Mechanism of Stem Cell Transplantation in the Treatment of Nervous System Diseases

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Abstract: Nervous system diseases are usually accompanied by neurological impairment or cognitive impairment, such as brain injury, Parkinson's syndrome, etc., which are difficult to treat by means of drug therapy. On the other hand, due to the fragile and mysterious nature of the nervous system, many neurological diseases that are difficult to diagnose are produced in the process of continuous development of human society. Stem cells that maintain the ability to divide and differentiate and regenerate and replenish organs in the body have become an important field of medical research. The special ability of stem cells enables them to be applied to various neurological diseases through transplantation techniques. In this paper, based on the research of different researchers on stem cell transplantation for the treatment of nervous system diseases, the corresponding mechanisms in the process of stem cell transplantation are summarized.

The human nervous system is the system that plays a leading role in the regulation of physiological and functional activities in the body. It mainly includes two kinds of nerve cells, neuron and glial cells, which have been regarded by the medical community as a permanent cell lacking regeneration. Therefore, medical research in the past believes that damage to the nervous system causes a large number of nerve cell deletions, and it is difficult to recover the damaged function because it cannot produce new cells for replacement. However, with the discovery and development of stem cells called "universal cells", new breakthroughs have been made in the treatment of human nervous system diseases. Because stem cells are part of the original cells retained during the development of the human body, they have the characteristics of self-replication and continuous proliferation, and can be differentiated into a variety of cells under certain conditions. This characteristic of stem cells changes the perception that nerve cells cannot be regenerated in the past studies, and brings hope to the treatment of human neurological diseases.

1. Theoretical study on stem cell transplantation therapy

Cells that exist in the body to maintain division and differentiation, and that can regenerate and replenish organs and tissues in the body are called stem cells. The research on stem cells was continuously awarded as the annual major scientific progress by the US Science magazine in 1998 and 1999, and was included in one of the six hot technology research fields in 2001. Because of the self-renewal and multi-directional differentiation of stem cells, it has a very wide application prospect, such as application in tissue engineering, drug screening and clinical cell transplantation for the treatment of diabetes, blood diseases, neurodegenerative diseases, etc. .

Stem cells were originally discovered in studies in mice because many of the cutting-edge medical research is carried out in mice that are also mammalian. In 1960, TILL and Ernest McCulloch, researchers at the Ontario Cancer Institute in Canada, observed an abnormality in cell colonies when studying the effects of radiation on mice, and discovered the characteristics of self-renewing cells and published them. The existence of stem cells was confirmed by subsequent scientists' research, and hematopoietic stem cells became the first stem cells to be discovered. The research by Till and McCulloch laid the foundation for all stem cell research conducted today.

Since the discovery of stem cells with self-replication and continuous proliferation, many

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scientists in the world have started its application research. In recent years, scientists from all over the world have made great progress in the clinical application of stem cells. A large number of studies have shown that stem cells can be used to treat diseases such as diabetes, stroke, heart disease, Alzheimer's disease, and Parkinson's syndrome. Scientists at the Israel Institute of Technology have developed human heart tissue from embryonic stem cells and can naturally behave and have electrophysiological properties and mechanical properties of newborn heart tissue. British scientists use bone marrow stem cells to develop kidney tissue that can be used to repair damaged kidneys. Swedish scientist Biorklund and colleagues transplanted the isolated neural stem cells into the brain of patients to treat Parkinson's disease. According to the postoperative follow-up observation, the transplanted nerve cells are still alive and produce dopamine to cause the corresponding symptoms. Significant improvement. Ramiya, a professor at the University of Florida, and colleagues found that transplanted diabetic mice can control blood sugar better by transplanting islet stem cells. These studies on stem cells have proven that stem cells have good prospects for the treatment of medical diseases and have created many opportunities for biomedical research.

2. Overview of research on neurological diseases

Nervous system diseases are diseases that occur in the central nervous system, the peripheral nervous system, and the autonomic nervous system, and are mainly manifested by sensory, motor, consciousness, and autonomic dysfunction. There are many kinds of causes that are likely to cause nervous system diseases. However, the etiology of many neurological diseases remains unclear until now. Common causes are infection, poisoning, genetic defects, nutritional disorders, immune damage, and metabolic disorders. Nervous system diseases mainly include cerebral palsy, Parkinson's syndrome, cerebral infarction, migraine headache, neurological deficit, etc. Neurological deficits caused by nervous system diseases and severe cognitive dysfunction are difficult points for clinical treatment, and neurological diseases The high rate of death and disability is a serious threat to people's health and life.

For the current application of neurological diseases, drug therapy is widely used, and some diseases are accompanied by partial psychological counseling. Parkinson's syndrome is a chronic central nervous system degenerative disease. Common symptoms include muscle stiffness, slow movement, and impaired posture reflex. The cause of the disease is disorder of the system caused by dopamine dysfunction, as shown in Figure 1. In the course of drug treatment, Parkinson's syndrome is relieved by promoting the release of dopamine, supplementing the dopaminergic transmitter, and inhibiting the release of acetylcholine. However, long-term medication can cause relatively large damage to the human body, such as blemishes, lack of energy, and insomnia.

