



Original Investigation | Neurology

Emerging boundaries in spinal cord injury treatment: a narrative review of neural stem cells, bioscaffold innovations and combinations techniques over traditional treatment approaches: A Narrative Review

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Key Points

Question:

How do bioengineering techniques improve neuroregeneration in SCIs? Can combination therapies enhance sensory and motor recovery beyond traditional treatments?

Findings:

SCIs result in permanent damage with current treatments providing limited recovery. Neural stem cells, bioscaffolds, and 3D bioprinting improve axonal growth and circuit restoration. Combination therapies yield better functional outcomes but face integration challenges.

Meaning:

Bioengineering approaches hold significant potential to transform SCI treatment by addressing limitations of conventional methods. Further research is crucial to optimize recovery and integration.

Abstract

Importance:

Spinal cord injuries (SCIs) lead to sensory, motor, and autonomic dysfunction due to primary axonal damage and secondary inflammatory processes. Current treatments focus on damage control and management, often leaving permanent functional impairments.

Objective:

To explore emerging bioengineering techniques and regenerative medicine principles, including neural stem cells, bioscaffolds, conductive biomaterials, and 3D bioprinting, to improve neuroregeneration and overcome limitations of conventional SCI treatments. Challenged by the limitation and the incapacity, scientists and researchers have developed a brain-computer interface technology (BCI) that enables direct communication between the brain and external computing devices independently of the peripheral nerves or muscles augmenting human capabilities in interacting with the physical environment.

Evidence Review

A narrative review of advancements in regenerative medicine, focusing on preclinical and clinical studies involving combination therapies. These include innovative materials and approaches that aim to enhance neurogenesis, axonal growth, and neuroelectrical circuit restoration.

Findings

Current treatments like surgical decompression and rehabilitation have limited efficacy in reversing SCIs. Bioengineering techniques such as neural stem cells and bioscaffolds promote neuroregeneration and provide structural support for cell survival and integration. Combination therapies demonstrate improved sensory and motor outcomes compared to standalone interventions, though challenges like limited recovery and functional integration remain.

Conclusions and Relevance:

Regenerative medicine offers promising avenues for SCI treatment by enhancing neuroregeneration and functional restoration. Combination therapies leveraging bioengineering innovations have shown beneficial outcomes, emphasizing the need for further research to overcome existing limitations.

