Journal of Education and Science (ISSN 1812-125X)

www.edusj.uomosul.edu.iq

The Relationship of Some Hormones, Enzymes and Proteins to ALzheimer′s Disease

S. A. Ayob [1] L. S. Alkhalidy [2] G. A. Taqa *[3]

[1, 3] Department of Dental Basic Sciences, College of Dentistry, University of Mosul, Mosul, Iraq
[2] Department of Environmental Health, College of Environmental Sciences, University of Mosul, Mosul, Iraq

Article information

Article history:
Received: July 25, 2024
Accepted: September 24, 2024
Available online: December 01, 2024

Keywords:
Apolipoprotein E (ApoE)
C-reactive protein
Choline acetyltransferase (ChAT)

Correspondence:
Ghada A. Taqa
ghadataqa@uomosul.edu.iq

Abstract

Alzheimer's disease involves environmental influences and genetic and biochemical factors that lead to the build-up of harmful proteins like amyloid and neurofibrillary tangles in brain. This accumulation can disturb the communication between nerve cells. Result in cognitive difficulties. This analysis emphasizes the importance of elements like air pollution and toxic metals in addition to discussing the influence of inflammation oxygen related stress and antioxidants, on disease progression. It also explores how specific hormones and enzymes influence the course of the disease. Alzheimer's stands out as a condition that leads to cognitive decline and affects nerve tissues in the brain extensively. It is identified through the development of tangles and the buildup of amyloid proteins outside cells that form plaques hindering communication among neurons. This inherited degenerative condition affects nerve function and results in a decrease, in abilities and memory loss. This review delves into biochemical pathways associated with Alzheimers disease; discussing the impact of air pollution and harmful metals along with inflammation and oxidative stress as well as the influence of antioxidants and certain hormones such as insulin and proteins like GO and insulin like growth factor (IGF) along with leptin in the process. It also touches upon the significance of enzymes like choline acetyltransferase and essential proteins in the disease pathway such, as C reactive protein interleukins and E methione. This research is crucial for gaining insights into the processes involved in Alzheimers disease and could help in crafting better prevention and treatment approaches, down the line.

DOI: 10.33899/edusj.2024.152177.1485,

1. Introduction

In the 2030s, projections show a rise of 65 million people to Alzheimer's disease compared to 1901 figures when the illness was first identified in a patient showing symptoms like memory loss and impaired motor skills with communication difficulties befallen on them inadvertently revealed brain cell shrinkage and build up of fats, in blood vessel autopsy analysis [1].

Subsequently, Alzheimer's disease was identified as a neurodegenerative disturbance classified by the formation of neurofibrillary tangles. There are two forms of Alzheimer's: earliest Alzheimer's, which disservices individuals under the age of sixty, and delayed Alzheimer's, which affects those over eighty years old and is commonly referred to as dementia [2]. The disease is complex and has various unknown causes. Potential contributing factors include genetics, ageing, environment,

lifestyle, and chronic diseases such as diabetes and obesity [3]. Research indicates that the brains of affected individuals contain unusual accumulations of specific proteins, which can be classified into two types: beta-amyloid protein (an abnormal, insoluble protein that forms protein "plaques") and tau protein (an abnormal protein that is one of the components of beta-amyloid) [4]. These proteins accumulate to form plaques in the brain, which develop slowly and initially cause memory loss for specific details. Over time, this memory loss progressively includes forgetting relatives and even daily tasks. These effects occur due to the prevention of proper neuronal communication and necessary nourishment. As the disease progresses, hormones and enzymes change, affecting other body systems [5].

Causes of Alzheimer's **disease:**

Several potential contributing causes of the condition can be summarized as follows:

1.1 General Causes:

1.1.1 Air-Pollution

The brain's frontal cortex is affected by numerous airborne pollutants released by industrial facilities, such as pb, ozone, NOx, SOx, and CO, among others [6]. These pollutants are considered a significant threat to human health. A study conducted by Schaefer et al. [7], revealed that exposure to toxic metals resulting from pollution leads to the formation of neurotoxic plaques, which are deposits of protein around deteriorated nerves containing microglial cells and activating the inflammatory response [8].

