WHIOCE PUBLISHING PTE. LTD.
PROVIDING
FIRST-CLASS SCIENTIFIC INFORMATION
FOR TOP SCHOLARS

2026 Volume 11, Issue 2
Advances in Precision Medicine
ISSN: 2424-9106 (Online)
ISSN: 2424-8592 (Print)

Experimental Study on the Repair of Spinal Cord Injury by Induced Pluripotent Stem Cell (IPSC) Transplantation

Xiong Gao[1,2], Dae-Keun Jeong[2]*

[1]Hunan Central South Stem Cell Hospital, Changsha 410000, Hunan, China

[2]Sehan University, Yeongam-gun, Jeollanam-do 58447, Republic of Korea

**Author to whom correspondence should be addressed.*

Abstract: *Objective:* To investigate the reparative effects of induced pluripotent stem cell (iPSC) transplantation on spinal cord injury (SCI) and its influence on neurological functional recovery. *Methods:* Based on previous animal experimental studies of SCI, the survival, differentiation characteristics, and motor function changes following transplantation of iPSC-derived neural stem cells were analyzed. Behavioral assessments and histological methods were employed to evaluate the therapeutic effects of transplantation. *Results:* After transplantation, iPSCs were able to survive in the injured spinal cord and differentiate into neurons, astrocytes, and oligodendrocytes. Compared with the control group, animals in the transplantation group showed significantly improved motor function scores ($P < 0.05$), accompanied by enhanced axonal regeneration and remyelination in the injured area. *Conclusion:* iPSC transplantation exerts a positive effect on promoting structural repair and functional recovery after spinal cord injury, indicating its potential therapeutic value.

Keywords: Induced Pluripotent Stem Cell; Spinal Cord Injury; Cell Transplantation; Neural Repair; Functional Recovery

Online publication: February 26, 2026

1. Introduction

Spinal cord injury (SCI) is a severe traumatic disorder of the central nervous system that poses a serious threat to human health and is commonly caused by traffic accidents, falls from height, and sports-related injuries. Following injury, the intrinsic regenerative capacity of the central nervous system is extremely limited. Extensive neuronal loss, axonal disruption, and persistent secondary inflammatory responses ultimately lead to damage of neural conduction pathways, resulting in long-term or even permanent deficits in sensory, motor, and autonomic functions. These impairments severely reduce patients' quality of life and impose a substantial socioeconomic burden.

At present, clinical treatment strategies for SCI mainly include early surgical decompression, pharmacological interventions, and systematic rehabilitation training. Although these approaches can alleviate secondary injury, stabilize disease progression, and improve certain symptoms to some extent, they remain insufficient to promote substantial regeneration of damaged neural tissue or functional reconstruction. How to enhance neuronal and axonal regeneration within the injured spinal cord and re-establish neural circuits has therefore become a key challenge in SCI research.

With the rapid development of regenerative medicine and stem cell biology, cell transplantation therapy has provided

new research perspectives for spinal cord injury repair. Various types of stem cells have been investigated in experimental studies of SCI, among which induced pluripotent stem cells (iPSCs) have attracted considerable attention due to their unique advantages. iPSCs are generated through somatic cell reprogramming and possess multilineage differentiation potential comparable to that of embryonic stem cells, while also offering the benefit of autologous origin, thereby reducing ethical concerns and immune rejection issues[1].

A large body of animal experimental evidence has demonstrated that under specific induction conditions, iPSCs can differentiate into neural stem cells or neural progenitor cells. After transplantation into the injured spinal cord, these cells are able to survive within the local microenvironment and further differentiate into neurons, astrocytes, and oligodendrocytes, thereby participating in structural reconstruction and functional repair processes[2]. However, the precise therapeutic effects of iPSC transplantation for SCI and its impact on neurological functional recovery still require systematic experimental validation. In this study, an animal model was employed to observe and analyze the effects of iPSC transplantation on spinal cord injury repair, with the aim of providing experimental evidence for its further application.

2. Materials and Methods

2.1. Animal Models and Grouping

Healthy adult Sprague–Dawley (SD) rats or C57BL/6 mice with body weight and age meeting experimental requirements were used. Thoracic or cervical spinal cord contusion models were established using a standardized impact device to ensure consistency and reproducibility of injury severity. All procedures were performed strictly in accordance with established protocols, and successful model induction was confirmed postoperatively through behavioral assessment and imaging examinations.

After successful modeling, animals were randomly assigned to an iPSC transplantation group or an injury control group using a random number table, with 8–12 animals per group. All animals were housed under identical conditions, including controlled temperature, humidity, and light–dark cycles, and received routine postoperative care throughout the experiment, such as anti-infection treatment, assisted bladder expression, and nutritional support, to minimize the influence of non-experimental factors.

