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Review

A Review on Etiology of Alzheimers Disease

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Abstract

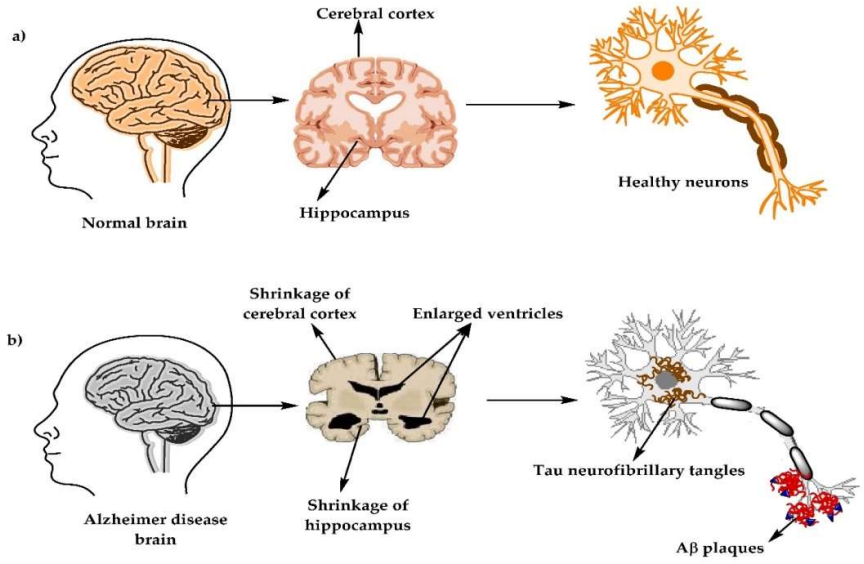
Alzheimers is one of the most common causes of dementia that influence nerve cells in various parts of the brain inflammation is a part of the first line of defence of the body against invasive pathogens and plays a crucial role in the tissue generation and repair. Alzheimer disease is the most common cause of a decline in cognitive ability. It is a neurodegenerative disorder that usually affects people over the age of 65 with the involvement of language, memory, attention, judgement and reasoning. Alzheimers disease is an unavoidable neurological disorder in which the death of brain cells causes memory loss and cognitive decline and ultimate dementia. It is a most common cause of the dementia in the people over the age 65 and 50% over the age of 85 years. It the manifests as a decline in short -term memory and cognition that impairs the daily behaviour. Most cases of the inherited disease are the sporadic, but the small minority of inherited forms allow gene identification which together with the neuropathology, yields important clues about the wider causes. Alzheimers disease is a complex age – related neurodegenerative disease. In this review carefully detail amyloid – β metabolism and its role in AD. We also consider the various genetical animal models used to evaluate therapeutics. The finally we consider the role of synthetic and the plant – based compounds in therapeutics.

Keywords: cognitive decline, neurodegenerative, dementia

INTRODUCTION

Dementia is a general term that refers to the decline in cognitive ability severe enough to interfere with activities of daily living alzheimers disease is the most common type of dementia, accounting for the at least two thirds of cases of dementia in peoples age 65 and older. Alzheimers disease is a neurodegenerative disease with the insidious onset and progressive impairment of behavioural and cognitive functions including memory, language, attention. There is no cure for alzheimers disease, although that they are treatments available that may improve some symptoms. Symptoms of alzheimers disease depends on the stages of the alzheimers disease. Neurodegenerative disorder are defined as hereditary, sporadic and age-related conditions which are characterized by cognitive decline, especially in learning and memory. these disorders are often associated with problems with movement (ataxia), or mental functioning (dementias).Alzheimers disease is named after the (German psychiatric Alois Alzheimer) it is the most common type of dementia and can be defined as a slowly

progressive neurodegenerative disease is characterized by neuritic plaques and neurofibrillary tangles as the result of amyloid – beta peptides accumulation in the most affected area of the brain, the medial temporal lobe and neocortical structures.



