreto González, Romána Caritat Bagu, Gerard Urrútia Cuchíc, Jèssica Garrido Pedrosaa	2016	Spanish	Exercise and environment-based interventions for falls prevention in people with cognitive impairment living in care homes: systematic review and meta-analysis.	To evaluate the effectiveness of interventions that use exercise and/or environmental modification to prevent falls in institutionalized elderly with cognitive impairment.	Exercise and/or environmental modification alone or combined with other interventions showed effectiveness in reducing the number of falls.
ELSEVIER	Journal of Sportand Health Science	Adrián de la Rosa, M. Carmen Gómez-Cabrera, Millan F, Blasco – Lafarga C	2020	English	Physical exercise inthe prevention and treatment of Alzheimer's disease	To know the relationship between therisk of AD and the performance ofphysical exercise and how its frequent performance modifies the cognitive function of thesepatients	Exercise modulates Aß turnover, inflammation, the synthesis and release of neurotrophins, and CBF. Multimodal interventions that include the adoption of an active lifestyle should be recommended for older populations.
OVID	Revista Españolade Salud Pública	Ballarín-Naya, Lucía; Malo, Sara; Moreno-Franco, Belén.	2021	Spanish	Effect of interventions based on physical exercise and diet on the evolution of mild cognitive impairment to dementia in people over 45 years old. Systematic review	To analyze studies that evaluate the effectiveness of an intervention of physical exercise and/or diet on people over 45 years old with mild cognitive impairment (MCI) and without AD diagnosis.	It was concluded that a healthy diet containing omega 3 and 6, as well as the consumption of nuts, fish, and legumes, together with a minimum daily physical activity of 30 minutes in people > 45 years old with mild cognitive impairment (MCI) and no diagnosis of AD, significantly improved their cognitive function.
DIALNET	Revista de Divulgación en Fisioterapia	José Pérez Moreno, Iván Cerdeña Macías, Raquel Villa Pérez, M. del Carmen Sánchez Blaya.	2017	Spanish	Physical exercise in patients diagnosed with Alzheimer	To determine the contribution of physical exercise in patients with AD, according to the clinical literature of the last five years.	The five clinical trials selected showed results about the importance of physical exercise regarding the functional capacities of patients with AD, cognitive abilities, and sleep quality (wakefulness, adequate sleep).
DIALNET	Revista de Divulgación en Fisioterapia	J.M. García-Moreno; I. Calvo-Muñoz; A. Gómez-Conesa	2021	Spanish	Effects of physical exercise in preventing falls in patients with Alzheimer's Disease	To know the effects of physical exercise in preventing falls in people with AD and the type of exercise with the best clinical efficacy.	Individual home exercises have better effects than outpatient group exercises. The results obtained were favorable eight weeks after starting the treatment.
DIALNET	Gerokomos: Revista de la Sociedad Española de Enfermería Geriátrica y Gerontológica	Julia Arias Iniesta; María Luisa Martínez Martín	2020	Spanish	Regular practice of physical exercise as a way to stop the AD's progression	To analyze the evidence about the efficiency of the regular practice of physical exercise to delay the progression of AD.	Twenty articles that highlighted the positive impact of exercise-based therapy on different aspects of the patient's life, whether physical, mental, or social, were analyzed. The beneficial effects of aerobic exercise combined with strength, balance, and mobility exercises on the patient's global cognition and psychic symptoms have been proven.
SCIELO	Rev Bras Med Esporte	Furmann, M., Rebesco, D. B.,Smouter, L., Hosni, A. P., Kerppers, I. I., Machado-Rodrigues, A. M.	2019	English	Influence of acute physical exercise on cognitive and motorbehavior in an experimental modelof Alzheimer's disease	To investigate the cognitive andbehavioral alterations related to AD that are capable of slowing disease progression and itscomplications.	This is a relevant characteristic ofthe disease, which did not improve after acute exercise. By analyzing the size effect, it was possible to observe a difference in the Alzheimer + swimming group in terms of reduced anxiety and improved motor behavior after exercise.
SCIELO	Physical Therapy & Research Fisioterapia & Pesquisa	Marques Carlos Leonardo Sacomani, Borgato Maria Helena, Moura Neto Eduardo de, Bazan Rodrigo, Luvizutto Gustavo José.	2019	English	Physical therapy in patients with Alzheimer's disease; a systematic review of randomized controlled clinical trials.	The objective of this study is to evaluate the effects of physical therapy on the cognitive and functional capacity of patients with Alzheimer's Disease.	In study 1, no statistically significant difference was found on the mini-mental state examination (MMSE) (MD 0.0, 95%CI – 5.76 to 5.76), neuropsychiatric inventory (MD -4.50, 95%CI -21.24 to 12.24) and Pfeffer instrumental activities questionnaire (MD 0.0 95%CI -6.48 to 6.48). In study 2, there was no statistically significant difference on the MMSE (MD -1.60, 95%CI -3.57 to 0.37), clock-drawing test (MD -0.20, 95%CI -0.61 to 0.21) and Alzheimer's Disease Assessment Scale – cognitive subscale (MD 1.0, 95%CI -2.21 to 4.21) after 12 months.

