Spinal Cord Injury: Developments in Using Stem Cells and Specialised Cells in Treating Spinal Cord Injuries

Modinat Olushanu, PhD

ABSTRACT

Spinal cord injury (SCI) is a severely debilitating condition that results in irreversible neurological deficits and significantly diminishes quality of life. Traditionally, treatment has primarily focused on symptom management and has offered limited functional recovery. Recent advancements in regenerative medicine and stem cell research have presented new possibilities for SCI patients. This review discusses key developments in SCI treatment, particularly stem cell transplantation, specialised cells, and combinational therapies. Mesenchymal stem cells (MSCs), neural stem cells (NSCs), induced pluripotent stem cells (iPSCs) and olfactory ensheathing cells (OECs) have shown promise in neural repair and functional recovery. Additionally, combining stem cell therapy with rehabilitation and neurotrophic factors enhances the therapeutic potential. However, achieving consistent and substantial functional recovery remains challenging and requires further research and large-scale clinical trials. This review underscores the need to translate these scientific advancements into clinical practice to improve the quality of life of SCI patients.

Keywords: Stem cells, MSCs, NSCs, iPSCs, OECs, Biomaterial, Scaffold, SCIs, Neurorehabilitation, Specialised cells, Functional recovery

Freelance Writer, London, United Kingdom

Correspondence to: Modinat Olushanu, modinat.liadi@gmail.com

Additional material is published online only. To view please visit the journal online.

Cite this as: Olushanu M. Spinal Cord Injury: Developments in Using Stem Cells and Specialised Cells in Treating Spinal Cord Injuries. Premier Journal of Science 2024;1:100005

DOI: https://doi.org/10.70389/PJS.100005

Received: 2 August 2024

Accepted: 13 August 2024

Published: 12 October 2024

Ethical approval: N/a

Consent: N/a

Funding: No industry funding

Conflicts of interest: The authors declare that they have no affiliations with or involvement in any organisation or entity with any financial interest in the subject matter or materials discussed in this manuscript.

Author contribution: Modinat Olushanu – Conceptualization, Writing – original draft, review and editing

Guarantor: Modinat Olushanu

Provenance and peer-review: Commissioned and externally peer-reviewed

Data availability statement: N/a

Introduction

According to the World Health Organization (WHO), it is estimated that between 250,000 and 500,000 people worldwide suffer from SCI annually.[1] The prevalence of SCI varies widely across different regions and populations and is often influenced by factors such as traffic accidents, workplace safety, and availability of medical care.[1,2]

SCI damage occurs in the spinal cord, resulting in the loss of functions such as mobility or sensation. The spinal cord, a vital part of the central nervous system, comprises nerve fibres that relay signals between the brain and the body.[3] Damage to the spinal cord can disrupt these signals, causing significant and often permanent changes in strength, sensation, and other functions below the injury site. SCIs can be caused by traumatic events, such as motor vehicle accidents, sports injuries, falls, and violence, or by nontraumatic factors.[3,4] SCIs are classified as complete or incomplete injuries: a complete injury results in no function below the injury level, whereas an incomplete injury preserves some function. The severity and impact of SCI are determined by the affected spinal cord level (cervical, thoracic, lumbar, or sacral).[4]

SCIs significantly impact individuals, resulting in physical, psychosocial, and economic challenges. These injuries often lead to the loss of movement and sensation, which can result in paralysis, such as tetraplegia or paraplegia.[5] Physical consequences may also include respiratory problems, spasticity, and persistent pain. Injuries to the cervical and thoracic regions can impede neural pathways, leading to respiratory difficulties such as ventilatory failure and pneumonia. Spasticity results in continuous muscle rigidity and hinders mobility, whereas chronic pain can manifest as neuropathic, musculoskeletal, or visceral discomfort.[6–8]

SCI can have a profound impact on an individual's emotional and psychological well-being, often leading to feelings of depression and anxiety as a result of sudden changes in physical capabilities. Furthermore, the financial strain caused by high medical expenses and loss of employment can exacerbate the challenges faced by individuals and their families.[9]

History of Treating SCI

The treatment of SCIs with stem cells and specialised cells can be traced back to early animal studies that examined the regenerative capabilities of various stem cell types, including MSCs, NSCs, and iPSCs. These studies have revealed the potential of these cells to improve motor and sensory functions and facilitate neural repair. Initial clinical trials conducted in the early 2000s focused on the safety and feasibility of MSC transplantation, demonstrating that MSCs derived from sources such as the bone marrow and adipose tissue are safe and can modulate immune responses and promote tissue repair.[10–13] Advances in iPSC technology in the 2010s have enabled the reprogramming of somatic cells into pluripotent stem cells, offering new avenues for neural repair.[14,15] NSCs derived from foetal tissues or iPSCs have been tested for their ability to differentiate into neurons and glial cells, aiding in neural repair and functional recovery.[14,16–18]

Specialised cell types, such as olfactory ensheathing cells (OECs) and stem cell-derived exosomes, have also been investigated for their regenerative potential.[19–22] OECs are known for their ability to support axonal growth, while exosome therapy offers a cell-free therapeutic approach by carrying neuroprotective and regenerative factors to the injury site.[20,21]

Despite promising results, challenges such as immune rejection, tumorigenesis, and the optimisation of cell delivery methods remain.[23,24] Recent studies have endeavoured to enhance these therapies and establish consistent guidelines for their clinical application, which could significantly advance the treatment of SCI and promote better patient outcomes.[25,26]

Stem Cell Transplantation

Mesenchymal Stem Cells (MSCs)

MSCs possess immunomodulatory and regenerative properties. Derived from bone marrow, adipose tissue, and umbilical cord, MSCs show potential in improving motor and sensory functions in SCI patients.[24,27] Levi et al. demonstrated the safety and feasibility of transplanting 20 million human central nervous system stem cells (HuCNS-SC) into the thoracic spinal cord of 12 patients with chronic motor-complete and sensory-incomplete SCI in a multi-site phase I/IIa clinical trial. The six-year study revealed no severe adverse effects or tumour formation, and while sensory improvements were observed in five patients, motor function recovery was not detected, emphasising the need for further research to enhance cell engraftment and integration.[28] Sykova et al. illustrated that MSCs from various sources have shown promise in treating neurodegenerative diseases such as SCI and ALS, owing to their multilineage differentiation potential and immunomodulatory properties.[29,30] They release neuroprotective cytokines, migrate to lesion sites, and enhance neural plasticity, leading to improved function in animal models.[27,31] Clinical studies have confirmed the safety and modest benefits of MSCs in promoting neural repair and functional recovery, particularly umbilical cord-derived MSCs with high neurotrophic factor secretion.[29,32,33,34] Tahmasebi et al.'s review, reflects that although improvements in sensory and bladder functions have been noted, the effects on motor function remain unclear, requiring further research to optimise and assess the application of these therapies in humans.[34]

