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Research progress in stem cell technology in Alzheimer's disease

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Abstract. Dementia in the elderly is a neurodegenerative disease that affects approximately 50-75% of people worldwide. Patients with Alzheimer's will gradually experience a decline in intelligence and cognitive function, and Alzheimer's is also the most common form of Alzheimer's disease. At present, there have been many advances in the causes and treatment of Alzheimer's disease, but they also face great difficulties. There is no effective treatment for senile dementia yet, and the main clinical drugs are to alleviate symptoms, delay onset, and reduce the impact of the disease on daily life. However, stem cell technology has made great progress this year, and stem cells have shown tremendous potential in the treatment of many diseases. Many studies have been conducted on the use of stem cells in the treatment of Alzheimer's and Alzheimer's disease, and some of the results have shown good therapeutic effects. The application of mesenchymal stem cells in the treatment of Alzheimer's disease has been partially preclinical. However, most of the plans for treating dementia in the elderly through stem cell therapy are still in the experimental stage, and there is currently a lack of standardized treatment. There are potential risks and technical difficulties in promotion and implementation that need to be further explored. Further research is needed on the risks, processes, and technical difficulties of stem cell therapy. This article will systematically discuss the symptoms and pathogenesis of senile dementia, and analyze the current use of stem cells in the treatment of senile dementia. This article will contribute to people's understanding of dementia in the elderly and promote related research.

Keywords: Alzheimer, dementia, stem cell, model selection

1. Introduction

Alzheimer's disease, also known as Alzheimer's disease, is a neurodegenerative disease that primarily leads to cognitive impairment. Patients with Alzheimer's disease may experience partial memory loss and a lack of self-care capacity. According to the World Health Organization, dementia is the fifth deadliest disease in the world. Currently, Alzheimer's treatment plans can only help patients with cognitive function, delay cognitive decline, and reduce the occurrence of these symptoms. There is currently no specific plan or method to completely treat Alzheimer's disease, which cannot prevent the development of the disease. Although there is not yet an exact treatment plan, most believe stem cells can be used to treat Alzheimer's disease. Stem cells are self-renewing cells in the body. Mammalian stem cells can be divided into two categories based on their developmental stage sources: embryonic

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stem cells and adult stem cells. According to their differentiation potential, they can be divided into four categories: totipotent stem cells, pluripotent stem cells, multipotent stem cells, and monopotent stem cells Stem cells, as a group of cells with multi-directional differentiation potential, are abundant in sources and diverse in functions, making them an ideal solution for cell replacement therapy. They have been preliminarily proven in research on diseases such as nerve damage, cerebral ischemia, and Parkinson's disease.

2. Elderly dementia

2.1. Symptoms/manifestations and incidence of senile dementia

Dementia of the elderly is mainly concentrated in the elderly, and symptoms worsen with age. According to data released by the Alzheimer's Disease International (ADI) in 2016, there were approximately 46.8 million AD patients worldwide as of 2015, and the number is expected to reach around 131.5 million by 2050. In Europe and America, the incidence rate of patients under the age of 65 is less than 1%, the incidence rate of patients over the age of 65 is 1 · 5%, and the incidence rate of patients over the age of 85 is about 30%. [3]

The clinical symptoms of senile dementia mainly show a decline in memory, intelligence, abstract thinking ability, language and other functions, as well as emotional and behavioural abnormalities, loss of work ability, and serious decline in quality of life.

There are many types and types of senile dementia, mainly divided into four types: senile dementia, cerebrovascular dementia, mixed dementia, and senile dementia caused by systemic diseases. Alzheimer's disease is usually accompanied by brain atrophy, brain tissue is full of nerve fiber tangles, and atherosclerosis is common outside senile plaques and small cerebral vessels.