1.1.2 Exposure To Toxic Metals

Biological and natural systems contain metals, categorized into three types: toxic, beneficial, and harmful. Toxic metals, which have no biological function and harm living systems (such as lead and aluminum), differ from essential beneficial metals, which are necessary for life and have physiological functions in organisms (such as copper, zinc, and iron) [9]. Aluminum is considered a toxic metal for the brain, and research indicates that exposure to aluminum causes disturbances in phosphorylation, aggregation, and the formation of hyperphosphorylated proteins through interactions with proteins like tau. Studies have shown that aluminum accumulation in areas responsible for memory and cognition leads to memory impairment (10). Additionally, calcium is a necessary metal affecting synaptic function and neuronal development. However, excessive calcium supplementation increases the danger of Alzheimer's by 3-7 times, especially in individuals with issues in white matter in the brain, potentially leading to mortality. Exposure to lead is related to Alzheimer's and increases the accumulation of the enzyme Aβ-secretase. Cadmium, a water-soluble carcinogen, can cross the BBB and cause neurological disorders such as memory loss. One study found that cadmium ions enhance tau protein's self-appropriation and the formation of plaques in the brain [11].

1.1.3 Infections

Chronic complaints in the central nervous system increase the risk of progressive Alzheimer's. Research by Miklossy and Ballin has shown that long-term bacterial infections can lead to neuronal cell death (apoptosis). This programmed cell death occurs in response to a series of cellular processes without releasing toxic substances into the surrounding environment, leading to neurofibrillary tangles and potentially causing destructive neurological disorders [12]. This process can result in decreased cognitive function and an increased risk of Alzheimer's disease. Animal exploring has indicated that inflammatory processes play a significant role in Alzheimer's disease and may be associated with increased cognitive impairment [13]. Studies on Alzheimer's patients have revealed elevated levels of cytokines such as IL-1 and their receptors (twelve proteins in this family) compared to control groups [14]. Scientists have suggested a potential link between the body’s inflammatory response and the onset of the disease. Alzheimer's causes changes in the levels of these proteins, which may occur due to ageing or systemic diseases [15].

1.1.4 Impact Of Oxidative Stress And Antioxidants

Oxidative stress happens due to an imbalance between the manufacture of reacting oxygen species and free radicals in the body. Oxidation-reduction processes in the body, decreased levels of trace metals, reduced grade of polyunsaturated fatty acids, and increased protein levels contribute to producing reactive oxygen species such as superoxide and hydrogen peroxide [16]. Alzheimer's research has underscored the significance of oxidative processes in the disease's development. During the examination of the cellular changes, oxidative stress was noted as a precursor to the appearance of neurofibrillary tangles, a hallmark of the disease. Although the primary source of oxidative stress in Alzheimer's is still unclear, the procedure likely relies heavily on the attendance of reactive shift metals, such as iron and copper [17]. Lower levels of antioxidants like boric acid, bilirubin, lycopene, alpha-carotene, vit- A, vit- C, and vit- E increase the susceptibility to Alzheimer. Recent research has shown that the action of antioxidants enzyme such as GS peroxidase and catalase is decreased in individuals with Alzheimer's. Studies conducted on mice have indicated that increased levels of glutathione (GSH) and superoxide dismutase (SOD) may reduce some of the classic signs and symptoms of Alzheimer's, such as memory loss and learning problems [18].

1.2 Specific Causes

Several specific factors in the body add to the advancement of Alzheimer's, including hormonal, enzymatic, and protein-related causes.

1.2.1 Insulin And Insulin-Like Growth Factor (IGF)

Elevated insulin levels are considered a risk factor for future Alzheimer's. Insulin, a hormone that maintains metabolic balance, plays a crucial role in regulating amyloid beta protein peptides and preventing neurofibrillary tangles (NFTs). High blood glucose levels stimulate the pancreas to produce more insulin. When cells cannot sense insulin, insulin resistance occurs, leading to elevated blood glucose levels. This, in turn, stimulates beta cells in the pancreas to release more insulin, potentially leading to type 2 diabetes (T2DM) [19]. Studies have shown that cerebrospinal fluid from Alzheimer's patients contains high levels of insulin. High insulin resistance leads to the accumulation of amyloid-beta protein, tau protein hyperphosphorylation, increased oxidative stress, and neurotoxicity [20]. Under normal conditions, chronically elevated insulin levels can lead to insulin resistance, directly contributing to increased plaque formation or neurofibrillary tangles through various mechanisms, resulting in memory impairment and reduced neuronal activity. Insulin-like growth factor (IGF) is closely related to oxidative stress as it disrupts metabolic balance and affects blood glucose regulation [21]. It leads to the formation of various reactive oxygen species (ROS), DNA impairment, and mitochondrial dysfunction, ultimately causing apoptosis, inflammation, and amyloid-beta accumulation [22].

