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# Treatment of Alzheimer's Disease

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**Abstract.** As a neurodegenerative disease, the pathogenesis of Alzheimer's disease is not completely clear Alzheimer's disease not only afflicts the patients themselves, but also causes harm to countless families. Therefore, the treatment of Alzheimer's disease urgently needs to be studied. This paper summarizes some existing methods for the treatment of Alzheimer's disease,which are described from the molecular mechanism of Alzheimer's disease, the symptoms and the future development of Alzheimer's patients. Based on the current studies on the therapeutic method of Alzheimer's disease, more targeted interventions will be developed in the future.

**Keywords:** Alzheimer’s disease, treatment, molecular mechanism, genetic engineering

## 1. Introduction

Alzheimer's disease (AD) is an age-related neurodegenerative disease. The symptoms of Alzheimer's disease are divided to 4 periods. The first phase is the preclinical or presymptomatic phase that lasts for many years, slight memory lapses and lesions of cortex and hippocampus are considered to be the characteristics of the disease.There is no dysfunction in everyday routines and no clinical features and symptoms of AD. The second phase is mainly in the mild or early AD. During this period, patients begin to have a variety of symptoms in daily life, such as inattention and memory loss, time and place perception loss, emotional changes and other symptoms In the third stage, moderate AD, the disease diffused through the cerebral cortex and causes increased memory lapses, difficulty recognizing family and friends, loss of impulse control, and difficulty reading, writing, and speaking. The final stage is severe AD or advanced stage, in which the disease spreads throughout the cortical region and severely accumulates neuroinflammatory plaques and tangles, leading to sexual and cognitive impairment The patient can not fully recognize his family, and has difficulty in swallowing and urinating, which results in the patient being bedridden for long periods. Ultimately, the patient will die due to these complications. The number of people suffering from AD is increasing year by year, an AD is the sixth leading cause of death in the United States and one of the only top 10 causes of death that is still increasing significantly. [9] However, there is no satisfactory treatment at present. This article lists some treatments for AD in recent years. There are several ways to treat AD from the molecular mechanism of AD, such as Cholinesterase Inhibitors, and Neuroprotective Agents. Treatments for Alzheimer's symptoms include Anti-Amyloid Therapy, Anti-tau Therapy. Through the summarization and comparison of these treatment methods, the future treatment directions that can be applied or developed are explored.

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## 2. Treatment plan for symptoms

### *2.1. Cholinesterase inhibitors*

According to the cholinergic hypothesis, AD is caused by the decrease in acetylcholine biosynthesis. Therefore, AD can be treated by inhibiting the degradation of acetylcholine or accelerating the synthesis of acetylcholine. Tacrine, a cholinesterase inhibitor, is the first generation of cholinesterase inhibitors, but it is limited by hepatotoxic side effects. Then there are donepezil, kabalatine, and galantamine, the former may be the most widely used drugs.[7]

*2.1.1. Donepezil.* This kind of drug is the main drug for the treatment of AD at present. It can reversibly combine with synaptic acetylcholine to increase the concentration of synaptic acetylcholine and alleviate the symptoms of AD, but it can not hinder the progress of AD [3].

*2.1.2. Rivastigmine.* Rivastin is a pseudo-irreversible inhibitor of acetylcholinesterase and butyylcholinesterase. Whenit works, it binds to two active sites of acetylcholinesterase, and the metabolism of acetylcholinesterase is blocked by it Patients with mild to moderate Alzheimer's disease will be treated with this drug. It can improve the cognitive ability of patients, but at the same time it has many side effects. Oral administration of the drug will cause untoward effect such as nausea, vomiting, indigestion, fatigue, anorexia and weight loss. These secondary actions are also the cause for drug withdrawal [3]. But these side effects can be solved artificially. Rivastigmine is often administered through transdermal patches, which is more controllable than oral pills and can solve side effects in a timely manner.

*2.1.3. Galantamine.* Galantamine is the second generation of cholinesterase inhibitors, were used to the treatment of AD. Galantamine is the standard drug for patients with moderate AD. The behavioral symptoms, living ability and ability of cognizance can be well improved by Gal.Its effect is little different from that of other acetylcholine inhibitors.Donepezil can increase the concentration of acetylcholine at the synapse.Its mechanism of action is reversible binding with acetylcholinesterase to inhibit the hydrolysis of acetylcholine.

### *2.2. Neuroprotective agents*

AD is a kind of neurodegenerative disease, and the purpose of neuroprotective agents is to delay the process of brain degenerative disease. antiepileptic drugs, NMDAR modification, and omega 3 polyunsaturated fatty acid supplements are Neuroprotective Agents.