References

- Kelly TH, Thompson T. The effects of methadone on operant behavior maintained with and without conditioned reinforcement in the pigeon. *Psychopharmacology (Berl)*. 1985;86(1-2):212-6. doi: 10.1007/BF00431712. PMID: 3927358.
- Li Z, Zhou T, Bao Z, Wu M, Mao Y. The Porous SilMA Hydrogel Scaffolds Carrying Dual-Sensitive Paclitaxel Nanoparticles Promote Neuronal Differentiation for Spinal Cord Injury Repair. *Tissue Eng Regen Med*. 2024 Aug;21(6):809-827. doi: 10.1007/s13770-024-00659-9. Epub 2024 Jul 15. PMID: 39004636; PMCID: PMC11286913.
- Wang Z, Li J, Xu T, Guo B, Xie Z, Li M. The Efficacy of Different Material Scaffold-Guided Cell Transplantation in the Treatment of Spinal Cord Injury in Rats: A Systematic Review and Network Meta-analysis. *Cell Mol Neurobiol*. 2024 May 4;44(1):43. doi: 10.1007/s10571-024-01465-6. PMID: 38703332; PMCID: PMC11069479.
- Liu Z, Lai J, Kong D, Zhao Y, Zhao J, Dai J, Zhang M. Advances in electroactive bioscaffolds for repairing spinal cord injury. *Biomed Mater*. 2024 Apr 30;19(3). doi: 10.1088/1748-605X/ad4079. PMID: 38636508.
- Yin W, Yang C, Liu D, Cha S, Cai L, Ye G, Song X, Zhang J, Qiu X. Mussel shell-derived pro-regenerative scaffold with conductive porous multi-scale-patterned microenvironment for spinal cord injury repair. *Biomed Mater*. 2024 Apr 30;19(3). doi: 10.1088/1748-605X/ad3f63. PMID: 38626779.
- Jiu J, Liu H, Li D, Li J, Liu L, Yang W, Yan L, Li S, Zhang J, Li X, Li JJ, Wang B. 3D bioprinting approaches for spinal cord injury repair. *Biofabrication*. 2024 Apr 22;16(3). doi: 10.1088/1758-5090/ad3a13. PMID: 38569491.
- Fan C, Cai H, Zhang L, Wu X, Yan J, Jin L, Hu B, He J, Chen Y, Zhao Y, Dai J. Constructing Linear-Oriented Pre-Vascularized Human Spinal Cord Tissues for Spinal Cord Injury Repair. *Adv Healthc Mater*. 2024 Jul;13(18):e2303388. doi: 10.1002/adhm.202303388. Epub 2024 Apr 4. PMID: 38537119.
- Zhang J, Li X, Guo L, Gao M, Wang Y, Xiong H, Xu T, Xu R. 3D hydrogel microfibers promote the differentiation of encapsulated neural stem cells and facilitate neuron protection and axon regrowth after complete transactional spinal cord injury. *Biofabrication*. 2024 May 9;16(3). doi: 10.1088/1758-5090/ad39a7. PMID: 38565133.
- Ghaffari N, Mokhtari T, Adabi M, Ebrahimi B, Kamali M, Gholaminejhad M, Hassanzadeh G. Neurological recovery and neurogenesis by curcumin sustained-release system cross-linked with an acellular spinal cord scaffold in rat spinal cord injury: Targeting NLRP3 inflammasome pathway. *Phytother Res*. 2024 Jun;38(6):2669-2686. doi: 10.1002/ptr.8179. Epub 2024 Mar 18. PMID: 38500263.
- Ozcicek I, Aysit N, Balcikanli Z, Ayturk NU, Aydeger A, Baydas G, Aydin MS, Altintas E, Erim UC. Development of BDNF/NGF/IKVAV Peptide Modified and Gold Nanoparticle Conductive PCL/PLGA Nerve Guidance Conduit for Regeneration of the Rat Spinal Cord Injury. *Macromol Biosci*. 2024 May;24(5):e2300453. doi: 10.1002/mabi.202300453. Epub 2024 Jan 18. PMID: 38224015.
- Yang Y, Fan R, Li H, Chen H, Gong H, Guo G. Polysaccharides as a promising platform for the treatment of spinal cord injury: A review. *Carbohydr Polym*. 2024 Mar 1;327:121672. doi: 10.1016/j.carbpol.2023.121672. Epub 2023 Dec 9. PMID: 38171685.