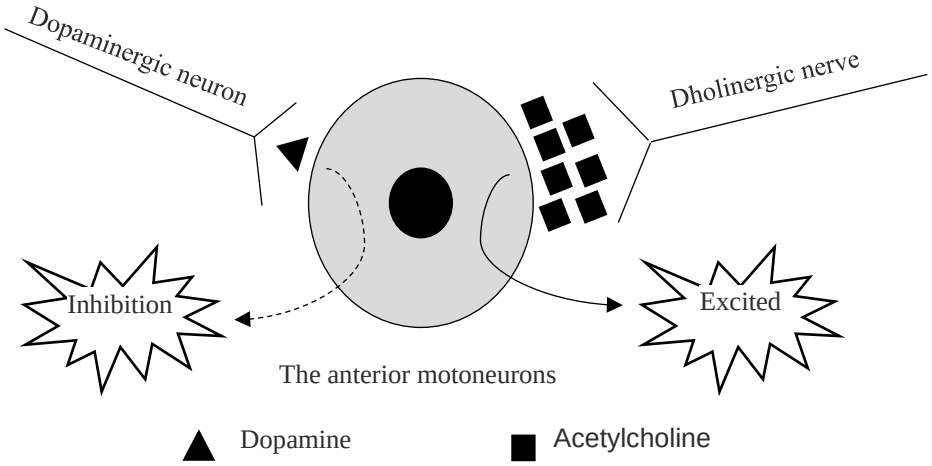

Figure 1 Parkinson's pathology

Some sleep disorders are also neurological diseases. There are two kinds of treatments for sleep

disorders: psychotherapy and drug therapy. Psychotherapy can help to alleviate people's insomnia, but some insomnia is accompanied by other diseases, so it is necessary to use drugs. Comprehensive Treatment. However, excessive dependence on drugs may cause symptoms such as memory loss, dizziness and fatigue, and drug dependence may occur in continuous medication. The medical treatment for other kinds of neurological diseases is also accompanied by the side effects of various medications, and the treatment of some nervous system diseases can only relieve the disease and cannot effectively eradicate the pathogenesis of the disease.

Through long-term experimental and clinical studies, it is found that the massive loss of neurons is an important pathological feature of many types of neurodegenerative diseases. Transplantation of neural stem cells for the treatment of neurodegenerative diseases has the advantage that conventional drugs and surgical treatments do not have the advantages, that is, transplanted stem cell proliferation. The newly produced neural cells can be integrated into the existing neural circuit and release various types of molecules to improve or even cure neurodegenerative diseases. The core of treatment is to improve from the root of the disease, the effect will be more obvious.

3. Stem cell transplantation for the treatment of neurological diseases

3.1 Stem cell transplantation for brain damage

Human brain damage diseases are a serious threat to human survival and health. Common brain damages are mainly ischemic brain damage and traumatic brain damage. Neuronal and oligodendrocytes are the most susceptible to ischemic brain damage because these two parts are sensitive to both cerebral ischemia and hypoxia. Traumatic brain injury is a change in the brain function that occurs after the brain is externally affected, resulting in pathological changes in brain damage. The existing conventional treatment is mainly supportive treatment, and can not directly block the occurrence of brain damage or help the direct regeneration of brain tissue. Scientists use animal experiments to study the therapeutic mechanism of cell transplantation brain injury. Some research shows that brain damage produces some secondary cytokines or molecular substances, which provide an environment for neural stem cells to survive. When neural stem cells are transplanted to the damaged site, they can grow, differentiate and embed into damaged brain tissue for repair. Avidsson et al. showed that only 0.2% of newborn neurons replaced neurons in the injured area, so the differentiation of endogenous neural stem cells by neural stem cell transplantation can effectively improve the repair effect of brain damage areas. Bao et al. experimented with experimental mice and found that transplantation of neural stem cells can promote the transformation of endogenous neural stem cells into nerve cells and promote the production of nerves. Han's research indicates that transplanted neural stem cells can secrete a variety of cytokines and trophic factors to repair nerve cells in areas of brain injury. Hardy et al. found that cytokines and trophic factors secreted by transplanted neurons can also stimulate damaged nerve tissue for self-repair.