*2.2.1. Antiepileptic drugs.* Antiepileptic drugs are considered as central nervous system inhibitors. Antiepileptic drugs are considered to be central nervous system inhibitors, and it may reduce cognitive function. In the experiments in mice, it was shown that it can reduce the deposition of a protein in cells and improve the cognitive ability of mice. Antiepileptic drugs also have the potential to enhance cognitive function in healthy elderly people. But the drugs currently in clinical trials also have some side effects. The subjects also suffered from fatigue and irritability while receiving treatment [8].

*2.2.2. NMDAR modification.* Glutamate is one of the main excitatory neurotransmitters in the central nervous system. NMDAR is a subtype of ionic glutamate receptor, which plays a key role in regulating synaptic plasticity, neuronal survival, learning and memory. (Figure 1) The level of glutamate in cerebrospinal fluid and NMDAR in the hippocampus and frontal cortex decreased in AD patients. Enhancement or regulation of NMDAR activity shows therapeutic potential in early AD.Sodium benzoate can inhibit reactive oxygen species and thus protect nerves.In a clinical trial, benzoate treatment improved cognitive function in women with moderate to severe AD [8].

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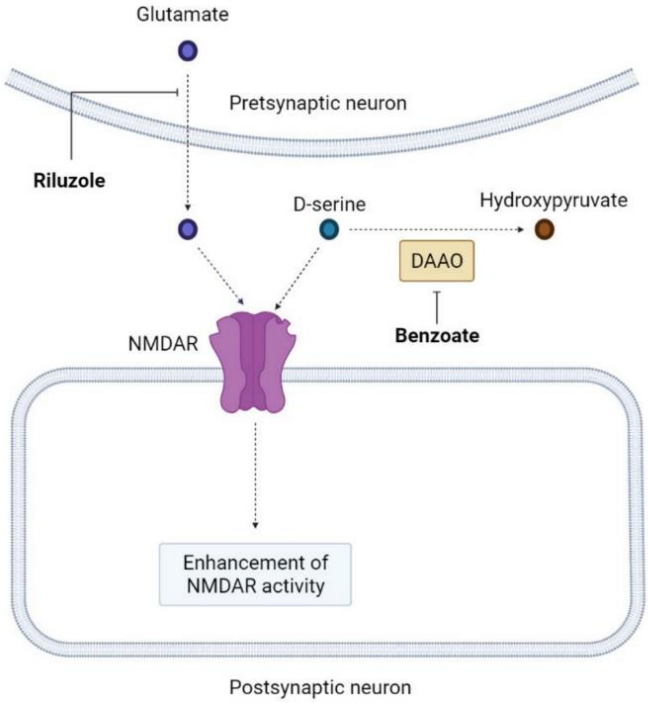



**Figure 1.** Nmdar Signaling Pathway [8].

*2.2.3. Omega 3 polyunsaturated fatty acid supplements.* Omega 3 polyunsaturated fatty acids include three subtypes: α-linolenic acid (ALA), eicosapentaenoic acid (EPA), and docosahexaenoic acid (DHA). Ingestion of these molecule have a positive effect on most brain diseases, as validated in the AD mouse model. This kind of molecule can improve the memory and learning ability of mice in the AD mouse model, and can effectively reduce the potential of AD in people with AD causing genes[8].

## 3. Treatment plan for the mechanism

The two major players in AD are commonly referred to as plaques and tangles. The cell membrane of neurons in the brain has some molecules called amyloid precursor protein(APP) on the cell membrane, these kinds of molecules have two parts, one is inside the cell, and the other is outside the cell. These molecules help neurons grow and repair after injury. APP is usually cut by some enzyme, which is called α-secretase and Y-secretase. If the cleaved polypeptide dissolves and disappears, it will not make effort on people's brain. But if β secretase and Y secretase act together to cut polypeptide, it will leave some protein fragments, which can't dissolve. This part of protein will form a monome called amyloid β, this kind of monome will get together and form βamyloid plaques. β amyloid plaques can block information transmission and precipitate in the cerebral vessels so cause AD.

The other culprit of AD is tangles. Tangles is formed because β Amyloid activated channels phosphorylate the TAU protein so that it can no longer support microtubules. TAU protein and microtubules cluster together causes to AD [2]. Mechanism-based therapy is to regulate the molecular process of AD.

