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DEEP BRAIN STIMULATION AS AN ALTERNATIVE TREATMENT FOR ALZHEIMER'S DISEASE

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Abstract: Aim: To describe through a literature review Alzheimer's disease and a new complementary therapy that allows an improvement in the individual's quality of life. **Methodology:** A bibliographic search was performed in the main health databases PUBMED and BVS Regional Portal, in which different studies, including laboratory studies, case reports, systematic reviews, narratives, and reviews, which were developed in living individuals, were included. Therefore, articles that did not address the topic in question, letters to the editor, opinion articles, duplicate literature in databases, and literature that did not address the variables under study were excluded. **Results:** According to the methodological analysis, it is observed that the average publication of articles in the Pubmed database was 2.33 and with a standard deviation of 1.11. While in BVS Regional Portal, the average was 1.0 and the standard deviation was 0.71. Thus, it is possible to verify that there was a significant variation in the number of articles in the two databases. **Conclusion:** It is concluded that deep brain stimulation applied to the fornix is a safe procedure, in addition to being a very promising alternative for patients who are refractory to other treatments. Therefore, there is a high benefit and safety in the use of the f-DPE technique in patients with AD.
Keywords: Deep Brain Stimulation; Fórnix, Brain; Alzheimer Disease; Clinical Diagnosis.

INTRODUCTION

Population growth and aging have increased the number of patients with Alzheimer's disease (AD) and other neurodegenerative comorbidities. The exponential growth of AD affects the development and creation of new therapeutic approaches, such as invasive brain technologies, aimed at improving the population's quality of life.[1]

Therefore, an alternative treatment that gained notoriety was deep brain stimulation (DBS-f), which in turn is a surgical technique in which an electrode is implanted in a specific region of the brain, then this electrode is coupled to a pulse generator, which resembles a cardiac pacemaker; it will send energy to the region of the brain that you want to stimulate, helping to re-establish the transmission of electrical impulses between neurons in that region. This surgical procedure proved to be effective for the treatment of various movement abnormalities, especially in Parkinson's disease, especially in cases of generalized dystonia. In addition, this technique has been explored in a variety of other neurological and psychiatric diseases with encouraging results. [2,3]

Recent studies show that there is an eventual improvement in the clinical picture of the patient with AD since it is possible to observe a clear evolution in the neuropsychomotor disability. Despite this, the search for methods capable of correlating physiological or behavioral effects from this technique that result in improvements in the treatment of AD is notorious. [4,5]

Findings in the literature show that fornix is the main target of ECP for AD since it has the potential to reduce neuronal loss rates, avoiding a possible worsening of the disease prognosis The exact mechanisms of action of ECP-f are not completely known, but studies have revealed the increased release of acetylcholine in the hippocampus, synaptic plasticity, with decreased inflammatory responses in the cortex and hippocampus to the use of ECP-f. [6]

In this context, observational studies demonstrate that ECP presents itself as an excellent alternative treatment for AD. However, there is still a lack of information on how the mechanism of action and/or the

pathophysiology of deep brain stimulation occurs in Alzheimer's disease. Therefore, the present study aims to describe, through a literature review, Alzheimer's disease and a new complementary therapy that allows an improvement in the individual's quality of life, since the cure is a process that is not possible in all patients. scenarios of neurodegenerative comorbidities.

METHODOLOGY

SELECTION OF STUDIES

A bibliographic search was performed in the main health databases Pubmed (www.pubmed.gov) and BVS (bvsalud.org), in which studies published from 2013 to 2022 were collected. In the first step, the list of retrieved articles was examined by reading titles and abstracts. In the second stage, the studies were selected by reading the content in full. Three authors (JDMM, MVML, and MGVF) performed steps 1 and 2. Experimental, clinical, case-control, randomized controlled, and laboratory cohort studies, case reports, systematic reviews, narratives, and literature, developed on living subjects, were included. Thus, articles that did not address the topic in question, letters to the editor, opinion articles, duplicate literature in databases, and literature that did not address the variables under study were excluded.