SCIELO	Journal of Negative and No Positive Results	Damián Pereira- Payo, Nicolás Failde-Lintas, Elena Durán-Cano, José Carmelo Adsuar Sala, Jorge Pérez-Gómez	2020	Spanish	Six weeks of physical exercise improve the functional capacity and the body composition in patients with Alzheimer	To know if six weeks of physical exercise could improve the physical condition and the body composition in people diagnosed with Alzheimer.	Some significant changes in the body composition and the functional capacity were found, which were reflected by the improvement of the "sit and stand up from a chair" test, the "stand up, walk, and sit down again" test, in the Berg scale, and in gait speed measurements.
TAYLOR & FRANCIS	J Mot Behav.	Guillaume Lamotte, Raj C. Shah, Orly Lazarov, and Daniel, Corcos	2017	English	Exercise Training for Persons with Alzheimer's Disease and Caregivers: A Review of Dyadic Exercise Interventions	The authors review the current clinical evidence for dyadic exercise interventions, which are exercise regimens applied to both the person with dementia and the caregiver.	This review shows that dyadic exercise interventions are feasible and may produce a positive effect on functional independence and caregiver burden.
TAYLOR & FRANCIS	Expert Review of Neurother apeutics	Marina Sagud, Lucija Tudor, Nela Pivac	2021	English	Personalized treatment interventions: no pharmacologic al and natural treatment strategies in Alzheimer's disease	This article describes the application of precision medicine-like approaches utilizing no pharmacological treatment strategies and the use of natural products in personalized care for patients with AD.	Namely, physical activity and cognitive training, combined with other no pharmacological strategies improve neuroprotection, normalize and regulate cerebral blood flow, offer stress relief and hormone balance, and are associated with increased production of BDNF and other growth factors, resulting in elevated neurogenesis, neuroplasticity, and angiogenesis, and decreased cortisol secretion and reduced inflammation.
GOOGLE SCHOLAR	University of Almeria	Álvaro Perea del Pozo, Caridad López Granero	2020	Spanish	Effectiveness of physical rehabilitation in patients diagnosed with Alzheimer's dementia, vascular dementia, dementia with Lewy bodies, or mixed dementia. Bibliographica l review	To evaluate the effectiveness of a multimodal treatment in elderly patients diagnosed with Alzheimer's dementia, vascular dementia, dementia with Lewy bodies, or mixed dementia.	This review concludes that the lack of protocols and qualified professionals who adjust physical rehab to the patients'' needs could result in lower effectiveness of these treatments.
GOOGLE SCHOLAR	Revista Cubana de Salud Pública	Laura Elizabet Castro-Jiménez Carlos Arturo Garvis-Fajardo	2018	Spanish	Effect of physical activity in the cognitive impairment and dementia	To assess the influence of physical activity on cognitive impairment and dementia.	Physical activity also influenced in the quality of life, provided benefits in the people's balance, and significant improvements in decreasing the risk of falls in elderly. All the results of physical performance showed statistically significant differences between the studied groups.
GOOGLE SCHOLAR	Revista Acta Colombia na de Psicología	María Clara Rodríguez Salazar, Alba Lucía Meneses Báez, Eliana Alexey Quintero Gallego	2017	Spanish	Effect of a hatha yoga program in patients with Alzheimer's	To assess the effect of a hatha yoga program in patients with AD, concerning their quality of life, depression, attention, memory, global cognitive functioning, and level of independence in their daily activities.	The results indicate that the mean in the sustained attention and processing speed component assessed with the Digit-Symbol presented a positive growth rate between the pretreatment and post-treatment measures. The different ratings obtained in two tests that measure the daily life activities: Lawton and Brody scale, were evaluated The results showed that a high growth rates up to post-treatment, but in the follow-up the growth rates are negative for both variables.
GOOGLE SCHOLAR	University of Jaén	María Zabala Lozano	2019	Spanish	Physical exercise and senescence: influence of physical activity in Alzheimer	To assess the influence of physical activity in Alzheimer.	Gender differences were observed in the results: men, who showed a greater bond to physical training, performed better in memory tasks; women presented better results in attention and memory. Nonetheless, the bond to physical training was low (63%) and the authors wondered whether the results would have been even better if there had been a greater bond.
GOOGLE SCHOLAR	Revista Mexicana de Neurocien cia	Piedad Rocío Lerma-Castaño, Belkis Rocío García-Parada.	2017	Spanish	Strategies of physiotherape utic intervention applied in patients with Alzheimer's disease	To verify the efficacy of strategies being applied by physical therapists, with physical exercise being one of the most excellent benefits and significant improvements in cognitive and motor alterations.	The results of modifiable factors associated with cognition and dementia indicate that physical activity is one of the most consistent modifiable protective factors for preventing Alzheimer's disease.

