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The relations between AD and DS and the therapies for curing this disease

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Abstract. Down syndrome is a disease that has relations with Alzheimer's disease. In this work, it mainly focus on the mechanism of additional 21st chromosome in Down syndrome patients causes the rise of Aβ protein (a protein would cause Alzheimer's disease). Two diseases that would reduce the life expectancy and loss of memory. This paper also discuss the exist therapy for curing Alzheimer's disease in Down syndrome by choline supply during pregnancy, using acetylcholinesterase for inhibiting and secondary prevention in experiment on Ts65Dn mice. Results show that though the samples size is small, some side effects are caused and there is no specific results show that those therapies is also useful in clinic trials, the great success is achieved in animal lines (near 50% to 60% of success). These therapies can play a significant role in the future and it can reduce the impact of Down syndrome and Alzheimer's disease in patients.

Keywords: Down syndrome, Alzheimer's disease, therapies of choline

1. Introduction

Down syndrome (DS), a genetic disorder that causes patients to have one more chromosome in the 21st chromosome pair. People who get Down syndrome disease always have problems with physical [1]. As more profound studies have been done recently, many researchers have found that Down syndrome is related to Alzheimer's disease. Alzheimer's disease is a typical progressive disease that worsens, and many patients with this disease may have problems with poor memory and even problems with communication [2]. Patients who have Alzheimer's disease may only have a 3 to 7-year life expectancy [3,4].

Alzheimer's disease is a disease that has existed for a long time, and the leading cause of this disease is the molecular mechanism of Tau protein aggregation in a particular position in the brain, such as the hippocampus, neocortex, and amygdala. However, 15% of patients have Alzheimer's because of a genetic mutation. While patients with Down syndrome(DS) have a higher risk of getting Alzheimer's disease(AD), this is because chromosome 21 always expresses APP, a kind of protein that leads to the occurrence of Aβ (a kind of protein that causes AD). Furthermore, one more trisomy 21 chromosome would over-express the APP [4], since the mRNA for producing protein APP is rising. Often, the risk of those DS patients increases as their age increases. Most patients above 40 years are constantly diagnosed with AD because there are a lot of neuritic plaques and neurofibrillary tangles [5.6.7] which are the disease can be found in the early year of 15 years old.

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2. Methodology

The method used is a literature review, searching for papers and pieces of literature using Google Scholar. The papers read are highly related to this research question, which comes from putting keywords to Google and then checking out the publish time, the types of articles, and the latest studies. The most famous publications will be used in this paper.

This paper will mainly focus on How Alzheimer's disease in Down syndrome is caused in the molecular level and in genetics and also will introduce the treatments for this disease by using choline in detail and mention other therapies, as well as the limitations of them at the end of this paper.

3. Therapies

3.1. Supplement of Additional Choline during Pregnancy

The experiment on the Ts65Dn mouse is carried out to prove that choline during pregnancy is an effective method for patients. Ts65Dn mouse is a kind of mouse that is used in experiments with trisomy chromosomes 16 and 17. Those mice show fundamental morphological, biochemical, and transcriptional changes similar to those seen in patients with DS and AD [8-13]. This means the Ach level is relatively low; this change can lead to neurons' differentiation and plasticity of synapse formation [14-16]. So, if there is an additional supply of choline, it can help with the AD in DS for babies.

Choline has many impacts on mice, including emotion reactivity and metabolism [17]. The experiment of the Ts65Dn mouse can show the impact of choline. Before the start of the experiment, mice had difficulties concentrating on things [18,19]. And researchers found that mice can pay attention to a thing more accurately if their mother took choline [19]. Moreover, choline also reduces negative emotion in mice, and they were less influenced by failure. Also, when researchers test the activity of liver, blood, frontal cortex, hippocampus, cerebellum and basal forebrain [20], they found the activity of those organs. For instance, liver activity improved by 60% and promoted cognitive function [20].

As most of us know, Down syndrome is a disease that can be detected before giving birth to a baby by amniocentesis so that doctors can find out whether there is an additional chromosome in this baby. However, the fact now is that there is no effective treatment for ID (intellectual disability and Alzheimer's disease) [17]. Fortunately, supplying additional choline during pregnancy improves the situation of Down Syndrome and Alzheimer's Disease, as a therapy for those who do not know if the baby can get the ID [17]. In the animal models, researchers found that those mice with DS may have neuron atrophy, and there is only a little choline in their hippocampus, as mentioned before [9,21-24] Cognitive disability is related to 2 kinds of choline in humans: one is explicit memory, and another one is the working memory. As a result, adding choline can prevent the decay of the cognitive and also the loss of memory.

3.2. Other Choline Therapy for Down Syndrome and Alzheimer's Disease

Instead of using choline during pregnancy or medicine that patients took for precaution, there is another acetylcholinesterase inhibitor for patients to use. And there is a study prove the availability and security of this kind of therapy. Patients who are selected need to take up 5mg placebo or donepezil randomly in the first 4 days and 10mg in following days [25]. Researchers take a record of patients Dementia Scale of Mentally Retarded Persons (DMRP) and Neuropsychiatric Inventory (NPI) [25]. This treatment also has a similar mechanism for curing by regulating the activities of cholinergic neurotransmitters [25]. There are three kinds of acetylcholinesterase inhibitor (AChE): donepezil (Aricept), rivastigmine (Exelon) and galantamine (Reminyl). But in this study these results indicate that donepezil has significant effects, which improves around 50% patients state of an illness [25]. However, further studies are needed to carry out since there are also some side effects for some patients such as insomnia and sleepy.

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3.3. Potential Secondary Prevention for Alzheimer's Disease in Down Syndrome

More results find that other secondary treatments can be used besides the choline. Many therapies focus on the AD disease and the later stages, but there are more expectations for the treatment for the earlier stage. It is now coming true because of advanced technology such as PET for patients with DS who have a higher risk of having Alzheimer's disease. Now, a research which is called the Down Syndrome Biomarker Initiative (DSBI) is working on this trial, which ranges from memory, learning and executive function and tries to deal with Alzheimer's disease in Down syndrome in the early stage [26].

4. Discussion for Therapies

There are only a limited number of treatments for Alzheimer's disease and Down syndrome. The study of additional maternal choline supplement has already shown great success in these experiments. However, though researchers found that it is valuable and beneficial on Ts65Dn mouse, it cannot prove that it can still work in the human body, though both mice and humans have similar brain structures. The use of cholinesterase also plays a significant role in this disease. The main problem is that the sample that can be used is limited because this experiment is based on humans, so it needs others' agreement. Another difficulty is that the patients have a higher possibility of getting complications.

5. Conclusion

Trisomy 21 might cause AD in older ages. However, the technology now can also help detect DS and AD, and the prevention of taking choline during pregnancy can be helpful for babies. Even for those who get AD in DS when growing up, another kind of cholinesterase can be used in the treatment. Though there still exist many obstacles that researchers should overcome, the treatment of AD in DS is ripening gradually now, so there will be fewer patients suffering from AD and DS now.

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