MOLECULAR BASIS OF ALZHEIMER'S DISEASE

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INTRODUCTION

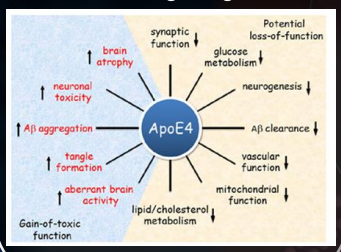
Alzheimer's disease (AD) is a neurodegenerative process in the Central Nervous System (CNS) characterized by a progressive neuronal death in several zones of the brain, in particular, cortical brain and hippocampus. The loss of immediate memory, a cognitive deterioration and behaviour disorders are also characteristics of Alzheimer's disease. The aetiology of the disease is already unknown and there is no existence of a treatment to stop the pathologic process. Several hypothesis have been made and some implications have been found with the intention to explain phenomena and what is going on AD.

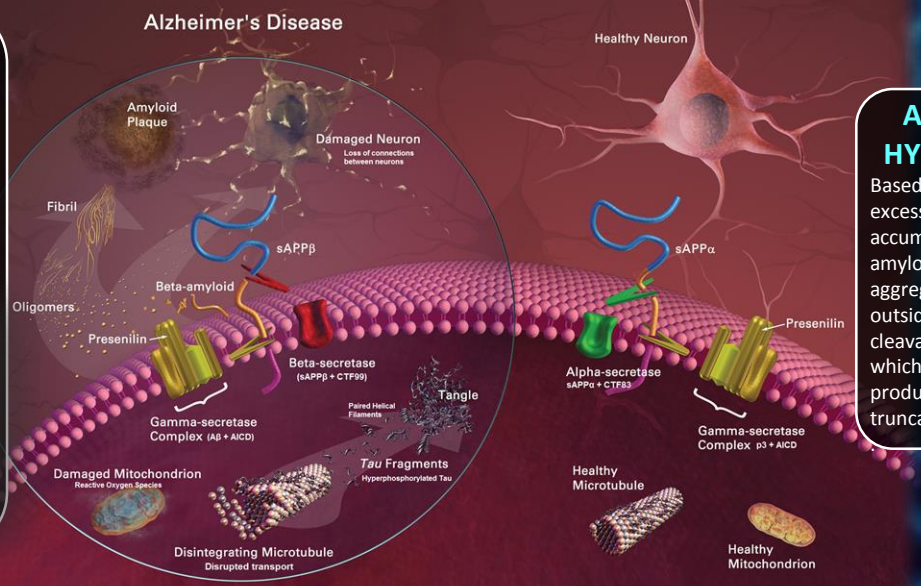
CHOLYNERGIC HYPOTHESIS

The loss of acetylcholine (ACh) neurons is a hallmark in AD. Ach in the synaptic cleft is catabolized by cholinesterases, implicated in behavioural functions including learning and memory.

APOE IMPLICATION

Mutation of ε4 allele in APOE gene coding for Apo-lipoprotein E stimulates AD causing accelerated cognitive decline with age and memory loss. ApoE is important in the metabolism of Aβ to carry it from the brain to systemic circulation for degrading.





AMYLOID HYPOTHESIS

Based on the excessive accumulation of amyloid-β peptide in aggregate forms outside neurons by cleavage of APP which results in in the production of truncated Aβ peptide.

PSEN IMPLICATION

Presenilins (code by PSEN) function as the catalytic subunit of γ-secretase. Some mutations in two conserved aspartate (thought to be part of the catalytic domain) cause loss of function.

TAU PROTEIN HYPOTHESIS

Tau's abnormal hyper-phosphorylation in AD results in toxic gain of function and formation of neurofibrillary tangles of paired helical filaments (PHF).

PREVENTION AND TREATMENT

There is no effective treatment against AD. Findings and research for strategies which target the cholinergic system has led to the development of cholinesterase inhibitors (AChEI) which diminish neuron loss (i.e. Rivastigmine). The synthesis of several antibodies or proteins that inhibit aggregation of β-amyloid or tau protein respectively has been useful to halt the decline in cognitive function and improve it but with some adverse effects (i.e. bapineuzumab, rember).

PROGRESS IN ALZHEIMER'S THERAPY

Alzheimer's therapies so far have revolved around retarding the progression of the disease rather than restoring the damaged neurons. However, the recent trend is to focus on removing the causes of the disease with stem cell-based therapies. If the causes of AD are understood more deeply and safer cell therapies are developed, AD could be conquered in the not too distant future.

CONCLUSIONS

Latest research direction of Alzheimer focuses on early diagnosis (biomarker's finding), given that the administered medication upon the initial manifestation of the disease can help to maintain the quasi-normal state of cognitive functions longer. Studies will show in the coming years the potential effectiveness of these strategies, which are the expectancy for the treatment of Alzheimer's disease.

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