Neural Stem Cells (NSCs)

NSCs can differentiate into neurons, astrocytes, and oligodendrocytes, making them suitable for repairing neural damage.[35–38] Additionally, it has been suggested that genetically modified NSCs could overcome certain limitations, such as low migration and survival rates, thereby enhancing their therapeutic potential.[39] Preclinical studies using NSCs derived from fetal tissues and iPSCs have shown promising results in promoting neurogenesis and functional recovery in animal models of SCI.[18,40–42] However, several challenges persist that must be addressed before the clinical application of this technology can be realised, including the regulation of cell differentiation and proliferation, as well as ensuring patient safety.[18,43] Further research is needed to optimise these therapies and ensure their efficacy and safety for potential use in humans.[41,42,44]

Another technology that has been explored is the conversion of human fibroblasts into NSCs using single zinc-finger transcription factors, which represents a significant advancement and provides deeper insights into neural development and potential therapeutic applications.[45,46] This method allows the generation of long-term self-renewable and multipotent NSCs, which are similar to control NSCs in terms of their characteristics and functionality. Induced NSCs exhibit the capacity to survive, migrate, and differentiate into neural phenotypes post-transplantation without tumour formation, which is crucial for any therapeutic application.[45] However, while this advancement is promising, it is important to consider the broader context of SCI treatment and the various approaches being explored. For instance, Yu et al. and Pereira et al. elaborate on the opportunities presented by NSCs derived from iPSCs and their capacity for cell transplantation therapy aimed at addressing SCI.[47,48] Lu et al. and Ao et al. emphasised the survival and integration of NSCs in severe SCIs and the potential synergistic effects of co-transplanting NSCs with other cell types, such as OECs, to promote regeneration and functional reconstruction.[49,50] Furthermore, Kiani et al. indicated the potential of employing human-induced neural stem cells (hiNSCs) for cell-based therapy in rats with spinal cord injury (SCI), as evidenced by the enhanced cell viability and locomotor function observed following transplantation.[51]

Induced Pluripotent Stem Cells (iPSCs)

iPSCs are a versatile source of stem cells that can be reprogrammed from somatic cells and differentiated into various cell types, including neural stem/progenitor cells (NS/PCs), which can be used for SCI treatment.[52–54] Research has demonstrated that iPSCs can survive, differentiate, and extend axons over long distances in the injured spinal cord, forming synapses with host neurons, which are crucial for functional recovery after SCI.[55,56] Recent studies have focused on preparing for first-in-human clinical trials using iPSC-derived neural stem/progenitor cells (NS/PCs) for subacute SCI.[57,58] These studies have addressed critical issues such as safety, tumourigenesis, and the practical challenges of cell preparation and transplantation.[54,58]

Olfactory Ensheathing Cells (OECs)

OECs have been identified as promising agents in treating SCIs because of their unique ability to support axonal growth and facilitate neural regeneration.[59,60] These cells, which share characteristics with both Schwann cells and astrocytes, can migrate within the damaged spinal cord, secrete neurotrophic factors, and potentially carry exogenous genes to promote neuronal regeneration.[61,62] Olfactory mucosa cells have been found to be effective in restoring motor function due to their capacity to remyelinate and regenerate axons. Furthermore, they express neurotrophic factors essential for nerve tissue recovery following SCI.[63] Additionally, OECs have been shown to interact with astrocytes, regulate inflammatory reactions, and contribute to myelination, which is a critical process in nerve repair.[59]

However, there are challenges in the application of OECs, such as inconsistency in therapeutic outcomes, which may be attributed to the variability in cell populations used for transplantation.[64] Moreover, while OECs have demonstrated neuroprotective and repair roles, the mechanisms by which they mediate anti-inflammatory effects remain a subject of debate.[65] The potential of OECs is further complicated by the need

DOI: https://doi.org/10.70389/PJS.100005 | Premier Journal of Science 2024;1:100005

for improved purification procedures to achieve their full therapeutic potential.[64]

In summary, OECs offer a multifaceted approach to SCI treatment by promoting axonal regeneration, myelination, and modulation of the inflammatory response. Despite promising evidence, further research is required to standardise cell preparations and fully understand the mechanisms of OEC-mediated repair to optimise their therapeutic application.[64,65]

Exosomes

Exosome therapy presents a novel cell-free approach to treating spinal cord injuries (SCIs) by capitalising on the intrinsic ability of exosomes to transport neuroprotective and regenerative factors to the site of injury. Exosomes are extracellular vesicles that facilitate intercellular communication and possess the potential to modify the injured spinal cord's environment by delivering bioactive molecules that promote neuroprotection and regeneration.[20,21,66] Numerous studies have demonstrated the therapeutic potential of exosomes. Zhou et al., in their study, revealed that exosomes derived from human placental MSCs possess the ability to promote recovery from SCIs by stimulating endogenous neurogenesis and improving locomotor and bladder functions via the MEK/ERK/CREB signalling pathway.[67] In addition, a study by Xue et al. showed that human umbilical cord mesenchymal stem cell (hUC-MSC)-derived small extracellular vesicles (sEVs) have the potential to repair disrupted blood-spinal cord barriers in SCI through the regulation of Endothelin-1 and the enhancement of tight junction proteins. These findings further support the idea that sEVs may offer a promising cell-free therapeutic strategy for treating SCI.[68] Another study demonstrated that exosomes derived from UC-MSCs enhanced motor function recovery and reduced inflammation by inhibiting the NF-κB/MAPK signalling pathway.[69] Lee et al. demonstrated that targeted delivery of MSC-derived nanovesicles (MF-NVs) enhances neuroprotection, anti-inflammation, and angiogenesis in SCI treatment, offering an effective cell-free therapeutic approach.[70] A study by Mu et al. showed that an emergency treatment strategy using MSC-derived exosomes encapsulated in fibrin glue resulted in significant functional recovery in SCI, suggesting potential benefits in urinary function recovery.[71]

Combination Therapies

Combining Different Types of Stem Cells

Recent research has suggested that combining different stem cell types may enhance therapeutic outcomes.[62] Co-transplantation of NSCs and MSCs has demonstrated synergistic effects, resulting in improved motor and sensory function. Furthermore, scaffolds and growth factors facilitate stem cell transplantation by establishing a favourable microenvironment that promotes tissue regeneration.[72–75] Notably, while the advantages of employing a combination of stem cells have been emphasised, the literature also recognises the intricacy of spinal SCI pathophysiology and the necessity for precision medicine approaches. This indicates that the efficacy of combined stem cell therapies may be contingent upon customised treatment to the unique features of the injury and the patient.[24,76,77]

Rehabilitation and Neurotrophic Factors

Integrating stem cell transplantation with rehabilitation and neurotrophic factors has yielded encouraging outcomes.

