Commentary

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A Commentary on Advances in Neural Stem Cell Therapy for Spinal Cord Injury

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Abstract

Spinal cord injury represents a severe form of neurological damage and neural stem cells have emerged as one of the most promising therapeutic options for repairing such injuries due to their remarkable capacity for self-renewal and differentiation into both neurons and glial cells. In this article, we aim to provide an in-depth review on the utilization of transplanted neural stem cells as well as endogenous neural stem cells in the treatment of spinal cord injuries. Additionally, we will address the challenges encountered in implementing neural stem cell therapy for these injuries while also discussing future directions that hold potential for further advancements in this field.

Keywords: Spinal cord injury; Neural stem cells; Endogenous neural stem cells

Introduction

Spinal Cord Injury (SCI) is a profound neurological disorder. Epidemiological studies conducted by the World Health Organization (WHO) and Western countries have revealed that the global incidence rate of SCI ranges from 10 to 40 cases per million individuals [1]. In SCI, primary injury refers to direct mechanical injury to the spinal cord, leading to irreversible neuronal death. Consequently, secondary damage caused by inflammatory reactions, local ischemia, and oxidative stress further exacerbates the consequences of primary injury. Neuronal death ultimately results in enduring functional impairments. Neural Stem Cells (NSCs), possessing self-renewal capacity and differentiation potential into neurons and glial cells, present an ideal strategy for replenishing neuronal populations following spinal cord injury. Herein, we will comprehensively review two aspects: exogenous transplantation of neural stem cells and regulation of endogenous neural stem cells.

Neural Stem Cells (NSCs) are multipotent stem cells with self-renewal capabilities with the ability to differentiate into neurons and glial cells [2]. They are widely employed as seed cells for exogenous cell transplantation in spinal cord injury research. The underlying mechanisms through which exogenous neural stem cells facilitate spinal cord injury repair primarily involve differentiation and paracrine secretion. In terms of differentiation, transplanted exogenous neural stem cells actively contribute to remyelination by differentiating into oligodendrocytes, establish crucial connections by differentiating into neurons, and form novel synaptic connections with host neurons, thereby effectively promoting the recovery process of spinal cord injuries [3,4]. However, NSC transplantation often leads to a reduced survival rate, primarily attributed to the special harmful microenvironment that follows SCI or the poor retention of transplanted cells at the injury site due to cerebrospinal fluid flow ability. Consequently, there has been a growing body of research focused on utilizing hydrogel or scaffold-loaded neural stem cells as transplant materials in recent years. The incorporation of hydrogels or scaffolds not only serves to shield transplanted cells from inhibitory microenvironments but also exerts control over their proliferation and differentiation by means of growth factors or employing stimuli such as sound, light or electricity.

Since the discovery of endogenous neural stem cells, research in this field has been continuously evolving with varying conclusions. In 2010, ependymal cells were extracted following SCI and found to be capable of being cultured into neurospheres *in vitro* with the ability to differentiate into neurons and glial cells [5]. It is widely accepted that Nestin-positive ependymal cells located near the central canal serve as a source for endogenous neural stem/progenitor-like cell populations within the spinal cord. However, a study conducted in 2017 revealed that ependymal cells are unable to differentiate into glial progenitors following SCI [6]. Interestingly, in 2022, Dai found in their study that GFAP-positive cells are the major cell type expressing Nestin and are more inclined to differentiate into astrocytes and participate in the formation of glial scars [7]. These discrepancies can be ascribed to divergences in modeling methodologies and research approaches, while also stimulating further investigation into the genesis of ENSC within the nervous systems. Currently, the primary approaches for regulating endogenous Neural Stem Cells (NSCs) involve drug intervention, gene therapy, exosomes and tissue scaffold transplantation. The

main objective is to modulate their proliferation from internal sources in order to obtain sufficient quantities required for repairing damaged tissues while guiding their differentiation towards neurons or oligodendrocytes. This process ultimately facilitates recovery from SCI.

The therapeutic approach aimed at neural stem cells has unparalleled hope for the treatment of spinal cord injuries, with even some preclinical trials demonstrating promising therapeutic outcomes. However, the ethical challenges associated with employing embryonic-derived neural stem cells hinder their widespread application in clinical settings. Hence, it is imperative to generate a safe and reliable induced neural stem cell line for exogenous transplantation therapy in spinal cord injury. Simultaneously, the sources, activation mode, and differentiation mechanisms of endogenous neural stem cells have not been fully elucidated. It is necessary to address these issues and find a method to regulate the activation and differentiation of neural stem cells for the endogenous repair of spinal cord injuries.

Conclusion

Neural stem cells possess the remarkable abilities of self-renewal and differentiation into both neurons and glial cells, offering promising prospects for functional recovery following spinal cord injury. By precisely regulating the differentiation of NSC promoting axonal regeneration and remyelination through their neuronal and oligodendrocytic differentiation can effectively facilitate the repair of intricate neural circuits. The continuous advancement in research on NSCs studies will contribute to further enhancing our understanding of SCI repair while fostering innovative strategies, ultimately enhancing the quality of life for individuals affected by SCI.

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Conflict of Interest

None

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