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NEURODEGENERATION IN ALZHEIMER'S DISEASE: MODERN TREATMENT STRATEGIES AND REHABILITATION TECHNOLOGIES

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Abstract: This literature review is devoted to a comprehensive analysis of modern approaches to the treatment and rehabilitation of patients with Alzheimer's disease. The paper examines the pathophysiological mechanisms of neurodegeneration and their influence on the formation of therapeutic strategies. A critical analysis of the effectiveness of pharmacological methods is presented, including acetylcholinesterase inhibitors, NMDA receptor antagonists, and the latest drugs aimed at modifying the course of the disease. Special attention is paid to non-pharmacological approaches: cognitive stimulation, physical activity, diet therapy, and digital rehabilitation technologies. Promising research directions are considered, including immunotherapy, targeted effects on tau protein and beta-amyloid, as well as the use of neuromodulation. Issues of a personalized approach to therapy and rehabilitation of patients at different stages of the disease are discussed. Based on the systematization of modern scientific data, recommendations for optimizing treatment and rehabilitation measures are formulated, and priority directions for further research in this field are determined.

Key words: Alzheimer's disease, neurodegeneration, therapeutic strategies, cognitive rehabilitation, disease modification, personalized medicine, neuroplasticity.

Introduction. This article is devoted to the study of existing and prospective methods of treatment and rehabilitation of Alzheimer's Disease. The analysis of data in the article shows that AD is currently one of the most common brain diseases in elderly people. Despite the high prevalence of this disease, there are currently no drugs capable of curing this pathology, but some existing therapeutic treatment methods at an early stage can delay the development of Alzheimer's Disease. Also, along with generally accepted standards of drug therapy, new methods of non-drug correction of Alzheimer's Disease symptoms have been actively discussed and developed recently. The ambiguity of opinions of Russian and foreign authors regarding the effectiveness of individual methods of influence and ways of their combined use dictates the need for further research in this area. This article also addresses the need to improve medical and rehabilitation care for patients with Alzheimer's Disease.

According to the World Health Organization and the International Association of Alzheimer's Disease Societies (Alzheimer's Disease International), the total number of patients worldwide suffering from dementia in 2013 was 44.5 million people, by 2030 it will grow to 75.5 million people, and by 2050 - to 135.5 million people. AD accounts for 50 to 70% of patients, but experts consider such statistics to be underestimated, as in underdeveloped countries this indicator is difficult to establish [1]. The average life expectancy of a person aged 65 and older diagnosed with AD ranges from 4 to 8 years. Some may live up to 20 years after the first signs of the disease. Despite a decrease in mortality from cardiovascular pathology (-8%), breast cancer (-2.6%), stroke (-10.6%), mortality in AD continues to rise, increasing by 11% per year. The most common cause of death in AD is pneumonia [5]. Currently, there are no known drugs to treat AD, but some therapeutic treatment methods at an early stage can delay its development [8].

