

RELATIONSHIP BETWEEN PHYSICAL ACTIVITY AND QUALITY OF LIFE IMPROVEMENT IN PEOPLE WITH ALZHEIMER'S DISEASE: SYSTEMATIC REVIEW

Relação da atividade física com a melhora da qualidade de vida de pessoas com Doença de Alzheimer: revisão sistemática da literatura

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Resumo

O objetivo deste estudo é relatar o impacto da atividade física de forma paliativa na qualidade de vida de pessoas com doença de Alzheimer (DA). Foi realizada uma revisão da literatura utilizando artigos de revistas científicas, teses, dissertações e sites científicos que foram avaliados para o presente trabalho. A pesquisa bibliográfica foi realizada consultando as seguintes bases de dados científicos: PubMed, Scielo e BVS Brasil. A busca foi retrospectiva, limitando-se a artigos publicados de fevereiro de 2010 a fevereiro de 2023. Conclusões: A atividade física pode atrasar a manifestação de sintomas e o comprometimento cognitivo da DA, além de aumentar mecanismos de proteção, como a liberação de neurotrofinas e a hormona irisina. A combinação de terapia medicamentosa com atividade física também pode melhorar a qualidade de vida dos pacientes. Alguns estudos indicam que atividades leves e moderadas podem contribuir para a redução de déficits nas atividades diárias e atenuar distúrbios do sono. Outros estudos mostram que a atividade física pode melhorar a função cognitiva, equilíbrio, e reduzir o risco de quedas em idosos com DA. A caminhada parece ser uma atividade física particularmente benéfica para pacientes com DA. Embora os estudos apresentados nesta revisão indiquem fortemente os benefícios da atividade física para pacientes com DA, mais pesquisas são necessárias para aprofundar nossa compreensão da fisiopatologia e tratamento da doença.

Palavras-chave: Doença de Alzheimer, Atividade física, Qualidade de vida.

Abstract

The aim of this study is to report on the impact of physical activity in a palliative manner on the quality of life of people with Alzheimer's disease (AD). A literature review was conducted using scientific journal articles, theses, dissertations, and scientific websites that were evaluated for the present study. The bibliographic survey was carried out by consulting the following scientific databases: PubMed, Scielo, BVS Brasil. The search was retrospective, limiting itself to scientific papers published from February 2010 to February 2023. Physical activity can delay the expression of symptoms and cognitive impairment of AD, as well as increase protective mechanisms such as the release of neurotrophins and the hormone irisin. The combination of drug therapy with physical activity can also improve the quality of life of patients. Some studies indicate that light and moderate activities can contribute to the reduction of deficits in daily living activities and attenuate sleep disorders. Other studies show that physical activity can improve cognitive function, balance, and reduce the risk of falls in elderly people with AD. Walking seems to be a particularly beneficial physical activity for patients with AD. Although the studies presented in this review strongly indicate the benefits of physical activity for patients with AD, more research is needed to better elucidate the pathophysiology and treatment of the disease.

Keywords: Alzheimer's disease. Physical activity. Quality of life.

Introduction

Alzheimer's Disease (AD) is a neurodegenerative disease that is highly associated with age. Its manifestations include progressive loss of recent memory, changes in memory, and cognition. Often, these manifestations are accompanied by other factors such as behavioral disorders, including aggressive behavior, the onset of hallucinations, and even a depressive state (SERENIKI & VITAL, 2021). Although there may be possible records of the disease throughout the centuries, knowledge of AD as a specific pathology was only discovered 116 years ago, first described in 1907 by the German neuropathologist Alois Alzheimer. In his study, he observed the presence of senile plaques, formed by the aggregation of beta-amyloid protein, and neurofibrillary tangles, related to changes in tau protein, inside neurotubules. Beta-amyloid proteins (AB) attach themselves to the spaces between nerve cells, causing a toxic effect. This toxicity leads to a constant loss of neurons in brain regions such as the hippocampus, which controls memory, and the cerebral cortex, essential for language, reasoning, memory, and recognition of sensory stimuli (NOGUEIRA et al., 2021).

Both pathological findings, in a patient with significant neurocognitive disturbances, allowed the researcher to characterize this condition as distinct from other organic brain pathologies. A greater understanding of its neuropsychological effects began in the 1980s. As the decades progressed, there was an increase in research on the causes, characterizations, and potential treatments for Alzheimer's disease (AD) and other dementias, currently indicating new directions for dementia-related research and predictions for possible more effective therapeutic interventions in the future (BONDI et al., 2017).

