

# Identify Protein that Contributes to the Neurotoxicity in Alzheimer's Disease

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## Abstract

Thinking ability of the brain is affected and this kind of mental health issue is known as Alzheimer's. The entire study is conducted with the causes and effects of Alzheimer's. The proteins which are involved in Alzheimer's have been discussed in this whole study. Amyloid and tau are the proteins which have huge influence have been described in the proposed study. Abnormal protein formation is built by BCAA that is known as the transportation system of amino acids. Abnormal formation of protein damages the building of tissue in the neighbourhood tissue of the brain and for this formation capabilities of the brain is badly affected. Many people are facing the issues of low thinking ability and Alzheimer's is responsible for these issues. Tau is another protein which is produced by alternative splicing. This protein is abundant in neurons that are part of the Central nerve system. Various chemicals are produced through the abundance of tau protein. Both secondary qualitative and quantitative analysis have been in the study to identify the proteins which have huge impact for the cause of Alzheimer's..

## Keywords

Alzheimer's, neurotransmitter, neurotoxicity, Protein.

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## INTRODUCTION

The building of abnormal proteins is the main cause of Alzheimer's and harms the human brain deadly. Several causes are responsible for building abnormal proteins in the human brain and this disease is the result of this building. Amyloid and tau, are proteins that have a big contribution to building abnormal proteins in human brain cells. Building abnormal proteins such as amyloid and tau affects the human brain and for this effect, the capability of chemical messengers is decreased in the human brain. Messaging and signalling of the human brain are affected and for this reason, the neurotransmitter level of the human brain is reduced. The capability of memory depends on neurotransmitter level and decreasing the capability of neurotransmitter level decreases memory power.

Several facts such as age, history of the family, down syndrome, and cardiovascular and head injuries have great contributions to increase risks of Alzheimer's disease. These factors promote the building of abnormal proteins in the human brain that are the causes of Alzheimer in the human brain. For example, a genetic change that is known as a down syndrome is responsible for building up amyloid protein and this protein has a big contribution to neurotoxicity. In the entire study, the contribution of amyloid and tau, as contributors to neurotoxicity in the human brain have been discussed. The thinking ability of memory is decreased due to disease and for this reason behaviour of normal humans is changed. In the early stage, symptoms are noticed at a minimum level and the progress of this disease is different in different human brains. A huge number of people are affected by Alzheimer's in India.

## LITERATURE REVIEW

### Associated proteins that lead to Alzheimer's disease

Alzheimer's is the disease totally depend on the various kinds of proteins and it also associated with the functioning of brain. It can affect memory, skills of thinking and also make an impact on the other kinds of abilities of the brain. This disease increases the risk of developing conditions and it includes depression, age increasing and lifestyle conditions and factors. This Alzheimer is one of the progressive conditions that is responsible for affecting multiple functions of the brain. The primary sign of Alzheimer's is minor memory problems and other symptoms are disorientation, confusion, decision making, lack of confidence, anxiety, hallucination, changes in personality and others. Beta-amyloid protein is inter connected with this disease and it make the impact on the different kinds of molecular forms that can collected between neurons [1]. This protein also known as amyloid precursor protein. On the other hand, beta amyloid 42 is a toxic protein. This protein hampers the brain function and is responsible for increasing the effects of disease.

In addition, Tau protein is another protein that influences the disease and generally this protein helps to stabilise the microtubules that are responsible for abnormal shaped and misfold. Accordingly, high plasmatic BCAA or branched-chain amino acids are used as dietary supplements and it is also linked with the metabolic risk factors that are connected with Alzheimer's disease. BCAA influences the transportation system of amino acids to the brain directly. From several studies it has been seen that tau protein becomes toxic while chemical molecules can accumulate in

the brain with its structures. It is also responsible for forming protein tangles that can destroy the other surrounding tissues [2]. In India 4 million people are facing Alzheimer's disease and all individuals are facing facetious symptoms reading this issue. In Alzheimer's disease, proteins are responsible for producing abnormal build-up of proteins in the brain's cells and it also changes the activity level of the enzymes that make a negative impact on the brain tissues. Lack of protein is called RbAp48 in the hippocampus that significantly plays a role in the memory loss that also affects the brain and body function of individuals.