Approaches to treatment and rehabilitation of AD. The latest generation drug, acetylcholinesterase (AChE) inhibitor - rivastigmine, trade name (exelon) - a pseudoreversible carbamate-type AChE inhibitor with selective action on acetylcholinesterase in the CNS, has successfully passed clinical trials in the USA and Europe in two large multicenter (double-blind) studies. Rivastigmine has significant advantages over other anticholinesterase agents: firstly, its metabolism occurs both in the liver and in the intestine, unlike other anticholinesterase agents. Secondly, rivastigmine is a "pseudo-irreversible" inhibitor of acetylcholinesterase and butyrylcholinesterase. Thirdly, its half-life is very short (1-2 hours for oral and 3-4 hours for transdermal administration), while donepezil has a long half-life - 70 hours, and galantamine - from 6 to 8 hours, but the duration of rivastigmine's action is longer, as acetylcholinesterase and butyrylcholinesterase are blocked for approximately 8.5 and 3.5 hours, respectively. However, despite the fact that a third of patients using rivastigmine had tangible advantages over other drugs from this group, one third of patients with AD showed worsening of disease symptoms during the first 6 months, and 29% of patients discontinued treatment due to its side effects [3]. For the treatment of AD at moderate and severe stages, memantine is used, which is a non-competitive antagonist of NMDA-glutamate receptors, slows down glutamatergic neurotransmission and the progression of neurodegenerative processes, has a neuromodulating effect, helps normalize mental activity, improves memory, increases the ability to concentrate attention, and correct motor disorders. Memantine was approved by the FDA for moderate and severe AD both as monotherapy and in combination with acetylcholinesterase agents. Their combination benefits patients with usually additive effects without any enhancement of side effects [11]. Neurotrophic factors play a key role in the development, differentiation, synaptogenesis, survival of brain neurons and in the processes of their adaptation to external influences. The discovery of the neurotrophic effects of cerebrolysin, similar to BDNF activity, has sparked new interest in this drug [7]. Cerebrolysin is a concentrate obtained from the cortical substance of pig brain. It contains low molecular weight (less than 10 kDa) biologically active neuropeptides, similar to neurotrophic factors (NGF, CNTF, GNTF, IGF-1, IGF-2), and free amino acids. The biologically active neuropeptides of the preparation are able to penetrate through the blood-brain barrier (BBB) and directly enter the nerve cells under conditions of peripheral administration, unlike nerve growth factors, whose large molecules hardly penetrate into the CNS. Due to the action of analogs of neurotrophins, cerebrolysin is able to activate: a complex of natural biological mechanisms regulated by neurotrophic factors, with which the cell continuously maintains normal processes of growth, development, functioning programmed in DNA; neuroprotection processes - a complex of mechanisms that protect the cell from damaging factors, as well as processes; neuroplasticity - the ability of neurons and neural networks to change functioning and existing connections (sprouting, arborization, synaptogenesis) in response to stimuli such as learning, new experience or damage; neurogenesis - the process of forming new cells of nervous tissue from stem cells. Antipsychotics and antidepressants remain the main drugs for the treatment of behavioral and psychological symptoms of dementia. Pharmacological approaches to the treatment of psychiatric symptoms in AD are very individual and variable, depending on comorbid diseases, stage of the disease and severity of symptoms [2]. Polypharmacy in elderly patients with dementia is common. Anticholinergic and sedative drugs are often used off-label. Unjustified prescription of antipsychotic drugs should be avoided in cognitively vulnerable elderly people due to their potential adverse cognitive effects [4]. Nobel Prize laureate in Physiology and Medicine Eric Kandel in his book "In Search of Memory: The Emergence of a New Science of Mind" considers the option of using SSRI antidepressants not only as drugs to relieve symptoms of depression, anxiety, increased tension, but also as means that affect the mechanism of neurogenesis. There are scientific works that show that the use of SSRI drugs enhances neurogenesis, but the mechanism of action remains unclear. Today, it can be clearly stated that 5-HT and BDNF are considered the main "players" in the mechanisms of neurogenesis and neuroplasticity [5]. Psychotherapy is actively used in the treatment and rehabilitation of AD. The most commonly used method for AD is cognitive psychotherapy. The method is well studied, represents the most reliable alternative and supplement to pharmacological treatment for dementia. Cognitive psychotherapy for AD is usually divided into 3 types: cognitive stimulation (CS), cognitive training (CT), and cognitive rehabilitation (CR) [10]. Several studies have reported