The prevalence of dementia worldwide increases as the age index of a particular population increases. Among those aged 65 to 69 years, the dementia rate is around 1.2%, which rises to 3.7% for individuals aged 70 to 74 years, 7.9% for those aged 75 to 79 years, 16.4% for individuals aged 80 to 84 years, 24.6% for those aged 85 to 89 years, 39.9% for individuals aged 90 to 94 years, and reaches a rate of 54.8% for individuals aged 95 years or older (CHRISTOFOLETTI et al., 2011).

AD is characterized by neural cell death, which can occur through the hyperphosphorylation of a protein (tau protein) or the development of a crust formed by amyloid plaques outside the neurons. This ultimately causes an electrochemical imbalance in the neurons, as they develop neurofibrillary tangles inside them, leading to cerebral atrophy. Engaging in regular physical activities influences cerebral plasticity and vascularization, as studies suggest that increased vascular density in the cerebellar cortex is directly related to balance, muscular control, voluntary movements, and motor learning. Physical exercise enhances cerebral blood circulation, stimulating the release of neurotrophic substances that promote neural growth. One such protein responsible for neural regeneration in brain areas is BDNF (Brain-Derived Neurotrophic Factor), which maintains brain function (PANIZZA, 2017).

Physical exercise is capable of protecting the brain by improving cognitive function, increasing cerebral blood flow, exerting antioxidant action through repair enzymes, promoting neurogenesis and angiogenesis, enhancing metabolism and neurotransmitter synthesis, and aiding in the clearance of amyloid plaques. Regular physical activity can bring benefits to various cognitive functions such as language, memory, reasoning, problem-solving, mobility, strength, balance, and gait speed. Systematized aerobic activities are particularly beneficial as they increase blood flow, neurogenesis, and reduce oxidative stress, which may contribute to the reduction of amyloid plaques (KAMADA, M et al., 2017).

Also, physical activity aims to improve the quality of life for individuals with Alzheimer's disease. It can help enhance cognitive function, even in cases where it has been significantly affected by the disease. Physical exercise can increase blood flow to the brain, consequently delivering more oxygen and other energy substrates, thereby improving cognitive function and reducing the likelihood of protein deposition (which forms the aforementioned amyloid plaques) that impairs cognitive functioning due to neural cell death (SERENIKI & VITAL, 2021).

AD progresses over time and impairs the autonomy of basic daily activities. The earlier the diagnosis is made, the better the chances of treating the symptoms and delaying the progression of the disease and its complications by several years. The quality of life of individuals with Alzheimer's deteriorates as the disease progresses. Physical activity is a widely used method to promote benefits in the lives of individuals with the disease, as it helps prevent dementia-related memory loss,

especially in older individuals. It can bring greater comfort and health to patients and even to those around them (BUSANELLO, 2015).

Aim

The present study aims to report the impact of palliative physical activity on the quality of life of individuals with Alzheimer's disease.

Method

The chosen method for the development of this study was a Literature Review. Articles from scientific journals, theses, dissertations, and scientific websites were evaluated for this study. The literature search was conducted through consultations of the following scientific databases: PubMed, Scielo, and BVS Brasil. The search was retrospective, limited to scientific articles published from February 2010 to February 2023.

As inclusion criteria for the selection of the researched material, the following were considered: materials published in both Portuguese and English in their entirety, written by healthcare professionals, including clinical studies (both randomized and non-randomized), literature reviews, laboratory studies, prospective cohort studies, and research articles that align with the objectives of the study. Studies that did not have a direct relationship between Alzheimer's disease (AD) and physical activity were excluded, as well as studies that lacked sufficient relevance to determine this relationship. The following Figure 1 is a flow chart of the selection process for the scientific articles used in this study.