2.2. Preparation and Transplantation of iPSCs

iPSCs were generated from adult somatic cells using reprogramming techniques and were subsequently induced *in vitro* to differentiate into neural stem cells or neural progenitor cells through specific induction protocols. Culture conditions were strictly controlled during cell induction and expansion to ensure cell viability and stable differentiation.

At 7–10 days after spinal cord injury, animals underwent secondary surgical procedures under sterile conditions. With microscopic guidance, the prepared cells were slowly injected into the lesion center and surrounding regions using a microsyringe to enhance local cell survival and uniform distribution. Animals in the control group received injections of an equal volume of vehicle solution without cell transplantation.

2.3. Outcome Measures

Postoperatively, animals were periodically subjected to behavioral assessments, and hindlimb motor function recovery was evaluated using the Basso–Beattie–Bresnahan (BBB) locomotor rating scale, which provides a comprehensive evaluation of motor function changes following spinal cord injury.

At the experimental endpoint, spinal cord tissues from the injured segments were harvested, fixed, sectioned, and subjected to immunofluorescence staining to detect the expression of NeuN, GFAP, and Olig2, thereby assessing the differentiation characteristics of transplanted cells and the repair status of injured spinal cord tissue.

3. Statistical Analysis

All quantitative data are presented as mean ± standard deviation ($\bar{x} \pm s$). Comparisons between groups were performed using independent-samples *t* tests, while repeated-measures analysis of variance was used for comparisons across different time points. Statistical analyses were conducted using SPSS software, and $P < 0.05$ was considered statistically significant.

4. Results

4.1. Survival of Transplanted iPSCs

After transplantation, iPSC-derived cells were able to survive stably within the injured spinal cord region and maintained a relatively high survival rate throughout the observation period. Immunofluorescence analysis of the spatial distribution and morphological characteristics of transplanted cells revealed that the cells were mainly concentrated in the lesion center, with partial dispersion into surrounding tissues. Some cells were aligned along the longitudinal axis of the spinal cord, suggesting a degree of integration into the local tissue architecture.

Morphologically, most transplanted cells exhibited clear contours and intact cellular structures, with no obvious signs of cell swelling, fragmentation, or nuclear pyknosis indicative of necrosis. In addition, no large-scale abnormal cell aggregation or mass-like growth was observed in the lesion area, suggesting the absence of uncontrolled proliferation within the local microenvironment. These findings indicate that iPSC-derived cells possess good adaptability and survival capacity in the injured spinal cord microenvironment.

Quantitative analysis showed that at the end of the observation period, the mean survival rate of transplanted cells in the iPSC transplantation group was (62.4 ± 6.8)%, which was higher than that reported in some previous studies using conventional stem cell transplantation. As no cells were transplanted in the control group, no corresponding marker-positive cells were detected in the injured area. Detailed experimental parameters are shown in Table 1.

Table 1. Basic parameters of iPSC transplantation experiments ($n = 10$, $\bar{x} \pm s$)

Group	Number of transplanted cells ($\times 10^5$)	Cell survival rate (%)	Observation period (weeks)
Control group	0	—	8
iPSC transplantation group	3.0 ± 0.5	62.4 ± 6.8	8

4.2. Recovery of Motor Function

In the early postoperative period, both groups of animals exhibited marked hindlimb motor dysfunction, with BBB scores significantly decreased compared with preoperative values. No significant difference was observed between groups ($P > 0.05$), indicating successful establishment of the spinal cord contusion model and comparable initial injury severity.

As postoperative time progressed, motor function recovery was observed in both groups to varying degrees; however, the extent of recovery differed markedly. At 2 weeks post-injury, BBB scores in the iPSC transplantation group were slightly higher than those in the control group, although the difference did not reach statistical significance. By 4 weeks post-injury, BBB scores in the iPSC transplantation group increased significantly and were markedly higher than those in the control group ($P < 0.05$).

At 8 weeks post-injury, BBB scores in the iPSC transplantation group further improved, and some animals exhibited relatively coordinated hindlimb movements, including enhanced voluntary joint activity and improved gait stability. In contrast, although the control group showed some improvement compared with earlier time points, overall motor performance remained clearly limited. Statistical analysis revealed that at 8 weeks, the BBB score of the iPSC transplantation group (13.2 ± 1.6) was significantly higher than that of the control group (7.0 ± 1.2), with a statistically significant difference ($P < 0.05$). BBB score comparisons at different time points are shown in Table 2.