1.2.2 Leptin

Recent years have revealed a connection between low leptin grades. Leptin is a hormone that regulates insulin sensitivity, bone formation, immunity, nervous system activity, energy metabolism, appetite, and reproduction. Most leptin is produced in white adipose tissue, but it can also be produced by skeletal muscles. Leptin can help combat several diseases, including Parkinson's, Alzheimer's, and epilepsy [23]. Reviewing has shown that memory loss in Alzheimer’s disease mouse models can be corrected by administering progressive leptin injections. Leptin can cross the BBB and reach the brain, where it helps mitigate the inflammatory effects of Aβ1-42 protein in Alzheimer's disease. The leptin receptor transports leptin from the periphery to the central nervous system throughout blood-brain barrier to improve neuronal function, so any disruption in this process can contribute to Alzheimer's disease [24].

1.2.3 Choline Acetyltransferase (ChAT)

Choline acetyltransferase (ChAT) is closely associated with memory through its role in acetylcholine transmission. ChAT plays a crucial role in the synthesis of acetylcholine (ACh) and significantly impacts cognitive functions. Acetylcholine is carried into storage compartments in the brain by a special transporter known as the acetylcholine transporter [25]. An essential enzyme that plays a role in various bodily functions like learning and memory retention as well as attention and sensory processing, among others. Recent studies have suggested a connection between Alzheimers disease and memory loss with the declining activity of choline acetyltransferase within neurons [26]. It is believed that beta amyloid can interfere with neurotransmission by impacting choline uptake and acetylcholine release. Furthermore, findings indicate a relationship between the deterioration of synapses and cognitive impairments. Choline acetyltransferase activity is notably lower in dementia cases than in nonvascular dementia cases [27].

1.2.4 Insulin Degrading Enzyme (IDE)

Insulin-degrading enzyme (IDE) functions to break down insulin and other proteins, such as beta amyloid, which is found in the brains of individuals with Alzheimer’s disease. Increased insulin levels in the bloodstream hinder IDE's ability to break down beta amyloid effectively [28]. A scenario that could result in the buildup of this protein and the development of plaques, to Alzheimers disease. Studies involving genetics have revealed that differences in IDE genes are connected to a likelihood of developing Alzheimer’s disease, and a decrease in the enzyme’s action could play a role in the disease’s progression. Gene variations in IDE have been tied to the symptoms of Alzheimer’s and an elevated chance of type 2 diabetes. An instability in IDE genes or other elements may result in a decline in IDE activity associated with increased insulin levels and a greater susceptibility to Alzheimer’s disease [29].

1.2.5 Apolipoprotein (ApoE)

apolipoprotein (known as apolipoprotein e or apoe for short) is vital in moving fats and cholesterol around the body. comes in three variations. apoe 2 apoe 3 and apoe 6. among these types, apoe 6 is linked with a chance of developing alzheimer’s disease. apoe 6 helps carry beta amyloid protein in the brain and encourages buildup, creating plaques that disrupt communication between nerve cells. individuals carrying the apolipoprotein e epsilon ε genotype, known as apoe epsilon ε, risk developing alzheimer’s disease. they may experience symptoms earlier than those with different apoe variants. additionally, apolipoprotein e plays a role in chylomicron lipoproteins and is vital for transporting lipids and cholesterol by interacting with various cell receptors due to its unique binding capabilities [30]. comprising 299 amino acids apolipoprotein e is responsible for

lipid transportation and repair mechanisms in the body. in patients with alzheimer, there is a correlation between amyloid beta accumulation and the apolipoprotein e gene variant known as apoe epsilon ε .in individuals with alzheimer's disease in the brain's regions apolipoprotein epsilon ε. ε enhances the development of clumps of proteins and twisted fibres within nerve cells while decreasing the activity of an enzyme called choline acetyltransferase. the impact of apolipoprotein epsilon is more significant in patients [31].