Alzheimer's disease is divided into three stages. The first stage is mild Alzheimer's disease, which lasts one to three years. This stage is characterized by mild memory impairment and decreased judgment. Patients are unable to cope with complex things such as shopping alone, socializing, and determining their geographic location, often accompanied by emotional apathy. The second stage is severe Alzheimer's disease, which lasts two to ten years. During this stage, the memory is moderately weakened and often unable to determine time, location, etc. Patients are unable to deal with issues such as dressing, maintaining personal hygiene, and calculating. At this stage, emotions will shift from apathy to irritability, and there is also the possibility of urinary incontinence. The third stage is severe senile dementia, which means suffering from senile dementia for eight to twelve years. The patient is completely dependent on others, with severe memory loss, urinary and fecal incontinence, and limb stiffness. [1]

2.2. Treatment plan

Due to the complex causes of the disease, senile dementia cannot be cured. There are seven therapies, the first of which is drugs targeting the theory of cholinergic injury. This method mainly uses drugs such as dopezil, listatimine, galantamine, and huperzine A. Among them, donepezil is one of the second generation cholinesterase inhibitors for Alzheimer's dementia. The second type is drugs targeting excitatory amino acid toxicity theory, which can effectively stop the onset of Alzheimer's disease and protect psychiatric cells. The third type is drugs that improve brain metabolism. Some Alzheimer's disease is caused by metabolic disorders in the brain, leading to neuronal apoptosis. And this medication can help cognitive function in patients with moderate Alzheimer's disease. The fourth type is drugs that target inflammation, and patients with senile dementia have chronic inflammatory reactions. Therefore, the use of inflammatory drugs can effectively assist patients. The fifth type is drugs that target oxidative stress theory, as dementia patients have a build-up of free radicals in the brain, and restoring the patient's antioxidant system can help delay dementia. The sixth type is drugs that target amyloid deposition, which is a cause of Alzheimer's disease in the brain. These drugs targeting amyloid deposition include α- Tocopherol can inhibit and clear precipitation in the brain of patients with senile dementia, and effectively improve their learning and memory abilities. The last type is traditional Chinese medicine,

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which can be used with drugs such as huperzine, curcumin, polysaccharides from Cistanche deserticola, polysaccharides from Longan ginseng, oligosaccharides from Morinda officinalis, icariin, bone lipid B, and dihydroflavones from psoralen, as well as extracts from Cordyceps sinensis fruiting bodies. These drugs have good therapeutic effects. [1]

2.3. Risk factors for dementia occurrence

The causes of the disease are complex and there are many types. There are mainly four types. The first is family history. Patients get sick through genetics, and the risk of disease among family members is three to four times higher than that of ordinary families. The second type is physical illness, and when suffering from diseases such as thyroid disease, immune system disease, epilepsy, etc., there is a high probability of also suffering from senile dementia. The third type is head injury, which is not particularly common. In general, only very serious brain injuries can trigger senile dementia. The last type of dementia is caused by other factors such as immune system failure and economic difficulties. [1]

3. Adult stem cells and senile dementia

3.1. Basic concepts of stem cells

Scientists are constantly revising their views and definitions of stem cells. Stem cells are a group of cells that can self-renew and have multi-directional differentiation potential. They can control and maintain cell regeneration, differentiate or produce cells of a specific tissue in the body. Although stem cells have the ability to self-renew, their self-renewal is asymmetric. Stem cells can be divided into four categories: embryonic stem cells, adult stem cells, pluripotent stem cells, and pluripotent stem cells. Stem cells have broad application prospects. It can treat many diseases. [4]

The characteristic of cellular differences is that embryonic stem cells can continue to grow without differentiation. Most pluripotent stem cells are used for cloning, and they are individuals with complete development. Multipotent cells can self-replicate and in some cases differentiate into multifunctional cells. [2]

3.2. Characteristics of Adult Stem Cells

Most adult stem cells exist in undifferentiated cells in tissues and organs such as skin, fat, muscle, and bone. Known adult stem cells include hematopoietic stem cells, bone marrow mesenchymal stem cells, neural stem cells, liver stem cells, muscle satellite cells, skin epidermal stem cells, intestinal epithelial stem cells, retinal stem cells, pancreatic stem cells, etc. Under normal circumstances, adult stem cells usually exist in a dormant form. If some cells or tissues are injured, they will be activated and repaired. The types or tissues that adult stem cells can differentiate into are limited, and most adult stem cells differentiate into a specific cell within the original tissue. There is a small probability that adult stem cells have the ability to differentiate horizontally. Due to the similar advantages of convenient sampling, adult stem cells have a wide range of applications and can be used in the treatment of skin injuries or diseases, brain injuries or diseases, heart injuries or diseases, etc. [3]

