Spinal Cord Injury (SCI) Research

Significant gains in spinal cord injury research throughout recent decades have greatly improved care and quality of life for people living with paralysis. A generation ago, any damage to the brain and spinal cord resulting in severely limited motor or sensory function was deemed untreatable. Now, scientists around the world are working on an array of potential therapies for people with paralysis, from developing drugs that prevent injury progression to promoting repair and reactivation of damaged nerves through cell transplant and activity-based training. As the functional changes caused by spinal cord injury have become better understood, research increasingly indicates that a cure for paralysis will likely not arrive in the form of a single drug or therapy; instead, a combination of treatments deployed at various stages of rehabilitation will be critical to countering damage and restoring function below the level of injury. Current research is centered around four key areas of spinal cord repair, including:

Neuroprotection: Traumatic spinal cord injury (SCI) occurs in two phases: the primary injury, caused by a sudden trauma that fractures or dislocates vertebrae, is then followed by a cascade of biochemical events that can significantly increase damage to the tissue surrounding the original injury. Researchers are currently studying how to prevent additional cell death and injury progression during this secondary phase. The steroid drug methylprednisolone sodium succinate (MPSS), sometimes prescribed after injury in hopes of improving motor and sensory outcomes, remains subject to debate among clinicians because of concerns about its effectiveness and potential complications. Some

neurosurgeons do not recommend its usage; others suggest that a 24-hour infusion of high dose MPSS be offered to adult patients who present within 8-hours of acute spinal cord injury, but not beyond this window due to a lack of demonstrated efficacy. Researchers are studying other potential acute treatment drugs, including riluzole, which may protect nerves from further secondary phase damage from excess glutamate. Decompression surgery, performed to relieve pressure within the spinal column, is also being studied to determine impact on neurological recovery; data indicates improved outcomes if surgery is performed within 24 hours after injury. The cooling of the spinal cord is another possible acute therapy treatment; hypothermia appears to slow down and reduce cell loss, but more research is needed to determine protocol, including the optimal timing and duration of cooling.

Regeneration: Promoting axon repair and regrowth after spinal cord injury remains critical for recovery. Damaged axons—the nerve pathways that carry messages up and down the spinal cord–interrupt the brain's communication with the spinal cord, resulting in lost function below injury level. Scientists continue to study potential treatments that facilitate the regeneration and sprouting of axons and counter factors in the central nervous system that inhibit regrowth. One avenue of research targets the glial scar, which forms around the lesion in a reaction occurring immediately after injury. The scar protects healthy tissue from the damaged area, but at the same time contains extracellular components that help discourage repair. The enzyme chondroitinase has shown promise in improving axonal sprouting and functional recovery after spinal cord injury in rodents. Studies using anti-Nogo antibodies to promote spinal cord cell growth by blocking inhibition have also yielded positive results. In 2021, NerveGen Pharma, a clinical stage biotech company, began a phase 1 trial of NVG-291 in Australia; the treatment aims to stimulate nerve repair by inhibiting the activity of the protein tyrosine phosphatase sigma, a neural receptor that blocks nerve regeneration following tissue damage. Other research efforts, including by the Miami Project to Cure Paralysis, are focused on how Schwann cells may help bridge and support nerve regeneration across the site of injury. And at Marquette University, the Blackmore Lab is currently working to improve neuronal growth capability using gene therapy; its recent work has identified novel combinations of transcription factors that drive enhanced axon growth in mature central nervous system neurons.

Cell replacement: Researchers continue to investigate the potential of stem cell therapy to treat paralysis. Scientists are currently studying how different types of cells, including bone marrow-derived mesenchymal stem cells, neural stem cells, induced pluripotent stem cells (adult stem cells altered in a lab to resemble embryonic stem cells) and non-stem cells such as olfactory ensheathing cells and Schwann cells can be used to promote connectivity and create a conducive environment for neural repair after spinal cord injury. Results of stem cell therapy studies have been cautiously encouraging but not because the new cells take on the identity of the lost or damaged ones. Rather, replacement cells seem to offer support and help nurture surviving cells.
Recent trials exploring potential future treatments include a phase1 study of NS1-566 by Biopharma (formerly Neuralstem) that grafted human-spinal-cord-derived neural stem cells in four individuals with chronic spinal injury; though the results demonstrated efficacy

and no detectable side effects, because of the small sample size, additional research is needed to more fully evaluate functional changes. The Mayo Clinic recently completed a phase 1 clinical trial of mesenchymal stem cell treatment with results indicating the potential for improved neurologic function; phase 2 of the trial, known as CELLTOP, began in 2020 with a focus on determining the characteristics (including age, severity of and time since injury) of individuals who respond to the therapy. And in 2021, researchers at Yale University and Sapporo Medical University reported gains in motor function in a preliminary trial: because results were not blinded and lacked placebo controls, more studies will be needed. While stem cell therapy may eventually yield gains for individuals living with paralysis, there is currently no approved stem cell treatment for spinal cord injury. The FDA cautions patients against seeking unproven and potentially harmful treatments from rogue stem-cell clinics that operate within the U.S. and around the world.