3.2 Stem cell transplantation for Parkinson's disease

Parkinson's syndrome is a neurodegenerative disease characterized by a variety of factors that cause damage to the brain's substantia nigra and striatal cells, resulting in reduced dopamine transmitter secretion. Existing treatments can only compensate for the various defects caused by degenerated cells, and cannot solve the problem fundamentally to restore denatured cells. In the past, researchers have implanted cells capable of secreting dopamine into the human body, replacing the function of neuronal loss. Among them, the better effect is the transplantation of substantia nigra cells in the embryo, but it is difficult to carry out a wide range due to the limited source of embryonic cells. Promotion, while other cell sources are difficult to function effectively. Neural stem cells can replace the mechanistic properties of damaged nerve cells, allowing scientists and patients to see new and effective means of treating Parkinson's disease. Existing research indicates that neural stem cells can be induced into dopaminergic neurons to compensate for lesions that improve the imbalance of dopamine secretion in the body. Arnhold et al. implanted neural stem

cells derived from embryonic stem cells into the striatum of experimental mice. After 2-4 weeks, some cells differentiated into neurons and integrated into surrounding nerve tissues. Park et al. transferred the gene of the neurotrophic factor into the mesenchymal stem cells of male rats, and then implanted the cells into healthy female mice. After 8 weeks, the substantia nigra neurons in the experimental group were observed. Higher than the control group, it indicates that the mesenchymal stem cells modified by genetic technology can survive in the experiment and activate the expression of the gene product to achieve the disease treatment. Svendsen et al. found through comparative experiments that genetic technology can be used to properly control stem cells, and then the cells can be implanted into the corresponding parts to produce the specific substances needed, and can be well fused with the surrounding host cells. These experimental studies have confirmed the culture of specific neuronal cells to replace degenerative brain substantia nigra and striatal cells, so that dopamine transmitter secretion is normal, and the possibility of treatment of Parkinson's syndrome is fundamentally completed.

3.3 Stem cell transplantation for the treatment of hereditary nervous system diseases

Many neurological genetic diseases are caused by genetic mutations, and genetic coding abnormalities cause lesions in the corresponding positions of the body. In the process of the development of genetic technology, the genetic genes of some hereditary neurological diseases have been clearly studied. For this part of the disease, the neural stem cells can be genetically modified first, and then the modified neural stem cells can be transplanted to The gene-stained cell site fuses the neural stem cells carrying the gene of interest to the host cells of the lesion, and encodes the normal protein required by the normal body, thereby treating a hereditary disease that is difficult to treat in the conventional sense. HD is an intractable and fatal autosomal dominant genetic disease. Hersch et al. used neural stem cells to treat patients with HD. After 18 months, they died unfortunately. The autopsy and histology showed no immunological rejection at the cell transplantation site. These transplanted cells replace the damaged neurons to reconstruct the connections between the neurons, so that there is no HD-specific neuronal protein accumulation in the lesion. Tamaki transplanted normal neural stem cells into the lesions of experimental mice lacking the PPT1 gene. Through continuous observation, it was found that the lesions of the rats were able to secrete PPT1, and the corresponding lesion symptoms were also improved. The clinical application of researchers such as Hersch and the experiments of Tamaki have proved that the use of decorated neural stem cells to repair and replace the cells in the genetic lesions has high research value and practical value.

4. Summary of the mechanism of stem cell transplantation for the treatment of neurological diseases

In past biological studies, neural stem cells that can be used to treat neurological diseases have the potential for self-renewal and multi-directional differentiation, overall plasticity, migration ability, and low immunogenicity. These biological characteristics of neural stem cells enable them to be transplanted. After that, the transformation and fusion with other cells are well done. Through the analysis of the results of various disease cases, we can find that the main mechanisms of stem cell treatment of neurological diseases are as follows: 1. Replacement. The newly acquired neural stem cells are directly transplanted to the corresponding lesions, so that the transplanted neural stem cells are differentiated according to the needs, and the damaged parts are effectively repaired. 2. Activation promotion. Neural stem cells transplanted to the lesion site can be differentiated into functional cells such as neurons and glial cells, which can secrete trophic factors to repair damaged parts and promote their regeneration. Or use appropriate inducing factors to promote differentiation of neural stem cells in the body, and also increase the therapeutic effect of transplanted neural stem cells. 3. Gene therapy. The use of genetic means to introduce a therapeutic target gene into neural stem cells, and then transplant the neural stem cells carrying the gene of interest to a location where the body's lesions exert a therapeutic effect, which can be used to repair spinal cord injury or other hereditary nervous system diseases. The above three mechanisms of stem cell transplantation for the

treatment of neurological diseases do not exist alone in actual application, but need to be rationally selected according to the degree of research and the specific conditions of the pathology.

5. Conclusion

The emergence and development of stem cell transplantation technology has brought hope for cure for many patients with incurable diseases. In recent years, medical scholars' research on stem cell transplantation technology has provided sufficient theoretical and technical support for the clinical application of stem cell transplantation technology. Diversified therapeutic mechanisms have made medical scholars have more choices in the face of a wide range of diseases. However, at this stage, people's research and understanding of stem cell transplantation technology is not so deep, and there is no clear recognition of its clinical application effects in various diseases, and its differential performance in individual human individuals has not been clearly defined. The results of the study, therefore, it is a reasonable process to study the situation of other diseases based on a clearer treatment mechanism. At the same time, the corresponding medical ethics should also be observed in the research process, and new medical ethics should be developed on the new medical technology.

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