Proceedings of the 2nd International Conference on Modern Medicine and Global Health
DOI: 10.54254/2753-8818/15/20240478

New directions in deep brain electrical stimulation for dementia and Alzheimer's disease - Advances in brain-computer interface technology

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Abstract. In *2022 Alzheimer's Disease Report*, World Health Organization (WHO) states that Alzheimer's disease and dementia have become the seventh most common causes of death in the U.S. However, there is currently no cure for Alzheimer's disease and dementia, therefore research into effective treatments for Alzheimer's disease is imminent. This paper introduces the incidence, pathogenesis, pathological mechanisms, and treatment of dementia and Alzheimer's disease, and describes the latest research direction for Alzheimer's disease - deep brain electrical signal stimulation. Although deep brain electrical signal stimulation is not commonly used to improve and treat cognitive function in Alzheimer's disease at this stage of the disease, it is a very promising research direction for repairing or re-stimulating brain function. This paper suggests that it may be possible to use the emerging technology of brain-computer interfaces (BCI), equipped with deep brain electrical stimulation systems, to synchronize the input and output of electrical signals to achieve the purpose of precisely determining the electrical stimulation points. Brain-computer interface technology can also be linked to artificial intelligence technology to build personalized brain models, completing the generalization of therapeutic technology.

Keywords: Alzheimer's Disease, Deep Brain Electrical Stimulation, Brain-Computer Interface Technology, Dementia.

1. Introduction

In 2022 report on Alzheimer's disease, WHO states that 6.5 million Americans aged 65 and over currently have Alzheimer's disease. By 2060, this number is likely to rise to 13.8 million people if there are no medical breakthroughs in preventing, slowing or curing Alzheimer's. Official death certificate records show that data last updated to 2019, 121,499 deaths from Alzheimer's disease. In 2019, Alzheimer's disease was officially listed as the Sixth most common cause of death in the United States, and in 2020 and 2021 it was listed as the seventh most common cause of death due to COVID-19's entry into the top 10 causes of death. Besides Alzheimer's disease remains the fifth most common cause of death for Americans 65 and older.From 2000 to 2019, deaths due to stroke, heart disease and AIDS declined, while reported deaths due to Alzheimer's disease increased by over 145 per cent [1]. Addressing Alzheimer's disease is urgent. At this stage, the study of Aducamab, a drug that is specific to the pathology of Alzheimer's disease, is in phase 3 clinical trials, and despite the side

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effects, it is believed that in the near future this drug could be introduced to the market and significantly slow down the exacerbation of Alzheimer's disease. However, in physical therapy, Alzheimer's disease is still very much a single therapy using transcranial magnetic stimulation, and it has been suggested in the literature that deep brain electrical stimulation can improve cognitive function in the brain and thus treat Alzheimer's disease. This paper uses the literature review method to search the literature on deep brain electrical stimulation for the curing of Alzheimer's disease since 2020, and summarizes and discusses the feasibility of this approach as well as proposes that brain-computer interface technology can be used as an alternative form of deep brain electrical stimulation to improve the shortcomings of deep brain electrical stimulation.

2. Dementia and Alzheimer's disease

Dementia is a chronic, generalized and usually irreversible decline in cognitive function. Dementia primarily impairs memory, that is usually caused by anatomical brain changes, has a slow start, and is usually irreversible. The most usual types of dementia are Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal lobe dementia, and HIV-related dementia. In this article, Alzheimer's disease is highlighted as a representative.

Alzheimer's disease is a condition that causes progressive cognitive deterioration. It is characterized by characteristic beta-amyloid deposits and neuro progenitor fibre tangles in the cerebral cortex and subcortical grey matter. The clinical symptoms of Alzheimer's disease are mainly short-term memory loss and deficits in other cognitive functions that tend to multiple aspects involved, such as impaired reasoning, poor judgment, language dysfunction, visuospatial dysfunction, and the prevalence of abnormal behaviour. Alzheimer's disease is slow and takes a long time to progress.

Alzheimer's disease, which accounts for 60~80% of dementia patients. In the United States, it is estimated that approximately 10% of people ≥65 years of age have Alzheimer's disease. The proportion of patients with Alzheimer's disease increases with age. The prevalence is twice as high in women as in men, which may be related to the fact that women live longer on average. In developed countries, as the elderly population grows, its prevalence increases accordingly [2].

However, with regard to conventional treatment options for dementia, physiotherapy is generally used in clinics to supplement medication. There is no specific drug for dementia such as Alzheimer's disease. Cholinesterase inhibitors may improve cognitive and memory impairment to some extent in some patients. In general, there are four available medications: donepezil, lisdexamfetamine, and galantamine. Due to the pathology of Alzheimer's disease, Aducamab, a human IgG1 anti-amyloid monoclonal antibody that specifically targets beta-amyloid oligomers associated with the pathophysiology of Alzheimer's disease, has been investigated and is now available as a monthly infusion used to treat Alzheimer's disease.. Anti-amyloid monoclonal antibody therapies, which also have side effects, include amyloid-associated imaging abnormalities (ARIA), including brain edema (ARIA-E) and/or microhaemorrhages and MRI signal changes in superficial ferritinosis (ARIA-H). Currently in the Phase 3 trial, 35.2% of patients receiving high-dose aducanumab experienced ARIA-E; ARIA-E typically occurs early in treatment and does not cause any symptoms. Yet, up to 0.9% of patients with ARIA had severe symptoms, including confusion, disorientation, gait disturbance, ataxia, visual disturbances, headache, nausea, and falls [3].