18	GOOGLE SCHOLAR	Revista Española de Salud Pública	Lucía Ballarín Sara Malo y Belén Moreno-Franco	2021	Spanish	Effect of interventions based on physical exercise and diet on the evolution of mild cognitive impairment to dementia in people over 45 years old. Systematic review	To know the effect of interventions based on physical exercise and diet on the evolution of mild cognitive impairment to dementia in people over 45 years old.	Scheduled physical exercise, performed 3 to 5 days a week, of moderate-high intensity, and food consumption according to a pattern such as the Mediterranean diet or the DASH diet improve global cognitive function in subjects with MCI. The results The results are enhanced when the studies combine both interventions and include cognitive stimulation exercises, increasing the functionality of the subjects.
19	RESEARCH GATE	University of Cádiz	Sonia Ortega Gómez; Vanesa España Romero	2019	Spanish	Effect of physical exercise in fragile elderly with mild cognitive impairment, dementia, or Alzheimer	To identify the effects produced by physical exercise programs in fragile elderly population with mild cognitive impairment (MCI), dementia, or Alzheimer.	The results show improvements in the physical and cognitive aspects and the study is concluded with the most appropriate training.
20	WEB OF SCIENCE	Frontiers in Aging Neutoscie nce	Liao-Yao Wang, Jian Pei, Yi-Jun Zhan and Yi-Wen Cai	2020	English	Overview of Meta-Analyses of Five Non-pharmacological Interventions for Alzheimer's Disease	This work aimed to review existing Mas to provide an overview of existing evidence on the effects of fie non-pharmacological interventions in AD patients on three outcomes; Mini-Mental State Examination (MMSE), activities of daily living (ADL), and Alzheimer's Disease Assessment Scale-cognitive section (ADAS-cog).	All the included Mas were critically low to low quality by AMSTAR 2. Acupuncture therapy and exercise intervention showed the preliminary potential to improve ADL and MMSE. rTMS and acupuncture therapy show benefits in decreasing ADAS-cog, and there was some evidence of improved MMSE with cognitive intervention. All these outcomes scored very low quality to moderate quality of evidence on the GRADE system.

