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NEURAL PLASTICITY AS A PREVENTION TO ALZHEIMER'S DISEASE: AN INTEGRATIVE REVIEW

PLASTICIDADE NEURONAL NA PREVENÇÃO DA DOENÇA DE ALZHEIMER: UMA REVISÃO ITEGRATIVA

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Plasticidade neuronal. Memória. Alzheimer.
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Resumo

Introdução: A plasticidade neuronal é a habilidade que o cérebro tem de desempenhar atividades e readaptar-se a partir de um estímulo provocado pelo meio externo. Relacionado à isso, tem-se que com o processo de envelhecimento do indivíduo, o organismo tende ao desenvolvimento de doenças, dentre elas, as que envolvem os processos cognitivos, como é o caso da Doença de Alzheimer, assim, este trabalho tem como objetivo discutir a importância da plasticidade neuronal e sua relação com o Alzheimer. Método: Foi realizada uma revisão integrativa a fim de analisar os estudos disponíveis nas bases de dados SciElo, PubMed, VHL e SciVerse Scopus, a partir dos descritores plasticidade neuronal, memória e Alzheimer. Foram utilizados artigos nos idiomas português e inglês, com período de publicação entre os anos 2000 e 2020. Resultados: Dois dos três estudos selecionados a partir dos critérios de inclusão constataram resultados positivos com relação à condição clínica, humor, aprendizagem e memorização dos idosos submetidos à realização de atividades que estimulassem a plasticidade neuronal, de forma a estimular o cérebro, memorizar, aprender ou reaprender algo novo. Para isso, foi introduzido à rotina dos pacientes o envolvimento da prática repetida de tarefas semelhantes à jogos realizadas no computador, a psicoeducação, além de variadas técnicas de mudança de comportamento e estilo de vida, incorporando-se também intervenções cognitivas com o auxílio de exercícios físicos. O último estudo utilizado não apresentou nenhum resultado significante que demonstrasse a eficácia da intervenção nos domínios múltiplos e do aconselhamento em saúde no desenvolvimento da plasticidade neuronal dos grupos estudados. Conclusão: Com o presente artigo, foi possível concluir que estimular o cérebro a novas atividades provoca a estimulação das sinapses nos processos de memorização e aprendizagem, contribuindo com a prevenção do aparecimento do Alzheimer.

Abstract

Neuronal plasticity is the brain's ability to perform activities and readapt itself from a stimulus caused by the external environment. Related to that, understands that with the human aging process, the organism tends to develop diseases, amongst them, those involving the cognitive processes, in case, like the Alzheimer´s Disease. Therefore, this work have the objective of discuss the importance of the neuronal plasticity and your relation with the Alzheimer's Disease. Method: An integrative review was made in order to analyze the available studies on SciElo, PubMed, VHL and SciVerse Scopus databases, from the neuronal plasticity, memory and Alzheimer descriptors. Articles in Portuguese and English languages were used, with the publication period between the years 2000 and 2020. Results: Two of the three studies about the inclusion criteria reported positive results with relation to the clinical condition, mood, learning and memorization of the elderly subjected to the realization of activities that stimulate the neuronal plasticity, so that stimulate the brain, memorize, learn or relearn something new. For that, was introduced to the patients' routine the involvement of repeated practice of tasks like games performed on the computer, the psychoeducation, beyond varied techniques of behavior changes and lifestyle, incorporating cognitive interventions with the aid of physical exercises. The last study used did not show any significant results that demonstrated the effectiveness of intervention in multiple domains and health counseling in the development of neuronal plasticity in the studied groups. Conclusion: With the present article, was possible conclude that stimulate the brain for new activities provokes the stimulation of synapses on the memorization and learn processes, contributing with the prevention of the onset of Alzheimer's Disease.

1 INTRODUCTION

The brain is part of the central nervous system (CNS), a complex structure that controls the entire human body, as it is composed of neurotransmitters, lobes, grooves, gyri, neurons, glial cells important because they dominate memory, speech, learning, movement, vision and hearing, that is, they coordinate internal and external areas of the organism (Lima, 2020).