In physical therapy, transcranial magnetic stimulation (TMS) has gained increasing recognition in both psychiatric and neurological disorders and in the field of rehabilitation. Currently, domestic and international studies have used it in the curing of Alzheimer's disease. TMS is a transcranial stimulation technique that regulates neurological function by inducing currents in the brain through an alternating magnetic field [4].

3. Electrical brain stimulation

Deep brain stimulation (DBS), through stereotactic technology, implant stimulating electrodes for high-frequency electrical stimulation at specific target points within the brain, thereby modulating the excitability of the corresponding nuclei for therapeutic purposes. This method can be used to treat motor

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neurological disorders (e.g., Parkinson's disease), and in some clinical studies is also promising for the curing of neuropsychiatric disorders (e.g., depression, obsessive-compulsive disorder), overeating, and obesity [5].

DBS has been used in the curing of Parkinson's Disease for 20 years, but is not widely known in practice. DBS is highly effective in the curing of Parkinson's Disease and can greatly enhance the quality of life of the patients. Alzheimer's disease is the same as Parkinson's disease. It is a neurodegenerative disease, which means that DBS may also be useful in the treatment of Alzheimer's disease, but only if the precise area of the brain to be stimulated needs to be identified in order to provide safe and effective treatment [6].

The research began with a DBS study at the University of Toronto in Canada, where electrical stimulation of the fornix region of the brain in a patient undergoing obesity treatment caused flashbacks of memories from his childhood and adolescence. And Alzheimer's disease is a process of progressive memory loss [7]. Thus, the team speculated that stimulation of the dome region of the brain might also be applicable to the curing of Alzheimer's disease [8].

The Charité Medical School in Berlin conducted a clinical pilot study of DBS of the cerebral fornix for the medical treatment of Alzheimer's disease. They subjected 46 patients with mild AD to bilateral DBS experiments targeting the fornix region, following a standardized stimulation protocol, between 2007 and 2019. Despite the unsatisfactory results of the study - only a small number of patients had improved cognitive function - the research team said that the choice of the spot in the brain to stimulate was very important, and that for some subjects who underwent electrical stimulation just a few millimetres off the spot, their cognitive function did not improve. However, based on this the team's further analysis showed that the intersection of the fornix and the stria terminalis in the brain may be the best area for DBS treatment, paving the way for further research and treatment [9].

4. New directions in Alzheimer's treatment

Based on the above research, it is believed that it is possible to achieve the goal of promoting brain function and thus treating Alzheimer's disease by finding the right brain area that should be electrically stimulated.

Brain-computer interface (BCI) is a new direction, BCI is a kind of instantaneous communication system connecting the brain and external devices, the key to BCI technology is the conversion of the user's input EEG signals to the computer into electrical signals that output controlled or commanded conversion algorithms, and the most important part of BCI research is tuning the ultimate adaptive relationship between the human brain and the brain-computer interface system, that is to say, finding the appropriate signal processing and conversion algorithms, so as to make the neuroelectric signals can be converted into real-time, fast and accurate neural signals through the BCI system, which can be used in the brain [10]. The electrical signals can be transformed into commands or operation signals that can be identified by the computer through the BCI system instantaneously, speedily and precisely. In other words, it links the human brain and the computer through electrodes, and realizes the capture of brain electrical signals and the visualization of brain electrical functions.

However, in the traditional brain-computer interface, the computer is used to receive the electrical signals from the brain as the input signal. Imagine that we may be able to use the electrical signals captured by the computer to pinpoint the specific locations of the brain areas that emit the electrical signals related to Alzheimer's disease, such as cognitive signals, memory signals, etc., and then we may be able to use the computer to send out high-frequency electrical stimulation to these precise locations, thus achieving the therapeutic effect of the Alzheimer's disease. and thus achieve the effect of treating Alzheimer's disease.

5. Conclusion

According to the above literature and research, the medical treatment of Alzheimer's disease is becoming more diversified. Pharmacological treatments are no longer limited to cholinesterase inhibitors to improve cognition, and anti-amyloid monoclonal antibody therapy has been studied in light

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of the characteristics of its pathology. In terms of physical therapy, it has been found that Parkinson's syndrome, which is also a neurodegenerative disease like Alzheimer's disease, can be improved by deep brain electrical stimulation, and many experiments have been conducted on stimulating brain function and treating Alzheimer's disease through deep brain electrical stimulation, and the results of the experiments have shown that deep brain electrical stimulation can stimulate brain function, but only a few subjects with Alzheimer's disease have their cognitive dysfunction improved. However, only a few subjects with Alzheimer's disease showed improvement in cognitive dysfunction. The reason for this is that the point of stimulation is very important, which directly determines whether DSE works or not.

The shortcoming of DSE is that it does not determine the point of stimulation, because it is like a double-blind test, which can only determine whether the point of stimulation is working or not by the subjective change of the patient's scale, but cannot guide people how to adjust the point of stimulation to the correct position. According to the research on brain-computer interface technology, people can understand that brain-computer interface technology is two-way, it can output signal and also input signal. However, the brain also relies on the sending and receiving of electrical signals to transmit information. We envision that we can receive cognitive signals from the brain through the brain-computer interface and trace back to the place where the signals are sent, so as to try to send out electrical signals to stimulate the brain area, which may be able to accurately locate the brain's electrical stimulation points.

Looking to future development, the brain-computer interface technology to stimulate the brain area can be combined with the hottest artificial intelligence technology, the development of the brain does not need humans to determine the location of the electrical stimulation of the brain, artificial intelligence can work independently, to establish a personalized brain model, for each patient to find their own electrical stimulation of the brain, so as to achieve the promotion and popularity of the technology to alleviate the morbidity and mortality of Alzheimer's disease remains high at this stage.

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