Journal of Research High School

Vol. 2024 (5) 354 – 357
ISSN 2688-3651 [online]

The Role of Genetics and Environmental Risk Factors in Alzheimer's Disease.

Shriya Katukuri[1 *], Neelima Katukuri[2]

[1]Lake Highland Preparatory School, Orlando, FL, USA
[2] University of Central Florida, Orlando, FL, USA
*Corresponding Author: katukurish@lhprep.org

Advisor: Dr. Neelima Katukuri, pneelu@gmail.com

Received June 25, 2023; Revised June 27, 2024; Accepted August 13, 2024

Abstract

Alzheimer's disease (AD) is defined clinically by a gradual decline in memory. More than 6 million Americans of all ages have Alzheimer's. An estimated 6.7 million Americans aged 65 and older are living with Alzheimer's in 2023. By 2050, the number of people aged 65 and older with Alzheimer's may grow to a projected. 12.7 million, barring the development of medical breakthroughs to prevent or cure AD. The role of genetics and environmental risk factors in AD need to be identified. People aged 65 and older survive an average of four to eight years after a diagnosis of Alzheimer's, yet some live as long as 20 years with Alzheimer's. This reflects the slow, uncertain progression of the disease. Identifying risk factors could ultimately help us to answer how to solve and prevent Alzheimer's dementia along with finding an effective treatment to fight Alzheimer's. The purpose of this study is to provide insight on the various genetic and environmental factors that contribute to Alzheimer's disease. The goals include identifying important genetic markers and environmental factors that contribute to the onset and progression of AD through a thorough examination of recent literature and empirical research findings. The approach entails analyzing and combining previous research to derive the main conclusions about the influence of different factors. In the end, this study aims to collect information that may guide approaches to Alzheimer's disease prevention.

Keywords: Alzheimer's disease, Genetics, Prevention

1. Introduction

Alzheimer's disease (AD) is defined clinically by a gradual decline in memory and other cognitive functions and neuropathologically by gross atrophy of the brain and the accumulation of extracellular amyloid plaques and intracellular neurofibrillary tangles" (Adani et al., 2020). Alzheimer's disease is defined by the accumulation of two hallmark pathological protein aggregates: amyloid-β peptide (Aβ) plaques and neurofibrillary tangles containing hyperphosphorylated tau, one postulate is that APOE affects these lesions. There are two different forms of Alzheimer's such as early-onset dementia and late-onset Alzheimer's. The two most common causes of Alzheimer's dementia are genetic and environmental/lifestyle factors. 60% to 80% of patients with Alzheimer's result from dementia, leading to memory loss and problems with behavior and thinking (Adani et al., 2020). Early-onset dementia (EOD) is defined as dementia with symptom onset before 65 years. The role of environmental risk factors in the etiology of EOD is still undefined (Adani et al., 2020). Genetic factors take on an important role in timing and determining the possibility of offspring inheriting Alzheimer's. The APOE ε4 allele remains the strongest genetic risk factor for sporadic Alzheimer's disease and the APOE ε2 allele the strongest genetic protective factor after multiple large-scale genome-wide association studies and genome-wide association meta-analyses. These genetic risk factors are important to learn, as this would help experts advance their knowledge to lower the risk of Alzheimer's in

Vol. 2024 (5) 354 – 357
ISSN 2688-3651 [online]

individuals. With over 3 million cases in the U.S per year, Alzheimer's deteriorates brain cells, creating a big impact on their daily life.