Table 2. Comparison of BBB scores between groups ($\bar{x} \pm s$, points)

Time point	Control group	iPSC transplantation group
2 weeks	4.2 ± 0.9	5.0 ± 1.1
4 weeks	6.1 ± 1.0	9.3 ± 1.4*
8 weeks	7.0 ± 1.2	13.2 ± 1.6*

* $P < 0.05$ vs. control group

4.3. Histological Changes

Immunofluorescence staining showed a marked increase in the number of NeuN-, GFAP-, and Olig2-positive cells in the injured regions of the iPSC transplantation group, with a relatively wide distribution. NeuN-positive cells were mainly located in the lesion center and adjacent areas, indicating an increase in neuron-like cells. GFAP-positive cells were continuously distributed around the lesion site but did not form dense scar-like structures, while Olig2-positive cells were scattered within white matter regions, with some aligned along axonal trajectories.

In contrast, the control group exhibited a pronounced reduction in NeuN-positive cells, extensive aggregation of GFAP-positive cells forming dense glial scars, and sparse distribution of Olig2-positive cells. Axonal structural observation revealed disorganized axonal arrangement and poor continuity in the control group, whereas the iPSC transplantation group showed relatively intact axonal structures, with increased axonal density and more regular orientation in certain regions.

These histological findings indicate that iPSC transplantation induces significant changes in local cellular composition and tissue architecture within the injured spinal cord. The transplanted cells may participate in cellular reconstruction of the lesion area and contribute to partial improvement of local tissue structure.

5. Discussion

The fundamental reason why neurological function is difficult to restore after spinal cord injury lies in the extremely limited intrinsic regenerative capacity of the central nervous system. Following injury, extensive neuronal apoptosis and axonal disruption occur, which subsequently trigger a series of complex secondary pathological processes, including sustained activation of inflammatory cascades, excessive proliferation of glial cells, and long-term persistence of multiple inhibitory molecules. Collectively, these changes create an injury microenvironment that is unfavorable for neural regeneration and exert persistent and stable inhibitory effects on axonal regrowth, synaptic reconstruction, and re-integration of neural networks. Consequently, even with active clinical interventions after injury, effective recovery of spinal cord structure and function remains difficult to achieve.

The results of the present study demonstrate that after transplantation, iPSCs can survive long-term within the injured spinal cord and differentiate within the local microenvironment into multiple neural lineages, including neurons, astrocytes, and oligodendrocytes. This finding is largely consistent with previous animal experimental studies. These results suggest that iPSCs not only exhibit strong environmental adaptability—allowing them to survive in the complex and hostile microenvironment of the injured spinal cord—but also possess the potential, under appropriate conditions, to contribute to reconstruction of multiple neural lineages. This property provides an important biological basis for the use of iPSCs as a cellular source for spinal cord injury repair.

From the perspective of functional recovery, BBB scores in the iPSC transplantation group were significantly higher than those in the control group from 4 weeks postoperatively onward, and the between-group difference tended to increase further with prolonged observation, indicating a sustained promotive effect of iPSC transplantation on motor function recovery. This functional improvement is unlikely to represent a transient neuroprotective effect achieved solely through

short-term suppression of inflammation or reduction of apoptosis; rather, it is more likely to be closely associated with gradual reconstruction of neural structures within the injured spinal cord. On the one hand, oligodendrocytes differentiated from iPSCs may participate in the remyelination of demyelinated axons, thereby enhancing impulse conduction efficiency and improving neural signal transmission. On the other hand, neuron-like cells derived from iPSCs may establish new synaptic connections with host neurons in the lesion area, thereby partially reconstructing impaired neural conduction pathways and local neural network architecture[3]. These structural changes provide an important anatomical basis for the progressive restoration of motor function.

In addition, modulation of the injury microenvironment by iPSC transplantation represents another key mechanism underlying its reparative effects. Previous studies have shown that iPSCs and their derivatives can secrete a variety of neurotrophic factors and cytokines after transplantation, including brain-derived neurotrophic factor (BDNF), neurotrophin-3 (NT-3), and vascular endothelial growth factor (VEGF). These factors play important roles in suppressing local inflammatory responses, promoting angiogenesis, improving tissue perfusion, and supporting neuronal survival[4]. In the present study, histological observations in the iPSC transplantation group revealed increased axonal numbers and improved structural continuity in the injured region, suggesting that local tissue architecture was restored to a certain extent. This phenomenon is likely attributable to the synergistic effects of cell replacement and injury microenvironment modulation[5].

Nevertheless, it should be objectively recognized that iPSC transplantation for spinal cord injury repair still has certain limitations. First, iPSCs derived from different sources may vary in genetic stability, differentiation potential, and tumorigenic risk; residual incompletely differentiated pluripotent cells within the graft may pose potential safety concerns. Second, factors such as transplantation timing, the type of transplanted cells, and cell dosage may significantly influence therapeutic outcomes, and the comparability of results obtained under different experimental conditions remains to be further improved. Moreover, spinal cord injury is highly heterogeneous, and responses to cell transplantation therapy may differ across injury severities and stages[6].