Rehabilitation enhances the effects of cell transplantation by promoting neural plasticity and functional recovery. Studies have shown that rehabilitation when combined with stem cell transplantation, can lead to significant improvements in functional recovery, particularly when initiated during the chronic phase of SCI.[78] This synergistic effect is thought to be the result of the rehabilitation's capacity to facilitate neuronal plasticity within transplanted stem cells and sensorimotor circuits, which is crucial for functional recovery.[79] Furthermore, it has been demonstrated that the integration of rehabilitation and neural progenitor cell (NPC) transplants leads to enhanced functional results because rehabilitation promotes the growth of host corticospinal axons into grafts.[78] This suggests that rehabilitation not only supports the integration of transplanted cells but also enhances endogenous repair mechanisms.

The use of neurotrophic factors, such as neurotrophin-3 (NT-3), in conjunction with stem cell therapies, has been shown to improve outcomes in patients with spinal cord injuries (SCI). The combination of these two therapies has demonstrated synergistic effects, leading to improved locomotor function and reduced SCI pathology.[80,81] In particular, the use of neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) and glial cell line-derived neurotrophic factor (GDNF), in conjunction with stem cell therapies has demonstrated the potential to mitigate damage and facilitate recovery in preclinical models of SCI.[80]

In conclusion, evidence suggests that neurotrophic factors, including NT-3, can effectively improve outcomes after SCIs when combined with stem cell treatments. This joint approach benefits from the neuroprotective and regenerative qualities of neurotrophins and the extensive therapeutic potential of stem cells, presenting a promising strategy for improving recovery in SCI.[77,80,81]

Clinical Trials and Outcomes

Safety and Feasibility

Clinical trials have established the safety and feasibility of stem cell transplantation in SCI. Rong et al. study highlights that stem cell transplantation has been performed at various stages of SCI and is safe and feasible, with the potential to alleviate inflammation and restore the function of damaged nerve cells.[82] Similarly, Digma et al. reported that early clinical trials demonstrated the safety and feasibility of stem cell transplantation in patients with SCI, with observed improvements in sensory and motor functions.[83] Silvestro et al. also supported these findings, indicating

that clinical trials have demonstrated the safety and efficacy of stem cell therapy in patients with SCI.[82–84] However, despite these positive indications, challenges and limitations remain to be addressed. Agosti et al. pointed out that, while stem cell therapies show promise, some potential adverse events and limitations necessitate careful optimisation of transplantation conditions.[85] Moreover, there is a need for a deeper understanding of SCI pathophysiology and concerns, such as tumourigenicity and immunogenicity, before its widespread clinical adoption. Goel et al. and Kan et al. echo the sentiment that more rigorous, large-scale clinical trials are needed to fully understand the safety, efficacy, and long-term viability of stem cell therapies for SCI.[85–87]

Efficacy

Although the safety of stem cell therapies has been well documented, their efficacy remains variable. The efficacy of these therapies is less consistent, as clinical studies have not always yielded encouraging results, and the translation of preclinical success to clinical practice has been challenging.[88] This discrepancy may be due to the heterogeneity of SCI pathophysiology, timing of intervention, and types of stem cells used.[76] Moreover, despite the promise shown in animal models, the limitations of preclinical data and the complexity of translating these findings into successful clinical outcomes have been acknowledged.[89]

Various studies have reported improvements in motor and sensory functions post-SCI have been reported in various studies, particularly with the use of MSCs and NSCs. MSCs have been shown to promote repair through immunomodulation, neuroprotection, and nerve regeneration,[24] whereas NSCs have demonstrated the ability to form synapses with host axons and extend new axons from the injury site.[79]

However, the extent of recovery is variable and dependent on factors such as the type of stem cells used, the severity of injury, and the therapeutic approach. The promising results from MSC and NSC therapies underscore the potential of stem cell-based interventions in SCI treatment, although further research is needed to optimise these therapies and understand their mechanisms of action.[24,90]

Discussion

Recent advancements in SCI treatment, particularly in stem cell therapies and combinational approaches, offer new hope for improving the quality of life for individuals with SCI.[76,89,91,92] Significant progress has been made in developing these therapies, demonstrating their potential to repair damaged spinal cord tissues and restore lost function.[22,93–95] However, ongoing research and clinical trials are crucial to overcome the existing challenges and fully realise the potential of these therapies. Addressing issues such as immune rejection, precise delivery methods, and ensuring stem cell treatments' long-term safety and efficacy remain essential.

Overcoming the Challenges

The advent of iPSC technology has mitigated ethical concerns, particularly with the use of embryonic stem cells (ESCs) and fetal tissues.[40] Although stem cells are not a complete solution for neural repair, their combination with other therapies, such as rehabilitation and nanotechnology, may enhance their effectiveness.[96]

Integrating innovative technologies and comprehensive treatment strategies is fundamental to advancing SCI treatment and achieving substantial functional recovery.[97–99] Technologies, such as biomaterials, scaffolding, and gene editing, are being explored to enhance the effectiveness of stem cell therapies. Biomaterials can provide a supportive environment for stem cells, promoting their survival and integration into the host tissues.[74,75,99–101]

Scaffolding techniques help guide the growth and organisation of new cells, whereas gene editing can be used to enhance the regenerative capacity of stem cells.[44,74,93,100] Moreover, integrating complementary technologies, such as neurorehabilitation, electrical stimulation, and pharmacological treatments, can maximise the benefits of stem cell therapy.[102,103] Neurorehabilitation can help patients relearn motor skills and improve functional outcomes. Electrical stimulation can enhance the activity of spinal circuits and promote nerve regeneration.[103–105] Pharmacological treatments can address inflammation and other secondary complications, creating a more favourable environment for stem cell therapy.[106]

Conclusion

Stem cell therapy for SCI is a promising field with great potential for improving patient outcomes. Collaborative efforts among stakeholders, including scientists, clinicians, and regulatory bodies, are vital to address the current challenges. Advances in stem cell biology and regenerative medicine have pushed the boundaries of what is possible. Future studies should focus on optimising stem cell therapy protocols to ensure the highest safety and efficacy standards. This includes determining the best types of stem cells to use, refining delivery methods, and establishing optimal timing for intervention.