improvements in overall cognitive functioning in patients with mild to moderate dementia after CS sessions. CS therapy has been proposed as a structured and methodologically substantiated protocol. To date, CS is considered a scientifically based method for the treatment of dementia in AD, including vascular dementia. Despite all the difficulties associated with conducting CS, interest in this method is growing [8]. Data on CT for people with dementia are less reliable. Studies have shown that CT can improve a patient's performance of tasks and exercises during sessions, but the results are not consolidated in everyday activities [1]. Studies have also shown that the connection between CS and CT did not lead to better results than individual interventions [18]. Cognitive rehabilitation is rarely used in AD, as the use of this method is difficult with this pathology [13]. Given the presence of psychiatric symptoms (hallucinations, delusions, low mood, anxiety, apathy, aggression, agitation, dissolution, wandering, socially or sexually unacceptable behavior) in the structure of dementia in AD, as well as the concern of patients and their relatives about the safety of drug treatment, it is advisable to use an individual and personally-oriented psychotherapeutic approach. Many recommendations have emphasized that the treatment of anxiety and depressive symptoms should be an integral part of the treatment of AD and other dementias [11]. Occupational therapy is also effective as a tool for reducing the psychiatric symptoms of dementia in AD, improving physical performance, quality of life, reducing emotional tension, improving mood [3]. Various phytotherapy techniques are actively used in the treatment of AD. The potential effects of essential oils are diverse, including promoting relaxation and sleep, pain relief. Studies have been conducted with positive results, using aromatherapy to eliminate psychiatric symptoms in AD, sleep disorders, and stimulate motivational behavior [2]. There is extensive literature reporting on the importance and benefits of music therapy for elderly patients including patients with dementia in AD. Studies have shown that sound can have a significant impact on the brain, activating a large number of cortical and subcortical areas [4]. Despite a large number of studies in this direction, there are also studies that refute the effectiveness of treating dementia in AD with music therapy [9]. In addition to drug therapy and psychotherapy, there are many simple ways to maintain independence and fight memory decline - such as electronic reminders, calendars, clocks, pill organizers. It has been confirmed that diet, physical exercise, and intensive social life help prevent cognitive decline [12]. Various diets are used in the treatment of AD, such as the ketogenic diet, MIND diet [24], etc. However, convincing evidence in numerous studies of the effectiveness of treatment with these methods as monotherapy has not been revealed. As for use in complex therapy, as an auxiliary method, it is a promising direction. It is known that environmental stimuli trigger the activation of BDNF and neurogenesis, stimulating neuronal plasticity. A number of studies have shown a connection between leisure and the incidence of AD. Individuals engaged in numerous leisure activities have a significantly lower risk of developing AD [11]. In the age of computer technology and the internet, telemedicine is actively developing all over the world. In the treatment of AD, telemedicine can indeed in the near future provide full-fledged home care, help people with AD maintain their independence and continue to live in their homes, receiving help and control around the clock while not wasting time on trips to the doctor, thereby improving their safety and relieving the burden on relatives and social services, improving clinical results and reducing the burden on the general medical network. Already in developed countries, telemedicine, in addition to diagnostic evaluation and remote examination by a doctor, is used for internet information groups and support groups, companion robots, remote monitoring of AD symptoms using smartphones, and teaching cognitive rehabilitation [7].

Promising treatment methods. One of the promising directions in the treatment of AD is immunotherapy. This method, directed against beta-amyloid protein, is a possible way to slow down the development of AD. Unlike conventional vaccination, which is carried out in advance, in the case of this disease, the vaccine is administered after the diagnosis has been established. According to the concept of researchers, the patient's immune system should recognize and attack amyloid deposits, reducing their size and alleviating the course of the disease. There are several directions of immunotherapy: Active immunotherapy. The basic concept of active immunization is to stimulate the immune system to recognize an antigen as a foreign protein to create a response to it. In the study, immunization of old mice effectively slowed the progression of plaque formation. The first human

study on active immunotherapy was conducted in 1999. The study included 372 patients. Despite significant "cleaning" of hippocampal plaques from beta-amyloid and a decrease in their density, as well as a decrease in phosphorylated tau protein compared to the control group of patients with AD, as well as improvements in cognitive indicators, the study was suspended at the 2nd stage, after four patients developed meningoencephalitis [3]. Today, there is a fourth strategy for active immunization - combined vaccination of the chaperone aSyn / Grp 94. In studies on mice using this strategy, strong suppression of microglial activation in the substantia nigra and striatum was observed in the CNS [8]. The fourth strategy of active immunization has been studied only in the first phase of clinical trials in humans. Passive immunotherapy. It is based on several stages:

1. Identification of the epitope (antigenic determinant) in the laboratory;
2. Generation of antibodies ex vivo;
3. Direct administration of the generated antibody to the patient.