### **Impact of Tau protein in Alzheimer's**

Tau protein is the group of highly six soluble proteins and it makes a huge impact on the Alzheimer's protein. This group of protein is produced by the alternative splicing from "microtubule associated protein tau" or MAPT. Generally, it has the basic and primary role to maintain the stability of axon's microtubules and they are also abundant in neurons of the central nervous system. In this context the cerebral cortex is highly abundant and there are various forms of chemical reaction that have occurred that make an impact on the disease. In this context it can be said that Tau substance also responsible to build up the Alzheimer's and also responsible for damaging the cells of brain that is essential for the memory and learning [3]. It has been seen that Tau also increase the enzyme activities of the enzymes and those are also act on the tau and it is known as "tau kinases". This is the reason for misfolded and clumps of tau protein and it is responsible for forming the neurofibrillary tangles.

On the other hand, this Tau protein also plays a major role in the healthy nerve cell as well and accordingly its able to create a barrier of the blood brain and also it plays a crucial role to maintain the microenvironment of CNS or central nervous system. Tau protein is essential for synaptic plasticity, genomic stability and cell signalling. In the adult human brain is able to express six kinds of isoform of the tau protein that is interconnected with the microtubule and messenger RNA. In addition, it can be described that emerging evidence is able to suggest that this type of substance may be responsible for the complexity interplay between beta-amyloid and abnormal tau protein and it has several factors [4]. Tau protein is collected with the spinal cord, neurons and others connecting tissues. On the other hand, it makes an impact on the central nervous system and its function also. Accordingly, some Alzheimer's disease and other frontotemporal disorders or become detached and damaged from the other axons. Sometimes dysfunctional Tau is more toxic for neurons and it can be responsible for death of individuals.

### **Effects of Alzheimer's in brain**

Alzheimer's disease is spread in the brain with a wide range and for this reason, multiple diagnosis processes are involved. Several types of research have been done on the range of spreading this disease in the brain. In many cases, it

is found that around 11 to 3 years are taken to diagnose this disease affected by Alzheimer's [5]. In another case, much more time is required to find the range of Alzheimer's that spreads in the brain. The people who are affected by Alzheimer's suffer from different kinds of health issues in their life. Dehydration is one of the major health issues that is caused by Alzheimer's. Multiple health objections have happened due to dehydration. Headache, tiredness and dry mouth are the major infections that occur by dehydration which is caused by Alzheimer's. Malnutrition is one of the big issues of people that are also caused by Alzheimer's. Weight losses, irritability, and fatigue are the major problems of people that occur due to malnutrition.

Alzheimer's has different kinds of impacts on human life. Life longs of Alzheimer-affected people depend on their age. In many cases, men who are affected by Alzheimer's live for 4.1 years after diagnosis. On the other hand, women live for 4.6 years after diagnosis affected by Alzheimer's. However, age is a factor that defers the living of people who are affected by Alzheimer's. People who are above 90 years old can live for 3.8 years after diagnosis of Alzheimer's [6]. On the other hand, people who are above 70 years old can live for about 10.7 years after diagnosis. A lifetime of Alzheimer's affected people depends on the diagnosis and for this reason, people who do not prefer diagnosis in the accurate time cannot manage to live the above-mentioned time period. Several therapies are designed to improve the mental health of people who are affected by Alzheimer's.

#### **Relation between Neurotoxicity and Reactive Astrocytes**

Alzheimer's is considered the most prevalent disease among older people and significantly the frequency of this disease is rising among these people. It is expected that around 66 to 76 million people are to be affected by Alzheimer's by the year 2030 [7]. Aggressive progression of tau protein in neurons promotes Alzheimer's in the human brain that decreases the capability of the human brain and for this reason, people suffer from various issues in their daily activities. Astrocyte cell culture is defined as progressing capability of brain cells that can control the effects of Alzheimer's. A proper technique is involved in building primary Astrocyte cell culture. Astrocytes work for electrolyte homeostasis and cell signalling. Primary astrocyte culture is used for making Astrocytes to increase responses of the brain that can promote the capability of memory. Several modifications are introduced in astrocyte cell culture and neuron-astrocyte co-culture is one of the modifications.