ETIOLOGY

Alzheimers disease is a gradual and progressive neurodegenerative disease caused by neuronal cell death. It is typically starts in the entorhinal cortex in the hippocampus. There is a genetic role identified for both early and late onset Alzheimer disease. Trisomy 21 is a risk factor for early-onset dementia. Several risk factors have been associated with the Alzheimer disease. Increasing age, it is the most important risk factor for Alzheimer disease. Traumatic head injury, depression, cardiovascular and cerebrovascular disease, higher parental age, smoking, family history of dementia, increased homocysteine levels and presence of APOE e4 allele are known to increase the risk of alzheimers disease.

ALZHEIMERS DISEASE

Alzheimers disease is a neurodegenerative disease that usually starts slowly and progressively worsens and it cause of 60-70% cases of the dementia. Alzheimer disease is the most common type of dementia this disease involves parts of the brain that controls thoughts memory&language.it is a brain disorder that slowly destroys the thinking skills and the eventually the ability to carry out the simplest task.it is a normal part of aging. this disease is named after DR. ALOIS ALZHEIMER in 1906 it has more than 6 million Americans many of them age 65and older are estimated to have alzheimers disease. there are more than 520,000 people in the UK with Alzheimer disease, and then worldwide at least 44 million people are living with dementia.

SYMPTOMS

Memory loss is the key symptoms of the alzheimers disease. Early signs include difficulty remembering recent events or conversations. But the memory gets worse and other symptoms developed as the disease progress. At first someone with the disease may the aware of having trouble remembering things and thinking clearly .as the symptoms of the get worse, a family member or friend may be the more likely to notice the issue.

MEMORY

Everyone has memory lapses at times, but the memory loss associated with the alzheimers disease. And persists and gets the worse. Over time, memory and loss the effects and the ability at function or at home.

THINKING AND REASONING

Alzheimers disease causes difficulty concentrating and thinking, especially about abstract concepts such as numbers.

PLANNING AND PERFORMING FAMILIAR TASKS

Routine activities that require completing steps in order becomes the struggle. this may include planning and cooking a meal or playing the favourite game.

CHANGES IN PERSONALITY AND BEHAVIOR

Brain changes that occur in alzheimers disease can affect moods and behaviors problems may include the following

- Depression
- Social withdrawl
- Mood swings
- Anger and aggression

CAUSES

The exact causes of alzheimers disease aren't fully understood. But at the basic level, brain proteins fail to function as the usual. This distrupts the work of brain cells, also called neurons, and the triggers a series of events. At first increasing forgetfulness or mild confusion may be the only symptoms of alzheimers disease that are noticeable. But over time, the disease robs you of more of your memory especially recent memories. The causes of alzheimers disease can be explained with the three types of hypotheses

CHOLINERGIC HYPOTHESIS

The cholinergic hypothesis of alzheimers disease came about due to the combined observations of deficits in choline acetyltransferase and acetylcholine and the factor that acetylcholine is important in the memory and learning.

AMYLOID HYPOTHESIS

Amyloidosis is the abnormal deposition of the amyloid proteins in the tissues, with altered amyloid proteins forming an insoluble β pleated sheet.

TAU HYPOTHESIS

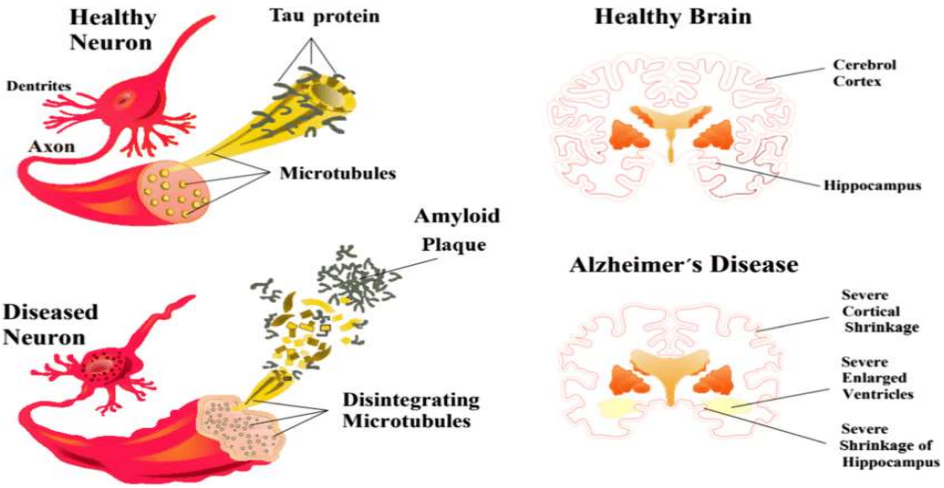
The tau hypothesis revolves around the presence of neurofibrillary tangles in alzheimers disease. At a result is increased phosphorylation of tau (originally bound to microtubules).