1.2.6 C - Reactive Protein (CRP)

cr preactive protein (cr p), a protein made by the liver when the body is inflamed, is found in the blood at levels during chronic inflammation, which may be linked to the onset of alzheimer's disease. studies suggest that sustained inflammation might aid in creating nerve plaques and tangles in the brain—a common hallmark of alzheimers [32]. high levels of crp have been linked to a risk of alzheimer's disease in older individuals. this liver produced immune protein is released during inflammation because of interleukin synthesis. crp supports the production of c reactive protein through a feedback loop. in addition to this creactive protein also boosts the production of aβ42. researchevidencesuggestthat increased levels could signal alzheimers disease potentially in individuals, over ninety years old [33].

1.2.7 Guanine Nucleotide-Binding Proteins (GO)

These proteins are part of guanine nucleotide binding proteins that serve as switches to relay messages inside cells effectively. Issues in G protein linked receptors (GPCRs) are connected to a range of health conditions like diabetes and cancer, as well as mental health problems such as depression and cardiovascular diseases [34]. The guanine nucleotide binding proteins comprise the Gβγ complex and the Gα subunit. You'll find the GO signaling molecule associated with G proteins in the brain region related to guanine nucleotides. Reports suggest that abnormal signalling through the APP-GO protein receptor imparts to the onset of Alzheimer. Accumulation of Aβ protein enhances the formation of the APP-GO protein complex [35].

1.2.8 Interleukins

Interleukins play a substantial role in increasing the risk of Alzheimer. Interleukins are produced by white blood cells, lymphocyte, monocytes, macrophages, and endothelial cells [36]. Interleukin 1 (IL-1) is one of the multi-functional cytokines that promotes immunity and reduces inflammation in the body. IL-1 activates T-cells and other inflammatory moderators, leading to an inflammatory response. Hyperphosphorylation of tau protein, resulting from interleukin activation, contributes to the development of neurofibrillary tangles (NFTs). Individuals with genetic polymorphisms in the IL-1 gene face a threefold increased risk of Alzheimer, and higher levels of interleukin have been established in the cerebrospinal fluid of Alzheimer's patients [37].

1.2.9 Presenilin Proteins

Presenilin proteins are related to Alzheimer and are located on the cell membrane. Human tissue contains two different types of presenilins: PSEN1 and PSEN2. The PSEN1 gene on chromosome 14 is linked to the PSEN2 gene on chromosome 1 [38]. Presenilins are involved in cellular differentiation and development, calcium signalling (Ca^{2+}), and γ-secretase activity. Presenilins 1 and 2 form part of the γ-secretase complex, which is implicated in proteolytic cleavage during cell division. γ-Secretase is essential for producing Aβ-42 . Presenilins 1 and 2 enhance the pathology of family Alzheimer by contributing to the cleavage of APP by β-secretase. Aβ-42 is more toxic than Aβ-40 and is also amyloidogenic [39].

1.2.10 Amyloid Precursor Protein (App)

APP is a glycoprotein that is part of the amyloid family and is found at synapses. The exact function of APP is not fully understood, but APP can produce Aβ, which has an antagonistic effect on neuronal protection and cell excitation regulation. While APP increases the entire number of synapses in the brain, high concentrations of APP lead to gradual increases in tau protein levels, ultimately contributing to Alzheimer [40]. APP is cleaved by α- and β-secretases. Additionally, APP interacts with membrane proteins such as G-protein-coupled receptors (GPCRs), which sense external stimuli and transmit signals across membranes. Aβ accumulation is directly associated with the onset of Alzheimer's disease. Aβ-42 aggregates more than Aβ-40 and is thus more harmful. It may lead to programmed cell death, synaptic loss, calcium imbalance, cytoskeletal disruption, pore formation, and ion leakage [41]. The final reason for APP's relationship with Alzheimer is that it also produces Aβ peptides, which lead to the forming of senile plaques, a hallmark of Alzheimer. Several oligomers formed from the aggregation of beta-amyloid protein eventually cluster to form plaques that disrupt normal function. Those patients have been found to have higher levels of Aβ-42 in their cerebrospinal fluid [42,43].

2. Conclusion:

Alzheimer is a complex condition influenced by environmental, biological, and genetic factors. It results from toxic metals, oxidative stress, inflammatory factors, and hormonal disruptions, leading to brain cell damage and cognitive decline. Internal factors like insulin and leptin levels trigger disease pathways. Addressing Alzheimer requires scientific research and early therapeutic interventions, focusing on preventive strategies and developing treatments to enhance patient quality of life and alleviate social and economic burdens.

