

pISSN: 3068-3203 | eISSN: 3067-8048

DOI: https://doi.org/10.70818/pjsn.v02i01.067



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The Role of Neuroplasticity in Recovery from Spinal Cord Injury: Mechanisms and Therapeutic Strategies

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ABSTRACT: Background: Spinal cord injury (SCI) leads to severe functional impairments, and neuroplasticity has been identified as a crucial mechanism in recovery. Understanding these mechanisms is essential for effective therapies. **Objective:** To evaluate the role of neuroplasticity in SCI recovery and to assess therapeutic strategies aimed at promoting neuroplastic changes for improving functional outcomes. Methods: This study was conducted at the Department of Neurology, Chinese PLA General Hospital, with a sample size of 188 SCI patients from January 2023 to June 2024. Patients underwent a combination of neuroplasticity-enhancing therapies, including physical rehabilitation, neuromodulation, and stem cell therapy. Functional outcomes were measured using the ASIA (American Spinal Injury Association) impairment scale, and neuroplastic changes were quantified through MRI and electrophysiological recordings. Data were analyzed using SPSS, with significance set at p<0.05. Results: Patients demonstrated significant functional improvements, with 72% showing an increase of 1-2 points on the ASIA scale after 6 months. Mean improvement in sensory scores was 32% (p = 0.003), while motor recovery showed an average improvement of 25% (p = 0.001). Standard deviation for motor recovery was 10.8, and sensory improvement was 8.4. In neuroplasticity markers, the volume of cortical reorganization was positively correlated with recovery, with an increase of 27% in cortical activation in motor regions (p = 0.002). Stem cell therapy combined with rehabilitation showed the highest efficacy, with a recovery rate of 80%, compared to 65% in the physical rehabilitation-only group (p = 0.01). *Conclusion*: Neuroplasticity plays a pivotal role in SCI recovery, with advanced therapeutic strategies significantly enhancing functional outcomes. The combination of rehabilitation and stem cell therapy offers the most promising results.

Keywords: Neuroplasticity, Spinal Cord Injury, Rehabilitation, Stem Cell Therapy, Cortical Remapping.

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Received: March 11, 2025 | Accepted: April 13, 2025 | Published: June 30, 2025

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INTRODUCTION

Spinal cord injury (SCI) represents one of the most devastating neurological conditions, often leading to permanent disability and significant impairment in motor, sensory, and autonomic functions. Despite extensive research, the recovery from SCI remains a major challenge, primarily due to the limited regenerative capacity of the adult spinal cord. Over the past few decades, however, a growing body of evidence has emerged suggesting that neuroplasticity—the ability of the nervous system to adapt, reorganize, and form new neural connectionsplays a central role in the recovery process following SCI [1]. Neuroplasticity encompasses a range of molecular, cellular, and synaptic mechanisms that allow for functional reorganization within the central nervous system (CNS) in response to injury or environmental changes [2]. These processes involve both the intrinsic capacity of surviving neurons to adapt and the modulation of their activity to promote recovery of lost functions. Recent advancements in neuroscience have provided crucial insights into how these mechanisms may

How to Cite: Shengyuan Yu. The Role of Neuroplasticity in Recovery from Spinal Cord Injury: Mechanisms and Therapeutic Strategies. Pac J Spine Neurosurg. 2024 Jan-Jun;2 (1): 5-14

be harnessed to develop more effective therapeutic strategies for SCI [3].

The complexity of neuroplastic changes following SCI is further compounded by the heterogeneity of the injury, which can vary in terms of the extent of damage to both the spinal cord tissue and the neural networks it connects. In the acute phase of SCI, the primary damage typically results from mechanical injury, leading to axonal disruption, hemorrhage, and inflammation, followed by a secondary cascade of cellular events such as oxidative stress, excitotoxicity, and glial scar formation [4]. While these processes initially protect the spinal cord by limiting further damage, they also inhibit neural regeneration, creating a formidable barrier to recovery. Nonetheless, recent studies have illuminated the plasticity of the spinal cord and the brain's ability to adapt in response to injury [5]. Neuroplasticity in SCI recovery is multifaceted and involves several key mechanisms. One critical process is the rewiring of neural circuits within the spinal cord itself, facilitated by the sprouting of surviving axons and the formation of new synaptic connections [6]. This can restore partial function, particularly in cases of incomplete SCI. Furthermore, neuroplasticity is not confined to the injured site alone; supraspinal structures, particularly the brain, also undergo significant reorganization to compensate for lost connections. This process, known as cortical remapping, has been observed in both animal models and humans, demonstrating that the brain can adapt its sensory and motor representations to accommodate the altered input from the spinal cord [7]. These adaptive changes are not always beneficial, as maladaptive plasticity can also occur, resulting in abnormal motor patterns or pain syndromes [8]. Thus, understanding the precise mechanisms underlying neuroplasticity is essential for designing therapeutic interventions that enhance functional recovery and minimize the negative effects of maladaptive plasticity.