PATHOGENESIS

Pathophysiology of AD debate the goes back to the alzheimers disease time 1907 when he observed the neuropathologically features of the disease. Amyloid plaques and hyperphosphorylated NFTs. several

hypotheses have been put forward on basis of the various causative factors in the order to explain this multifactorial disorder that the cholinergic hypothesis. Aβ hypothesis tau hypothesis and inflammation hypothesis. A continue exit between the pathophysiology of the aging and that the AD pathological hallomarks of AD have been identified, however these features occur in the brain of cognitively intact persons for example in a study which as neuropathologists were blinded to clinical data, they identified 76% of the brain cognitively intact elderly patients as demonstrating AD.

AD affects the 3 processes that keep the neurons healthy communication, metabolism, and repair certain nerve cells in the brain stop working lose connections with other nerve cells in the brain stop working lose connections with other the nerve cells and finally they die. The accumulation of SPs primarily precedes the clinical onset of the AD NFTs loss of neurons, and loss of synapse accompany the progression of cognitive decline.



DIAGNOSIS

Clinical examination: the clinical diagnosis of AD is usually made during the mild stage of the disease. Using the above listed signs.

Lumbar function: levels of the tau and phosphorylated tau in the cerebrospinal fluid are often elevated in AD, whereas amyloid levels are usually low; at the present, however , routine measurement of CSF .

Imaging studies: imaging studies are particularly important for the ruling out potentially treatable causes of the progressive cognitive decline such as chronic subdural hematoma or normal – pressure hydrocephalus. To receive the diagnosis of the alzheimers disease a person will be an experienced memory loss and cognitive decline or behavioral changes that they affecting their ability to daily life. There is a single test for the alzheimers diseases if the doctor suspects that the presence of the condition they will ask the person -sometimes their family or caregivers – about their symptoms, experienced and medical history.

TREATMENT

Treatment of alzheimers disease there is no cure of alzheimers disease it is not the possible to reverse the death of brain cells. Treatment can however the relieve its symptoms and improve quality of life for the person and their family and caregivers

- ❖ Effective management of any conditions occurring alongside alzheimers.
- ❖ Activities and day care programmes.
- ❖ Involvement of support groups and services.

Drug therapy: Two types of medications used to treat alzheimers disease acetylcholinesterase inhibitors and N-methyl D-aspartate antagonists two types work in different ways. Cholinesterase inhibitor: there is lower level of the chemical called acetylcholine in the brain of a person with alzheimers disease. Acetyl choline performance the function of sending messages between nerve cells. cholinesterase inhibitor aims to increase acetylcholine availability in synaptic neurotransmission in order to treat memory.

PREVENTION

- Stopping smoking

- Keeping alcohol to a minimum.
- Eating a healthy, balanced diet.
- Exercising for at least 150minutes every week – with moderate intensity aerobic activity such as walking, swimming or jogging.
- Making sure your blood pressure is checked and controlled through regular health.

THROUGH DIET

Nutritional support could slow the progression of dementia and probably improve the quality of life of AD patients without any effect on survival rate. Foods like fish, fruits, vegetables, nuts, or even Indian spices have been verified to decrease the risk of AD up to 45%. As mention above in our review fructose should be consume less than 25 g/day. There are some researches that suggest decrease in Alzheimer symptoms with good level of magnesium in brain. Vitamin D too exerts beneficial effect on AD by its immune boosting and anti-inflammatory properties. Diet rich in vitamin B12, omega-3 too should be consumed.

Folic acid increases concentrations of ω-3 PUFAs (polyunsaturated fatty acids) such as eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) that are known to be useful in the prevention/treatment of dementia and Alzheimer's disease. Both EPA and DHA enhance NO generation, suppress production of pro-inflammatory cytokines, and enhance brain acetylcholine levels, a neurotransmitter whose levels are decreased in Alzheimer's disease.