3. Acknowledgements

Thanks to the College of Dentistry, University of Mosul, and Department of Dental Basic Sciences for their support in conducting this study.

4. References

[1] Santos, C.Y.; Snyder, P.J.; Wu, W.C.; Zhang, M.; Echeverria, A.; Alber, J. Pathophysiologic relationship between ALzheimer′s disease, cerebrovascular disease, and cardiovascular risk: A review and synthesis. ALzheimer′s Dement., vol .7, pp. 69–87, 2017, doi: 10.1016/j.dadm.2017.01.005

[2] Abubakar, M. B., Sanusi, K. O., Ugusman, A., Mohamed, W., Kamal, H., Ibrahim, N. H., ... & Kumar, J.. ALZheimer′s disease: An update and insights into pathophysiology. Frontiers in Aging Neuroscience,. vol. 14, PP.742408. 2022, doi: 10.3389/fnagi.2022.74240

[3] Cacace R, Sleegers K, Van Broeckhoven C. Molecular genetics of early-onset ALzheimer′s disease revisitAlzheimers Dement., vol. 12, PP.733–48, 2016, doi:10.1016/j.jalz.2016.01.012

\

[4] Chen, Y., & Yu, Y.. Tau and neuroinflammation in ALzheimer′s disease: interplay mechanisms and clinical translation. Journal of Neuroinflammation,. vol.201, no.1,pp 1-21, 2023 https://pubmed.ncbi.nlm.nih.gov/37452321/

[5] Livingston G, Huntley J, Sommerlad A, Ames D, Ballard C, Banerjee S, Brayne C, Burns A, Cohen-Mansfield Cooper C, et al. Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. Lancet.vol. 396,pp.413–46, 2020, doi: 10.1016/S0140-6736(20)30367-6

[6] Cho, H. S., Huang, L. K., Lee, Y. T., Chan, L., & Hong, C. T. Suboptimal baseline serum vitamin B12 is associated with cognitive decline in people with Alzheimer's disease undergoing cholinesterase inhibitor treatment. Frontiers in Neurology,vol. 9, pp. 325 ,2018,doi: 10.3389/fneur.2018.00325.

[7] Shaffer RM, Li G, Adar SD, et al. Fine Particulate Matter and Markers of Alzheimer's Disease Neuropathology at Aulopsy in a Community-Based Cohort. J Alzheimers Dis., Vol. 79, no. 4, pp.1761–1773, 2021, doi: 10.3233/JAD-201005

[8] Christensen, G. M., Li, Z., Liang, D., Ebelt, S., Gearing, M., Levey, A. I., ... & Huels, A. Fine particulate air pollution and neuropathology markers of Alzheimer's disease in donors with and without APOE ε4 alleles–results from an at autopsy cohort. medRxiv., vol. 224, 2023, doi: 10.1101/2023.04.07.23288288

[9] Croze, M.L.; Zimmer, L. Ozone atmospheric pollution and ALZheimer′s disease: From epidemiological facts to molecular mechanisms. J. ALzheimer′s Dis. Jad,.vol. 62,pp.503–522, 2018, doi: 10.3233/JAD-170857.

[10] Colomina, M.T.; Peris-Sampedro, F. Aluminum and ALzheimer′s disease. Adv. Neurobiol., vol. 18,pp. 183–197. 2017 . https://pubmed.ncbi.nlm.nih.gov/28889268/

[11] Sang, C., Philbert, S. A., Hartland, D., Unwin, R., Dowsey, A. W., Xu, J., & Cooper, G. J.. Coenzyme A- dependent tricarboxylic acid cycle enzymes are decreased in ALZheimer′s disease consistent with cerebral pantothenate deficiency. Frontiers in aging neuroscience.vol.14, pp. 893159, 2022, doi: 10.3389/fnagi.2022.89315

[12] Huat, T.J.; Camats-Perna, J.; Newcombe, E.A.; Valmas, N.; Kitazawa, M.; Medeiros, R. Metal toxicity links to ALzheimer′s disease and neuroinflammation. J. Mol. Biol. vol.431, pp. 1843–1868, 2019, doi:org/10.1016/j.jmb.2019.01.018.

[13] Beata, B. K., Wojciech, J., Johannes, K., Piotr, L., & Barbara, M.. ALzheimer′s disease—biochemical and psychological background for diagnosis and treatment. International Journal of Molecular Sciences. vol.24, no.2 ,pp. 1059, 2023, doi: 10.3390/ijms24021059.