This approach has been successful in the clinic for the treatment of a number of diseases, including autoimmune disorders, cancer, and transplant rejection. Experience in using monoclonal antibody therapy for human therapy began to be used for the treatment of neurological disorders, including for AD [1].

Conclusion. Thus, data have been obtained on the high prevalence of Alzheimer's Disease and the insufficient effectiveness of individual methods of influence and ways of their combined use in this pathology. Given the increasing life expectancy of people and the absence of correct medications that can significantly reduce the symptoms of AD, it is necessary to develop new methods of treatment and rehabilitation for this contingent of patients.

References

1. Gavrilova S.I. Pre-dementia stage of Alzheimer's disease: modern approaches to diagnosis and pharmacotherapy // Doctor.Ru. 2017. № 8 (137). P. 44–49 / Gavrilova SI. Predementnaya stadiya bolezni Al'tsgeymera: sovremennye podkhody k diagnostike i farmakoterapii [Pre-dementia stage of Alzheimer's disease: modern approaches to diagnosis and pharmacotherapy]. Doktor.Ru. 2017;8(137):44-9.
2. Gavrilova S.I. Guide to geriatric psychiatry. M.: Pulse, 2011. 380 p. / Gavrilov's SI. Rukovodstvo po geriatricheskoy psikhiatrii [Guide to geriatric psychiatry]. Moscow: Pulse; 2011. Russian.
3. Atri A. Current and future treatments in Alzheimer's disease // Semin Neurol. 2019. Vol. 39. P. 227–240 / Atri A. Current and future treatments in Alzheimer's disease. Semin Neurol. 2019;39:227-40.
4. Kamalova Malika Ilkhomovna, Islamov Shavkat Eriyigitovich, Khaidarov Nodir Kadyrovich. Morphological Features Of Microvascular Tissue Of The Brain At Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 2020. 2(10), 53-59
5. M. I. Kamalova, N.K.Khaidarov, Sh.E.Islamov, Pathomorphological Features of hemorrhagic brain strokes, Journal of Biomedicine and Practice 2020, Special issue, pp. 101-105
6. Kamalova, M. I., Eriyigitovich, I. S., & Khaydarov, N. K. (2020). MORPHOLOGICAL CHANGES OF CEREBRAL VESSELS IN ISCHEMIC STROKE. Journal of Biomedicine and Practice, 6(5).
7. Kamalova, M. I., & Khaidarov, N. K. (2020). PREVENTION AND RISK FACTORS FOR BRAIN INFARCTION (LITERATURE REVIEW). Journal of Neurology and Neurosurgical Research 1(2).
8. Malika, K. I., Nodir, H. K., & Shavkat, I. E. (2020). MODERN UNDERSTANDING OF RISK FACTORS AND PREVENTION OF BRAIN INFARCTION (LITERATURE REVIEW). Journal of Neurology and Neurosurgical Research, 3(1).

9. Khaidarov Nodir Kadyrovich, Shomurodov Kahramon Erkinovich, & Kamalova Malika Ilhomovna. (2021). Microscopic Examination Of Postcapillary Cerebral Venues In Hemorrhagic Stroke. The American Journal of Medical Sciences and Pharmaceutical Research, 3(08), 69–73.
10. Shomurodov K.E. Peculiarities of cytokine balance in gingival fluid at odontogenic phlegmon of maxillofacial area // The doctor-aspirant. - 2010. - 42(5.1). - C. 187-192.
11. Taylor M.K., Sullivan D.K., Mahnken J.D., Burns J.M., Russell H. Swerdlow Feasibility and efficacy data from a ketogenic diet intervention in Alzheimer's disease // Alzheimer's & Dementia: Translational Research & Clinical Interventions. 2018. Vol. 4. P. 28–36
12. Gitlin L.N., Arthur P., Piersol C., Hessels V., Wu S.S., Dai Y. Targeting behavioral symptoms and functional decline in dementia: a randomized clinical trial // J Am Geriatr Soc. 2018. Vol. 66. P. 339–345.
13. Hukins D., Macleod U., Boland J.W. Identifying potentially inappropriate prescribing in older people with dementia: a systematic review // Eur J Clin Pharmacol. 2019. Vol. 75. P. 467–481