### *3.1. Reduce tau phosphorylation*

This section describes the treatment with reducing tau phosphorylation through mild hyperthermia sauna-like conditions or menthol. This treatment works on tau protein, the principle is that high temperature can affect the activity of tau protein phosphorylation kinase. Under the high-temperature condition, the phosphorylation degree of tau protein decreased due to the decrease of tau protein phosphorylation kinase activity. The decrease of tau protein phosphorylation inhibited the production

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of tangles. During the sauna, the increase of body temperature broke the balance between phosphorylase and kinase, resulting in the dephosphorylation of tau protein [6].

### *3.2. Anti-amyloid therapy*

*3.2.1. Secretase inhibitors.* Secretase inhibitors are used to inhibit β Secretase and Y secretase activity. The decrease in the activities of these two secretory enzymes can reduce the deposition of amyloid in the brain. This method is feasible in terms of pathogenesis but they have a lot of side effects in clinical trials. Several BACE1 inhibitors have reached phase III clinical trials however these drugs have little effect on patients with mild cognitive impairment (MCI), and mild to moderate AD and may even aggravate the loss of cognitive function. The last inhibitor was discontinued in phase III because it showed high risk in the early stages of AD. Y secretase inhibitor had a bad effect on patients' cognition, so it was stopped [8]. At present, there are still many problems in the application of inhibitors, so the application of these drugs is controversial.

*3.2.2. Aβ aggregation inhibitors.* As the beta-protein deposition contributes to AD, AD is often treated with aggregation inhibitors that inhibit protein deposition [8]. But this method has many disadvantages, these compounds are small molecules, so they have little effect on protein deposition. Some compounds have poor permeability through the blood-brain barrier, so it is hard for them to get into the brain.

### *3.3. Anti-tau therapy*

Hyperphosphorylation of tau leads to the deposition of tau and microtubules, leading to the formation of tangles. So we can treat AD by inhibiting tangle formation [8].

*3.3.1. Phosphatase modifiers*. Phosphatase Modifiers can reduce tau protein phosphorylation, but many problems have been found in clinical trials [8]. For example, Sodium selenate is a PP2A activator. According to Yu, the use of sodium selenate was not found to have any effect on cognitive performance in patients with mild to moderate AD [8].

*3.3.2. Kinase inhibitors.* Kinase inhibitors can reduce the phosphorylation degree of tau protein. Some of these drugs have not been put into clinical trials but two types of GSK3β inhibitors, tideglusib and lithium have been researched in AD [8]. Tideglusib did not show clinical benefits in the phase II trial of mild to moderate AD, and its short-term administration resulted in the side effects of increased reversible transaminase.

*3.3.3. Tau aggregation inhibitors.* Tau protein aggregation inhibitor can keep the interaction and aggregation of tau protein in vivo. The two drugs used in clinical trials are methylene blue and curcumin [8].

Methylene blue is the earliest tau aggregation inhibitor and it is dual in the treatment of AD. Yu (2021) claim MB shows improvement in cognitive function in patients with early to middle AD. But at the same time, MB accelerated the formation of neurotoxic tau oligomers. So there are still some huge contradictions in drug administration [8].

Moreover, curcumin is a coloring agent and food additive. Although curcumin can inhibit the aggregation of tau protein, it has not shown any improvement in cognitive function in clinical trials and even decreased the cognitive function of patients [8].

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## 4. New treatment for AD

### *4.1. Disease-modifying therapeutics (DMT)*

Disease-Modifying Therapeutics (DMT) is different from the previous method. This method is not intended to improve or delay the onset of AD from the mechanism, but to reduce the symptoms [3]. At present, its application is still in the clinical trial stage.

### *4.2. Chaperone*

Protein misfolding can also cause AD when it accumulates in cells, at this time, we need molecular chaperones to change the conformation of proteins and guide the correct folding of proteins [3]. This is also a new idea for us to treat and maintain AD.

### *4.3. Natural extract*

After a long time of scientific research, some naturally extracted compounds have the potential for the treatment of AD, because these natural extracts can protect the nerves [3]. Some natural extracts have entered the stage of clinical trials. In vitro and in vivo studies have proved that natural compounds have the potential to treat AD, which makes some of them enter the stage of clinical trials. Nicotine is the first natural compound to enter the clinical trial for AD. Later, other compounds such as vitamin C, e and d have attracted more attention and interest because of their protective effects on neuroinflammation and oxidative damage.

### *4.4. Brain stimulation*

*4.4.1.Deep-brain stimulation.* DBS is an advanced treatment commonly used in surgery [8]. According to Yu, DBS can improve the cognitive ability and glucose metabolism of mild AD patients [8]. In patients with mild AD, DBS can improve the cognitive ability of patients over 65 years old. However, it has a negative effect on the cognitive ability of some young patients with AD.