Therapeutic strategies targeting neuroplasticity in SCI recovery have become a major focus of recent research. Rehabilitation approaches, such as physical therapy, electrical stimulation, and neuromodulation, aim to promote the activation of neuroplastic processes by enhancing the intrinsic capacity for reorganization and compensatory mechanisms [9]. Additionally, molecular therapies are being explored to augment neuroplasticity by targeting specific pathways that govern axon growth, synaptic plasticity, and inflammation. For instance, the modulation of neurotrophins, such as brain-derived neurotrophic factor (BDNF), has been shown to promote axonal regeneration and functional recovery after SCI [10]. Furthermore, recent advances in stem cell therapy hold promise in facilitating repair and regeneration of damaged spinal cord tissue by promoting cell survival, differentiation, and integration into existing neural circuits [11]. The interplay between neuroplasticity and injury severity is a critical factor in determining the potential for recovery. In cases of complete SCI, where extensive tissue damage occurs, neuroplasticity alone is unlikely to fully restore function. However, in cases of incomplete SCI, the ability of the CNS to reorganize itself and compensate for lost connections may result in significant functional improvements [12]. The extent of neuroplasticity also varies with the timing of intervention, with early rehabilitation often yielding better outcomes than delayed treatment [13]. Furthermore, the chronic phase of SCI presents additional challenges, as the long-term presence of glial scars, the accumulation of inhibitory factors, and the loss of neuronal connectivity may limit the extent of plasticity [14]. While the therapeutic potential of neuroplasticity is immense, several challenges remain in translating these findings into clinical practice. One major obstacle is the complexity of the neuroplastic changes that occur in response to SCI. These changes are not always predictable and can vary depending on the type of injury, the individual's age, and the presence of comorbid conditions. Additionally, the long-term effects of therapeutic interventions aimed at enhancing neuroplasticity remain unclear. There is a need for further research to identify the optimal timing, intensity, and duration of interventions to maximize recovery. Moreover, the risk of maladaptive plasticity, such as spasticity, chronic pain, or abnormal motor control, must be carefully considered in the design of treatment strategies [15].

Aims and Objective

The aim of this study is to investigate the role of neuroplasticity in the recovery process following spinal cord injury (SCI). The objective is to assess the effectiveness of various therapeutic strategies, including rehabilitation, neuromodulation, and stem cell therapy, in promoting neuroplastic changes and improving functional outcomes in SCI patients.

MATERIAL AND METHODS

Study Design

This study employed a prospective, observational design conducted at the Department of Neurology, Chinese PLA General Hospital, from January 2023 to June 2024. A total of 188 SCI patients were enrolled. The study aimed to explore the role of neuroplasticity in recovery following SCI, assessing therapeutic interventions, including physical rehabilitation, neuromodulation, and stem cell therapy. Functional recovery was evaluated using the ASIA impairment scale, while neuroplastic changes were quantified through MRI and electrophysiological tests. Data were collected pre- and post-intervention to assess the efficacy of treatments and their impact on neuroplasticity.

Inclusion Criteria

Participants included in the study were adult patients aged 18 to 65 years with confirmed SCI, classified between AIS A and D according to the American Spinal Injury Association Impairment Scale. Patients must have had SCI for no longer than 12 months, ensuring the potential for neuroplastic recovery. Participants were required to provide written informed consent and were expected to undergo all therapeutic interventions and follow-up assessments.

Exclusion Criteria

Patients were excluded from the study if they had pre-existing neurological disorders unrelated to SCI, significant psychiatric conditions, or active infections that could interfere with recovery. Individuals with prior spinal surgeries, those receiving pharmacological treatments that could affect neuroplasticity, or those unable to comply with rehabilitation protocols were also excluded. Patients with other severe medical comorbidities, such as uncontrolled cardiovascular disease, were not eligible to ensure a focused analysis on SCI-related recovery.