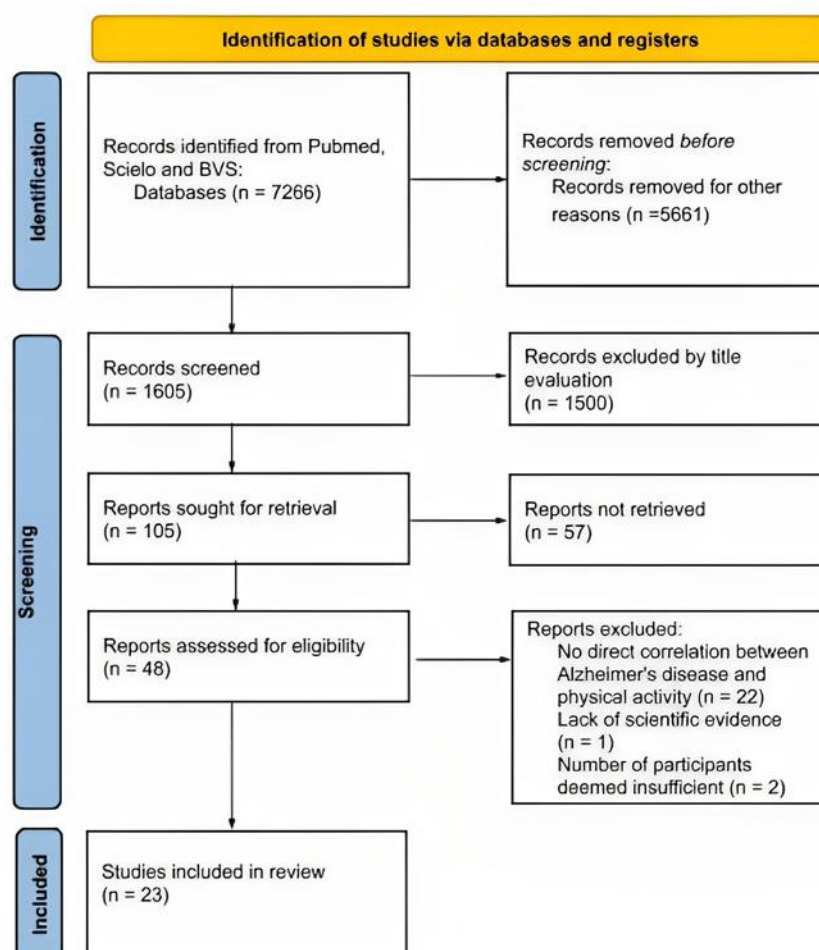


Figure 1 - Selection process.

Source: Data collected by the authors.

Results

Due to population aging, it is believed that currently in Brazil approximately 1.2 million people live with some form of dementia, with the majority still not having received a proper diagnosis. Around 100,000 new cases are diagnosed per year. Globally, the number of people diagnosed with Alzheimer's disease (AD) is approximately 50 million (BRASIL, 2021).

AD is a disease that can affect the entire world. It is estimated that approximately 6.2 million Americans aged 65 and older currently live with AD. It is believed that this number will increase to 13.8 million by 2060, posing challenges to the development of medical advancements to prevent, slow down, or cure AD. In 2019, there were 121,499 recorded deaths from the disease, making Alzheimer's the sixth leading cause of death in the US and the fifth leading cause of death among Americans aged 65 and older. Over a span of 20 years (2000 to 2019), deaths from AD increased by about 145% in the US, due to high healthcare costs, low caregiver demand, and an increasing number of individuals with AD (The Alzheimer's Association, 2021). According to estimates from Alzheimer's Disease International, these numbers could reach 74.7 million by 2030 and 131.5 million by 2050, due to population aging, highlighting a global health crisis and the need to seek measures to address it (ALZHEIMER'S DISEASE INTERNATIONAL, 2018).

The development of AD is divided into three stages. The initial stage is called mild, characterized by observed episodic memory loss, difficulty in acquiring new tasks, decreased judgment capacity, gait disturbances such as reduced speed and step length, decreased calculation ability and visuospatial skills, decreased strength in the upper and lower limbs, and changes in postural control, which directly influence the increased number of falls in cognitively impaired older adults. In the second stage, known as moderate, aphasia occurs, which is the weakening or loss of the ability to comprehend, manipulate, and express language, leading to difficulty in naming people and objects, difficulty in choosing words to express feelings, ideas, and desires, accompanied by apraxia, which is when the brain cannot correctly perform and instruct body movements. In the third and final stage of AD, the terminal stage, aggressive changes occur, such as alterations in sleep patterns, behavioral changes such as irritability and aggression, psychotic symptoms, inability to walk, speak, and perform self-care. In the final stage, AD patients are unable to perform any task independently (ZIDAN et al. 2012).