Regard to memory, it is part of an important psychological process of the body because it is responsible for storing important information, both in the short and long term. In addition, memory is associated with the learning process of something new, as the individual needs to go through the memorization process to be able to execute something, whether it be driving or making a recipe (Junior and Faria, 2015).

In this sense, neuroplasticity has a crucial role in this process, because with the effectiveness of synapses, the individual learns or relearns to perform or execute something when there is the stimulation and reinforcement of this connection between neurons. In other words, the neuroplasticity or neuronal plasticity is the brain's ability to project and perform a given activity through stimuli received from the environment (Arthur et al., 2010).

With the human aging process, the organism becomes more conducive to the appearance of diseases, as is the case of Alzheimer's Disease (AD). According to Santana et al, 2019, AD is the neurodegenerative disease that most affects individuals today, as its prevalence is less than 1% before age 65, but this proportion can increase considerably among individuals aged 65, reaching around 10%. In elderly people aged 85 or over, this proportion can reach up to 40% of this age group. Thus, it is estimated that AD affects more than 47 million people worldwide, taking into account that it can come in a unique way or associated with another disease (Camara, 2019).

Alzheimer's does not have a specific etiology, but when seen on imaging, the main findings are cortical atrophy, that is, loss of tissue, in addition to an intense synaptic degeneration and significant increase in the deposition of senile plaques and neurofibrillary tangles in the cerebral cortex. These changes caused in the human brain can trigger a decrease in the individual's cognitive performance and end up developing a dementia condition (Santos, Rodrigues and Monteiro, 2020).

Although AD has been reported for decades in the literature, as well as being considered the most prevalent neurodegenerative disease in the world population, with the knowledge that neuronal plasticity is important in the learning and memorization process, it is necessary to understand how this reinforcement of synapses can influence the non-appearance of Alzheimer's, in addition to preventing severe disease progression. Thus, being able to understand means of prevention in order to provide patients with a better quality of life.

Distarte, the present study aimed to evaluate and discuss the importance of neuronal plasticity and its relationship with the patient with Alzheimer's, starting from the following question: Why is the process of memory and learning important to prevent the onset or progression of Alzheimer's?

2 METHODOLOGY

The research is a integrative review which includes the analysis of studies, allowing the synthesis of the state of knowledge on a given subject (Mendes, Silveira and Galvão, 2008). The methodological path followed the following phases: definition of the problem to be studied, selection of the sample in the literature, characterization of the articles, critical

analysis of the results included, discussion of the results and presentation of the integrative review (Souza, Silva and Carvalho, 2010).

The electronic search was carried out from 10 to 30 November 2020, in the Scientific Electronic Library Online (SciElo), Virtual Health Library (VHL), PubMed and SciVerse Scopus databases. For the research of the studies, the following descriptors were used: "neuronal plasticity", "memory", "Alzheimer" according to the Health Sciences Descriptors (DeCS), where it was possible to select articles published between the period of 2000 and 2020, in which the choice of articles was made initially by reading the title and abstract, and after that, reading in full. As inclusion criteria, articles were selected in Portuguese and English, published in the dated period and published in full and that addressed the proposed theme. Thesis, dissertations and letters to the editor were excluded from the research.

Data collection was performed through the included articles and information was selected for a characterization of the study: author, year of publication, study location, type of study, type of questionnaire for the evaluation of female sexual function, results found.

Figure 1. Flowchart of article selection for research.