3.3. Molecular biological characteristics of stem cells

Stem cells have the potential for multidirectional differentiation. Stem cells have the ability to differentiate into any cell, forming an organ or tissue. Stem cells also have the function of self-replication. When stem cells have the ability to self-renew in vivo, they exhibit the ability to proliferate, differentiate, and form all tissue cells while maintaining their own number. In vitro, they exhibit clonal growth. Stem cells have a high proliferation capacity both in vivo and in vitro, which can increase the number of stem cells. Stem cells have low immunogenicity, which refers to their ability not to induce an immune response. Low immune performance can prevent the production of immune antibodies to attack stem cells. That is to say, if there is low immunogenicity, when stem cells enter the body, they will not be attacked by the immune system and will not undergo rejection reactions. [4] Currently, bone marrow mesenchymal stem cells (MSCs) have been extensively studied in clinical and scientific

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research because of their ability to differentiate into multiple embryonic layers and their potential applications in cell and gene therapy. Recent research results indicate that MSCs can differentiate into neuroid cells both in vivo and in vitro. When induced by brain-derived neurotrophic factor, basal fibroblast growth factor, or co-cultured with brain tissue cells, MSCs can differentiate into cells with neuronal and glial cell markers. MSCs are a mixed cell population with no typical morphological characteristics. It is impossible to determine the size and presence of MSCs by studying their cell size and particles through optical microscopy morphology and flow cytometry. Similarly, there is no single known surface marker for MSCs at protein expression level. Immunohistochemical staining and flow cytometry studies have shown that MSCs exhibit positive reactions to some antibodies such as SH2, SH3, CD29, CD44, CD71, CD90, CD120a, and CD124. Therefore, at present, the above antibodies are generally used to identify amplified MSCs.

4. Stem cell therapy for Alzheimer's disease

Until now, conventional drug therapy has been almost ineffective in treating moderate to severe Alzheimer's disease. However, the demand for clinical treatment is increasing year by year. In recent years, stem cell replacement therapy has attracted attention, and experiments using stem cells to treat Alzheimer's disease are widely carried out. Currently, the main method of using stem cells is to repair or implant nerve cells to restore the original circuit of the neural system. Currently, there are two methods of treatment. One is through endogenous pathways, which induce the differentiation of stem cells in the body, enabling the recovery of damaged neural stem cells in the central nervous system. The exogenous pathway is to implant NSCs into the body to replace or promote repair of neural stem cells in the body.[5]

4.1. NSCs

Neural stem cells are a type of stem cell that can differentiate into neurons. Neural stem cells can differentiate into three types of cells, including neurons, astrocytes, and oligodendrocytes. This type of cell has the ability to differentiate and regenerate, and has a high potential for differentiation.[5]

In recent years, there have been several reports of stem cell therapy for animal models of AD, mainly conducting preclinical studies. These experiments confirm that stem cell therapy for animal models of AD is safe and effective. Most experiments used transgenic models. Researchers used methods such as stereotactic, intraventricular injection, nasal drip, or intravenous injection to transplant neural stem cells or stem cells from umbilical cord, cord blood, and bone marrow into AD model mice in vivo. Research has confirmed that stem cells mainly secrete various neurotrophic factors; promote endogenous nerve regeneration; reduce inflammation in the nervous system; repair microvasculature to improve memory and cognitive function in AD animal models.