Data Collection

Data were collected at three distinct time points: pre-intervention, immediately after 6 months of therapy, and at a 12-month follow-up. The primary outcome measures included the ASIA Impairment Scale to assess motor and sensory function, along with advanced neuroimaging (MRI) and electrophysiological tests to measure neuroplastic changes in the CNS. Patient demographics, injury characteristics, and therapy details were also documented.

Data Analysis

Data were analyzed using SPSS version 26.0. Descriptive statistics were employed to summarize baseline characteristics, with comparisons of outcomes using paired t-tests for pre- and post-intervention results. Continuous variables, such as sensory and motor scores, were analyzed for normal distribution and presented with mean, standard deviation (SD), and p-values. A significance level of p<0.05 was considered statistically significant. Correlations between neuroplasticity markers and functional recovery were assessed using Pearson's correlation coefficient.

Procedure

Upon inclusion, participants underwent an initial baseline assessment, including demographic data collection and clinical evaluations of SCI severity. baseline testing, patients Following received individualized therapy, consisting of daily physical rehabilitation, weekly neuromodulation sessions, and biweekly stem cell therapy injections. Neuroplasticityenhancing therapies targeted both functional restoration and tissue regeneration, using evidence-based protocols. Each patient was closely monitored for adverse effects and progression during the treatment period. Functional and neuroplastic outcomes were assessed after 6 months of combined therapy, followed by follow-up evaluations at 12 months. MRI scans assessed cortical reorganization, and electrophysiological recordings were used to measure central nervous system changes. During follow-up, patients' progress was analyzed for signs of neuroplastic changes, with a focus on motor and sensory recovery. The data collection team maintained strict confidentiality, ensuring compliance with ethical standards throughout the study. All outcomes were recorded, analyzed, and compared to determine the impact of neuroplasticity therapies on recovery rates.

Ethical Considerations

This study was approved by the Institutional Review Board (IRB) of Chinese PLA General Hospital. Written informed consent was obtained from all participants prior to inclusion. Ethical guidelines were followed in accordance with the Declaration of Helsinki, ensuring patient privacy and confidentiality. Any adverse events were promptly reported and managed.

RESULTS



Figure 1: Demographic Characteristics

The distribution of the study sample shows a significant prevalence of patients aged between 31 and 40 years. Most of the participants were male (60%), and over half were employed at the time of their injury. The differences in the proportions of age, gender, and occupation groups were statistically significant with pvalues below 0.05.

Category	Baseline (Frequency)	6-Month Follow-Up (Frequency)	Change (%)	P-Value
AIS A	132	105	-20.45%	0.01
AIS B	39	49	+25.64%	0.04
AIS C	17	32	+88.24%	0.02
AIS D	0	2	+100%	0.06

Table 1: ASIA Impairment Scale Scores at Baseline and 6-Month Follow-Up

A significant improvement was observed in patients' ASIA scores, with 40% of participants showing at least one level of improvement. The AIS C category saw the highest increase, suggesting that neuroplasticityenhancing therapies facilitated substantial motor recovery.

Table 2: Sen	sory Recovery	Post-Intervention	

Body Region	Pre-Therapy Sensory Score	Post-Therapy Sensory Score	Mean Improvement	Р-
	(%)	(%)	(%)	Value
Upper Limbs	28%	60%	35%	0.003
Lower Limbs	25%	53%	28%	0.05
Torso	32%	50%	18%	0.12
Perineum	20%	40%	20%	0.07

The data indicates that the upper limbs experienced the most significant sensory recovery after therapy. Statistically significant improvements were found in both the upper and lower limbs, while sensory recovery in the torso and perineum showed less pronounced improvements.

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Table 3: Motor Recovery in Spinal Cord Injury Patients								
Treatment Group	Pre-Therapy	Motor	Score	Post-Therapy	Motor	Score	Improvement	Р-
	(Mean)			(Mean)			(%)	Value
Rehabilitation	20			24			20%	0.04
Only								
Stem Cell + Rehab	22			30			36%	0.001

Motor recovery was significantly better in the stem cell therapy group, with a 36% improvement compared to the 20% improvement in the rehabilitationonly group. These findings suggest that combining stem cell therapy with rehabilitation may be more effective in improving motor function.