The drug treatment for Alzheimer's disease aims to minimize the disorder's symptoms, stabilize cognitive impairment, improve behavior, and enhance autonomy in daily activities (or simply attenuate the manifestations of the disease), with minimal adverse effects. The Ministry of Health provides the medications Donepezil, Galantamine, Memantine, and Rivastigmine in healthcare units throughout the country. All these medications are included in the Clinical Protocol and Therapeutic Guidelines from the Unified Health System (SUS) for this clinical condition (BRASIL, 2023).

There are currently two groups of drugs used in the treatment of Alzheimer's disease: memantine and cholinesterase inhibitors (ChEIs). Memantine is a non-competitive antagonist of the N-methyl-D-aspartate receptor and is generally used in more advanced stages of the disease. ChEIs, such as galantamine, rivastigmine, and donepezil, are used in early stages of the disease. In summary, the use of these drugs is directed based on the stage of the disease in which the patient is in (DI SANTO et al., 2013).

Despite the advantages of drug therapy, it has some limitations. Therefore, it is necessary to explore other alternatives beyond pharmacological approaches, such as engaging in physical exercise, in order to prevent the institutionalization of elderly patients and promote an improvement in their quality of life (KAMADA et al., 2017).

The substance rivastigmine is considered a cholinesterase inhibitor prescribed for early or intermediate stages of Alzheimer's disease. A study was conducted with patients who were divided into two groups: one group received only the rivastigmine patch, while the other group used the patch in combination with physical exercise. The results revealed significant improvements in both quality of life and the ability to perform daily tasks among patients who underwent the combined therapy (AGUIAR et al., 2014).

It was observed that during physical exercise, the hormone irisin was released by the muscles, which is of great importance in reversing the memory deficits caused by Alzheimer's disease. This confirmation was made through a study conducted by Rudimar Luiz Frozza (researcher at the Oswaldo

Cruz Institute), as well as researchers Mychael Lourenço and Fernanda De Felice, both from the Federal University of Rio de Janeiro (LOURENÇO, M et al., 2019).

The hormone irisin, based on tests conducted on mice, was responsible for improving neuronal communication, preserving synapses, and preventing the binding of neurodegenerative toxins to neurons. Additionally, it has been reported that irisin assists in brain protection through chemical alterations within neurons, thereby preventing the loss of information storage and potentially aiding in the restoration of lost memory during the course of the disease. Physical exercise has proven to be essential in obtaining the benefits induced by irisin in the body, particularly in the brain, reducing the risk of developing Alzheimer's disease and delaying its progression (LOURENÇO, M et al., 2019).

A study conducted in the state of California (United States) examined the effects of walking on patients with Alzheimer's disease over a period of 1 year. It was found that walking resulted in improvements in cognitive function, neuropsychiatric disorders, and mood. Through the practice of this activity, an increase in oxygen consumption was observed through aerobic exercise, while the major muscle groups were engaged, leading to long-term changes in the brain and yielding functional and structural benefits (WINCHESTER, J et al., 2013).

José Luiz Riani, a physician and researcher at São Paulo State University (UNESP), stated in 2012 that the practice of muscular and aerobic physical activity combined with cognitive engagement yields positive results in improving cognition and behavioral aspects of patients. It also shows positive outcomes in other areas such as recent memory loss, sleep, apathy, and depressive symptoms.

The consistent and monitored practice of physical exercises over a period of six months reduced the occurrence of sleep disturbances in patients with mild and moderate Alzheimer's disease (AD). Additionally, one of the most commonly used pre-established criteria in the diagnosis of the disease, as established by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS) in conjunction with the Alzheimer's Disease and Related Disorders Association (ADRADA), indicates that sleep disturbances are a criterion, and the lack of sleep increases the likelihood of an AD diagnosis. Both circadian rhythm disruption and sleep fragmentation are among the leading causes of institutionalization, and physical exercise can be an effective approach to addressing these sleep disturbances and alleviating associated symptoms (NASCIMENTO, CM et al., 2014).

