When Proteins Clump: The Origin of Alzheimer's

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Key points:

- Introduction
- Beta Amyloid and Tau proteins
- Effects
- Risk factors
- Symptoms
- Conclusion

Introduction

Alzheimer's disease is the most common cause of dementia and one of the leading neurodegenerative disorders worldwide. First described by Alois Alzheimer in 1906 after observing progressive memory loss and cognitive decline in a middle-aged patient, the disease has since become a major global health concern. Over the past century, advances in research have significantly improved our understanding of its causes, diagnosis, and progression. Despite these developments, Alzheimer's disease remains a progressive and incurable condition that primarily affects memory, thinking, and daily functioning.[1,2]

Role of Beta-Amyloid

The formation of beta-amyloid (Aβ) peptides begins with the amyloid precursor protein (APP), a transmembrane protein encoded by the **APP** gene on chromosome 21. Under the amyloidogenic pathway, APP is sequentially cleaved by β-secretase and γ-secretase, producing beta-amyloid peptides, particularly **Aβ42**, which is highly prone to aggregation. These peptides accumulate to form oligomers, fibrils, and extracellular amyloid plaques, a hallmark of Alzheimer's disease. The buildup of beta-amyloid disrupts neuronal communication, triggers inflammation, and contributes to progressive neuronal damage and cognitive decline.[3]

Role of Tau Proteins

Tau is a microtubule-associated protein that helps maintain the structural stability of neurons and supports intracellular transport. Under normal conditions, it stabilizes the neuronal cytoskeleton, but in Alzheimer's disease, abnormal phosphorylation and other modifications cause tau to detach from microtubules and aggregate into neurofibrillary tangles. These toxic aggregates disrupt neuronal function, impair axonal transport, and contribute to progressive neurodegeneration. Tau proteins released from damaged neurons may also spread to neighboring cells, promoting disease progression.[3–5]

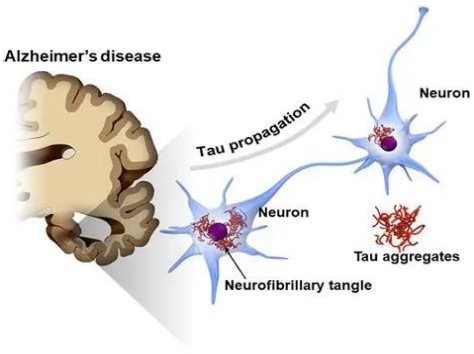


Figure 1: *Role of Tau Protein.*[5]

Effects of Beta-Amyloid and Tau Aggregates

The accumulation of beta-amyloid plaques and tau neurofibrillary tangles disrupts several essential neuronal functions. Both proteins impair mitochondrial activity, reducing ATP production and increasing oxidative stress, which contributes to neuronal injury and cell death. They also damage synapses by interfering with neurotransmitter release and disrupting normal neuronal communication, leading to progressive cognitive decline.[6]

In addition, beta-amyloid and tau activate microglial cells and trigger a chronic inflammatory response within the brain. Persistent neuroinflammation, together with altered calcium homeostasis and impaired synaptic function, accelerates neuronal degeneration and the progression of Alzheimer's disease.[6,7]

Risk Factors

Alzheimer's disease develops through a combination of genetic, vascular, and environmental factors. Genetic variants such as APOE ε4 increase the risk by impairing the clearance of beta-amyloid and promoting tau pathology, while mutations affecting TREM2 reduce the ability of microglia to remove amyloid deposits. Individuals with Down syndrome (trisomy 21) are also at increased risk because of excess amyloid precursor protein production. Advancing age remains the strongest risk factor, while obesity, cardiovascular disease, unhealthy diet, and environmental exposures may further contribute to disease development.[3,8]

Symptoms

Alzheimer's disease usually begins with subtle memory impairment and gradually progresses to affect thinking, language, and daily functioning. Common symptoms include short-term memory loss, difficulty with problem-solving, confusion, poor judgment, and impaired decision-making. As the disease advances, patients may develop anxiety, depression, agitation, sleep disturbances, hallucinations, and delusions. In the later stages, severe cognitive decline leads to complete dependence on caregivers for everyday activities.[9-11]

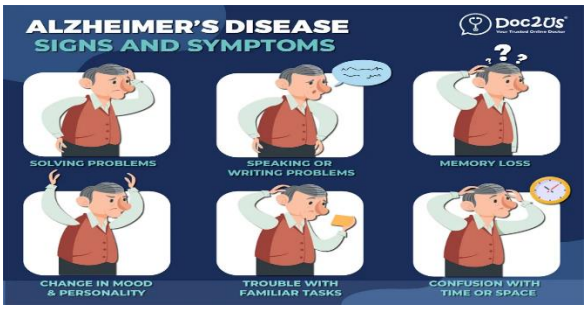


Figure 2: *Alzheimers Disease*.[10]

Conclusion

Alzheimer's disease is a progressive neurodegenerative disorder driven largely by the accumulation of beta-amyloid plaques and tau neurofibrillary tangles. These pathological changes disrupt neuronal function, promote inflammation, and lead to progressive cognitive decline. Although tau pathology shows a stronger correlation with disease severity and cognitive impairment, both beta-amyloid and tau play complementary roles in disease progression. Continued research into these mechanisms is essential for improving early diagnosis, developing targeted therapies, and ultimately enhancing patient outcomes.[12]

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