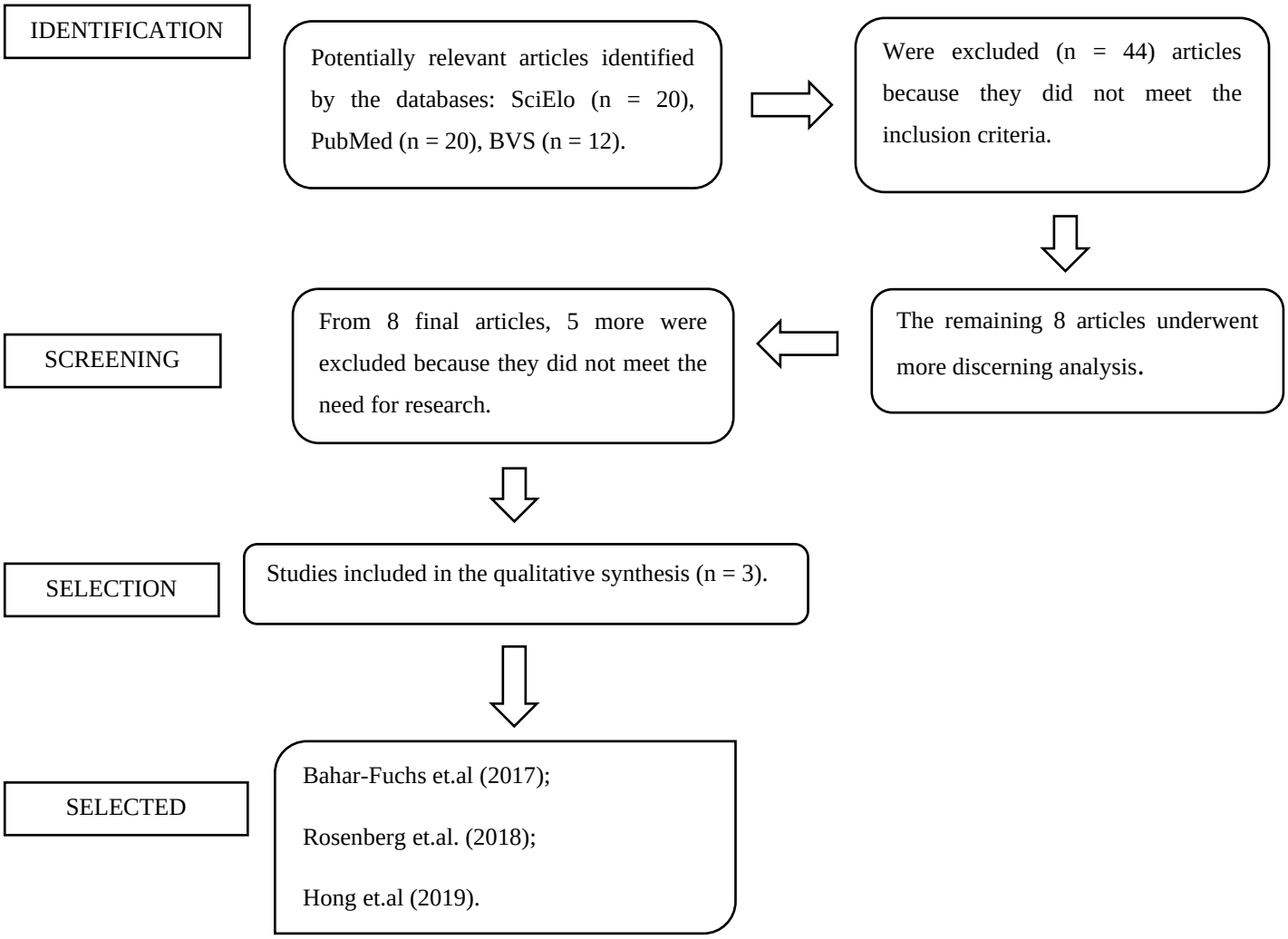

Table 1. Methodological characteristics of the selected studies, from 2017 to 2020.

