ALZHEIMER'S DISEASE: MODERN PERCEPTIONS OF THE DISEASE

Nenko Ivanov[2], Anita Nikolova[2], Silvia Yaneva[2], Aleksandra Christova[2], Aneliya Kostadinova[1]

*1 – Institute of Biophysics and Biomedical Engineering, Bulg. Acad. Sci., Acad. G. Bonchev str., bl. 21, 1113-Sofia, Bulgaria 2 –Faculty of Biology, Sofia University, 8 Dragan Tzankov Blvd, 1164 Sofia, Bulgaria, *Corresponding author: aneliakk@yahoo.com**

Abstract

In our decade the most relevant topics in the sphere of science are the ones for treating cancer, finding cure for diabetes and the development in the field of bioengineering. One particular disease however seems forgotten and the hope for finding a cure is more like a dream not only for the affected but for their close ones as well. This is the Alzheimer's disease and that is the reason we assembled this report to present a little bit more about the past of the disease, what we know today and to think about its future.

***Key words**: Alzheimer, amyloid beta protein, acid sphingomyelinase*

Introduction

The history of Alzheimer's,

Alois Alzheimer was born 1864 in South Germany. He graduated medical school in 1887. Interested in the research of the human brain cortex he started working in the psychiatric hospital in Frankfurt. Not long after he became an assistant to the famous psychiatrist prof. Emil Kraepelin in the Medical school of Munich where he had the opportunity to combine both his research and medical practice. There he created a brain research facility. In the years to come he conducted series of experiments and issued a lot of publications but his name gained popularity in 1907 after a lecture where he presented the extraordinary disease in the cortex of the brain. The Alzheimer's disease was named after its founder proposed by prof. Kraepelin. And the first human to ever be diagnosed was a 50 year old woman named Auguste Deter. She suffered from memory loss, disorientation and was delusional. Aguste died at age of 56 following the consequences of her disease. After dr. Alzheimer's death only his name is left to mark the disease that still has no cure even to this day.

Alzheimer's disease (AD)

Alzheimer's is incurable, degenerative and terminal disease. Even though every patient experiences it in a different way there are a lot of common symptoms. The first ones are often mistaken with anxiety and stress. In early stages the incapability of acquiring new memories and the difficulty of remembering old ones are the most common symptoms. If suspicions for AD occur, the diagnose has to be confirmed after a series of cognitive tests and evaluation of the behavior of the patient often followed by brain scanner when it's possible.

With the advancement of the disease new symptoms like confusion, irritability and aggression are shown. Quick change in mood, facing difficulties when trying to speak and loss of long term memory lead to weakening the senses of the patient. Gradually other body functions are stunned which in the end results in death. Individually it's impossible to predict how the disease is going

to proceed because its duration varies with different patients. Alzheimer's disease may develop indefinitely before the first symptoms are shown and that's what makes early diagnostic for the disease nearly impossible. The average life span after diagnosis is around 7 years. Less than 3% of the affected live longer than 14 years after diagnostic

Root causes for Alzheimer's disease and what we know so far

Alzheimer's disease is determined not only by one biochemical error in the neurons, but by many acting together. It's widely believed that the main reason behind Alzheimer's is the accumulation of amyloid plagues in the brain tissue. The amyloid beta protein is causing the formation of the so called amyloid plagues and the disturbance in cell functioning. Initially the accumulations are extracellular but later on they reach the neural ends and disturb the normal function the synapses. Another pathogenic mechanism is the decreased production of ATP (adenosine triphosphate), the main energy supplying compound for the function of the brain. As a result there are serious changes in the transport and exchange of ions between neurons and the extracellular matrix, the rush of extracellular ions intracellularly which results in cell damage and death. There is the acetylcholine theory for the pathogenesis of the disease, which takes into account the decrease in the acetylcholine media and the impossibility for acetylcholine esterase to take place in the decomposition of the amyloid beta protein.

Acid sphingomyelinase (ASM)

Till now no one knows exactly how AD begins, scientists understand it to be a complex interaction between genes and the environment. In conducted studies, a team of researchers from Kyungpook National University discovered how the brains of Alzheimer's patients have elevated levels of an enzyme called acid sphingomyelinase, or ASM for short. This enzyme, which is expressed by almost all cell types, normally works in harmony with other enzymes and proteins for proper cell metabolism; yet at the wrong levels, it breaks down membrane lipids in the myelin sheath that coats nerve endings.

Although the research team had been aware of a link between ASM and Alzheimer's, they wanted to know if it might be directly causing AD. So they examined ASM and the activities and levels of various lipids in brain tissue samples from Alzheimer's patients and a group of unaffected individuals. As expected, they confirmed a significantly higher level of ASM in patients with AD compared with normal individuals. Then, they took their experiment one step further and looked at ASM levels in samples from individuals with Parkinson's disease. What did they observe? ASM was not elevated in samples from Parkinson's patients so they decided that it must be a signature of Alzheimer's disease alone.

Next, the team of researchers ran experiments to figure out how ASM and AD co-exist. This time the team turned to mice with Alzheimer's-like disease and elevated levels of ASM activity. After testing and analysis, the researchers found the additional ASM appeared to clog up the autophagy machinery in the brain cells of the mice. In turn, this resulted in an accumulation of waste. When they reduced the levels of ASM in the mice by using the drug amitriptyline-

hydrochloride, the researchers were able to restore proper autophagy and this lessened the brain damage in the mice. Eventually, the mice even showed improved learning and memory.

Treatment

At this point there is no effective way for treating AD. The available therapies can't stop the progression of the disease. Even the drug used by Lee Jk and his team on mice in the experiment described above is not a potential solution. The amitriptyline-hydrochloride is a strong psychotic drug which could lead to more complications in humans. Medicaments like Donepezil and Galantamin are part in a group of drugs called acetylcholinesterase inhibitors. They are used to slow down the symptoms and to delay the terminal stages of the disease. Our team set the goal of finding different plant extracts to help support the curing of AD. We have plans for the future and those plans are connected with one specific plant named huperzia serrata which is used in traditional Chinese medicine for hundreds of years for curing schizophrenia. In recent years it is also used in test drugs for Alzheimer's as well. We would like to perfume experiments with cell membranes from where AD is currently starting from. To study in details the cell signaling pathways and to find an adequate solution to the problem.

Conclusion

It's important to raise the issue for Alzheimer's treatment. Since the discovery of the disease more than 100 years ago there is no significant progress in terms of finding a cure. The statistics shows that by the year 2050 every 10^{th} will suffer from AD or will show the symptoms of the disease. The available treatment for Alzheimer's is as expensive as chemotherapy in cancer treatment but AD is still more neglected. It's time to give the problem the needed attention and with concentrated effort to find a solution which will be effective in the long run.

Reference:

[1] History of Alzheimer's „Alzheimer Bulgaria,"

[2] Alzheimer's Disease & Dementia | Alzheimer's Association website

[3] Medical Daily Magazine

[4] Lee JK, Jin HK, Park MH, et al. Acid sphingomyelinase modulates the autophagic process by controlling lysosomal biogenesis in Alzheimer's disease. *JEM.* 2014.