References

1 Laura Sminkey. Spinal cord injury: as many as 500 000 people suffer each year. WHO Geneva. 2013. Available from: https://www.who.int/news/item/02-12-2013-spinal-cord-injury-as-many-as-500-000-people-suffer-each-year
2 Bickenbach J, Officer A, Shakespeare T, von Groote P, World Health Organization, The International Spinal Cord Society. International perspectives on spinal cord injury / edited by Jerome Bickenbach ... [et al]. Geneva: World Health Organization; 2013. Available from: https://iris.who.int/handle/10665/94190
3 Mayo Clinic Staff. Spinal Cord Injury. Mayoclinic.org. Available from: https://www.mayoclinic.org/diseases-conditions/spinal-cord-injury/symptoms-causes/syc-20377890
4 Spinal Cord Injury. NINDS. Available from: https://www.ninds.nih.gov/health-information/disorders/spinal-cord-injury
5 Cleveland Clinic. Spinal Cord Injury. Cleveland Clinic. Available from: https://my.clevelandclinic.org/health/diseases/12098-spinal-cord-injury
6 Hadjipavlou G, Cortese AM, Ramaswamy B. Spinal cord injury and chronic pain. BJA Educ. 2016;16(8):264–8. Available from: https://doi.org/10.1093/bjaed/mkv073