Cortical Volume Before and After Therapy

Figure 2: Cortical Reorganization as Measured by MRI

Cortical reorganization was significantly greater in the stem cell therapy group, with a 35% increase in cortical volume compared to 16.67% in the rehabilitationonly group. These results support the hypothesis that stem cell therapy may enhance neuroplastic changes in the brain's motor regions.

Table 4: Maladaptive Hasticity and Adverse Events							
Adverse Event	Frequency	Percentage (%)	P-Value				
Spasticity	23	12.23%	0.03				
Chronic Pain	34	18.09%	0.01				
None	131	69.68%	0.05				

Maladaptive plasticity was observed in 12% of patients who developed spasticity and 18% who experienced chronic pain. These issues were more prevalent among patients with more severe injuries at baseline, underlining the complexity of neuroplasticity in SCI recovery.

DISCUSSION

This study sought to explore the role of neuroplasticity in the recovery process, particularly focusing on the effects of combined neuroplasticityenhancing therapies, including stem cell therapy, rehabilitation, and neuromodulation [16]. The results demonstrated significant improvements in sensory and motor function, cortical reorganization, and neuroplastic changes, confirming the importance of neuroplasticity in SCI recovery. This discussion will place our findings in the context of existing literature, comparing and contrasting them with other studies to further elucidate the underlying mechanisms and therapeutic implications of neuroplasticity in SCI rehabilitation.

Neuroplasticity in SCI Recovery: A Review of Mechanisms

Neuroplasticity encompasses a range of adaptive changes within the nervous system following injury, including axonal sprouting, synaptic rearrangement, and cortical reorganization. In the case of SCI, neuroplastic changes occur both within the spinal cord and in the brain, particularly in areas responsible for motor and sensory control. The spinal cord's capacity for self-repair is limited, but neuroplasticity facilitates functional compensation by reorganizing neural circuits to restore partial motor and sensory function [17]. Our study observed significant improvements in sensory function, with a 32% mean improvement across patients, particularly in the upper limbs. This finding aligns with other studies that have shown that neuroplasticity in the form of sensory cortical reorganization plays a crucial role in sensory recovery after SCI. For instance, Eisdorfer et al., reported that sensory remapping in the primary sensory cortex is often observed following incomplete SCI and rehabilitation, allowing patients to regain some sensory awareness [18]. Furthermore, the greater improvement in the upper limbs in our study is consistent with findings from Symeonides et al., who found that cortical remapping is more pronounced in the upper limb regions, which are generally more flexible in terms of functional reorganization [19]. In terms of motor recovery, our study found a 25% improvement in motor function, with patients receiving a combined therapy of stem cell transplantation and rehabilitation demonstrating the most significant recovery. This result is consistent with previous studies that have examined the role of stem cells in enhancing neuroplasticity and promoting motor function recovery. For example, Zhou *et al.*, found that stem cell therapy, when combined with physical rehabilitation, led to improved motor function by promoting neuronal survival and axon regeneration [20]. The role of neurotrophins such as BDNF in promoting axonal growth and functional recovery after SCI has been extensively studied. Our findings are also supported by clinical trials that have shown stem cell therapies can facilitate neuroplastic changes in the spinal cord and improve motor outcomes in patients with SCI.

Therapeutic Strategies and Neuroplasticity Enhancement

Our study focused on the synergistic effects of stem cell therapy, neuromodulation, and rehabilitation on neuroplasticity and functional recovery in SCI patients. The results indicated that combined therapy significantly enhanced sensory and motor recovery, which is in line with several studies exploring multimodal therapeutic strategies. Sánchez et al., demonstrated that activity-based rehabilitation (such as locomotor training) could stimulate neuroplasticity and promote functional recovery, particularly in incomplete SCI [21]. Furthermore, physical rehabilitation and neuromodulation have been shown to activate neuroplastic changes in both the spinal cord and brain, enhancing sensory and motor function. The effectiveness of combined rehabilitation and stem cell therapy in promoting neuroplasticity was evident in our study, with patients receiving this regimen showing a 36% improvement in motor function, compared to 20% in those who only underwent rehabilitation. These findings are consistent with research that suggests stem cell transplantation, when combined with rehabilitation, can provide optimal conditions for neuroplastic changes. For instance, studies by Liao et al., and Zhang et al., demonstrated that the combination of stem cells and rehabilitation not only promotes neuronal regeneration but also enhances cortical reorganization and improves functional outcomes, including motor and sensory recovery [22, 23]. Moreover, our study found a significant correlation between cortical reorganization and motor recovery (r = 0.82, p = 0.002), supporting the idea that cortical plasticity is closely linked to functional recovery. In line with this, several studies have demonstrated that reorganization, measured cortical as through neuroimaging, correlates with functional improvements in SCI patients. Kong et al., found that patients who experienced cortical remapping following SCI rehabilitation exhibited significant improvements in motor function [24]. Similarly, our study showed that patients with greater cortical reorganization had more pronounced motor recovery, suggesting that neuroplasticity in the brain's motor cortex plays a crucial role in facilitating functional outcomes post-SCI.

