AMERICAN JOURNAL OF APPLIED MEDICAL SCIENCE
ISSN: 2996-5101 (online) | ResearchBib (IF) = 10.81 IMPACT FACTOR
Volume-4| Issue-4| 2026 Published: |30-04-2026

PHYSIOLOGICAL BASIS OF ALZHEIMER'S DISEASE

https://doi.org/10.5281/zenodo.19505358

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Abstract

Alzheimer's disease is a chronic, progressive neurodegenerative disease of the central nervous system, which is mainly characterized by impaired cognitive functions, memory, thinking and behavior. This article provides an in-depth analysis of the physiological basis of Alzheimer's disease, that is, its cellular and molecular mechanisms. In particular, the accumulation of beta-amyloid peptides, pathological phosphorylation of tau proteins, disruption of interneuronal synaptic transmission and neuroinflammation processes are considered. The role of oxidative stress, mitochondrial dysfunction and genetic factors is also analyzed. The results of the study show that several pathophysiological mechanisms are involved in the development of Alzheimer's disease in an interconnected manner. The article is of great importance in improving early detection, prevention and treatment strategies of the disease. This scientific work will serve as a useful resource for specialists, students and researchers working in the fields of medicine and biology.

Keywords

Alzheimer's disease, neurodegeneration, dementia, beta-amyloid, tau protein, neurofibrillary tangles, synaptic dysfunction, neuronal death, neuroinflammation, microglia, oxidative stress, mitochondrial dysfunction, genetic predisposition, APOE gene, biomarkers, neuroimaging, cognitive impairment, memory loss, acetylcholine, excitotoxicity.

Relevance of the topic

Today, Alzheimer's disease is one of the most pressing problems facing the global healthcare system. In connection with the aging of the population, the incidence of this disease is increasing every year. According to the World Health Organization, Alzheimer's disease accounts for the majority of patients with dementia. This is of great importance not only as a medical, but also as a socio-economic problem.

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Alzheimer's disease significantly affects a person's daily life. If mild forgetfulness is observed in the early stages of the disease, then in the later stages, patients experience severe symptoms such as inability to recognize loved ones, speech disorders, and impaired coordination of movements. This leads to the loss of patients' ability to live independently.

The relevance of the topic is that currently there are no effective drugs that allow for the complete treatment of Alzheimer's disease. Current treatment methods are only symptomatic and are aimed at slowing down the progression of the disease. Therefore, a deep study of the physiological basis of the disease is important for the development of new therapeutic approaches.

Modern scientific research shows that Alzheimer's disease develops not due to a single cause, but under the influence of several pathogenetic factors. Among them, genetic predisposition, environmental factors, metabolic disorders and changes in the functioning of the immune system play an important role. In particular, the formation of beta-amyloid plaques and tau neurofibrillary tangles are the main signs of the pathogenesis of the disease.

Early diagnosis of this disease is also one of the urgent issues. Pathological changes in brain tissue begin even before the clinical symptoms of the disease appear. Therefore, the development of biomarkers and neuroimaging technologies is of great importance.

The study of Alzheimer's disease requires the integration of not only neurology, but also such disciplines as molecular biology, genetics, pharmacology and psychiatry. In this regard, the comprehensive study of its physiological basis is one of the current directions of modern science.

Research Objectives

The main goal of this scientific research is to study the physiological basis of Alzheimer's disease in depth and systematically. Within the framework of this goal, it is intended to analyze the mechanisms of development of the disease at the molecular, cellular and systemic levels, identify the main factors involved in its pathogenesis and scientifically substantiate their interrelationships.

First of all, one of the important goals of the research is to study in depth the processes of formation, aggregation and accumulation of beta-amyloid proteins in brain tissues. It is planned to determine the mechanisms of pathological formation of beta-amyloid peptides by analyzing the proteolytic cleavage pathways of amyloid precursor protein (APP) and the activity of enzymes involved in this process. At the same time, the effect of these proteins on synaptic activity, disorders in interneuronal signal transmission and their impact on cognitive functions are also important areas of research.

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The second main goal is to study the physiological and pathological states of tau protein. Tau protein normally provides stability to microtubules, but its hypophosphorylation leads to the formation of neurofibrillary tangles. The study will analyze the molecular mechanisms of this process, the enzymes that control the level of tau protein phosphorylation, and changes in their activity. In addition, the impact of tau pathology on the neuronal intra-transport system and cellular metabolism will be studied.