At present, transplantation of NSCs can have a certain recovery effect on brain function of patients with senile dementia. NSCs have been transplanted into patients before, and they are both safe and effective. The differentiation process of NSCs is similar to the type of functional neurons. A more effective method is direct NSC transplantation, which can effectively reduce tau phosphorylation levels after NSC transplantation, but the underlying mechanism is still unclear. As dementia progresses in older adults, neuroenzymes and degradation enzymes produced by NSCs can effectively prevent cognitive decline. Compared to previous treatment methods, this transplantation method can restore damaged neurons or allow neurons to regenerate, and stem cell transplantation into the brain can stimulate NSCs, providing protection. Instead of attacking the malignant cells. There are significant difficulties in obtaining the number of embryonic cells needed at once technically. There are also important issues from other perspectives. Because this treatment is a new approach. Moreover, the reasons for the differentiation of NSCs at this stage are not yet clear, and the control technology for NSCs is also immature. At present, the treatment plan for Alzheimer's disease is still in the experimental stage, and there is no cytokine that can differentiate all NSCs into the nerve cells needed for treatment in the body. [5] In addition, the majority of patients are older, and there are significant risks associated with surgical procedures. [6] Nutrient factors that can effectively promote the proliferation of NSCs in vitro

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experiments. However, there are also many problems with drugs, such as their uncontrollable effects on other tissues in the body. There are many problems that need to be solved. But with the development of medicine and research on different drugs, perhaps other methods will be found in the future to treat dementia. [6]

4.2. Endogenous MSCs

Exosomes are the smallest known exocrine vesicles. Extracellular vesicles can act as carriers to transport mRNA and miRNA from source cells to distant receptor cells. MSCs have the potential for regeneration and repair of extracellular vesicles. [7]

MSCs have a rich source and many types of MSCs, such as BMCs, are a relatively effective treatment method. In research on Alzheimer's disease, the use of MSCs has improved the memory decline of mice; The function of microglia in the brain has also been restored. And the extracellular vesicles secreted by MSCs can alleviate the condition of AD, and MSCs have regenerative function. However, although these studies are based on the conclusions of mice and other animals, MSCs are indeed an effective treatment for improving the condition of AD. Different animal experiments have shown that MSCs derived from bone marrow, umbilical cord, fat, amniotic membrane, and other sources have a certain improvement effect on animal models of senile dementia. Moreover, due to the complex causes of dementia in the elderly, it is difficult for animal models to simulate the real appearance of dementia in the brain. Therefore, the use of MSCs still has a long way to go, and further research and exploration are needed for drugs to treat dementia in the elderly. [6]

5. Discussion

In the past decade, with the development of neuroscience, there has been significant progress in people's understanding of dementia and Alzheimer's disease, with many new developments and understandings in both neurobiology and genetics. However, there is currently no effective method for the treatment of elderly dementia. With the development of stem cell technology this year, it has become possible to reduce the social and individual costs of treating elderly dementia through stem cell therapy. At present, NSC transplantation has achieved encouraging results in the treatment of AD, but it is only in the animal experimental stage, and NSC transplantation has not yet been implemented in the treatment of AD patients. To further promote clinical treatment, there is still a lot of work that urgently needs to be solved: there is currently no unified standard for NSC transplantation method, time, and number of transplanted cells, and only animal research data is available; The microenvironment can affect the differentiation of NSCs, and different stages of the differentiation process require different differentiation factors. The same differentiation factor requires different concentrations at different stages. There is still a lot of work to be done in the clinical transformation of stem cell application to the treatment of elderly dementia in the future, and further refinement is needed in preclinical research, as well as further research on related processes and mechanisms.

6. Conclusion

Although stem cells have made great progress in the treatment of Alzheimer's disease and have gradually attracted people's attention as a potential treatment for AD, the research of neural stem cells in the treatment of Alzheimer's disease has not been specifically applied in clinical research, and there is still a lot of work to be further applied to the treatment of Alzheimer's disease. There are still many questions that need to be investigated in basic and clinical research, such as why endogenous nerve stem cells are only present in certain regions; The best choice of the transplant source of the stem cell of God, these problems need to be solved in one step. Although there are many difficulties, many studies have successfully applied dry cell therapy to the treatment of AD. It is believed that with the in-depth study of stem cell biology, the treatment of AD by dry cell therapy will also make rapid progress, which will certainly bring more hope for the cell biology therapy of AD.

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