In many types of research, astrocytes have been considered as the possible solution that can bring change to Alzheimer's. L-Deprenyl is one kind of enzyme that is found in astrocytes. In modern bio-science, this enzyme is approached in vitro and this enzyme distributes the activities in different ways [8]. In many cases, it is found that AD and MAO-B, both are increasing in the human body during the enhancement of astrocytes. This enhancement is one of the processes to observe the progress of AD. Evidence of L-dependency in AD encourages researchers to use it in AD. Considering this

fact, most biomarkers accept it in AD. The growth of neurons affects the progress of AD and for this reason, neuron-astrocyte is used for decreasing the effects of AD. In many cases, neuron astrocytes are considered superior for decreasing the effects of AD.

### Contribution of amyloid for Alzheimer's disease

Amyloid splices are related to neurotoxicity that progresses Alzheimer's. Amyloid protein is considered a single-pass transmembrane protein that has high-level effects on the brain. The entire amyloid is divided in two ways such as non-amyloid and full-length amyloid. The non-amyloid part of amyloid protein is considered alpha and the other part is known as beta [9]. Beta-amyloid protein enzyme that is called BACE1. In the initial stage, Amyloid beta is toxic with the help of BACE1. The produced toxic affects the function of the existing proteins of the brain and as a result, abnormal protein form is rising. In this disease, neurons are badly affected and for this reason the capability of the brain in storing memory is decreased. Communication occurs between neuron to neuron and amyloid affects this communication between the neurons. Different molecules are involved in amyloid. These molecules are directly connected with neurons.

Large proteins are broken down and many toxic proteins are formed. This formation of toxic protein progresses to abnormal protein level in the brain. The enhancement of protein affects the main function of neurons and as a result capability of the brain is affected. Neurotoxicity is directly produced by amyloid beta in the brain and for this production memory skills are affected badly [10]. Memory power of the brain is reduced and this reduction is increased by the production of neurotoxicity. The presence of amyloid protein helps to increase the level of homeostasis. The enhancement level of homeostasis plays an important role in producing excitotoxicity as an outcome in the brain. This outcome reduces the buffering capacity of the human brain and for this reason the capability of the brain is affected. On the other hand, amyloid beta leads to collaboration between the central nervous system and receptors. Outcoming excitotoxicity affects this collaboration and for this reason, the overall capability of the central nervous system is affected.

### METHODOLOGY

Online journals, magazines, and websites are the sources of secondary qualitative data. In the proposed study, online journals are used as the sources of required data, and for this reason, secondary qualitative data have been used in the proposed study. Sources of secondary data are easily accessible for researchers and for this reason these sources can be used for collecting data with a low budget and time. A wide range of data is available under secondary qualitative data and researchers have the choice to consider data sources as per requirements [11]. Considering the facts, secondary qualitative data has been chosen in this proposed study. Most data sources in secondary qualitative data are available online

and for this reason, researchers can collect data from the sources in a short time. This short time process of collecting data helps to reduce the time of overall research. Considering secondary qualitative data, researchers can manage time in the entire research.

Consumption of more time in research increases the overall cost of research and that has a financial impact on researchers. Collecting secondary data reduces the overall time period and as a result, researchers have the opportunity to manage the budget of the entire research. Secondary qualitative data have been used in previous research and for this reason authenticity of data is proven. Researchers can make authentic research using secondary qualitative data. Authentic data helps to make authentic research papers and for this reason, researchers consider this kind of data [12]. Rich sources of data increase the authenticity of research papers and secondary data have rich sources. Researchers have the opportunity to improve the authenticity of research using rich data sources and for this reason in this study, secondary qualitative data sources have been considered as sources of data collection. Structured sources of data are present in secondary data collection.