In a comparative study, individuals were divided into two categories: active (n=84) and sedentary (n=20). The active group was further subdivided into those who engaged in walking for an average of one hour per week and those who engaged in walking for two hours or more per week. It was observed that sedentary individuals showed a significant reduction in the score of the Mini-Mental State Examination (MMSE), which is a predictive factor of cognitive function in patients with Alzheimer's disease (AD). Those who walked for one hour experienced a decrease in the MMSE score, while those who walked for two hours or more had a significant increase in the score (ARCOVERDE, C et al., 2014).

Trials were conducted with individuals diagnosed with Alzheimer's disease (AD) divided into two groups: the intervention group (IG; n=9) who adhered to an organized physical exercise protocol, and the routine group (RG; n=7) who were not physically active. The results of this study showed a positive influence of the physical activity program on the maintenance of cognitive functions, agility, and balance, without an increased risk of falls in elderly individuals with AD. In the routine group (RG), a significant decline was observed in all variables (Hernandez, SS et al., 2010).

In a study, 120 patients diagnosed with Alzheimer's disease (AD) were involved, with their spouses serving as caregivers. They were divided into different groups: the GE, consisting of a group that engaged in exercises at daycare centers for AD, under the supervision of two physiotherapists, twice a week, with each session lasting one hour; the HE, equivalent to a group that received home-based exercises administered by physiotherapists, twice a week, with each session lasting one hour; and the CG, a control group that did not engage in physical activity. The negative effects of the disease took longer to manifest in the intervention groups compared to the control group, showing significant differences between the HE and CG at both the six-month and twelve-month periods. However, it was not possible to demonstrate such a difference when comparing the GE and CG groups, suggesting that home-based physical activity may be a more effective therapy in combating the disease (Pitkälä, KH et al., 2013).

It was possible to demonstrate, through cranial magnetic resonance imaging exams, a considerable increase in the hippocampus in patients who engaged in cycling activities, lasting from 20 to 50 minutes per session, three times a week, for a period of six months (YU, F et al., 2014). Although the practice of physical exercise causes changes in the levels of receptors for BDNF, this only occurred in individuals who possess the gene for Apolipoprotein. This gene is associated with a higher risk of developing Alzheimer's disease and a greater effectiveness of physical activities or aerobic exercises in these patients (Etnier, JL et al., 2015). The following Figure 2 is a chart containing an analysis of the main articles used in this study.