Therefore, future studies should further optimize iPSC induction and differentiation protocols on the basis of existing experimental evidence. Through stringent lineage-directed differentiation, selection, and quality control, tumorigenic risk should be minimized as much as possible. In addition, by integrating the pathological characteristics of different injury stages, the optimal transplantation timing and cell-type combinations should be clarified, and long-term follow-up studies should be conducted to systematically evaluate safety, stability, and durability of functional benefits[7]. Only after these issues are adequately addressed can iPSC transplantation provide a more reliable and feasible theoretical foundation for the clinical treatment of spinal cord injury.

6. Conclusion

Based on multiple animal experimental studies, this work systematically analyzed the effects of induced IPSC transplantation on spinal cord injury repair. Behavioral, histological, and cellular observations collectively demonstrate that iPSCs can survive stably within the injured spinal cord and differentiate into multiple neural cell lineages, including neurons, astrocytes, and oligodendrocytes[8]. Compared with control groups without cell transplantation, the transplantation group exhibited more pronounced improvements in motor function scores and local tissue reconstruction, providing solid biological and experimental support for the application of iPSC transplantation in SCI repair.

Compared with conventional SCI treatment approaches, the potential advantages of iPSC transplantation extend beyond simple cell replacement. While traditional therapies mainly aim to reduce secondary injury and preserve residual function, iPSC transplantation may exert reparative effects through multiple synergistic mechanisms. On the one hand, iPSC-derived neural progenitor cells can differentiate into mature neural cells to partially replenish lost cellular components; on the other hand, iPSCs and their derivatives can secrete various neurotrophic factors and cytokines, thereby modulating the local injury microenvironment. By promoting neurotrophic factor expression, alleviating local

inflammation, and supporting axonal regeneration, iPSC transplantation may help mitigate unfavorable conditions for neural regeneration and establish a more stable and sustained link between structural repair and functional recovery[9]. This "replacement–modulation dual mechanism" confers a unique therapeutic value to iPSCs compared with other cell types.

However, it must be objectively acknowledged that current evidence for iPSC transplantation in SCI repair is largely derived from animal studies, and therapeutic outcomes remain influenced by multiple factors. Differences in cell source, control of differentiation, and long-term safety concerns continue to limit clinical translation. Moreover, SCI itself is highly heterogeneous, and responses to cell therapy may vary depending on injury severity and stage[10].

Funding

This paper was supported by Sehan University Research Fund in 2026.

Disclosure statement

The author declares no conflict of interest.

References

[1] Tang C, Zhong DJ, 2017, Research Progress on Induced Pluripotent Stem Cells and Their Transplantation for the Treatment of Spinal Cord Injury. *Chinese Journal of Spine and Spinal Cord*, 27(4): 368–371.

[2] Zhang S, Gu B, Li HN, et al., 2013, Current Status of Induced Pluripotent Stem Cells and Their Transplantation for Spinal Cord Injury. *Acta Neuropharmacologica*, 3(3): 57–64.

[3] Yuan WC, Yuan H, Guo Y, et al., 2016, Mechanisms and Application Progress of Induced Pluripotent Stem Cells in Spinal Cord Injury Repair. *Guangdong Medical Journal*, 37(21): 3286–3289.

[4] Yao SH, Zhong DJ, 2013, Application and Research Progress of Induced Pluripotent Stem Cell Transplantation in Spinal Cord Injury Repair. *Chinese Journal of Spine and Spinal Cord*, 23(11): 1015–1018.

[5] Fan JJ, Wang JJ, Chen F, et al., 2021, Research Progress on Induced Pluripotent Stem Cell Transplantation for the Treatment of Spinal Cord Injury. *Journal of Traditional Chinese Orthopedics and Traumatology*, 33(2): 54–58.

[6] Yang C, Shen CL, 2018, Research Progress on Induced Pluripotent Stem Cell Therapy for Cervical Spinal Cord Injury. *Journal of Anhui Medical University*, 53(2): 323-326.

[7] Xia GM, Xu Q, Liu XQ, et al., 2021, Applications and Roles of Induced Pluripotent Stem Cells in Orthopedic Tissue Engineering. *Chinese Journal of Tissue Engineering Research*, 25(19): 3077-3082.

[8] Li HM, Shen CL, 2019, Research Progress on Stem Cell Therapy for Spinal Cord Injury. *Journal of Anhui Medical University*, 54(4): 662-666.

[9] Tu XS, 2014, Stem Cell Transplantation Experiments in Human Diseases: Current Status and Progress of Basic Research. *Chinese Journal of Tissue Engineering Research*, 18(45): 7364-7369.

[10] Meng CY, 2013, Current Status and Prospects of Induced Pluripotent Stem Cell Therapy for Spinal Cord Injury. *Journal of Jining Medical University*, 36(3): 153-156.