DATA SOURCE

Through bibliographic research, 30 articles were selected, all of which were extracted from Pubmed (www.pubmed.gov) and BVS Regional Portal (bvsalud.org). The following specific medical subject titles and keywords were used: *Deep Brain Stimulation* (DeCS/MeSH Terms), *Fornix, Brain* (DeCS/MeSH Terms), *Alzheimer Disease* (DeCS/MeSH Terms), *Clinical Diagnosis* (DeCS/MeSH Terms).

Database	Mean ± Standard Deviation	CI 95%
Pubmed	2.33 ± 1.11[a]	(1.22–3.44)
BVS	1.0± 0.71[b]	(0.29–1.71)

Table. 1 - Mean ± standard deviation and coefficient interval of the number of studies in the main health databases.

According to the tabulation of evaluated works, it can be observed that the average number of articles published in the period from 2013 to 2022 in the Pubmed database was 2.33, with a standard deviation of 1.11; on the other hand, on the VHL portal, a score of 1.0 was obtained, with a standard deviation of 0.71. Therefore, it was possible to verify that there was a significant variation in the number of articles between the groups of health data.

RESULTS

Given careful research and tabulation of the respective articles, the result was that in many cases deep brain stimulation applied to the fornix is a safe procedure, in addition to being a very promising alternative for patients who are refractory to other treatments, especially in older patients. of 65 years. The most relevant results of ECP-f demonstrated progress in recalling memories, increased energy metabolism, and brain structural changes.

DISCUSSION

A randomized study involving 42 AD patients, accessing the fornix of these patients by ECP, indicated that although there were no signs of cognitive improvement in the patients who received the f-DPE, 48% of them reported the presence of memory flashbacks right at the beginning of stimulation. Patients reported richly detailed experiences, which became greater the more the stimulation voltage was increased.[7] Corroborating the

previous study, an analysis proposed by Germann et al. (2021), demonstrated that when performing f-DBS on 39 patients and 46% of them experienced flashback phenomena at least once during the process. [8]

In addition, in a randomized clinical trial carried out on 42 patients for two years, safety in the use of the f-DPE method in individuals with AD, where only rare study volunteers had serious adverse side effects and the greatest benefits were proven at ages more advanced.[9] Studies claim that bilateral f-DBS can be performed safely and is well tolerated among patients. [10-12] A significant increase in glucose metabolism was also observed in several brain regions in patients who received f-DPE. However, the increase was not significant in the first 12 months of the study. [13,15]

Subsequently, a one-year article used f-DBS in 42 patients who had AD and evaluated the benefits of stimulation related to the patient's age. The result was that f-DBS had greater benefits when performed in patients older than 65 years. Most patients under 65 years old showed little or no benefit. [16]

Sankar and Collaborators. (2015),[17] observed that, at least in certain patients, f-ECP may have a trophic effect. Whereas, 2 out of 6 AD patients who received f-ECP continuously during a one-year study had increased hippocampal volume, and yet a slower rate of atrophy in both the fornix and mammillary bodies.

Numerous limitations on the subject still exist, among them a special one gaining notoriety, being the ethical challenge inherent to research involving individuals with cognitive dysfunctions. Due to impaired or expected future loss of decision-making capacity, there are losses in the ability to consent, especially regarding the choice of treatments and participation in clinical trials and studies in general.

CONCLUSION

It can be concluded from this study that

Most studies have shown benefits and safety in the use of the f-DPE technique in patients with AD. The main findings observed were the recall of memories, increased energy metabolism in various brain regions, and brain structural changes, with volume expansions located in areas known for atrophy in AD. However, for this procedure to be used in clinical practice, further studies will be needed to prospectively observe cases that present chronic conditions of f-DPE in patients with AD.

INTEREST CONFLICTS

The author declares that there were no conflicts of interest.

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