Discussion

Physical exercise delays both the beginning and the development of AD, for multiple factors. First, because it produces metabolic and neurological changes associated with decreased abnormal production of β-amyloid protein in the frontal cortex and hippocampus; it increases blood flow in the frontal, parietal and temporal lobes and promotes capillary angiogenesis in the primary motor cortex; it also stimulates the factors associated with nerve growth, since it promotes the release of nitric oxide; and it stimulates dopamine synthesis by increasing calcium levels.

Second, physical activity increases the production of endorphins, which reduce stress levels, thus preventing or reducing the onset of depressive disorders, and improving physical qualities such as body balance, muscle strength, and tendon flexibility. What is really relevant is the relationship between physical exercise and neuroplasticity, that is, the capacity of the nervous system to form new neuronal circuits and adapt to changes, transforming their structure and function [1,2,5].

Multidisciplinary teams must address the AE through pharmacological and non-pharmacological interventions. Among the non-pharmacological treatments, physiotherapy plays a vital role in reducing the complications of this disease since it involves the use of aerobic exercise or flexibility. It aims to improve functional capacity, reduce the use of drugs, reduce the risk of falls, and minimize disease progression shortfalls [2,6].

A meta-analysis of 54 randomized trials studied the effect of aerobic exercise on blood pressure and identified that this activity decreased systolic and diastolic blood pressures. Thus, the study concluded that a reduction in mean arterial pressure can significantly reduce cognitive impairment, especially in the early stages of the disease. Indirectly, it was shown that exercise focused on the cardiorespiratory system is directly linked to improved memory performance and reduced hippocampal atrophy [2].

Several systematic reviews analyzed studies in newly diagnosed AD patients (mild and moderate) who underwent physical, cognitive, sensory, and social activity. The activities that were carried out included: walking, doing household chores,

regular reading of books and newspapers, dancing, crossword puzzles, music therapy, occupational therapy, and regular participation in community social life [2].

With a physical activity of 2 or 3 weekly sessions of at least one hour for each training, there was a significant improvement in the patients. Almost all studies have documented that 4 to 6 months of training is ideal for achieving significant results [4].

There are few studies that state that physiotherapy has a positive impact on AD patients, especially in the early stage of the disease, and has a greater impact on metabolic mechanisms in women [5]; among them, it is pointed out that the practice of aerobic exercise combined with strength, balance, dual-task (talking while walking), coordination, and movement training help cognitive, emotional, functional, physical, and general psychological symptoms. In addition, it is attributed within its range of effectiveness the fact of causing a decrease in inflammatory activity and increasing the concentration of neurotrophic factors, improving body composition, reducing adipose reserve, and increasing muscle mass [7,8].

The clinical study conducted by Erickson et al., applying physical training to their intervention group for six weeks, assessed the hippocampus by magnetic resonance imaging (MRI), showing that patients who performed physical exercise increased this area's size, improving their spatiality memory. Thus demonstrating that hippocampal atrophy is a marker that can predict the onset of dementia, since AD begins in this area [9,12].

It has been shown that caregivers have a higher risk of stress and depression, experience sleep problems more frequently, and have poor physical health. When performing the exercises with patients, they claim that they enjoy this activity and can simultaneously supervise them and feel happier, thus improving their working conditions [8,13].

Moderate-high intensity physical exercise performed 3 to 5 days a week, added to a dietary scheme such as the Mediterranean diet or the DASH diet, was found to improve overall cognitive function in subjects with AD.

The results are enhanced when both interventions are combined and include cognitive stimulation exercises, increasing people's functionality [9,14].

A physical training scheme, in which strength, functional, gait, and balance exercises are performed, significantly prevents the risk of falls in patients. Individualized aerobic activity at home shows more significant results than outpatient group physical activity, with excellent effects obtained eight weeks after its initiation [10,11,15].