References

- Szymoniuk M, Mazurek M, Dryla A, Kamieniak P. The application of 3D-bioprinted scaffolds for neuronal regeneration after traumatic spinal cord injury - A systematic review of preclinical in vivo studies. *Exp Neurol*. 2023 May;363:114366. doi: 10.1016/j.expneurol.2023.114366. Epub 2023 Feb 28. PMID: 36858280.
- Sousa JPM, Stratakis E, Mano J, Marques PAAP. Anisotropic 3D scaffolds for spinal cord guided repair: Current concepts. *Biomater Adv*. 2023 May;148:213353. doi: 10.1016/j.bioadv.2023.213353. Epub 2023 Feb 23. PMID: 36848743.
- Chen X, Wang Y, Zhou G, Hu X, Han S, Gao J. The combination of nanoscaffolds and stem cell transplantation: Paving a promising road for spinal cord injury regeneration. *Biomed Pharmacother*. 2021 Nov;143:112233. doi: 10.1016/j.biopha.2021.112233. Epub 2021 Sep 30. PMID: 34649357.
- Yu Q, Liao M, Sun C, Zhang Q, Deng W, Cao X, Wang Q, Omari-Siaw E, Bi S, Zhang Z, Yu J, Xu X. LBO-EMSC Hydrogel Serves a Dual Function in Spinal Cord Injury Restoration *via* the PI3K-Akt-mTOR Pathway. *ACS Appl Mater Interfaces*. 2021 Oct 20;13(41):48365-48377. doi: 10.1021/acsami.1c12013. Epub 2021 Oct 11. PMID: 34633177.
- Kim SH, Hwang K, Lee HA, Kim J, Cho M, Kim M, Shin JE, Lee H, Park KI, Jang JH. Pastable, Adhesive, Injectable, Nanofibrous, and Tunable (PAINT) Biphasic Hybrid Matrices as Versatile Therapeutic Carriers. *ACS Appl Mater Interfaces*. 2021 Sep 15;13(36):42429-42441. doi: 10.1021/acsami.1c10818. Epub 2021 Sep 2. PMID: 34472351.
- Deng WS, Yang K, Liang B, Liu YF, Chen XY, Zhang S. Collagen/heparin sulfate scaffold combined with mesenchymal stem cells treatment for canines with spinal cord injury: A pilot feasibility study. *J Orthop Surg (Hong Kong)*. 2021 May-Aug;29(2):23094990211012293. doi: 10.1177/23094990211012293. PMID: 34060363.
- Mneimneh AT, Mehanna MM. Collagen-based scaffolds: An auspicious tool to support repair, recovery, and regeneration post spinal cord injury. *Int J Pharm*. 2021 May 15;601:120559. doi: 10.1016/j.ijpharm.2021.120559. Epub 2021 Apr 5. PMID: 33831486.
- Li XH, Zhu X, Liu XY, Xu HH, Jiang W, Wang JJ, Chen F, Zhang S, Li RX, Chen XY, Tu Y. The corticospinal tract structure of collagen/silk fibroin scaffold implants using 3D printing promotes functional recovery after complete spinal cord transection in rats. *J Mater Sci Mater Med*. 2021 Mar 22;32(4):31. doi: 10.1007/s10856-021-06500-2. PMID: 33751254; PMCID: PMC7985105.
- Santi S, Corridori I, Pugno NM, Motta A, Migliaresi C. Injectable Scaffold-Systems for the Regeneration of Spinal Cord: Advances of the Past Decade. *ACS Biomater Sci Eng*. 2021 Mar 8;7(3):983-999. doi: 10.1021/acsbiomaterials.0c01779. Epub 2021 Feb 1. PMID: 33523634.
- El Waly B, Escarrat V, Perez-Sanchez J, Kaur J, Pelletier F, Collazos-Castro JE, Debarbieux F. Intravital Assessment of Cells Responses to Conducting Polymer-Coated Carbon Microfibres for Bridging Spinal Cord Injury. *Cells*. 2021 Jan 5;10(1):73. doi: 10.3390/cells10010073. PMID: 33466339; PMCID: PMC7824803.