2. Environmental and Genetic Factors of Alzheimer's:

In review of literature almost 4784 studies revealed that there is a clear connection between environmental risk factors and dementia. Risk factors were considered in six categories: air quality, toxic heavy metals, other metals, along with geographical variation, occupational-related exposures, and miscellaneous environmental factors. Few studies took a life course approach. There is at least moderate evidence implicating the following risk factors: air pollution; aluminum; silicon; selenium; pesticides; vitamin D deficiency; and electric and magnetic fields (Serrano-Pozo et al., 2021). Aluminum in drinking water and electromagnetic fields including occupational exposure to solvents and pesticides were all important, (Killin et al., 2016). In two prospective cohort studies: a 15-year prospective cohort study of 1806 healthy men and women in Umeå, Sweden, and a retrospective cohort study of almost 13,000 individuals identified from the comprehensive Taiwanese health insurance database passively followed up for a decade it was noted that higher levels of nitrogen oxides were observed to be associated with increased risk of dementia (Killin et al., 2016). In a cross-sectional study of almost 6000 people in five provinces of China, tobacco smoke was shown to be associated with increased risk of dementia. A prospective cohort study of almost four thousand older adults in south-west France (the PAQUID study) – found that levels of aluminium consumption in drinking water in excess of 0.1 mg per day were associated with a doubling of dementia risk and a three-fold increase in the risk of Alzheimer's dementia" (Serrano-Pozo et al., 2021). The research investigated and studied many different metals to see which ones were associated with dementia, and through multiple studies, they have reached the conclusion that Aluminum has the biggest impact on whether one develops dementia. Two reviews concluded that exposure to pesticides was associated with an increased risk of dementia which was corroborated by the prospective Canadian Study of Health and Aging. Studies showed that fertilizers, pesticides, and other chemicals were considered to strengthen the risk of developing dementia (Adani, G. et al., 2020, Serrano-Pozo, A. et al., 2021). Three high-quality prospective studies examined the association between vitamin D and dementia, and all found that lower vitamin D levels at baseline were associated with an increased risk of developing dementia. (Serrano-Pozo, A. et al., 2021). Even after multiple large-scale genome-wide association studies (GWAS) and GWAS meta-analyses1, the ε4 allele of the APOE gene (compared to the most common ε3 allele) continues to be the strongest genetic risk factor associated with sporadic Alzheimer's disease since its discovery in 1993. Moreover, the relatively rare APOE ε2 allele remains by far the strongest genetic protective factor against sporadic Alzheimer's disease, emphasizing the importance of APOE's role in Alzheimer's disease pathogenesis.

3. Discussion:

3.1 Environmental Factors of Alzheimer's and Dementia.

Environmental risk factors for Alzheimer's and dementia play a huge role in determining whether an individual would have this syndrome/disease or not. As a matter of fact, the consideration of environmental exposures as potential risk factors for dementia and other neurodegenerative diseases has considerably increased in recent years (Adani, G. et al., 2020). These environmental factors include airborne and metallic factors that work towards the risk of Alzheimer's.

3.2 Airborne Factors

Air quality is one of the environmental risk factors that is associated with dementia, along with higher nitrogen oxide and tobacco smoke are shown to be associated with increased risk of dementia. Potential treatments include incorporating air filtration systems within indoor environments to help reduce airborne pollutants as well as encouraging policies to implement reduced emissions from vehicles and factories.

Vol. 2024 (5) 354 – 357
ISSN 2688-3651 [online]

3.3 Occupational Related/Metallic Factors

Aluminum, fertilizers and pesticides exposure using herbicides and fungicides and lower vitamin D levels at baseline were associated with an increased risk of dementia. Potential treatments include encouraging maintaining optimal vitamin D levels to help mitigate the risk associated with Alzheimer's while also practicing minimizing the use of fertilizers or pesticides that contain aluminum.

3.4 Genetic Risk Factors of Alzheimer's and Dementia

Along with factors external to the human body, genetic risks also exist that increase the risk of Alzheimer's. Genetic risk factors are by far one of the most important factors to take into consideration. Genetic susceptibility clearly appears to play an etiologic role for EOD, including APP and PSEN1/2 gene mutations for Alzheimer's dementia (AD) and MAPT, GNR, and C9ORF72 for frontotemporal dementia (FTD). Those who have a parent or sibling with Alzheimer's are more likely to develop the disease than those who do not have a first-degree relative with Alzheimer's. Those who have more than one first-degree relative with Alzheimer's are at an even higher risk. When diseases like Alzheimer's and other dementias tend to run in families, either genetics (hereditary factors), environmental factors, or both may play a role. The main two types of genes that are risk inducing are APOE and PSEN.

