IMPACT OF PROTEIN MISFOLDING IN ALZHEIMER'S DISEASE

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Abstract:

Protein Misfolding can be explained as the major process of forming from primary to secondary to tertiary, but in a mismatched way. Amyloid diseases can be described as the accumulation of misfolded protein. The most important one is Alzheimer's disorder, which is associated with neuro retrogressive impact on brain cells and dementia. This review article explains briefly the protein associated with Alzheimer's disease. As these are related to mutations, compare the relationship between mutations and protein functions.

Keywords: Alzheimer's disease, Protein Misfolding, Amyloid forerunner protein

How to Cite this Article?

Dash B. Impact of protein misfolding in Alzheimer's disease. Int J Adv Res Med Nurs Health Sci [Internet]. 2025 Jan-Jun [cited 2025 Jun 27];3(3):97-100. Available from: http://www.ijarmnhs.in

Introduction:

The formation of misfolded protein due to the arrangement of various peptide bonds, disulfide bonds, and ionic bonds is a key factor in various human disorders, including Parkinson's disease, abnormality in RBC, and Alzheimer's disease (AD)[1]. These abnormal proteins gather inside or outside the tissues. The structural alterations lead to inhibiting the normal function of physiological function of protein and help to form cytotoxicity. Amyloid peptides are associated with a subset of misfolded proteins. We can observe the misfolded protein by using advanced microscopic techniques [2].

Alzheimer's disorder is a major impact on neurodegeneration; it deals with memory loss. In recent scenarios, over 5 million Americans have been affected by AD.[3] It indirectly creates a burden on socioeconomic resources. Researchers analyzed the various pathological and biochemical aspects

of this disease. Due to a lack of effective treatment and an alteration in modifying treatment process. We are unable to cure this disease, and it is also associated with genetic inheritance. Proper analysis of this disease deals with the proper detection of misfolded protein. These abnormal proteins gather in senile plaques and neurofibrillary tangles. To increase the oxidative damage and to reduce the activity of the brain's cell[4,5,6].

To represent AD etiology, we should know about the misfolded Ab species, metal ion dyshomeostasis/ miscompartmentalization [7]. The Amyloid-Containing protein (APP) is an important component of the formation of plaques inside the brain, along with the Ab peptide. It indirectly deals with neuropathogenesis and various cell-signalling pathways[8] . It is made up of 38-43 amino acid.[9,10,11]. The major isoforms of this protein are APP695, APP751, and APP770, but APP695 plays a major role in AD. Based on research studies, APP releases ferroxidase enzyme similar to ceruloplasmin, and responsible for increasing the level of Fe in the case of AD. Other factors involved in protein misfolding are presenilin , nicastrin, and presenilin enhancer-2 (PEN-2) [12]. The common full-length peptides, Ab1–40 and Ab1–42, are produced through the amyloidogenic pathway (the amino acid sequence of Ab1–42 is DAEFRHDSGYEVHHQKLVFFA EDVGSNKGAIIGLMVGGVVIA)[13]. The accumulation of Ab molecules inside the neural tissues enhances the misfolding of APP protein and enhances the hydrophilic property, minimizing unfavorable interactions with the aqueous environment. Metal ions have a significant role in physiological processes inside the body. It involves various structural, catalytic, and cellular communicating actions. An example of a major metal involved in this disease is Cu(I/II) and Zn(II). These are the signalling molecules in the neurons and synapses. For example, Zn(II) is formed during the formation of glutamate neuronal stimulation and used by calcium channels.

Other vital metals that are associated with protein misfolding, iron, cupper and zinc ion have been detected to be linked to the various diagnosis of AD[14,15].

Conclusion:

AD is an aging-associated amyloid diseases that have various functions but is analyzed by the formation of amyloid protein collection containing misfolded Ab peptides and IAPP, so on. As explained in this review, the formation of AD's misfolding has been partially elucidated, with recent studies based on research showing the environmental condition and formulation mismatched APP protein and its various impacts with metal ions. On the other side, various

biophysical experiments are used to examine various mechanisms of amyloid aggregation and atomic-level interaction.

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