AUTHOR	GROUP	INTERVENTION	VARIABLES	RESULTS
Bahar-Fuchs et.al (2017)	Group of elderly people with cognitive impairment (n = 11). Group of elderly people with neuropsychiatric symptoms related to mood (n = 9). Groups with elderly people with both characteristics (n = 25).	Period of 8 to 12 weeks and follow-up for three months. Involvement of repeated practices in tasks performed on the computer similar to games, psychoeducation and a variety of behavior change techniques.	Change in global cognitive ability after intervention. Change in the self-report of memory functioning, perception of memory deficits, mood and independence in activities of daily living.	Improvement in satisfaction with memory in all groups. Elderly with primary cognitive impairment improves memory and learning assessment measures.
Rosenberg et.al. (2018).	1260 elderly people aged 60 to 77 years at risk of dementia.	Participants were randomized for intervention in multiple domains (diet, exercise, cognition and vascular risk management) and health counseling.	Change in cognition.	No results were significant found.
Hong et.al (2019).	Group of elderly people who has received cognitive stimulation and lifestyle changes. Group of elderly people who only changed their lifestyle and group 3 did not perform any intervention.	Cognitive intervention with the aid of physical exercise and lifestyle changes.	Scores on the computerized tests of the Cambridge Neuropsychological Test Automated Battery. Test scores that assess general cognition, memory, visuospatial and cognitive functions.	Phonemic fluency, verbal memory, quality of life and mood were the best in the group of older adults than cognitive stimulation and lifestyle changes.

3 RESULTS

A summary of the electronic search for articles carried out in November 2020, in the selected databases, is shown in Figure 1. Initially, 52 articles were identified, of which 44 were excluded because they did not meet the inclusion criteria after reading the title and Summary. Of these, 8 were read in full and subjected to a careful evaluation, of which five were excluded for not meeting the inclusion criteria, leaving 3 that adequately met all the inclusion criteria, thus being selected for this integrative review.

The description of the articles that verified how the memory and learning process are important to prevent the onset or progression of AD is presented in table 1. Of the 3 selected articles, all are experimental. Articles were identified in South Korea, the United States and Finland.

4 DISCUSSION

Alzheimer's disease (AD) is a neurodegenerative disease that affects a large part of the world population, where its stages are divided into: mild, moderate and severe (Ximenes, Rico and Pedreira, 2014). According to Gallucci, Tamelini and Forlenza (2005) in this division of stages of the disease, the symptoms come in a varied and more intense form according to the progress of the disease. This division may be classified: Light stage - lasting two to three years, with episodic memory loss and learning difficulties. In the intermediate stage, which can last from two to ten years, aphasia, agnosia, apraxia, and anomie progressively occur, in addition to musculoskeletal changes caused by disorders in the extrapyramidal system, such as changes in posture, increase without muscle tone, impairment gait and imbalance (Araújo and Nicoli, 2010). In the severe stage, which lasts from 8 to 12 years, all brain functions are affected, in addition to behavioral changes, non-sleep and activities of daily living (Ximenes, Rico and Pedreira, 2014).

Over the years, researchers have sought to understand how the brain memorizes and relearns something new, that is, how neuronal plasticity occurs, as it has been one of the most studied areas in recent years, as studies seek to understand functionality, paths nervous, synaptic responses resulting from massive sprouting and reactive synaptogenesis in intact and uninjured axons (Raineteau et al., 2001).

Thus, these changes that occur in the CNS, lead to compromised emotional state, loss of synapses and neuronal death, in addition to drastically worsening the cognitive decline of these patients, thus leading to the main symptom, causing mortality due to treatment difficulties and brain damage. irreversible (Kocahan and Dogan, 2017). Observing the studies included in this review, it is possible to verify that all were carried out with elderly people aged 60 or over, the choice by the elderly may be due to the higher prevalence and / or risk of dementia in this group. In addition, regardless of the presence or absence of neurological disease, the elderly may have progressive loss of some unit or cognitive function due to changes in the CNS such as loss of memory, planning and processing speed (Soares et al., 2015).

Cognitive stimulation has been considered as a means of intervention to promote the improvement of neuroplasticity, considering that there is an evident relationship between learning, memory and cognition (Bahar-Fuchs et al., 2017). Early AD already compromises the individual's memory, the studies found for this review a multimodal intervention to trigger the decrease in the progression of this pathology (Bahar-Fuchs et al., 2017; Rosenberg at al., 2018; Hong et al., 2019).