7 Berlowitz DJ, Wadsworth B, Ross J. Respiratory problems and management in people with spinal cord injury. Breathe. 2016;12(4):328–40. Available from: http://breathe.ersjournals.com/lookup/doi/10.1183/20734735.012616
8 Reyes, M.R., & Chiodo, A. Spasticity and Spinal Cord Injury. MSKTC. Available from: https://msktc.org/sci/factsheets/spasticity-and-spinal-cord-injury
9 Budd MA, Gater DR, Channell I. Psychosocial consequences of spinal cord injury: a narrative review. J Pers Med. 2022;12(7).
10 Undale AH, Westendorf JJ, Yaszemski MJ, Khosla S. Mesenchymal stem cells for bone repair and metabolic bone diseases. Mayo Clin Proc. 2009;84(10):893–902. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0025619611605065
11 Galderisi U, Peluso G, Di Bernardo G. Clinical trials based on mesenchymal stromal cells are exponentially increasing: where are we in recent years? Stem Cell Rev Rep. 2022;18(1):23–36. Available from: https://doi.org/10.1007/s12015-021-10231-w
12 Nguyen NHT, Phan HT, Le PM, Nguyen LHT, Do TT, Phan TPT, et al. Safety and efficacy of autologous adipose tissue-derived stem cell transplantation in aging-related low-grade inflammation patients: a single-group, open-label, phase I clinical trial. Trials. 2024;25(1):309. Available from: https://doi.org/10.1186/s13063-024-08128-3
13 Orozco Delclós L, Soler Rich R, Arriaza Loureda R, Moreno García A, Gómez Barrena E. Efficacy and safety of autologous or allogeneic mesenchymal stromal cells from adult adipose tissue expanded and combined with tricalcium phosphate biomaterial for the surgical treatment of atrophic nonunion of long bones: a phase II clinical trial. J Transl Med. 2024;22(1):493. Available from: https://doi.org/10.1186/s12967-024-05280-x
14 Wang A, Tang Z, Park IH, Zhu Y, Patel S, Daley GQ, et al. Induced pluripotent stem cells for neural tissue engineering. Biomaterials. 2011;32(22):5023–32. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0142961211003681
15 Biswas D, Jiang P. Chemically induced reprogramming of somatic cells to pluripotent stem cells and neural cells. Int J Mol Sci. 2016;17:226.
16 Jensen MB, Yan H, Krishnaney-Davison R, Al Sawaf A, Zhang SC. Survival and differentiation of transplanted neural stem cells derived from human induced pluripotent stem cells in a rat stroke model. J Stroke Cerebrovasc Dis. 2013;22(4):304–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1052305711002503
17 Choi HW, Hong YJ, Kim JS, Song H, Cho SG, Bae H, et al. In vivo differentiation of induced pluripotent stem cells into neural stem cells by chimera formation. Zambidis ET, editor. PLOS ONE. 2017;12(1):e0170735. Available from: https://dx.plos.org/10.1371/journal.pone.0170735
18 Salewski RP, Mitchell RA, Li L, Shen C, Milekovskaia M, Nagy A, et al. Transplantation of induced pluripotent stem cell-derived neural stem cells mediate functional recovery following thoracic spinal cord injury through remyelination of axons. Stem Cells Transl Med. 2015;4(7):743–54. Available from: https://academic.oup.com/stcltm/article/4/7/743-754/6397338
19 Zhang Y, Wang WT, Gong CR, Li C, Shi M. Combination of olfactory ensheathing cells and human umbilical cord mesenchymal stem cell-derived exosomes promotes sciatic nerve regeneration. Neural Regen Res. 2020;15(10):1903. Available from: https://journals.lww.com/10.4103/1673-5374.280330
20 Chou RH, Lu CY, Wei-Lee, Fan JR, Yu YL, Shyu WC. The potential therapeutic applications of olfactory ensheathing cells in regenerative medicine. Cell Transplant. 2014;23(4–5):567–71. Available from: http://journals.sagepub.com/doi/10.3727/096368914X678508
21 Denaro S, D'Aprile S, Alberghina C, Pavone AM, Torrisi F, Giallongo S, et al. Neurotrophic and immunomodulatory effects of olfactory ensheathing cells as a strategy for neuroprotection and regeneration. Front Immunol. 2022;13:1098212. Available from: https://www.frontiersin.org/articles/10.3389/fimmu.2022.1098212/full
22 Costăchescu B, Niculescu AG, Dabija MG, Teleanu RI, Grumezescu AM, Eva L. Novel Strategies for spinal cord regeneration. Int J Mol Sci. 2022;23(9):4552. Available from: https://www.mdpi.com/1422-0067/23/9/4552
23 Peyvandi H, Abbaszadeh HA, Peyvandi A, Niknazar S, Khoramgah MS, Darabi S, et al. Cell Therapy; a new and safe strategy for the treatment of spinal cord injury: a review. J Otorhinolaryngol Facial Plast Surg. 2019;5(1). Available from: https://doi.org/10.22037/orlfps.v5i1.27202
24 Chen SY, Yang RL, Wu XC, Zhao DZ, Fu SP, Lin FQ, et al. Mesenchymal Stem cell transplantation: neuroprotection and nerve regeneration after spinal cord injury. J Inflamm Res. 2023;16:4763–76. Available from: https://www.dovepress.com/mesenchymal-stem-cell-transplantation-neuroprotection-and-nerve-regene-peer-reviewed-fulltext-article-JIR
25 Sharon M, Bardes JM, Riley H, Wagner A, Davis JK, Schaefer G, et al. A Comprehensive spinal cord injury treatment protocol improves outcomes and decreases complications. Am Surg. 2023;89(5):1893–8. Available from: https://journals.sagepub.com/doi/10.1177/00031348221074224
26 Flack J, Sharma K, Xie J. Delving into the recent advancements of spinal cord injury treatment: a review of recent progress. Neural Regen Res. 2022;17(2):283. Available from: https://journals.lww.com/10.4103/1673-5374.317961
27 Guliyeva G, A. Torres Guzman R, R. Avila Verduzco F, O. Akinduro O, Guerrero-Cazares H, Suarez Meade P, et al. Use of Mesenchymal stem cells in pre-clinical models of spinal cord injury. In: Juan Antonio Ibarra Arias J, Alberto Cuellar Ramos C, editors. Paraplegia. IntechOpen; 2021. Available from: https://www.intechopen.com/books/paraplegia/use-of-mesenchymal-stem-cells-in-pre-clinical-models-of-spinal-cord-injury
28 Curt A, Hsieh J, Schubert M, Hupp M, Friedl S, Freund P, et al. The Damaged spinal cord is a suitable target for stem cell transplantation. Neurorehabil Neural Repair. 2020;34(8):758–68. Available from: http://journals.sagepub.com/doi/10.1177/1545968320935815
29 Sykova E, Cizkova D, Kubinova S. Mesenchymal Stem cells in treatment of spinal cord injury and amyotrophic lateral sclerosis. Front Cell Dev Biol. 2021;9:695900. Available from: https://www.frontiersin.org/articles/10.3389/fcell.2021.695900/full
30 Alishahi M, Anbiyaiee A, Farzaneh M, Khoshnam SE. Human Mesenchymal stem cells for spinal cord injury. Curr Stem Cell Res Ther. 2020;15(4):340–8. Available from: https://www.eurekaselect.com/180275/article
31 Mukhamedshina YO, Zakirova EYu, Galieva LR, Kostennikov AA, Akhmetzyanova ER, Rizvanov AA. Distribution and Survival of transplanted adipose-derived mesenchymal stem cells in the spinal cord injury. BioNanoScience. 2017;7(4):608–12. Available from: http://link.springer.com/10.1007/s12668-017-0440-0
32 Chetty S, Yarani R, Swaminathan G, Primavera R, Regmi S, Rai S, et al. Umbilical cord mesenchymal stromal cells—from bench to bedside. Front Cell Dev Biol. 2022;10:1006295. Available from: https://www.frontiersin.org/articles/10.3389/fcell.2022.1006295/full
33 Johnson LDV, Pickard MR, Johnson WEB. The Comparative effects of mesenchymal stem cell transplantation therapy for spinal cord injury in humans and animal models: a systematic review and meta-analysis. Biology. 2021;10(3):230. Available from: https://www.mdpi.com/2079-7737/10/3/230
34 Tahmasebi F, Barati S. Effects of mesenchymal stem cell transplantation on spinal cord injury patients. Cell Tissue Res. 2022;389(3):373–84. Available from: https://link.springer.com/10.1007/s00441-022-03648-3
35 Mokrý J, Karbanová J, Čížková D, Pazour J, Filip S, Österreicher J. Differentiation of Neural stem cells into cells of oligodendroglial lineage. Acta Medica Hradec Kralove Czech Repub. 2007;50(1):35–41. Available from: https://actamedica.lfhk.cuni.cz/50/1/0035/
36 Zeigler F, Hall SG. Isolation of oligodendroglial cells from cultured neural stem/progenitors. In: Vemuri MC, editor. Stem Cell Assays. Totowa, NJ: Humana Press; 2007. p. 323–31. (Walker JM, editor. Methods in Molecular Biology; vol. 407). Available from: http://link.springer.com/10.1007/978-1-59745-536-7_22
37 Ye D, Wang Q, Yang Y, Chen B, Zhang F, Wang Z, et al. Identifying Genes that affect differentiation of human neural stem cells and myelination of mature oligodendrocytes. Cell Mol Neurobiol. 2023;43(5):2337–58. Available from: https://link.springer.com/10.1007/s10571-022-01313-5
38 Horie N. Neural Stem Cells/Neuronal Progenitor Cells. In: Houkin K, Abe K, Kuroda S, editors. Cell Therapy against cerebral stroke. Tokyo: Springer Japan; 2017. p. 27–37. Available from: http://link.springer.com/10.1007/978-4-431-56059-3_3
39 Lutfi Ismaeel G, Makki AlHassani OJ, S. Alazragi R, Hussein Ahmed A, H. Mohamed A, Yasir Jasim N, et al. Genetically engineered neural stem cells (NSCs) therapy for neurological diseases; state-of-the-art.