The Role of Maladaptive Plasticity: Challenges in SCI Recovery

While neuroplasticity holds promise for SCI recovery, maladaptive plasticity remains a significant challenge. Maladaptive plasticity refers to the abnormal reorganization of neural circuits that can lead to adverse outcomes, such as spasticity, chronic pain, or abnormal movement patterns. In our study, 12% of patients experienced spasticity, and 18% reported chronic pain at the 6-month follow-up. These findings are consistent with other studies that have highlighted the risk of maladaptive plasticity in SCI recovery. For example, Freyermuth et al., described how the formation of glial scars and the overactivation of inhibitory pathways can limit the efficacy of neuroplasticity and lead to maladaptive plasticity [25]. Spasticity and chronic pain are common complications of SCI and are thought to arise from changes in spinal cord circuits and abnormal sensory processing in the brain. Our study found that patients with more severe baseline injuries were more likely to develop maladaptive plasticity, which aligns with the findings of Clifford et al., who observed that severe SCI is often associated with a higher incidence of spasticity and chronic pain [26]. Interestingly, our study also found a significant association between maladaptive plasticity and the severity of SCI at baseline (p = 0.01). This suggests that the potential for maladaptive plasticity may be more pronounced in patients with complete SCI (AIS A), as they may have more extensive damage to spinal cord circuits. These findings highlight the need for targeted therapeutic strategies that not only promote adaptive plasticity but also minimize the risk of maladaptive changes.

Cortical Reorganization and its Implications for SCI Rehabilitation

Cortical reorganization is a key component of neuroplasticity and is crucial for the recovery of motor and sensory functions following SCI. Our study demonstrated a 27% increase in cortical activation in the motor regions of the brain after 6 months of therapy, which is consistent with findings from other studies that have explored cortical reorganization in SCI patients. As shown by Piskin et al., cortical plasticity plays an essential role in compensating for lost motor function, with areas of the brain taking over functions previously controlled by damaged regions [27]. The enhanced cortical reorganization observed in our study suggests that neuroplasticity in the motor cortex contributes significantly to motor recovery after SCI. Cortical reorganization is facilitated by neuroplasticity-enhancing therapies such as neuromodulation and rehabilitation, which have been shown to activate cortical motor areas. For example, the use of transcranial magnetic stimulation (TMS) has been shown to enhance cortical reorganization and improve motor function in SCI patients. Our findings align with those of Chen et al., who demonstrated that neuromodulation therapies, such as TMS, could stimulate cortical remapping and promote recovery of motor function in SCI patients [28]. The combination of rehabilitation and neuromodulation, as used in our study, may therefore provide an optimal therapeutic strategy to enhance cortical reorganization and facilitate functional recovery.

Conclusion: Implications for Future SCI Rehabilitation Strategies

In conclusion, our study provides strong evidence that neuroplasticity plays a crucial role in the recovery of motor and sensory function after SCI. The significant improvements in sensory and motor function, as well as cortical reorganization, observed in our study support the concept that neuroplasticity can be harnessed through targeted therapeutic strategies. The combined use of stem cell therapy, rehabilitation, and neuromodulation was particularly effective in enhancing recovery, highlighting the potential for multimodal approaches to SCI rehabilitation. However, the risk of maladaptive plasticity, such as spasticity and chronic pain, underscores the need for carefully designed therapies that promote adaptive neuroplasticity while minimizing adverse effects. Our findings are consistent with previous studies that have emphasized the importance of neuroplasticity in SCI recovery and support the growing body of evidence suggesting that stem cell therapy and rehabilitation can enhance functional outcomes. Nevertheless, further research is needed to optimize therapeutic protocols, understand the mechanisms underlying neuroplasticity in

SCI, and develop personalized treatment strategies that maximize recovery and minimize the risks of maladaptive plasticity.

Funding: No funding sources **Conflict of interest:** None declared

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