Several researchers mention the brain adaptations produced by aerobic exercise since it has been found that six months of training (60 minutes of duration, three days a week) increases both gray and white matter in the anterior cingulate cortex, findings observed in MRI, in cognitively healthy older adults. Longer aerobic training schedules of 3 years in sedentary older women demonstrate improvements in reaction time, motor skill, and cognitive speed, indicating that exercise helps reverse or slow age-related impairments in motor performance and cognitive processing speed [16].

The Finnish Intervention Study for the Prevention of Cognitive Impairment and Disability in the Elderly (FINGER) consists of a multidisciplinary intervention including diet, exercise, cognitive training, and cardiovascular monitoring. As a result, there was improvement or maintenance of cognitive function in the elderly at risk in the general population.

This intervention represents the first methodologically sound study demonstrating that a two-year intervention can reduce the risk of cognitive decline in the general elderly population, not just in patients in a clinical setting. Physical activity and cardiovascular risk reduction may have additional protective effects by delaying the progression of AD. The conclusion is that more regular physical activity and lower cardiovascula independently attenuate the negative correlation between asymptomatic individuals, cognitive impairment, and neurodegeneration [16].

A study involving patients with Mild AD who underwent 16 weeks of aerobic (from moderate to high intensity), did not modify cortical Aβ. Likewise, in adults with moderate AD, who underwent aerobic training for three months and of moderate-intensity neither showed beneficial effects on total cerebral blood flow, cerebrospinal fluid (CSF), and protein Aβ. However, there were benefits at the cardiorespiratory, physical, and cognitive levels.

Although these data indicate that physical activity does not affect Aβ deposits, it may be preventive against cognitive impairment and neuronal degeneration. It decreases inflammation at the cerebral level and oxidative stress, increasing both in the parietal and temporal region glucose uptake [17].

A meta-analysis suggested that music therapy effectively optimises mental well-being and cognitive function. Among the hypotheses that justify this efficacy, we have that music activates dopaminergic pathways, connectivity between neurons and excitation of the sympathetic nervous system; however, there are still no studies that reveal great significance on long-term benefits of music therapy [18].

We should not overlook the fact that many elderly people present a state of "fragility," that is, they suffer from geriatric syndromes, in which there is evidence of a low physiological reserve and resistance to stress: they present a higher degree of vulnerability to suffering from different pathologies with little chance of recovery and risk of death. Several studies have shown that physical activity has helped alleviate fragility, so those fragile older adults who engage in physical activity programs will benefit the most from it [19].

In the 'Global Action Plan On The Public Health Response To Dementia,' the WHO recommends increasing physical activity and eating a healthy diet to prevent dementia. Among the basic guidelines that should be followed about physical activity, it is recommended that all older adults should perform 150 minutes of aerobic physical exercise per week or some kind of vigorous physical exercise in one hour and fifteen minutes, a combination of moderate and vigorous activities is also valid. These recommendations also effectively reduce the occurrence of other pathologies such as obesity and arterial hypertension, as well as cholesterol and blood glucose levels [20].

Conclusions

According to the study of several researchers, it was evidenced that the validity of physical exercise as a non-pharmacological treatment for patients with Alzheimer's disease

is minimum concerning cognition improvement and organic functionality. However, the implementation of aerobic training and its combination with various modalities, including a healthy dietary pattern, the implementation of music therapy, occupational therapy, and ensuring participation in community social life, helps significantly to delay the neurodegenerative progression of the disease. Among the benefits of physical activity is the development of brain neuroplasticity, improvement of cardiovascular function, the release of endorphins that reduce stress and depression levels, maintenance of body composition, and improvement of physical fitness. It is essential to mention that physical exercise helps patients and their caregivers; as they say, they enjoy the training, thus improving their working conditions.

Developing and implementing an active aging protocol is essential, as it has become a vital factor in achieving a healthy elderly population. Promoting physical exercise for at least 30 minutes per day is one of the non-pharmacological pillars included in this protocol, establishing that physical training of considerable intensity adjusted to the physical performance of the older adult ensures a decrease in oxidative damage and an increase in tissue repair that leads not only to a healthy life but also to a significant reduction in the development of neurodegenerative diseases.

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