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Research Progress of Neural Stem Cell Transplantation Combined with Biological Scaffold in the Treatment of Spinal Cord Injury

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Abstract: SCI is a kind of nerve injury disease caused by direct or indirect factors. The result is the damage of motor mechanism and the partial or total loss of sensory function below the injury site. The researchers found that planting neural stem cells in a biological scaffold and then colonizing the site of SCI greatly improved the survival rate of stem cells and promoted the repair of injury. However, different biomaterials have different differences. In order to better promote the recovery of function after SCI, it is important to select an appropriate scaffold combination.

Keywords: Neural Stem Cell; Biological Scaffold; Spinal Cord Injury

Introduction

Due to the low cure rate and high disability rate of SCI, exploring an effective treatment method to improve patients' function is the current research direction.[1,2] A large number of experimental studies have been carried out using neural stem cell transplantation. The mechanism of neural stem cell transplantation is mainly that neural tissue can differentiate into normal direction through stem cells. It has unique advantages in axon growth, synaptic remodeling and myelin formation. In view of the local inhibition of microenvironment and the lack of neurotrophic factors, it promotes the synthesis and secretion of local nutrients and improves the microenvironment.[3,4,5,6] However, the implantation of exogenous stem cells will lead to transplantation rejection, and the survival rate of stem cells is very low. The regeneration direction of axons cannot grow in the normal direction, so it is difficult to establish an effective synaptic connection with the host neurons, and the regenerated axons are difficult to grow outward from the transplantation area beyond the inhibition of glial scar. [7]

With the rise of tissue structure engineering, researchers found that stem cell transplantation combined with biomaterials has a certain prospect in the treatment of spinal cord injury. They found that biomaterials and stem cells have good biocompatibility and good degradation performance, which can improve the survival rate of stem cells, colonization and differentiation of transplanted cells to a certain extent, and separate the implanted stem cells from the host tissue, Thus, it provides an independent microenvironment for stem cell differentiation and proliferation, which is conducive to the release of exogenous cytokines without affecting the activity of endogenous factors. It can better bridge the gap of lesions and provide a bridge across glial scar for transplanted stem cell colonization.[8,9,10,11]

1. Neural stem cells

Neural stem cells are derived from neural tissue. They are one of the cells with the highest degree of differentiation and the strongest regeneration ability among seed cells. They can differentiate into neurons, astrocytes and oligodendrocytes, and play a vital role in the regeneration of the nervous system.[12, 13] studies have found that neural stem cells have the ability of unlimited proliferation and the potential of multi-directional differentiation. After transplantation, they can play a corresponding role by secreting corresponding nutritional factors instead of the cells at the injury, so as to promote the growth of neurons in the required direction and promote axon regeneration and neural tissue repair.[14]

2. Disadvantages of neural stem cell transplantation

The study found that the mechanisms related to axon regeneration are extremely complex, the microenvironment after spinal cord injury is relatively complex, and it is difficult for stem cell transplantation to create a good microenvironment. In the study of stem cell transplantation, it was also found that some of them have the risk of tumorigenesis caused by immune rejection and ectopic diffusion. [15] Moreover, cell transplantation alone has the disadvantages of low cell survival rate and uncontrollable differentiation direction.[16]

At present, further research should be done to find more effective application methods for different SCI patients in different periods, so as to provide effective personalized treatment schemes for the rehabilitation of different SCI patients.