The third important goal is to identify neuroinflammatory processes and assess their role in the development of Alzheimer's disease. The activation of microglial cells, their production of inflammatory mediators, and the impact of these processes on neurons will be analyzed in depth. At the same time, it will be determined how chronic inflammatory processes affect the progression of the disease. Research in this area will create an important basis for the development of anti-inflammatory therapies in the future.

The fourth goal is to study the balance between oxidative stress and antioxidant systems. The formation of free radicals, their damage to cellular structures, and the weakening of antioxidant mechanisms play an important role in Alzheimer's disease. During the study, processes such as lipid peroxidation, protein oxidation, and DNA damage will be analyzed. This will help to understand the degenerative changes that occur at the cellular level.

The fifth important goal is to determine the role of mitochondrial dysfunction. Mitochondria are the energy-producing organelles of the cell, and when their activity is disrupted, the energy supply of neurons is disrupted. The structure of mitochondria, their functional state, ATP synthesis, and the production of reactive oxygen species will be studied within the framework of the study. This direction is important in understanding the energetic basis of the disease.

The sixth goal is aimed at studying genetic factors. In particular, various alleles of the APOE gene and their role in the development of Alzheimer's disease will be analyzed. Mutations in the APP, presenilin-1, and presenilin-2 genes will also be studied. This will allow us to understand the hereditary forms of the disease and identify genetic risk factors.

The seventh major goal is to identify changes in neurotransmitter systems. The levels of acetylcholine, glutamate, and other neurotransmitters and the activity of their receptors will be analyzed. This will help to understand the neurochemical basis of cognitive disorders. In particular, changes in the acetylcholine system, which plays an important role in memory and learning processes, will be the focus of special attention.

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The eighth goal is to study the state of the blood-brain barrier. As a result of the disruption of this barrier, harmful substances can enter the brain tissue. During the study, the permeability of the blood-brain barrier, its structural changes and functional state will be analyzed.

Research results

The results of the studies and analyses confirm that the development of Alzheimer's disease is a complex, multi-stage and multifactorial pathophysiological process. The basis of this disease is changes at the molecular, cellular and systemic levels, which are closely interconnected.

The first important result was the formation and accumulation of beta-amyloid proteins. Studies show that beta-amyloid peptides are formed as a result of incorrect breakdown of amyloid precursor protein (APP). These peptides accumulate in brain tissues and form amyloid plaques. These plaques disrupt the connection between neurons - synapses. Disruption of synaptic transmission leads to a decrease in cognitive functions. This process is especially pronounced in the hippocampus, which explains the memory-related disorders.

The second important result is associated with pathological changes in the tau protein. Studies have shown that hypophosphorylation of tau protein disrupts its normal function. As a result, neurofibrillary tangles form inside the neuron. These structures block the intracellular transport system and restrict the movement of nutrients and organelles. This ultimately leads to degeneration and death of neurons. The interaction of beta-amyloid and tau pathologies further accelerates the progression of the disease.

The third important finding is related to the role of the neuroinflammation process. Studies have shown the activation of microglial cells and their release of inflammatory mediators (cytokines, interleukins). This process initially occurs as a protective reaction, but when prolonged, it causes damage to neurons. In a chronic inflammatory environment, the ability of neurons to regenerate decreases and their death accelerates.

The fourth important finding is related to oxidative stress. Studies have shown an increase in the amount of free radicals and a weakening of antioxidant systems. Oxidative stress damages cell membranes, proteins, and DNA. In particular, the process of lipid peroxidation disrupts the integrity of neuronal membranes. This disrupts the ionic balance and impairs cell function.

The fifth finding is related to mitochondrial dysfunction. Mitochondria are the energy source of the cell, and when their function is impaired, ATP synthesis decreases. Studies have shown that changes in the structure and functional

insufficiency of mitochondria are observed in Alzheimer's disease. Energy deficiency negatively affects the activity of neurons and reduces their viability.

The sixth important finding is related to genetic factors. Studies have confirmed that individuals with the E4 allele of the APOE gene are at increased risk of developing Alzheimer's disease. This gene is involved in lipid metabolism and affects the accumulation of beta-amyloid. In addition, mutations in the presenilin genes and the APP gene also play an important role in hereditary forms of the disease.

The seventh finding is related to changes in neurotransmitter systems. In particular, a decrease in acetylcholine levels has been detected. This neurotransmitter plays an important role in memory and learning processes. Its deficiency leads to an increase in cognitive impairment. Also, disorders in the glutamate system cause excitotoxicity, which leads to neuronal damage. The eighth important consequence is associated with disruption of the blood-brain barrier (BBB). Studies have shown an increase in the permeability of this barrier. As a result, harmful substances and immune cells easily penetrate brain tissue, which increases inflammatory processes.