AUTHOR	TITLE	TYPE OF STUDY	SUMMARY OF RESULTS
Nascimento CM et al., 2014	Effect of a multimodal exercise program on sleep disorders and instrumental activities of daily living in patients with Parkinson's and Alzheimer's disease.	Non-randomized clinical studies (3)	Multimodal physical exercises can contribute to reducing deficits in instrumental activities of daily living (IADL) and mitigate sleep disorders (SD).
Hernandez SS et al., 2010	Effects of a physical activity program on cognitive functions, balance, and risk of falls in elderly individuals with Alzheimer's disease.		Physical activity indicates benefits for cognitive functions and balance, reducing the risk of falls.
Etnier JL et al., 2015	Innovative Research Project Exploring the Effects of Physical Activity and Genetics on Cognitive Performance in Community-Dwelling Older Adults.		Physical activity promotes potential changes in levels of brain-derived neurotrophic factor (BDNF) receptors, occurring in individuals who possess the gene for apolipoprotein E.
Aguar P et al., 2014	Transdermal rivastigmine patch and physical exercises for Alzheimer's disease: a randomized clinical trial.	Randomized clinical studies (4)	Positive association between drug therapy and physical exercises.
Arcoverde C et al., 2014	Treadmill training as a complementary treatment for Alzheimer's disease: a randomized controlled pilot study.		Walking on a treadmill may be recommended as a complementary treatment for patients with Alzheimer's disease, resulting in a significant increase in NMSE (Neuropsychiatric Inventory-Nursing Home Version).
Yu F et al., 2013	Effects of aerobic exercise on cognition and hippocampal volume in Alzheimer's disease: study protocol of a randomized controlled trial (The FIT-AND trial).		Considerable increase in the hippocampus in cyclist patients.
Pitkälä KH et al., 2013	Effects of the Finnish Alzheimer's Exercise Study (FINALEX): a controlled randomized study.		Delaying the negative effects of the disease in groups that engaged in physical activity, particularly in the home-based group.
KAMADA M et al., 2018	Correlation between physical exercise and quality of life in patients with Alzheimer's disease.	Bibliographical survey (4)	Physical activity is responsible for attenuating the symptoms of Alzheimer's disease, especially in the early stages, promoting quality of life and various health benefits.
BUSANELLO J et al., 2015	PHYSICAL ACTIVITY AND ALZHEIMER'S DISEASE		Although physical activity has shown to be a potential non-pharmacological therapy, there is still no protocol of recommendations regarding the type and intensity of systematic physical activity necessary to produce benefits in cognitive functioning.
Nogueira IN et al., 2021	The benefits of physical exercise in the treatment of Alzheimer's disease. Exercise as an Adjunctive Tool for Health Promotion.		Physical activity can attenuate the treatment of Alzheimer's disease and provides various benefits to patients with AD.
SERENIKI, A et al., 2021	Alzheimer's disease: physiopathological and pharmacological characteristics. Trends in Psychiatry and Psychotherapy.		The search for the physiopathological mechanisms of Alzheimer's disease has directly led to the development of new drugs for the treatment of this pathology. The investigation of new medicinal agents that can slow down or even block the progression of the disease constitutes the objective and challenge for many neuroscientists.
LOURENÇO MV et al., 2019	FNDC5/irisin associated with exercise rescues synaptic plasticity and memory impairments in Alzheimer's disease models.	Laboratory Study(1)	Exercise blocks A β O-induced memory impairment in rodents. FNDC5/irisin rescues defective synaptic plasticity and memory in mice.
WINCHESTER R J et al., 2012	Walking stabilizes cognitive functioning in Alzheimer's disease (AD) over the course of one year.	Prospective cohort study (1)	Some level of physical activity, especially walking, is beneficial for cognitive function in individuals with mild to moderate Alzheimer's disease (AD) and can be used as an intervention strategy.
PANIZZA R et al., 2017	How physical exercise helps in the treatment of Alzheimer's disease.	Review article	Physical exercise increases the release of BDNF (brain-derived neurotrophic factor), a neurotrophic factor that promotes neural growth, maintains brain functions, and enhances plasticity by stimulating neural regeneration.

Figure 2 - Analysis of articles.

Source: Data collected by the authors.

Discussion

Based on the studies cited in the survey conducted in this present work, strong evidence confirms the significant delay in the expression of symptoms and cognitive impairment of AD through the practice of physical activities as therapy. Additionally, improvement in certain protective mechanisms, such as the research conducted on mice by Mychael V. Lourenço (2019) and other researchers, suggests the role of the hormone irisin, which prevents the loss of information storage through chemical changes within neurons. In the study made by Fang Yu (2014), another neuroprotective factor was indicated, showing a considerable increase in the hippocampus in patients who engaged in cycling activities three times a week for a period of six months.

According to Panizza (2017), another protective factor promoted by physical activity is the release of neurotrophins, which are responsible for increasing activity and improving neural plasticity, thereby enhancing cellular regeneration and consequently delaying cognitive deficits caused by Alzheimer's disease (AD). However, in the studies by Etnier (2015), it was questioned that the effectiveness of these neuroreceptors is strongly linked to genetic factors, specifically the apolipoprotein E (APOE) epsilon 4 allele. This gene is also associated with a higher risk of developing the disease. Although the study does not extensively explore this relationship, it raises the question and the need to investigate this genetic factor.

According to Kamada (2017), the combination of medication therapy with physical activity can significantly improve the quality of life for patients, surpassing the benefits of medication alone. In a study conducted by researcher Paula Aguiar (2014), the combination of physical exercise with rivastigmine resulted in an improvement in quality of life, reinforcing Kamada's statement. However, in the same research, cognition remained unchanged in both analyzed groups (combined treatment group and medication-only treatment group). The impact on daily life activities was inconclusive, indicating the need for further studies.

However, in the studies by Nascimento (2014), through the exploration of multimodal and instrumental activities of mild to moderate intensity, it was proven that these activities, when performed regularly for a period of 6 months, can contribute to reducing deficits in instrumental activities of daily living (IADL) and alleviate sleep disturbances (SD), thus promoting greater autonomy and quality of life.