[14] Guo L, Zhong MB, Zhang L, Zhang B, Cai D. Sex differences in ALzheimer′s disease: Insights from the multiomics landscape. Biological Psychiatry.vol.19,no.1,pp. 61-71. 2021,doi: /10.1016/j.biopsych.2021.02.968.

[15] Fulop, T.; Itzhaki, R.F.; Balin, B.J.; Miklossy, J.; Barron, A.E. of microbes development of ALZheimer′s disease: State of the art—An international symposium presented at the 2017 IAGG congress in San Francisco. Front. Genet. vol.9, pp.362, 2018, doi:10.3389/fgene.2018.00362.

[16] Muzambi, R.; Bhaskaran, K.; Brayne, C.; Smeeth, L.; Warren-Gash, C. Common bacterial infections and risk of incident cognitive decline or dementia: A systematic review protocol. BMJ Open.vol. 9,no.9. ,pp.e030874,2019. https://bmjopen.bmj.com/content/9/9/e030874

[17] Rottkamp, C. A., Nunomura, A., Raina, A. K., Sayre, L. M., Perry, G., & Smith, M. A.. Oxidative stress, antioxidants, and Alzheimer disease. Alzheimer Disease & Associated Disorders., vol. 14, no.1, pp. S62-S66, 2000. https://pubmed.ncbi.nlm.nih.gov/10850732/

.

[18] Heydemann, A. An overview of murine high fat diet as a model for type 2 Diabetes mellitus. J. Diabetes Res.vol.2016, no.1,pp. 2902351. 2016, doi:10.1155/2016/2902351 .

[19] Stanley, M., Macauley, S. L., and Holtzman, D. M.. Changes in insulin and insulin signaling in ALzheimer′s disease: cause or consequence? J. Exp. Med.vol. 213,pp. 1375–1385. 2016, doi: 10.1084/jem.20160493.

[20] Tokarz, V. L., MacDonald, P. E., and Klip, A.. The cell biology of systemic insulin function. J. Cell Biol.vol. 217,pp. 2273–2289. 2018, doi:10.1083/jcb.201802095

[21] Kusters, C., Horvath, S., Sinsheimer, J., & Ritz, B.. Sex hormones and ALZheimer′s disease: A Mendelian randomization approach. Journal of the Neurological Sciences,vol. 429, 2021, doi:10.1016/j.jns.2021.118981.

[22] Hurrle, S., and Hsu, W. H.. The etiology of Ox¡dative stress in insulin resistance. Biomed. J., vol.40, pp. 257–262, 2017, doi: 10.1016/j.bj.2017.06.007.

[23] Hamilton K, Harvey J. The neuronal actions of leptin and the implications for treating ALzheimer′s disease. Pharmaceuticals (Basel). vol.14,no.1,pp.52, 2021,doi:10.3390/ph14010052

[24] Tong JQ, Zhang J, Hao M, Yang J, Han YF, Liu XJ, et al. Leptin attenuates the detrimental effects of β-amyloid on spatial memory and hippocampal later-phase long-term potentiation in rats. Horm Behav., vol.73,pp.125–30. 2015,doi:10.1016/j.yhbeh.2015.06.013.

[25] Piccardo P., King D., Brown D., Barron R.M. Variable tau accumulation in murine models with abnormal prion protein deposits. J. Neurol. Sci.,vol. 38,pp.142–150, 2017, doi:10.1016/j.jns.2017.10.040.

[26] Sharma, S. K., Chorell, E., Steneberg, P., Vernersson-Lindahl, E., Edlund, H., and Wittung-Stafshede, P.. Insulin-degrading enzyme prevents α-synuclein fibril formation in a nonproteolytical manner. Sci. Rep. vol.5,pp.12531, 2015. doi:10.1016/j.bbadis.2018.03.023.

[27] Nieznanska H., Bandyszewska M., Surewicz K., Zajkowski T., Surewicz W.K., Nieznanski K. Identification of prion protein-derived peptides of potential use in ALzheimer′s disease therapy. Biochim. Biophys. Acta Mol. Basis Dis. vol.1864, no.6 ,pp.2143–2153,2018. https://pubmed.ncbi.nlm.nih.gov/29604335/

[28] Twohig, D., Rodriguez-Vieitez, E., Sando, S. B., Berge, G., Lauridsen, C., Møller, I., et al.. The relevance of cerebrospinal fluid α-synuclein Levels to sporadic and familial ALZheimer′s disease. Acta Neuropathol. Commun.vol. 6, no.1,pp. 130. 2018,doi:10.1186/s40478-018-0624-z .