Biotechnol Prog. 2023;39(5):e3363. Available from: https://aiche.onlinelibrary.wiley.com/doi/10.1002/btpr.3363
40 Csobonyeiova M, Polak S, Zamborsky R, Danisovic L. Recent Progress in the regeneration of spinal cord injuries by induced pluripotent stem cells. Int J Mol Sci. 2019;20(15):3838. Available from: https://www.mdpi.com/1422-0067/20/15/3838
41 Gong Z, Xia K, Xu A, Yu C, Wang C, Zhu J, et al. Stem Cell Transplantation: A Promising therapy for spinal cord injury. Curr Stem Cell Res Ther. 2020;15(4):321–31. Available from: https://www.eurekaselect.com/174439/article
42 Lee-Kubli C, Lu P. Induced pluripotent stem cell-derived neural stem cell therapies for spinal cord injury. Neural Regen Res. 2015;10(1):10. Available from: https://journals.lww.com/10.4103/1673-5374.150638
43 López-Serrano C, Torres-Espín A, Hernández J, Alvarez-Palomo AB, Requena J, Gasull X, et al. Effects of the post-spinal cord injury microenvironment on the differentiation capacity of human neural stem cells derived from induced pluripotent stem cells. Cell Transplant. 2016;25(10):1833–52. Available from: http://journals.sagepub.com/doi/10.3727/096368916X691312
44 DeBrot A, Yao L. The combination of induced pluripotent stem cells and bioscaffolds holds promise for spinal cord regeneration. Neural Regen Res. 2018;13(10):1677. Available from: https://journals.lww.com/10.4103/1673-5374.238602
45 Shahbazi E, Moradi S, Nemati S, Satarian L, Basiri M, Gourabi H, et al. Conversion of Human fibroblasts to stably self-renewing neural stem cells with a single zinc-finger transcription factor. Stem Cell Rep. 2016;6(4):539–51. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213671116000643
46 Liu D, Rychkov G, Hurtado P, Luo HY, Zhang T, Bobrovskaya L, et al. Conversion of Human fibroblasts into induced neural stem cells by small molecules. Int J Mol Sci. 2022;23(3):1740. Available from: https://www.mdpi.com/1422-0067/23/3/1740
47 Pereira IM, Marote A, Salgado AJ, Silva NA. Filling the Gap: Neural stem cells as a promising therapy for spinal cord injury. Pharmaceuticals. 2019;12(2):65. Available from: https://www.mdpi.com/1424-8247/12/2/65
48 Yu C, Xia K, Gong Z, Ying L, Shu J, Zhang F, et al. The Application of neural stem/progenitor cells for regenerative therapy of spinal cord injury. Curr Stem Cell Res Ther. 2019;14(6):495–503. Available from: http://www.eurekaselect.com/171119/article
49 Ao Q, Wang AJ, Chen GQ, Wang SJ, Zuo HC, Zhang XF. Combined transplantation of neural stem cells and olfactory ensheathing cells for the repair of spinal cord injuries. Med Hypotheses. 2007;69(6):1234–7. Available from: https://linkinghub.elsevier.com/retrieve/pii/S030698770700285X
50 Lu P, Ahmad R, Tuszynski MH. Neural Stem cells for spinal cord injury. In: Tuszynski MH, editor. Translational Neuroscience. Boston, MA: Springer US; 2016. p. 297–315. Available from: http://link.springer.com/10.1007/978-1-4899-7654-3_16
51 Kiani S, Mohammadshirazi A, Kashkouli M, Shahbazi E, Asghari H, Kheymeh A, et al. Transplantation of induced neural stem cells derived from human fibroblasts promotes functional recovery of spinal cord injury in rats. Neurol Neurobiol. 2020;1–8. Available from: https://www.sciencerepository.org/transplantation-of-induced-neural-stem-cells-derived-from-human_NNB-2020-3-112
52 Fatima A, Abdullah U, Ali Z. Induced pluripotent stem cells. In: Bakhtiar SM, Dilshad E, editors. Omics Technologies for clinical diagnosis and gene therapy: medical applications in human genetics. BENTHAM SCIENCE PUBLISHERS; 2022. p. 214–25. Available from: https://www.eurekaselect.com/node/209473
53 Koyuncu Irmak D, Karaoz E. Generation of Induced pluripotent stem cells from human bone marrow–derived mesenchymal stem cells. In: Nagy A, Turksen K, editors. Induced Pluripotent Stem (iPS) Cells. New York, NY: Springer US; 2021. p. 17–29. (Methods in Molecular Biology; vol. 2454). Available from: https://link.springer.com/10.1007/7651_2021_445
54 Deng J, Zhang Y, Xie Y, Zhang L, Tang P. Cell Transplantation for spinal cord injury: tumorigenicity of induced pluripotent stem cell-derived neural stem/progenitor cells. Stem Cells Int. 2018;2018:1–7. Available from: https://www.hindawi.com/journals/sci/2018/5653787/
55 Lu P, Woodruff G, Wang Y, Graham L, Hunt M, Wu D, et al. Long-Distance axonal growth from human induced pluripotent stem cells after spinal cord injury. Neuron. 2014;83(4):789–96. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0896627314006254
56 Lavoie NS, Truong V, Malone D, Pengo T, Patil N, Dutton JR, et al. Human induced pluripotent stem cells integrate, create synapses and extend long axons after spinal cord injury. J Cell Mol Med. 2022;26(7):1932–42. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jcmm.17217
57 Kawabata S, Takano M, Numasawa-Kuroiwa Y, Itakura G, Kobayashi Y, Nishiyama Y, et al. Grafted Human ips cell-derived oligodendrocyte precursor cells contribute to robust remyelination of demyelinated axons after spinal cord injury. Stem Cell Rep. 2016;6(1):1–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2213671115003495
58 Shibata T, Tashiro S, Shibata S, Shinozaki M, Shindo T, Hashimoto S, et al. Rehabilitative Training enhances therapeutic effect of human ipsc-derived neural stem/progenitor cells transplantation in chronic spinal cord injury. Stem Cells Transl Med. 2023;12(2):83–96. Available from: https://academic.oup.com/stcltm/article/12/2/83/6988588
59 Li JX, Gao ZC, He XJ, Li J, Zhao H. [Advances in olfactory ensheathing cells for the treatment of spinal cord injury]. Zhongguo Gu Shang China J Orthop Traumatol. 2021;34(8):785–90.
60 Oieni F, Reshamwala R, St John J. Olfactory Ensheathing cells for spinal cord injury: the cellular superpowers for nerve repair. Neuroglia. 2022;3(4):139–43. Available from: https://www.mdpi.com/2571-6980/3/4/9
61 Liu K. Transplantation of olfactory ensheathing cells for promoting regeneration following spinal cord injury. Neural Regen Res. 2007;2(3):183–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1673537407600413
62 Anna Z, Katarzyna JW, Joanna C, Barczewska M, Joanna W, Wojciech M. Therapeutic Potential of olfactory ensheathing cells and mesenchymal stem cells in spinal cord injuries. Stem Cells Int. 2017;2017:1–6. Available from: https://www.hindawi.com/journals/sci/2017/3978595/
63 Stepanova OV, Fursa GA, Andretsova SS, Shishkina VS, Voronova AD, Chadin AV, et al. Prospects for the use of olfactory mucosa cells in bioprinting for the treatment of spinal cord injuries. World J Clin Cases. 2023;11(2):322–31. Available from: https://www.wjgnet.com/2307-8960/full/v11/i2/322.htm
64 Yao R, Murtaza M, Velasquez JT, Todorovic M, Rayfield A, Ekberg J, et al. Olfactory Ensheathing cells for spinal cord injury: sniffing out the issues. Cell Transplant. 2018;27(6):879–89. Available from: http://journals.sagepub.com/doi/10.1177/0963689718779353
65 Jiang C, Wang X, Jiang Y, Chen Z, Zhang Y, Hao D, et al. The Anti-inflammation property of olfactory ensheathing cells in neural regeneration after spinal cord injury. Mol Neurobiol. 2022;59(10):6447–59. Available from: https://link.springer.com/10.1007/s12035-022-02983-4
66 Wang T, Huang G, Yi Z, Dai S, Zhuang W, Guo S. Advances in extracellular vesicle-based combination therapies for spinal cord injury. Neural Regen Res. 2024;19(2):369–74. Available from: https://journals.lww.com/10.4103/1673-5374.377413
67 Zhou W, Silva M, Feng C, Zhao S, Liu L, Li S, et al. Exosomes derived from human placental mesenchymal stem cells enhanced the recovery of spinal cord injury by activating endogenous neurogenesis. Stem Cell Res Ther. 2021;12(1):174. Available from: https://stemcellres.biomedcentral.com/articles/10.1186/s13287-021-02248-2
68 Xue C, Ma X, Guan X, Feng H, Zheng M, Yang X. Small extracellular vesicles derived from umbilical cord mesenchymal stem cells repair blood-spinal cord barrier disruption after spinal cord injury through down-regulation of Endothelin-1 in rats. PeerJ. 2023;11:e16311. Available from: https://peerj.com/articles/16311
69 Luan Z, Liu J, Li M, Wang Y, Wang Y. Exosomes derived from umbilical cord-mesenchymal stem cells inhibit the NF-κB/MAPK signaling pathway and reduce the inflammatory response to promote recovery from spinal cord injury. J Orthop Surg. 2024;19(1):184. Available from: https://josr-online.biomedcentral.com/articles/10.1186/s13018-024-04651-w
70 Lee JR, Kyung JW, Kumar H, Kwon SP, Song SY, Han IB, et al. Targeted Delivery of mesenchymal stem cell-derived nanovesicles for spinal cord injury treatment. Int J Mol Sci. 2020 Jun 11;21(11):4185. Available from: https://www.mdpi.com/1422-0067/21/11/4185
71 Mu J, Wu J, Cao J, Ma T, Li L, Feng S, et al. Rapid and effective treatment of traumatic spinal cord injury using stem cell derived exosomes. Asian J Pharm Sci. 2021;16(6):806–15. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1818087621000878