Câmara (2019), points out that the highest prevalence in Alzheimer's findings is the ε4 allele of apolipoprotein E, as it consist of the accumulation of beta-amyloid protein (APP) plaques, hyperphosphorylated neurofibrillary tangles, inflammation mediated by neuroglia, dysregulation of neurotransmitter signaling, cerebral atrophy and neuronal changes, thus influencing the appearance of these patients' symptoms.

A study evaluating the group of elderly people who underwent cognitive stimulation with changes in lifestyle shows improvement in verbal memory when compared to groups of elderly people who have only undergone lifestyle changes or who have not undergone any form of intervention (Hong et al., 2019). Cognitive stimulation is a non-pharmacological approach that aims to activate existing functions to allow them to compensate as compromised, for example, reality-oriented therapy, through the use of newspapers, videos, among others (Camara et al., 2009).

Cognitive performance is related to the maintenance and learning of motor skills. With aging, more attention is needed, with concern about the ability to adapt to environmental changes. This adaptation is related to cognition and brain plasticity, responsible for the production of motor control and the compensation of disturbances caused by external stimuli.

In this process of relationship between memory and learning, LTP and LTD are also found, known as Long Term Potentiation and Long Term Depression, respectively, long and short term memory. Long Term Potetiation (LPT) is an increase in synaptic efficacy, involving both pre- and post-synaptic changes, which can last for hours or weeks, thus causing greater memory correction (Willis, 2000)..

In LTP there is an important role for this correction, since the excitatory amino acid neurotransmitters act in non-NMDA receptors (non-N-methyl-D-aspartate), promoting an increase in the range of action of the strongest potentials or a phosphorylation of protein substrates bridge to lasting changes in synaptic efficacy (Kleppisch et al., 2003).

While in Long Term Depression (LTD), there is a reduction depending on the activity of the synapses, making it last for hours or a few days, varying according to the stimulus pressed. LTD occurs in several areas of the CNS with varied mechanisms depending on the region of the brain and is characterized mainly in the hippocampus and cerebellum, with the neurotransmitter most often L-glutamate (Silverio and Rosat, 2006).

In general, LTP and LTD have similar characteristics, as both involve an initial activation of some types of receptors to glutamic acid, the main excitatory neurotransmitter, going through the same steps as the entry into the post-synaptic calcium cell, followed by activation of several enzymes dependent on this ion, thus allowing a download of phosphate ions from one protein to another and the subsequent activation of DNA transcription, leads to protein synthesis in the ribosomes of the activated neuron cytoplasm, and this protein system is important for both genesis of LTP as for LTD (Myskiw et al., 2013).

In this way, the synaptic marking process is understood, because when a learning modification resulting from a hippocampal LTP or LTD occurs by another learning resulting in the same way, the consequence of the production of new proteins occurs close to the synapse that was stimulated first thus, other proteins, synthesized near another synapse in the same hippocampal cell, migrate to the previous synapse and "capture" the proteins synthesized therein (Izquierdo et al., 2013).

Thus, it is understood that neuroplasticity has different effects according to age, but that in any one of them, it is an important process for learning by reinforcing synapses (Bastos et al., 2017).

Therefore, these findings are in line with the results obtained in two of the three selected articles, where the improvement of the clinical condition, mood, learning and memorization, occurred through neuronal plasticity, since the connection synapses and reinforcements stimulated between them, stimulate the brain to memorize and learn or relearn something new whenever necessary, thus improving the situation of these patients.

Given the above, it is observed that the theme of this study has relevance, in view of the restricted link between neuronal plasticity and the decrease in cognitive loss, especially in the elderly. However, further research needs to be carried out in order to fill some scientific gaps, such as the brain's plasticity ability to reach the speed of processing and learning the memory.

5 CONCLUSION

Thus, it is concluded that stimulating the brain to new activities and events, causes the brain synapses to be stimulated to a new execution memorization, reinforcing the learning and memorization, contributing to prevent the onset of Alzheimer's, besides stimulating the brain to prevent severe disease progression, slowing cognitive and memory loss.

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