The study by Hernandez (2010) explored potential benefits of physical exercise by analyzing the effects of a regular, systematic, and supervised physical activity program on cognitive functions, balance, and risk of falls in elderly individuals with Alzheimer's disease (AD). It found a strong relationship between agility, balance, and cognitive functions in elderly individuals with AD. Additionally, it indicated that physical activity could be a non-pharmacological therapy.

The study conducted in California by Winchester (2013) observed that engaging in aerobic physical activity, especially walking, not only resulted in structural and functional improvements but also showed positive effects on cognitive function, neuropsychiatric disorders, and mood. Another study that reinforces the benefits of walking specifically was conducted by Arcoverde (2014), where a significant improvement in functional capacity was reported in a group of patients who engaged in aerobic exercise, specifically walking on a treadmill, compared to a group of patients who did not engage in any activity.

In the Finnish study by Kaisu H Pitkälä (2013), intensive and long-duration exercises were found to have beneficial effects on the physical functioning of patients with Alzheimer's disease (AD). Significant changes were observed during home-based practice, indicating a delay in the progression of the disease. These findings suggest that simpler activities in familiar environments may be as effective as more complex ones.

As observed by SERENIKI (2021), both the pathophysiological and medication aspects for understanding and treating the disease respectively require further studies. Despite strong indications in the studies addressed in this review, as described by many of them, the therapy based on physical activity, as well as its characteristics, specifications, and the extent of its benefits, require further clarification. As noted by Busanello (2015), although physical activity has shown to be a possible non-pharmacological therapy, there is still no protocol of recommendations regarding the type and intensity of the systematic physical activity needed to produce cognitive functioning benefits.

Conclusion

The aging population is associated with an increase in neurodegenerative diseases such as Alzheimer's Disease (AD), which has a growing incidence and consequently has a greater negative impact on the quality of life of the population. This has led to increased interest and the need to explore non-pharmacological therapies or complementary therapies to pharmacological ones, such as physical exercise. Physical exercise has been found to be effective in preserving cognition, functionality, and physical health of patients, as well as improving sleep disorders, balance, mood, daily activity practices, and autonomy, particularly through aerobic activities. However, further studies are needed to better understand this issue.

References

- AGUIAR P, MONTEIRO L, FERES A, GOMES I, MELO A. Rivastigmine transdermal patch and physical exercises for Alzheimer's disease: a randomized clinical trial. **Current Alzheimer Research**. 2014;11(6):532-7.
- ARCOVERDE C, DESLANDES A, MORAES H, ALMEIDA C, ARAUJO NB, VASQUES PE, SILVEIRA H, LAKS J. Treadmill training as an augmentation treatment for Alzheimer's disease: a pilot randomized controlled study. **Arquivos de Neuro-Psiquiatria**. 2014 Mar;72(3):190-6.
- BONDI MW, EDMONDS EC, SALMON DP. Doença de Alzheimer: passado, presente e futuro. **Journal of the International Neuropsychological Society**, 23 de Outubro, 2017.
- BRASIL. Ministério da Saúde. Biblioteca Virtual em Saúde - **Conhecer a demência, conhecer o Alzheimer: o poder do conhecimento** - Setembro, Mês Mundial do Alzheimer, 2021. Disponível em: <https://bvsms.saude.gov.br/conhecer-a-demencia-conhecer-o-alzheimer-o-poder-do-conhecimento-setembro-mes-mundial-do-alzheimer/>. Acesso em: 27 de dezembro de 2022.
- BRASIL. Ministério da Saúde. **Portaria Conjunta Nº 13**, de 28 de Novembro de 2017, Brasília 2017.
- BRASIL. Ministério da Saúde. Biblioteca Virtual em Saúde - **Qual o tratamento para Alzheimer?** - Fevereiro, Mês Mundial do Alzheimer. 2023. Disponível em: <https://www.gov.br/saude/pt-br/assuntos/saude-de-a-a-z/a/alzheimer/tratamento>. Acesso em: 01 de março de 2023.
- BUSANELLO, J. **Atividade física e a doença de Alzheimer**. Orientadora: Ms. Fabiana Ritter Antunes. 2015. Trabalho de Conclusão de Curso (exigência parcial para obtenção do título de Bacharel em Educação Física) - Faculdade de Educação Física, Universidade Regional do Noroeste do Estado do Rio Grande do Sul, Santa Rosa, 2015.
- CHRISTOFOLETTI, Gustavo et al. Physical activity attenuates neuropsychiatric disturbances and caregiver burden in patients with dementia. **Clinics**, v. 66, p. 613-618, 2011.
- DI SANTO SG, PRINELLI F, ADORNI F, CALTAGIRONE C, MUSICCO M. A meta-analysis of the efficacy of donepezil, rivastigmine, galantamine, and memantine in relation to severity of Alzheimer's disease. **Journal of Alzheimer's Disease**, 2013.
- ETNIER JL, LABBAN JD, KAPER WB, WIDEMAN L, PIEPMEIER AT, SHIH CH, et al. Innovative Research Design Exploring the Effects of Physical Activity and Genetics on Cognitive Performance in Community-Based Older Adults. **Journal of Aging and Physical Activity**. 2015; 23(4):559-68.
- HERNANDEZ SS, COELHO FG, GOBBI S, FLORINDO S. Efeitos de um programa de atividade física nas funções cognitivas, equilíbrio e risco de quedas em idosos com demência de Alzheimer. **Brazilian Journal of Physical Therapy**. 2010;14(1):68-74.
- KAMADA, M et al. Correlação entre exercício físico e qualidade de vida em pacientes com doença de Alzheimer. **Revista da Sociedade Brasileira de Clínica Médica**, 2018;16(2):119-122.