Researchers have the opportunity to consider the data sources as per their requirements and for this reason, most researchers consider secondary data sources in research to collect proper data. On the other hand, researchers have not any control over the data quality, and of this researchers cannot manage the quality of study. Quantitative data sources are much more authentic and for this reason, researchers approach quantitative data sources in research [13]. In the proposed research secondary quantitative data have been used as a data collection procedure. Chemical, cell line, propidium iodide, LC-MS, protein extraction, and level-free quantitative data have been used in the proposed study as materials. Sodium metaarsenite, lead chloride, and methyl mercury chloride, these chemicals are used in the method. In the model of hippocampal neuronal cells, HT-22 cells are used which is part of numerous studies.

Eagle's medium that is maintained by Dulbecco is used to maintain HT-22 cells. Different kinds of elements such as fetal bovine serum, penicillin, and streptomycin are used in forming the cell HT-22 [14]. Propidium iodide is used for the metals that are present in proteins that have a bad impact on increasing amyloid in the brain. Protein identification is the main bottom of this study and for this purpose Mascot search engine has been used. Different kinds of MS spectra are used in Progenesis software that helps to identify different kinds of proteins that have an impact in increasing Alzheimer's in the human brain. Two different kinds of criteria such as trypsin are to be considered as an enzyme, and different kinds of modifications, oxidation, allowing two cleavages are considered in the proposed study. Statistical analysis has been approached in the proposed study to identify proteins that are involved in the cause of Alzheimer's. Quantitative data has been considered in the t-test method and for this purpose, Microsoft Excel has been used. Data is filtered in

this process which helps to bring changes in the approached method.

The Meaboat 3.0 program is considered an unsupervised data filter and for this reason, this program has been used in this process for filtering unsupervised data. In statistical data analysis, filtering unsupervised data is approached as a common principle to direct the entire process in the right way. In the interpretation of biology analysis, mainly three steps are involved. The steps are first, identification of the statistical significance of the protein that is chosen for the identification. Progressive QI software has been used in the method of identification of the protein [15]. Quantitative analysis is used under Progenesis QI software. In this entire method, 3140 proteins are identified among 27088 peptide ions. The proteins which have two unique peptides are chosen as the identified proteins through the method of protein identification.

### DISCUSSION

The entire is based on the impact of various proteins that are the causes of Alzheimer's. Thinking ability and memory power are badly affected by Alzheimer's. The human brain is affected by the progressive movement of this disease. The function of the brain is affected by Alzheimer's and several symptoms are involved with this disease [16]. In the initial stage, insufficient decision-making ability and confusion in thinking have happened with people who are affected by this disease. Beta-amyloid molecular proteins are directly connected with Alzheimer's. The functions of the brain are affected by the toxins which are produced by beta-amyloid protein. The toxicity helps to increase the effects of Alzheimer's in the human brain and for this reason capabilities of the human brain are decreased in order to improve thinking skills and memory level. Many people are under the impact of Alzheimer's and the effect of this disease is rising immensely worldwide. Several health issues are identified due to the impact of Alzheimer's on the human brain.

Primary astrocytes cell nature is used to decrease the impact of toxic proteins in the brain and this initiative helps to reduce the bad impact of Alzheimer's. Different kinds of health issues are identified among the people who are affected by Alzheimer's. Dehydration is one of the major health issues which happens due to Alzheimer's. Quantitative analysis shows the protein identification from the method that helps to understand the impact of proteins that are the causes of Alzheimer's. Eagle's medium model is used to identify HT-22 cells and this model is maintained by Dulbecco [17]. The method that is considered in the proposed study identifies 3140 proteins out of 27088. Non-Amyloid and full length of amyloid, the two types of proteins that are included in amyloid. Beta-amyloid is one kind of full-length amyloid protein that has a huge impact on Alzheimer's. Toxins come from this protein and this toxicity plays an important role to affect the human brain and its capabilities. BACE1 is an enzyme that is produced by the beta-amyloid

protein and is toxic that affects the brain.