[29] Lee, S., Tong, M., Hang, S., Deochand, C., and de la Monte, S. CSF and indices of insulin resistance, Ox¡dative stress and neuro-inflammation in early versus late ALzheimer′s disease. J. ALZheimer′s Dis. Park.vol. 3,pp.128,2013, doi: 10.4172/2161-0460.1000128.

[30] Patassini, S., Begley, P., Xu, J., Church, S. J., Kureishy, N., Reid, S. J., et al.. Cerebral vitamin B5 (D-Pantothenic Acid) deficiency as a potential cause of metabolic perturbation and neurodegeneration in Huntington's disease. Metabolites .vol. 9,pp.113, 2019,doi:10.3390/metabo9060113.

[31] Wang S., Zhang J., Pan T. for ALzheimer′s Disease Neuroimaging Initiative. APOE ε4 is associated with higher Levels of CSF SNAP-25 in prodromal ALZheimer′s disease. Neurosci. Lett.vol. 685, pp. 109–113, 2018,doi:10.1016/j.neulet.2018.08.029.

[32] Foster, T. C., Kyritsopoulos, C., and Kumar, A.. Central for NMDA receptors in redox mediated impairment of synaptic function during aging and ALZheimer′s disease. Behav. Res.vol. 322,pp. 223–232, 2017,doi:10.1016/j.bbr.2016.05.012.

[33]Kumar, D., Sharma, A., & Sharma, L.). A comprehensive review of ALzheimer′s association with related proteins: Pathological and therapeutic significance. Current Neuropharmacology., vol.18, no.8, pp.674-695, 2020 , doi:10.2174/1570159X18666200203101828

[34]Olajide, O. J., Suvanto, M. E., and Chapman, C. A.. Molecular mechanisms of neurodegeneration entorhinal cortex that underlie its selective vulnerability during the pathogenesis of ALZheimer′s disease. Biol. Open. vol.10, 2021, doi:10.1242/bio.056796.

[35]. Bignante E.A., Ponce N.E., Heredia F., Musso J., Krawczyk M.C., Millán J., Pigino G.F., Inestrosa N.C., Boccia M.M., Lorenzo A. APP/Go protein Gβγ-complex signaling mediates Aβ degeneration and cognitive impairment in ALzheimer′s disease models. Neurobiol. Aging.vol. 64, pp,44–57. 2018,doi:10.1016/j.neurobiolaging.2017.12.013.

[36]. Taha, I. G., Mahmoud, E. S., & Ayob, S. A. (2024). Separation and partial purification of lecithin: cholesterol acyltransferase from serum of obese women with a study of the effect of oily and nano-extract of Castanea fruit in activating the enzyme. Advancements in Life Sciences,vol. 11,no. 3, pp. 619-623. 2024,
doi. 10.62940/als.v11i3.2618 .

[37] Lyra e Silva, N. M., Gonçalves, R. A., Pascoal, T. A., Lima-Filho, R. A., Resende, E. D. P. F., Vieira, E. L., ... & De Felice, F. G.. Pro-inflammatory interleukin-6 signaling links cognitive impairments and peripheral metabolic alterations in ALZheimer′s disease. Translational psychiatry.vol.11, no. 1, pp. 251. 2021, doi:10.1038/s41398-021-01349-z.

[38] Koyama, A.; Hashimoto, M.; Tanaka, H.; Fujise, N.; Matsushita, M.; Miyagawa, Y.; Hatada, Y.; Fukuhara, R.; Hasegawa, N.; Todani, S.; et al. Malnutrition in ALzheimer′s disease, dementia with lewy bodies, and frontotemporal lobar degeneration: Comparison using serum albumin, total protein, and hemoglobin level. PLoS ONE.vol.11, pp. e0157053, 2016, doi:10.1371/journal.pone.0157053.

[39] Lanoiselee, H.M.; Nicolas, G.; Wallon, D.; Rovelet-Lecrux, A.; Lacour, M.; Rousseau, S.; Richard, A.C.; Pasquier, F.; Rollin-Sillaire, A.; Martinaud, O.; et al. APP, PSEN1, and PSEN2 mutations in early-onset Alzheimer disease: A genetic screening study of familial and sporadic cases. PLoS Med.vol. 14, pp. e1002270, 2017, doi:10.1371/journal. pmed.100227.