THROUGH ASTROCYTES

In a study conducted on cultured adult and neonatal mouse, astrocytes were transplanted into the hippocampus of AD mice. Seven days later, these astrocytes were found mainly near Aβ deposits and internalize human Aβ immuno-reactive material in vivo. This study supports the role of astrocytes as an active Aβ clearing cells in the brain, which may have important implications for future development of therapeutic strategies for AD.

THROUGH STEM-CELLS

The neural stem cell transplantation induces a robust enhancement of BDNF-mediated hippocampal synaptic density and rescues the spatial learning and memory deficits of AD mice, without altering Aβ deposits. This study suggested that modulation of neurotrophin levels could provide a viable approach in the development of stem cell-based therapies to treat AD in future.

Researchers transplanted the human umbilical cord blood derived mesenchymal stem cells into the hippocampus of the AD mice they found reduction in neuronal apoptosis which rescues memory deficits of host mice.

INDUCED PLURIPOTENT STEM CELLS

Not all stem cells are the identical. Some stem cells can build any kind of cell in the body. These are called 'pluripotent' stem cells and are found in early embryos. They are the initial point for every kind of cell in the body. These embryonic stem cells can be reserved for many years in a laboratory, because they can keep dividing, producing more stem cells which are also pluripotent.

CONCLUSION

In this review we have stated some rationale and possible strategies for the treatment of AD. Various studies have shown that the causative metabolic pathways include's extracellular amyloid plaques, intracellular neurofibrillary tangles, synaptic deterioration, and neuronal death which ultimately leads to AD as a neurodegenerative disorder. About 70% of AD risk at any given age is attributable through genetics. The most common genetic risk factor for AD is the epsilon 4 allele of the gene for apolipoprotein E (ApoE). Apart from the genetic and molecular aspect vitamin D deficient diet, active form of which regulates nerve growth factor seems to be another cause of AD. Also, in AD brain glucose metabolism decrease causing diabetes 3 reasons of which are still not clear. Finally, we would like to conclude that biomarkers and stem cell therapy could be emerging techniques in early diagnosing & treatment of AD. An effective treatment for sporadic Alzheimer’s disease rests on the translation of the disease pathways we have discussed, as well as additional molecular mechanisms or new risk genes (e.g.,apolipoprotein J) defined by gene-expression profiling and whole-genome association studies,181,182 into specific pharmacologic targets. Examples of recently discovered

proteins encoded by these risk genes and mechanisms include apolipoprotein J (clusterin), another Aβ chaperone,183 TOMM40, a transporter of proteins across the mitochondrial membrane, and Sortillin-related receptor, which functions to partition amyloid precursor protein away from β-secretase and γ-secretase; this is consistent with observations that levels are reduced in the brains of patients with Alzheimer's disease and mild cognitive impairment.184,185 Another potential risk factor for sporadic Alzheimer's disease, general aesthesia, promotes tau insolubility and Aβ oligomerization,186,187 deficiency of oestrogen in the brains of postmenopausal women,188 and chronic activation of the glucocorticoid axis.189 However, their underlying mechanisms are diverse, and whether any of these factors lead to amyloid deposition and tauopathy in humans is unknown. Prospective studies also show that cognitive leisure activity and training can lower the risk of dementia190; findings from these studies provide support for the concept of building a "cognitive reserve." The figure in the Supplementary Appendix (available with the full text of this article at NEJM.org) summarizes the heterogeneity of pathways that could initiate and drive Alzheimer's disease. There is no single linear chain of events. Complicating matters, some changes are not pathologic but reactionary or protective. Thus, the development of a multitargeted approach to prevent or symptomatically treat Alzheimer's disease, as used in current practice for other multigenic disorders, is needed.191 Recent studies point to brain atrophy and other pathologic conditions, not severe amyloid or tangle load, in accounting for dementia in the oldest old (persons 80 years of age or older).192 It remains possible that many of these mechanisms, including the amyloid hypothesis, are minor or wrong and that some critical aging-related process is the disease trigger.