*4.4.2.Vagus nerve stimulation.* Vagus nerve stimulation can be divided into invasive and non-invasive methods. Yu claims that invasive treatment can improve the symptoms of patients with AD. Invasive VNS is approved for the treatment of epilepsy and refractory depression [8]. Studies have shown that non-invasive can improve the associative memory of the healthy elderly. At present, it is considered that this method has the potential to treat AIDS, but its application is still in the stage of clinical trials.

### *4.5. Genetic engineering*

After large-scale research and experiments, it is found that APOE4 is closely related to the pathogenesis of AD and is the genetic factor of AD, while APOE2 is the strongest genetic protective factor. It is found that APOE4 has the strongest pathogenicity, so there is a new idea to treat AD by transforming the APOE4 gene into APOE2 or APOE3 [10].

However, this kind of therapy is still rare in clinics, because it has many obstacles compared with the treatment methods that directly act on the molecular mechanism. First, further development of small molecules capable of reliably changing the conformation of APOE4 to APOE3 or APOE2 is difficult. Second, the new data implicating a variety of non-Aβand non-tau targets in APOE pathophysiology raises new questions. Although this research is full of challenges at present, it is still an important idea for the treatment of AD.

## 5. Conclusion

The prevalence of AD is gradually increasing, but due to the complexity of AD, the pathogenesis of AD is not fully understood. Moreover, there are few treatment methods for AD, usually only a few medications are available to alleviate the symptoms of AD. Currently approved AD treatment is limited to cholinesterase inhibitors and memantine or a combination of these drugs [4]. Some specific

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drugs based on molecular mechanism have failed to pass phase III clinical trials due to side effects and other reasons, and they still cannot be administered on a large scale. [5] Future research can focus on preventive measures, such as protecting cell membranes from amyloid toxicity, reducing chronic inflammation and oxidative stress, and improving overall health and well-being through active lifestyle choices, which may slow the invasion of AD, provided that the intervention starts early enough in the disease process. [1] In addition, while focusing on the research and development of AD treatment methods, more attention should be paid to the mental health of AD patients, because this is a multi-faceted and complex disease.We can improve genetic engineering technology and promote its application in the treatment of Alzheimer's disease.At present, this article also has some problems, such as the lack of data support in some experiments, which can be supplemented by subsequent experiments.

## References

[1] Hane, F. T., Robinson, M., Lee, B. Y., Bai, O., Leonenko, Z., Albert, M. S., (2017), Recent Progress in Alzheimer's Disease Research, Part 3: Diagnosis and Treatment, *J Alzheimers Dis*, **57(3)**, 645-665. doi: 10.3233/JAD-160907. PMID: 28269772; PMCID: PMC5389048.

[2] Chu, L. W. (2012). Alzheimer's disease: early diagnosis and treatment. *Hong Kong Med J,* **18(3)**, 228-237.

[3] Breijyeh, Z., & Karaman, R. (2020). Comprehensive review on Alzheimer's disease: causes and treatment. *Molecules*, **25(24)**, 5789.

[4] Cummings, J. L., Tong, G., & Ballard, C. (2019). Treatment combinations for Alzheimer's disease: current and future pharmacotherapy options. *Journal of Alzheimer's Disease*, **67(3)**, 779-794.

[5] Weller, J., & Budson, A. (2018). Current understanding of Alzheimer's disease diagnosis and treatment. F1000Research, 7.

[6] Guisle, I., Canet, G., Pétry, S., Fereydouni-Forouzandeh, P., Morin, F., Kérauden, R., ... & Planel, E. (2022). Sauna-like conditions or menthol treatment reduce tau phosphorylation through mild hyperthermia. *Neurobiology of Aging*, **113**, 118-130.

[7] Briggs, R., Kennelly, S. P., & O'Neill, D. (2016). Drug treatments in Alzheimer's disease. *Clinical Medicine*, **16(3)**, 247.

[8] Yu, T. W., Lane, H. Y., & Lin, C. H. (2021). Novel therapeutic approaches for Alzheimer's disease: An updated review. *International Journal of Molecular Sciences*, **22(15)**, 8208.

[9] Atri, A. (2019). The Alzheimer's disease clinical spectrum: diagnosis and management. *Medical Clinics*, **103(2)**, 263-293.

[10] Serrano-Pozo, A., Das, S., & Hyman, B. T. (2021). APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches. *The Lancet Neurology*, **20(1)**, 68-80.