[40] Zetterberg H, Skillbäck T, Mattsson N, Trojanowski JQ, Portelius E, Shaw LM, et al. Association of Cerebrospinal Fluid Neurofilament Light Concentration With Alzheimer Disease Progression. JAMA Neurol.vol.73, no. 1, pp.60-67. 2016, doi:10.1001/jamaneurol.2015.3037.

[41] Rolland, M., Powell, R., Jacquier-Sarlin, M., Boisseau, S., Reynaud-Dulaurier, R., Martinez-Hernandez, J., et al.. Effect of Aβ oligomers on neuronal APP triggers a vicious cycle leading to the propagation of synaptic plasticity alterations to healthy neurons. J. Neurosci.vol. 40, no.27,pp. 5161–5176, 2020, doi:10.1523/JNEUROSCI.2501-19

[42] Taqa, G. A., and Idrees, I. R. Evaluation the effect of amitriptyline and/or ashwagandha on body weight in male rats. Al-Salam Journal for Medical Science, 2023. 2(1), 28-33. doi.org/10.55145/ajbms.2023.1.1.005

[43] Ayob,S.A.,Saleh,O.W.,Alhussary,B,N.,Taqa,G.A. The Antioxidative Role of Moringa Oil extract in Modulating Histological and Biochemical Changes in the Salivary Glands of Rats Under Oxidative Stress Induction ,vol.21,no.4,pp.136-145,2024,

علاقة بعض الهرمونات والإنزيمات والبروتينات بمرض الزهايمر

شيماء عباس ايوب[1] لقاء سعيد الخالدي [2] غادة عبد الرحمن طاقة[3]

[1,3] قسم العلوم الأساسية لطب الأسنان، كلية طب الأسنان، جامعة الموصل، الموصل، العراق
[2] قسم الصحة البيئية ، كلية العلوم البيئية، جامعة الموصل، الموصل ، العراق

المستخلص:

يتضمن مرض الزهيمر تأثيرات بيئية وعوامل وراثية وكيميائية حيوية تؤدي إلى تراكم البروتينات الضارة مثل الأميلويد والتشابكات العصبية الليفية في الدماغ. يمكن أن يؤدي هذا التراكم إلى إزعاج الاتصال بين الخلايا العصبية. ينتج عنه صعوبات معرفية. يؤكد هذا التحليل على أهمية عناصر مثل تلوث الهواء والمعادن السامة بالإضافة إلى مناقشة تأثير الإجهاد المرتبط بالأكسجين والالتهاب ومضادات الأكسدة على تطور المرض. كما يستكشف كيف تؤثر الهرمونات والإنزيمات المحددة على مسار المرض. يبرز الزهيمر كحالة تؤدي إلى التدهور المعرفي وتؤثر على الأنسجة العصبية في الدماغ على نطاق واسع. يتم التعرف عليه من خلال تطور التشابكات وتراكم بروتينات الأميلويد خارج الخلايا التي تشكل لويحات تعيق الاتصال بين الخلايا العصبية. تؤثر هذه الحالة التنكسية الموروثة على وظيفة الأعصاب وتؤدي إلى انخفاض في القدرات وفقدان الذاكرة. يتعمق هذا الاستعراض في المسارات الكيميائية الحيوية المرتبطة بمرض الزهيمر. يتناول هذا البحث تأثير تلوث الهواء والمعادن الضارة إلى جانب الالتهاب والإجهاد التأكسدي بالإضافة إلى تأثير مضادات الأكسدة وبعض الهرمونات مثل الأنسولين والبروتينات مثل GO وعامل النمو المشابه للأنسولين (IGF) إلى جانب اللبتين في هذه العملية. كما يتطرق إلى أهمية الإنزيمات مثل أسيتيل ترانسفيراز الكولين والبروتينات الأساسية في مسار المرض مثل إنترلوكينات البروتين التفاعليE والميثيونC . يعد هذا البحث أمرًا بالغ الأهمية لاكتساب رؤى حول العمليات المشاركة في مرض الزهيمر ويمكن أن يساعد في صياغة طرق أفضل للوقاية والعلاج في المستقبل.