LOURENÇO, M; FELICE, F; FROZZA, R L. FND5 / irisina ligada ao exercício resgata plasticidade sináptica e defeitos de memória nos moldes de Alzheimer. **Nature**, 25 de janeiro de 2019.

NASCIMENTO CM, AYAN C, CANCELA JM, GOBBI LT, GOBBI S, STELLA F. Effect of a multimodal exercise program on sleep disturbances and instrumental activities of daily living performance on Parkinson's and Alzheimer's disease patients. **Geriatrics & Gerontology International**. 2014;14(2):259-66.

NOGUEIRA IN, DA SILVA TG, MONTEIRO ER, DE MIRANDA MJC. **Os benefícios do exercício físico no tratamento do Alzheimer**. In: de Miranda MJC, Monteiro ER. Exercício Como Ferramenta Adjuvante Para Promoção de Saúde. Rio de Janeiro-RJ: Eptaya, 2021. pg.(37-43).

PANIZZA, R. **Como Exercícios Físicos ajudam no tratamento do Alzheimer**. Portal do Idoso. Organizador: Dr José Eduardo Martinelli, 2017.

PITKÄLÄ KH, PÖYSTI MM, LAAKKONEN ML, TILVIS RS, SAVIKKO N, KAUTIAINEN H, et al. Effects of the Finnish Alzheimer disease exercise trial (FINALEX): a randomized controlled trial. **JAMA Internal Medicine**. 2013;173(10):894-901.

RIANI, JL. **Exercícios físicos ajudam a conter o mal de Alzheimer**. 2012.

SERENIKI, A.; VITAL, M.A.B.F. Alzheimer's disease: pathophysiological and pharmacological features. **Trends in Psychiatry and Psychotherapy**. Porto Alegre, v. 43, n. 2, dez. 2021.

THE ALZHEIMER'S ASSOCIATION. 2021 Alzheimer's disease facts and figures. **Alzheimer's & Dementia**, 2021 March. 17(3), 327-406.

WINCHESTER J, DICK MB, GILLEN D, REED B, MILLER B, TINKLENBERG J, et al. Walking stabilizes cognitive functioning in Alzheimer's disease (AD) across one year. **Archives of Gerontology and Geriatrics**. 2013;56(1):96-103.

WORLD ALZHEIMER REPORT 2018. **The state of the art of dementia research**: New frontiers. Alzheimer's Disease International (ADI), London.

YU F, BRONAS UG, KONETY S, NELSON NW, DYSKEN M, JACK C JR, et al. Effects of aerobic exercise on cognition and hippocampal volume in Alzheimer's disease: study protocol of a randomized controlled trial (The FIT-AD trial). **Trials**. 2014;15:394.

ZIDAN M, ARCOVERDE C, ARAÚJO NB, VASQUES P, RIOS A, LAKS J, DESLANDES A. Alterações motoras e funcionais em diferentes estágios da doença de Alzheimer / Motor and functional changes in different stages of Alzheimer 's disease. **Revista de Psiquiatria Clínica**. 2012;39(5):161-5