From the above-mentioned literature, it can be stated that the disease Alzheimer's is mainly dependent on distinct protein materials. The enhancement of Alzheimer's disease gradually impacted on skills, thinking capability, and working capacity of the Brain [18]. The risk factors associated with this disease are the deterioration of lifestyles of elderly individuals. The disease mainly occurs above the age 65 and it negatively impacts the brains of individuals. Minor memory loss is the fundamental sign of Alzheimer's and some other types of severe syndromes are hallucination, anxiety, and depression. On the other hand, the interconnection of Beta-amyloid protein with Alzheimer's can be highly observed in this case. Neurons are interconnected with each other and react with the protein and it also forms amyloid precursor protein. Additionally, the study provided the concept of Beta Amyloid protein and it can be stated that Beta Amyloid is one kind of toxic element which is responsible for the formation of the disease Alzheimer. Additionally, Tan can be considered as another identical protein factor that also contributes in the formation of the disease Alzheimer's.

Tan protein mainly encompasses six different soluble protein groups and also contributes to the emergence of Alzheimer's disease. The splicing activity of the protein group can form MAPT and it has the capability to maintain the microtubules of axons present in the central nervous system of individuals [19]. Therefore, Tau is the fundamental protein factor that can cause further damage to cells, which hinders the thinking, learning and decision-making capability of people. Activities of Tau protein led to the formation of Tau kinase, which further misfold the protein in the Brain. As a result, neurofibrillary tangles can be generated and certain types of clumps can be generated. In contrast, Tau protein can deliberately form a blood-brain barrier for the further maintenance of the central nervous system.

### CONCLUSION

Various proteins are the reason for the disease Alzheimer's. People suffer from different kinds of issues such as low thinking capabilities; low memory power are happened due to Alzheimer's. Possibility of developing decision-making capabilities are affected due to bad impact of Alzheimer's and people cannot grow their mental ability in thinking critical subject. Impacts of this disease are rising after diagnosis and people are affected more after affected by this disease. Memory problem is considered as primary problem that affects regular life of human life. Decision making ability is reduced and confidence level of human is also decreased. Beta amyloid is one of the proteins which has huge impact to increase impact of Alzheimer's in human brain. Beta amyloid 42 is a toxic protein that affects the capabilities of the human brain and for this reason the working capabilities of the human brain is badly affected. These effects are the causes of the reduced thinking ability of the human brain.

Tau protein is another protein that has a huge impact on increasing the effects of Alzheimer's on the human brain. BCAA is branch chained that operates transportation of amino acids and toxic products affects this transportation system. This cause influences overall formation of protein and for this reason abnormal protein is built in brain that is the cause of Alzheimer's. It is found in study that around four million people are directly involved in Alzheimer's impact and these people are facing lower memory power and poor thinking ability. Tau is another protein that has also huge impact on occurring Alzheimer's. Six soluble proteins are included in a group that is known as tau protein. Tau protein plays important role for ensuring stability of axon's microtubules. This disease spread in several states and people are affected in various classification. After diagnosis people are affected in different ways due to this disease.

Age of people is one of the important factors that has huge influences on the effects of Alzheimer's. The people who are above the age of 70 years can live for 10.7 years after diagnosis. 90 years above people can live for 3.8 years after diagnosis and are affected by this disease. Amyloid protein is divided into two parts such as non-amyloid and full-length amyloid. These two types of amyloids have a huge impact on increasing toxicity in the human brain and for this reason the capabilities of the brain are decreased. This reduction plays an important role in decreasing the ability of memory power and thinking ability. BACE1 is a toxic that is produced by full length amyloid and for this toxic abnormal formation of protein is rising. This kind of increasing protein formation is the main reason for decreasing thinking ability of the human brain. On the other hand, beta amyloid plays a key role in producing neurotoxicity. Capability of the brain is also damaged due to neurotoxicity and for this reason the thinking ability of humans is badly affected.

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