3.5 APOE in Alzheimer's and Dementia

Apolipoprotein E (APOE) is one of the main risk genes for inheriting Alzheimer's and is most researched by experts (Alzheimer's Association 2022). APOE-e4 is the first risk gene identified and remains the gene with the strongest impact on risk with 40-65% of people diagnosed with Alzheimer's have APOE-e4 gene. APOE-e4 is one of three common forms of the APOE gene; the others are APOE-e2 and APOE-e3. Those who inherit one copy of APOE-e4 from their mother or father have an increased risk of developing Alzheimer's.

3.6 PSEN in Alzheimer's and Dementia

Along with APOE (allele), PSEN is a risk gene for developing Alzheimer's that is highly researched and studied. PSEN1 is located at chromosome 14q24.3, while its homologue, PSEN2, is located at chromosome 1q31-q42. PSEN1 and PSEN2 localize in the endoplasmic reticulum and Golgi apparatus, where they play an important role in protein processing. As many as 185 dominant pathogenic mutations have been identified in PSEN1, accounting for approximately 80% of early-onset familial AD cases. (Karch et al., 2014) There are still many biological mysteries to be answered about Alzheimer's such as how plaques and tangles are found in the brain and how brain cells die once amyloid plaque gets deposited (Reitz., 2015). To help reduce the genetic risk factors associated with both types of genes, it is encouraged to create lifestyle modifications such as daily exercise and healthy diets (ex. Mediterranean diet) to potentially decrease the onset of Alzheimer's.

4. Conclusion:

The discovery of common and unusual variations that contribute to AD risk has opened several new avenues for research into the processes underlying AD (Nierenberg, C., 2016). The next-generation sequencing research have identified genes involved in numerous previously unknown pathways involved in AD pathogenesis: lipid metabolism, immunological response, and endocytosis/synaptic function Although there is still much to learn about the risk factors associated with EOD and late-onset Alzheimer's, advances in technology and research could ultimately help us to answer how to solve and prevent Alzheimer's dementia along with finding an effective treatment to fight Alzheimer's. It is important to know that there is still further research needed to fully understand the environmental exposures and genetic factors that are related to dementia and Alzheimer's through potential studies of genetic interactions and longitudinal studies. Understanding the vital roles that environmental factors, such airborne effects and environmental exposures, and genetic factors, like APOE and PSEN mutations, play in the development and risk of Alzheimer's

Vol. 2024 (5) 354 – 357
ISSN 2688-3651 [online]

disease is crucial. In order to effectively tackle this complex neurodegenerative disease, comprehensive measures focused at prevention and early interventions are critical.

References

Adani, G. et al. (2020). Environmental Risk Factors for Early-Onset Alzheimer's Dementia and Frontotemporal Dementia: A Case-Control Study in Northern Italy. *International journal of environmental research and public health*, 17(21), 7941. https://doi.org/10.3390/ijerph17217941

BBB Accredited Charity. (n.d.). *Is alzheimer's genetic?* Alzheimer's Disease and Dementia. Retrieved August 3, 2022, from https://www.alz.org/alzheimers-dementia/what-is-alzheimers/causes-and-risk-factors/genetics

Google Search for "Alzheimer's" (2022).

Karch, C. et al. (2014). Alzheimer's disease genetics: from the bench to the clinic. Neuron, 83(1), 11–26. https://doi.org/10.1016/j.neuron.2014.05.041

Killin, L. et al. (2016). Environmental risk factors for dementia: a systematic review. *BMC geriatrics*, 16(1), 175. https://doi.org/10.1186/s12877-016-0342-y

Nierenberg, C. (2016). 6 Big Mysteries of Alzheimer's Disease. Livescience.Com. https://www.livescience.com/56253-biggest-mysteries-of-alzheimers-disease.html

Reitz C. (2015). Genetic diagnosis and prognosis of Alzheimer's disease: challenges and opportunities. Expert review of molecular diagnostics, 15(3), 339–348. https://doi.org/10.1586/14737159.2015.1002469

Serrano-Pozo, A. et al. (2021). APOE and Alzheimer's disease: advances in genetics, pathophysiology, and therapeutic approaches. *The Lancet. Neurology*, 20(1), 68–80. https://doi.org/10.1016/S1474-4422(20)30412-9