References

- Liu L, Wan J, Dai M, Ye X, Liu C, Tang C, Zhu L. Effects of oxygen generating scaffolds on cell survival and functional recovery following acute spinal cord injury in rats. *J Mater Sci Mater Med*. 2020 Nov 28;31(12):115. doi: 10.1007/s10856-020-06453-y. PMID: 33247423.
- Ghane N, Beigi MH, Labbaf S, Nasr-Esfahani MH, Kiani A. Design of hydrogel-based scaffolds for the treatment of spinal cord injuries. *J Mater Chem B*. 2020 Dec 21;8(47):10712-10738. doi: 10.1039/d0tb01842b. Epub 2020 Nov 6. PMID: 33155614.
- Xi K, Gu Y, Tang J, Chen H, Xu Y, Wu L, Cai F, Deng L, Yang H, Shi Q, Cui W, Chen L. Microenvironment-responsive immunoregulatory electrospun fibers for promoting nerve function recovery. *Nat Commun*. 2020 Sep 9;11(1):4504. doi: 10.1038/s41467-020-18265-3. Erratum in: *Nat Commun*. 2021 May 11;12(1):2882. doi: 10.1038/s41467-021-23438-9. PMID: 32908131; PMCID: PMC7481196.
- Chen W, Zhang Y, Yang S, Sun J, Qiu H, Hu X, Niu X, Xiao Z, Zhao Y, Zhou Y, Dai J, Chu T. NeuroRegen Scaffolds Combined with Autologous Bone Marrow Mononuclear Cells for the Repair of Acute Complete Spinal Cord Injury: A 3-Year Clinical Study. *Cell Transplant*. 2020 Jan-Dec;29:963689720950637. doi: 10.1177/0963689720950637. PMID: 32862715; PMCID: PMC7784506.
- Yao L, DeBrot A. Preparation of Bioscaffolds Delivering Stem Cells for Neural Regeneration. *Methods Mol Biol*. 2020;2155:63-70. doi: 10.1007/978-1-0716-0655-1_5. PMID: 32474867.
- Cnops V, Chin JS, Milbreta U, Chew SY. Biofunctional scaffolds with high packing density of aligned electrospun fibers support neural regeneration. *J Biomed Mater Res A*. 2020 Dec;108(12):2473-2483. doi: 10.1002/jbm.a.36998. Epub 2020 Jul 23. PMID: 32418345.
- Bedir T, Ulag S, Ustundag CB, Gunduz O. 3D bioprinting applications in neural tissue engineering for spinal cord injury repair. *Mater Sci Eng C Mater Biol Appl*. 2020 May;110:110741. doi: 10.1016/j.msec.2020.110741. Epub 2020 Feb 19. PMID: 32204049.
- Chen X, Wu J, Sun R, Zhao Y, Li Y, Pan J, Chen Y, Wang X. Tubular scaffold with microchannels and an H-shaped lumen loaded with bone marrow stromal cells promotes neuroregeneration and inhibits apoptosis after spinal cord injury. *J Tissue Eng Regen Med*. 2020 Mar;14(3):397-411. doi: 10.1002/term.2996. Epub 2020 Jan 29. PMID: 31821733; PMCID: PMC7155140.
- Blando S, Anchesi I, Mazzon E, Gugliandolo A. Can a Scaffold Enriched with Mesenchymal Stem Cells Be a Good Treatment for Spinal Cord Injury? *Int J Mol Sci*. 2022 Jul 7;23(14):7545. doi: 10.3390/ijms23147545. PMID: 35886890; PMCID: PMC9319719.
- Xiao Z, Tang F, Zhao Y, Han G, Yin N, Li X, Chen B, Han S, Jiang X, Yun C, Zhao C, Cheng S, Zhang S, Dai J. Significant Improvement of Acute Complete Spinal Cord Injury Patients Diagnosed by a Combined Criteria Implanted with NeuroRegen Scaffolds and Mesenchymal Stem Cells. *Cell Transplant*. 2018 Jun;27(6):907-915. doi: 10.1177/0963689718766279. Epub 2018 Jun 5. PMID: 29871514; PMCID: PMC6050906.