REFERENCES

1. Barnes DE, Yaffe K. The projected effect of risk factor reduction on Alzheimers disease prevalence [published online a head of print July 19, 2011]. Lancet Neurol. 2011;10(9):819-28. doi: 10.1016/S1474-4422(11)70072-2, PMID 21775213.
2. Bekris LM, Yu CE, Bird TD, Tsuang DW. Genetics of Alzheimers disease. J Geriatr Psychiatry Neurol. 2010;23(4):213-27. doi: 10.1177/0891988710383571.
3. Bellenguez C, Grenier, Boley B, Lambert JC. Genetics of Alzheimers disease: where are, and where we are going. Curr Opin Neurobial. 2022;61:40-8.
4. Chiang K, Koo EH. Emerging therapeutics for Alzheimers disease. Annu Rev Pharmacol Toxicol. 2014;54:381-405. doi: 10.1146/annurev-pharmtox-011613-135932, PMID 24392696.
5. De Rojas I, Moreno-Grau S, Tesi N, Grenier-Boley B, Andrade V, Jansen IE et al. common variants in Alzheimers disease and risk stratification by polygenic risk scores. Nat Commun. 2021;12(1):3417. doi: 10.1038/s41467-021-22491-8, PMID 34099642.
6. Dubois B, Feldman HH, Jacova C, et al. Reasearch criteria for the diagnosis of Alzheimers disease: revising the NINCIDS-ADRDA criteria, Lancet Neural. 2007;6:734-46.
7. Kunkle BW, Grenier-Boley B, Sims R, Bis JC, Damotte V, Naj AC et al. genetic meta – analysis of diagnosed Alzheimers disease identifies new risk loci and implicates Aβ, tau, immunity and lipid processing. Nat Genet. 2019;51(3):414-30. doi: 10.1038/s41588-019-0358-2, PMID 30820047.
8. Lambert JC, Ibrahim-Verbaas CA, Harold D, Naj AC, Sims R, Bellenguez C et al. Meta – analysis of 74,046 individuals identifies 11 new susceptibility loci for Alzheimers disease. Nat Genet. 2013;45(12):1452-8. doi: 10.1038/ng.2802, PMID 24162737.
9. Liu JZ, Erlich Y, Pickrell JK. Case-Control association mapping by proxy using family history of disease. Nat Genet. 2017;49(3):325-31. doi: 10.1038/ng.3766, PMID 28092683.
10. Marioni RE, Harris SE, Zhang Q, McRae AF, Hagenaars SP, Hill WD et al. GWAS on family history of Alzheimers disease. Transl Psychiatry. 2018;8(1):99. doi: 10.1038/s41398-018-0150-6, PMID 29777097.
11. Mellon EA, Pilkinton DT, Clark CM, Elliott MA, Witschey WR, Borthakur A et al. Sodium MR Imaging Detection of Mild Alzheimers disease; Preliminary Study. A.J.N.R Am J Neurorad. 2009;30(5):978-84. doi: 10.3174/ajnr.A1495, PMID 19213826.
12. Povova J, Ambroz P, Bar M, Pavukova V, et al. Epidemiological of and risk factor for Alzheimers disease: a review. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub. 2012;156:108-nets''. Discovery Health . Web . 2010.
13. Santana I, Farinha S, et al. The epidermology of dementia and Alzheimers disease in Portugal: estimations of prevalence and treatment costs. Acta Med Port. 2015;28:182-8.
14. Singh SK, Srivastav S, Yadav AK, Srikrishna S, Perry G. Overview of Alzheimers disease and some therapeutic approaches targeting abeta by using several synthetic and herbal compounds. Oxid Med Cell Longev. 2016;2016:7361613. doi: 10.1155/2016/7361613, PMID 27034741.
15. Zec RF, Burkett NR. Non – pharmacological and pharmacological treatment of the cognitive and behavioural symptoms of Alzheimers disease. Neuro Rehabilitation. 2008; 23(5):425-38. PMID 18957729.

16. Wallace L. the ou O, Rockwood K, and rew MK, relationship between frailty and Alzheimers biomarkers as coping review. Alzheimers Dement (AMST). 2018;10:394-401.
17. Vevma M, Wills Z, Chu CT. excitatory dendritic mitochondrial calcium toxicity:implications for Parkinson's and other neuro degenerative disease front Neurosci. 2018;12:523.