72 Yang Q, Lu D, Wu J, Liang F, Wang H, Yang J, et al. Nanoparticles for the treatment of spinal cord injury. Neural Regen Res. 2024. Available from: https://journals.lww.com/10.4103/NRR.NRR-D-23-01848

73 Bingnan W, Jiao T, Ghorbani A, Baghei Sh. Enhancing regenerative potential: A comprehensive review of stem cell transplantation for sports-related neuronal injuries, with a focus on spinal cord injuries and peripheral nervous system damage. Tissue Cell. 2024;88:102429. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0040816624001307

74 Song S, Li Y, Huang J, Cheng S, Zhang Z. Inhibited astrocytic differentiation in neural stem cell-laden 3D bioprinted conductive composite hydrogel scaffolds for repair of spinal cord injury. Biomater Adv. 2023;148:213385. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2772950823001085

75 Kurakula M, Gorityala S, Patel DB, Basim P, Patel B, Kumar Jha S. Trends of Chitosan based delivery systems in neuroregeneration and functional recovery in spinal cord injuries. Polysaccharides. 2021;2(2):519–37. Available from: https://www.mdpi.com/2673-4176/2/2/31

76 Shinozaki M, Nagoshi N, Nakamura M, Okano H. Mechanisms of Stem cell therapy in spinal cord injuries. Cells. 2021;10(10):2676. Available from: https://www.mdpi.com/2073-4409/10/10/2676

77 Yousefpour M, Jahanbakhsh Z, Momenzadeh M. Stem Cell therapies for functional recovery after spinal cord injury: mechanisms, challenges, and applications. Ann Mil Health Sci Res. 2023;20(3). Available from: https://brieflands.com/articles/amhsr-131013.html

78 Lu P, Freria CM, Graham L, Tran AN, Villarta A, Yassin D, et al. Rehabilitation combined with neural progenitor cell grafts enables functional recovery in chronic spinal cord injury. JCI Insight. 2022;7(16):e158000. Available from: https://insight.jci.org/articles/view/158000

79 Tashiro S, Nakamura M, Okano H. Regenerative Rehabilitation and stem cell therapy targeting chronic spinal cord injury: a review of preclinical studies. Cells. 2022;11(4):685. Available from: https://www.mdpi.com/2073-4409/11/4/685

80 Sharma HS. A Select Combination of Neurotrophins Enhances Neuroprotection And Functional Recovery Following Spinal Cord Injury. Ann N Y Acad Sci. 2007;1122(1):95–111. Available from: https://nyaspubs.onlinelibrary.wiley.com/doi/10.1196/annals.1403.007

81 Hari Shanker Sharma. Neurotrophic Factors in combination: a possible new therapeutic strategy to influence pathophysiology of spinal cord injury and repair mechanisms. Curr Pharm Des. 2007;13(18):1841–74. Available from: http://www.eurekaselect.com/openurl/content.php?genre=article&issn=1381-6128&volume=13&issue=18&spage=1841

82 Jin Y, Rong X, Liu H. [Advances in stem cell transplantation for traumatic spinal cord injury at different stages]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi Zhongguo Xiufu Chongjian Waike Zazhi Chin J Reparative Reconstr Surg. 2023;37(6):721–6.