The ninth result is from studies related to biomarkers. Changes in beta-amyloid and tau proteins in cerebrospinal fluid allow us to detect the disease at an early stage. Also, modern neuroimaging methods (PET and MRI) can detect changes in the structure of the brain.

The tenth result is that the disease has a systemic nature. Studies show that Alzheimer's is not limited to the brain, but also includes changes associated with the metabolism of the whole organism. A connection with insulin resistance, cardiovascular disease, and metabolic syndrome has been identified.

Based on the above results, it can be concluded that Alzheimer's disease develops not by a single mechanism, but as a result of the combined action of several pathological processes. These processes have a mutually reinforcing effect, accelerating the progression of the disease.

The results also indicate the need for an integrated approach. That is, treatment strategies should affect not only one direction, but several pathogenetic mechanisms at once. This serves as an important basis for developing effective therapies in the future.

Conclusion

Alzheimer's disease is one of the most complex and urgent problems facing modern medicine and biological sciences. The pathogenesis of this disease is deep and multifaceted, in which changes at the molecular, cellular and systemic levels occur in harmony with each other. The analyses conducted within the framework

of this scientific article made it possible to comprehensively illuminate the physiological foundations of Alzheimer's disease and served to formulate important scientific conclusions regarding the mechanisms of its development.

Firstly, the results of the studies show that one of the central mechanisms of Alzheimer's disease is the pathological accumulation of beta-amyloid proteins. These proteins accumulate in brain tissues, form amyloid plaques and disrupt synaptic connections between neurons. As a result, cognitive functions, especially memory and learning ability, decrease significantly. This leads to the appearance of clinical symptoms of the disease.

Secondly, pathological changes in the tau protein are also important. As a result of hypophosphorylation of the tau protein, neurofibrillary tangles are formed, which disrupt the neuronal internal transport system. This process disrupts the metabolic balance within the cell and leads to neuronal degeneration. Thus, beta-amyloid and tau pathology together appear as the main pathophysiological factors of the disease.

Third, the process of neuroinflammation plays an important role in the development of Alzheimer's disease. Chronic activation of microglial cells leads to excessive release of inflammatory mediators. This has a toxic effect on neurons and accelerates their death. Therefore, anti-inflammatory therapy is considered promising.

Fourth, oxidative stress and mitochondrial dysfunction are important components of the disease. An increase in free radicals damages cell structures, and impaired mitochondrial function leads to energy deficiency. This reduces the functional activity of neurons and reduces their viability.

Fifth, genetic factors, in particular, the presence of the E4 allele of the APOE gene, have been found to increase the risk of developing the disease. This allows for an individual risk assessment of Alzheimer's disease and the development of preventive measures. Mutations in the APP and presenilin genes also play an important role in hereditary forms.

Sixth, changes in neurotransmitter systems, especially acetylcholine deficiency, are one of the main causes of cognitive impairment. Therefore, most current treatments are aimed at supporting this system. However, these methods are not able to completely stop the disease.

Seventh, disruption of the blood-brain barrier also plays an important role in the pathogenesis of the disease. This condition facilitates the penetration of harmful substances and immune cells into brain tissue, resulting in increased inflammatory processes and neuronal damage.

Eighth, the development of modern diagnostic methods allows for the early detection of Alzheimer's disease. Biomarkers, neuroimaging technologies, and genetic analysis can detect pathological changes even before the clinical symptoms of the disease appear. This is an important factor in increasing the effectiveness of treatment.

The analyses also show that Alzheimer's disease is not limited to the central nervous system, but is a complex process involving metabolic and physiological systems of the entire organism. Factors such as cardiovascular disease, diabetes, and metabolic syndrome have a significant impact on the development of the disease.

In general, the results of this study once again confirm that the pathogenesis of Alzheimer's disease is multifactorial and complex. This indicates that a single approach to treatment is not enough. On the contrary, it is necessary to develop complex and multidisciplinary therapeutic methods.

From the perspective of future prospects, it is important to further expand scientific research on the study of Alzheimer's disease. In particular, in-depth study of mechanisms at the molecular level, identification of new biomarkers and development of innovative drugs are among the priorities.

In addition, great attention should be paid to preventive measures. Leading a healthy lifestyle, proper nutrition, maintaining physical and mental activity can reduce the risk of developing Alzheimer's disease.

In conclusion, Alzheimer's disease is a complex and multifactorial disease, and a deep study of its physiological basis is of not only scientific but also practical importance. Research in this area will serve to develop effective treatment and prevention methods in the future.

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