References

- Agosti E, Zeppieri M, Pagnoni A, Fontanella MM, Fiorindi A, Ius T, Panciani PP. Current status and future perspectives on stem cell transplantation for spinal cord injury. *World J Transplant.* 2024 Mar 18;14(1):89674. doi: 10.5500/wjt.v14.i1.89674. PMID: 38576751; PMCID: PMC10989472.
- Rath N, Balain B. Spinal cord injury-The role of surgical treatment for neurological improvement. *J Clin Orthop Trauma.* 2017 Apr-Jun;8(2):99-102. doi: 10.1016/j.jcot.2017.06.016. Epub 2017 Jun 16. PMID: 28720984; PMCID: PMC5498753.
- Rath N, Balain B. Spinal cord injury-The role of surgical treatment for neurological improvement. *J Clin Orthop Trauma.* 2017 Apr-Jun;8(2):99-102. doi: 10.1016/j.jcot.2017.06.016. Epub 2017 Jun 16. PMID: 28720984; PMCID: PMC5498753.
- Rath N, Balain B. Spinal cord injury-The role of surgical treatment for neurological improvement. *J Clin Orthop Trauma.* 2017 Apr-Jun;8(2):99-102. doi: 10.1016/j.jcot.2017.06.016. Epub 2017 Jun 16. PMID: 28720984; PMCID: PMC5498753.
- Suzuki H, Imajo Y, Funaba M, Ikeda H, Nishida N, Sakai T. Current Concepts of Biomaterial Scaffolds and Regenerative Therapy for Spinal Cord Injury. *Int J Mol Sci.* 2023 Jan 28;24(3):2528. doi: 10.3390/ijms24032528. PMID: 36768846; PMCID: PMC9917245.
- Feng C, Deng L, Yong YY, Wu JM, Qin DL, Yu L, Zhou XG, Wu AG. The Application of Biomaterials in Spinal Cord Injury. *Int J Mol Sci.* 2023 Jan 3;24(1):816. doi: 10.3390/ijms24010816. PMID: 36614259; PMCID: PMC9821025.
- Harder M, Baumberger M, Pannek J, Decker J, Bersch I. Rehabilitation nach einer Querschnittlähmung : Aktuelle Trends und Grundlagen [Rehabilitation after Spinal Cord Injury : Current trends and principles]. *Unfallchirurgie (Heidelb).* 2023 Oct;126(10):764-773. German. doi: 10.1007/s00113-023-01360-7. Epub 2023 Aug 22. PMID: 37608182.
- Scheel-Sailer A, Selb M, Gmünder HP, Baumberger M, Curt A, Hund-Georgiadis M, Jordan X, Stucki G; Swiss SCI/D Rehabilitation Interest Group. Towards the implementation of clinical quality management at the national level: description of current types of rehabilitation services for spinal cord injury/disorder in Switzerland using an interdisciplinary consensus process. *Eur J Phys Rehabil Med.* 2022 Apr;58(2):190-198. doi: 10.23736/S1973-9087.21.06923-9. Epub 2021 May 18. PMID: 34002976; PMCID: PMC9980538.
- Blando S, Anchesi I, Mazzon E, Gugliandolo A. Can a Scaffold Enriched with Mesenchymal Stem Cells Be a Good Treatment for Spinal Cord Injury? *Int J Mol Sci.* 2022 Jul 7;23(14):7545. doi: 10.3390/ijms23147545. PMID: 35886890; PMCID: PMC9319719.
- Xiao Z, Tang F, Zhao Y, Han G, Yin N, Li X, Chen B, Han S, Jiang X, Yun C, Zhao C, Cheng S, Zhang S, Dai J. Significant Improvement of Acute Complete Spinal Cord Injury Patients Diagnosed by a Combined Criteria Implanted with NeuroRegen Scaffolds and Mesenchymal Stem Cells. *Cell Transplant.* 2018 Jun;27(6):907-915. doi: 10.1177/0963689718766279. Epub 2018 Jun 5. PMID: 29871514; PMCID: PMC6050906.

References

Jiu J, Liu H, Li D, Li J, Liu L, Yang W, Yan L, Li S, Zhang J, Li X, Li JJ, Wang B. 3D bioprinting approaches for spinal cord injury repair. *Biofabrication*. 2024 Apr 22;16(3). doi: 10.1088/1758-5090/ad3a13. PMID: 38569491.

Bedir T, Ulag S, Ustundag CB, Gunduz O. 3D bioprinting applications in neural tissue engineering for spinal cord injury repair. *Mater Sci Eng C Mater Biol Appl*. 2020 May;110:110741. doi: 10.1016/j.msec.2020.110741. Epub 2020 Feb 19. PMID: 32204049.

Li Z, Zhou T, Bao Z, Wu M, Mao Y. The Porous SilMA Hydrogel Scaffolds Carrying Dual-Sensitive Paclitaxel Nanoparticles Promote Neuronal Differentiation for Spinal Cord Injury Repair. *Tissue Eng Regen Med*. 2024 Aug;21(6):809-827. doi: 10.1007/s13770-024-00659-9. Epub 2024 Jul 15. PMID: 39004636; PMCID: PMC11286913.

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