3. Types and characteristics of biological scaffolds

At present, the research of biological scaffold materials mainly focuses on the different structures of scaffolds. Natural scaffolds have suitable biodegradability, strong morphological remodeling and low toxicity to the body, but the mechanical properties of natural scaffolds are relatively poor, which can not provide sufficient mechanical support for cell climbing, and the degradation speed is fast; Synthetic scaffolds have good mechanical properties and can be synthesized easily, but their cell compatibility is poor. The acidic environment formed in the degradation process shows certain restrictions and damage to cell survival and growth. Composite scaffolds are composed of natural materials and synthetic materials, which have common advantages, but the cost is expensive. [17,18,19,20,21]

4. Treatment of SCI based on neural stem cell transplantation combined with biological scaffold

4.1 Neural stem cell transplantation combined with biological scaffold

Cao Zongrui et al. [22] observed that the collagen / heparin sulfate scaffold has good biological performance and stable structure. After planting the neural stem cells in the collagen / heparin sulfate scaffold and filling it in the spinal cord injury, they found that it showed a microenvironment suitable for regeneration, which can partially re-establish the neuronal pathway at the spinal cord injury of rats, promote the regeneration of nerve fibers at the stage, and partially improve the function of rats. Wang et al. [23] co cultured neural stem cells with chitosan gelatin scaffolds and found that neural stem cells can better adhere and grow on chitosan gelatin scaffolds and differentiate towards neurons and astrocytes, which slightly alleviates the recovery of limbs after spinal cord injury. Qi Guodong et al. [24] used stably subcultured neural stem cells and SCAs with removed cells and intact matrix to construct spinal cord tissue engineering. By observing the adhesion, growth and differentiation of neural stem cells on the scaffold, it was found that the adhesion state of neural stem cells in the scaffold combination group was better and could gradually differentiate into neurons and glial cells with plump cell bodies and clear axons on the scaffold, Stable connections can be established between differentiated neuronal axons, and the formed axons can also go deep into the pores of scaffold matrix.

4.2 Combined biological scaffolds based on neural stem cells from various sources and derivatives

It was found that after the transplantation of 3D printing scaffolds combined with UC derived iPSCs NSCs in rats, it was observed that the motor and sensory functions of rats recovered, and the spinal nerve fibers of the damaged segments grew well under electron microscope. [25] Zhou et al. [26] filled the injury area of rats with polycaprolactone scaffolds prepared by the combination of xuewang's cells and neural stem cells derived from induced pluripotent stem cells. The observation results showed that neural stem cells grew better on the scaffolds than those in the simple stem cell transplantation group, and this combination significantly reduced the spatial range of the lesion cavity and promoted the improvement of the motor system function of rats' lower limbs.

In a word, the effect of scaffold combined with stem cell transplantation group is better than that of simple transplantation group in all aspects of SCI in most cases. At present, the research direction of combined transplantation is relatively diversified and there are great differences. More suitable combination methods need to be further explored in the future.

5. Summary and Prospect

The low cure rate and high disability rate of spinal cord injury have brought a heavy economic burden. The survival rate of simple stem cell transplantation is very low. Moreover, due to the continuous flow of cerebrospinal fluid in the spinal cord, it is difficult for cells to colonize the injury site, which not only reduces the therapeutic effect of stem cells, but also is likely to cause the risk of ectopic proliferation, It is also a difficult problem to solve at present that it is unable to differentiate directionally and difficult to cross glial scar.Some progress has been made in the treatment of spinal cord with biological scaffolds combined with stem cell transplantation. It has significantly improved the survival rate of stem cells, adjusted the microenvironment, supported and filled the lesion cavity to reduce the cavity in the injury area, induced its directional growth, slowly released the secreted neurotrophic factors, and is more conducive to crossing the glial scar, Promote the recovery of motor function after injury. Selecting reasonable scaffolds and the combination method that is easier to repair the injury can better inhibit cell apoptosis, provide connection for the axons at the damaged site, enable the seed cells to fully release and proliferate, and provide a suitable environment for promoting the recovery of spinal cord nerve function. However, different biomaterials have different strength and structure, and the ability of immune rejection, mechanical strength to support tissue growth and biodegradability after implantation need to be fully considered. In the future research on the combination mode, it is necessary to formulate the corresponding combination treatment scheme according to the characteristics of each stage of spinal cord injury, and choose the implantation mode with the least injury and better treatment effect is also the focus of the combination treatment scheme in the future.

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