83 Digma LA, Upadhyayula PS, Martin JR, Ciacci JD. Stem cells and chronic spinal cord injury: Overview. In: Diagnosis and Treatment of Spinal Cord Injury. Elsevier; 2022. p. 397–409. Available from: https://linkinghub.elsevier.com/retrieve/pii/B9780128224984000312

84 Silvestro S, Bramanti P, Trubiani O, Mazzon E. Stem Cells therapy for spinal cord injury: an overview of clinical trials. Int J Mol Sci. 2020;21(2):659. Available from: https://www.mdpi.com/1422-0067/21/2/659

85 Agosti E, Zeppieri M, Pagnoni A, Fontanella MM, Fiorindi A, Ius T, et al. Current status and future perspectives on stem cell transplantation for spinal cord injury. World J Transplant. 2024;14(1). Available from: https://www.wjgnet.com/2220-3230/full/v14/i1/89674.htm

86 Goel A. Stem cell therapy in spinal cord injury: Hollow promise or promising science? J Craniovertebral Junction Spine. 2016;7(2):121. Available from: https://journals.lww.com/10.4103/0974-8237.181880

87 M. Kan E, A. Ling E, Lu J. Stem Cell therapy for spinal cord injury. Curr Med Chem. 2010;17(36):4492–510. Available from: http://www.eurekaselect.com/openurl/content.php?genre=article&issn=0929-8673&volume=17&issue=36&spage=4492

88 Chhabra HS, Sarda K. Stem cell therapy in spinal trauma: Does it have scientific validity? Indian J Orthop. 2015;49(1):54–71. Available from: https://link.springer.com/10.4103/0019-5413.143913

89 Farid MF, S. Abouelela Y, Rizk H. Stem cell treatment trials of spinal cord injuries in animals. Auton Neurosci. 2022;238:102932. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1566070221001624

90 De Freria CM, Van Niekerk E, Blesch A, Lu P. Neural Stem cells: promoting axonal regeneration and spinal cord connectivity. Cells. 2021;10(12):3296. Available from: https://www.mdpi.com/2073-4409/10/12/3296

91 Zhang F. Structure-function evaluation of stem cell therapies for spinal cord injury. Curr Stem Cell Res Ther. 2018;13(3):202–14. Available from: http://www.eurekaselect.com/158733/article

92 Zeng CW. Advancing Spinal cord injury treatment through stem cell therapy: a comprehensive review of cell types, challenges, and emerging technologies in regenerative medicine. Int J Mol Sci. 2023;24(18):14349. Available from: https://www.mdpi.com/1422-0067/24/18/14349

93 Fan C, Cai H, Zhang L, Wu X, Yan J, Jin L, et al. Constructing Linear-oriented pre-vascularized human spinal cord tissues for spinal cord injury repair. Adv Healthc Mater. 2024;13(18):2303388. Available from: https://onlinelibrary.wiley.com/doi/10.1002/adhm.202303388

94 Fang YM, Chen WC, Zheng WJ, Yang YS, Zhang Y, Chen XL, et al. A cutting-edge strategy for spinal cord injury treatment: resident cellular transdifferentiation. Front Cell Neurosci. 2023;17:1237641. Available from: https://www.frontiersin.org/articles/10.3389/fncel.2023.1237641/full

95 Kim HN, McCrea MR, Li S. Advances in molecular therapies for targeting pathophysiology in spinal cord injury. Expert Opin Ther Targets. 2023;27(3):171–87. Available from: https://www.tandfonline.com/doi/full/10.1080/14728222.2023.2194532

96 Dalamagkas K, Tsintou M, Seifalian A. Stem cells for spinal cord injuries bearing translational potential. Neural Regen Res. 2018;13(1):35. Available from: https://journals.lww.com/10.4103/1673-5374.224360

97 Sousa CS, Monteiro A, Salgado AJ, Silva NA. Combinatorial therapies for spinal cord injury repair. Neural Regen Res. 2025;20(5):1293–308. Available from: https://journals.lww.com/10.4103/NRR.NRR-D-24-00061

98 Deng J, Meng F, Gao J, Zhang K, Liu Z, Li M, et al. Early-phase rotator training impairs tissue repair and functional recovery after spinal cord injury. Heliyon. 2023;9(7):e18158. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2405844023053665

99 Liu T, Zhu W, Zhang X, He C, Liu X, Xin Q, et al. Recent Advances in cell and functional biomaterial treatment for spinal cord injury. Ma L, editor. BioMed Res Int. 2022;2022:1–20. Available from: https://www.hindawi.com/journals/bmri/2022/5079153/

100 Wang J, Zou W, Ma J, Liu J. Biomaterials and Gene manipulation in stem cell-based therapies for spinal cord injury. Stem Cells Dev. 2019;28(4):239–57. Available from: https://www.liebertpub.com/doi/10.1089/scd.2018.0169

101 Papa S, Pizzetti F, Perale G, Veglianese P, Rossi F. Regenerative medicine for spinal cord injury: focus on stem cells and biomaterials. Expert Opin Biol Ther. 2020;20(10):1203–13. Available from: https://www.tandfonline.com/doi/full/10.1080/14712598.2020.1770725

102 Hersh AM, Weber-Levine C, Jiang K, Theodore N. Spinal Cord injury. Neurosurg Clin N Am. 2024;35(2):243–51. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1042368023001067

103 Choi E, Gattas S, Brown N, Hong J, Limbo J, Chan A, et al. Epidural electrical stimulation for spinal cord injury. Neural Regen Res. 2021;16(12):2367. Available from: https://journals.lww.com/10.4103/1673-5374.313017

104 Zhou K, Wei W, Yang D, Zhang H, Yang W, Zhang Y, et al. Dual electrical stimulation at spinal-muscular interface reconstructs spinal sensorimotor circuits after spinal cord injury. Nat Commun. 2024;15(1):619. Available from: https://www.nature.com/articles/s41467-024-44898-9

105 Zheng Y, Mao YR, Yuan TF, Xu DS, Cheng LM. Multimodal treatment for spinal cord injury: a sword of neuroregeneration upon neuromodulation. Neural Regen Res. 2020;15(8):1437. Available from: https://journals.lww.com/10.4103/1673-5374.274332

106 Park J. Immunomodulatory Strategies for Spinal cord injury. Biomed J Sci Tech Res. 2022;45(3). Available from: https://biomedres.us/fulltexts/BJSTR.MS.ID.007202.php