Rehabilitation and plasticity: Research conducted over the past few decades spotlights the importance of physical rehabilitation on improving function and quality of life after spinal cord injury. Intensive, activity-based training, including robotic and body-weight support treadmill training, and overground and standing training, can help reorganize and reactivate dormant nerve circuits, leading to gains in mobility and autonomic function. Scientists continue to study how physiological changes in the nervous system are fostered by high-intensity training compared to standard rehabilitation programs. Activity-based training used in combination with advanced therapeutic technologies such as electrical stimulation has also become a central focus of current spinal cord injury research. The purpose of electrical stimulation—deployed through electrodes placed on the skin's surface or through surgical implantation over the spinal cord–is to replicate signals sent by the brain along the spinal cord prior to injury; in this treatment, electrical pulses activate neural circuits and cause muscle contraction. The application of electrical stimulation on its own and in combination with activity-based training has yielded multiple gains in mobility and autonomic function for individuals with chronic injury and remains a potentially crucial component of future treatments for paralysis. Recent and current research efforts include a clinical trial underway at the University of Louisville's Kentucky Spinal Cord Injury Research Center that is studying the impact of epidural stimulation on standing, restoring voluntary movement, improving bowel and bladder management, and regulating blood pressure; a study at the University of Washington's Restorative Technologies Laboratory assessing the effects of non-invasive electrical stimulation and physical and occupational therapy on upper extremity function; and multiple studies at the Cleveland Functional Electrical Stimulation Center, a consortium of nationally recognized health systems, investigating the use of stimulation to restore cough, improve pelvic health and prevent pressure sores.

Sources: National Institute of Neurological Disorders and Stroke (NINDS), Craig Hospital, Christopher & Dana Reeve Foundation's Paralysis Resource Guide 2020, Mayo Clinic, Shepherd Center, Congress of Neurological Surgeons, *Nature*, *The Lancet, Global Spine Journal.*

Websites

Christopher & Dana Reeve Foundation: Research

www.ChristopherReeve.org/Research
This page has information on research into treatments and cures for spinal cord injury including information on epidural stimulation of the spine.

Administration for Community Living (ACL): National Institute on Disability and Rehabilitation Research (NIDILRR)'s Research Program
https://www.acl.gov/programs/research-and-development
This page describes the NIDILRR's research program, which is conducted via a network of individual research projects and centers of excellence throughout the country. Most NIDRR grantees are universities or providers of rehabilitation or related services.

American Institutes for Research's Center on Knowledge Translation for Disability and Rehabilitation Research (CKTDRR)
https://ktdrr.org/
The organization aims to make it easier to find and understand the results of research in the disability and rehabilitation field. KTDRR is funded by the National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR) (https://acl.gov/NIDILRR.).

Canadian/American Spinal Research Organization
http://csro.com/
126 Westwood Lane
Richmond Hill, ON
L4C 6Y3
and
2430 Military Road, Box # 271
Niagara Falls, NY, 14304-1745
Phone: 905-508-4000,
Toll-free: 800-361-4004
The CSRO is dedicated to the improvement of the physical quality of life for persons with a spinal cord injury and those with related neurological deficits, through targeted medical and scientific research.

Craig H. Neilsen Foundation
http://www.chnfoundation.org/
http://chnfoundation.org/what-we-fund/
16633 Ventura Blvd., Suite 352
Encino, CA 91436
Phone: 818-762-8533
This foundation funds research grants that support scientific, charitable and educational organizations conducting spinal cord injury research, training in spinal cord medicine and providing services to assist individuals and families affected by spinal cord injury.

Disability Research and Dissemination Center
https://www.disabilityresearchcenter.com/dissemination/

The American Association on Health and Disability (AAHD http://www.aahd.us/) and the University of South Carolina offer the DRDC Dissemination Core which communicates current scientific, programmatic, and policy information.

Miami Project to Cure Paralysis
https://www.themiamiproject.org
1095 NW 14th Terrace
Miami, FL 33136
Phone: 305-243-6001, 800-STAND UP (Toll-free, 800-782-6387)
E-mail: miamiproject@med.miami.edu
The Miami Project is the world's largest comprehensive spinal cord injury research center, dedicated to finding more effective treatments and, ultimately, a cure for paralysis.

National Institute of Neurological Disorders and Stroke: Spinal Cord Injury – Hope Through Research
https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Spinal-Cord-Injury-Hope-Through-Research
This page has comprehensive information on spinal cord injury, including treatment, rehabilitation and research.

Paralyzed Veterans of America Research Foundation
www.pva.org
http://www.pva.org/research-foundation
Lindsay Perlman
Associate Director, Research and Education
Phone: 202-416-7611
Email: LindsayP@pva.org
The PVA Research Foundation supports innovative research and fellowships that improve the lives of those with spinal cord injury and disease.

Reeve-Irvine Research Center
http://www.reeve.uci.edu
The mission of the Reeve-Irvine Research Center is to find new treatments for spinal cord injury through the collaborative research and educational efforts of prominent scientists and clinicians both at the University of California, Irvine and around the world.

Rutgers University: W.M. Keck Center for Collaborative Neuroscience
http://keck.rutgers.edu/
The Spinal Cord Injury Project
604 Allison Road, D-251
Piscataway, NJ 08854
Phone: 848-445-2061 or 848-445-9553
E-mail: SCIProject@rutgers.edu The mission of the W. M. Keck Center for Collaborative Neuroscience is the development of effective treatment for acute and chronic spinal cord injuries and to move these discoveries from laboratory to human lives as rapidly as possible.

Spinal Cord Injury Rehabilitation Evidence (SCIRE)
http://www.scireproject.com/
SCIRE is a Canadian project that synthesizes research on SCI rehabilitation for health care professionals, scientists,
policymakers and consumers.

University of Alabama at Birmingham-Spinal Cord Injury Model System (UAB-SCIMS)
https://www.uab.edu/medicine/sci/
The UAB-SCIMS information network provides an overview of research, health issues and quality of life for people with spinal cord injuries.

University of Louisville Kentucky Spinal Cord Injury Research Center
https://louisville.edu/kscirc
511 South Floyd St., Room 616
Louisville, KY 40202
Office: (502) 852-8060
The University of Louisville's Kentucky Spinal Cord Injury Research Center is working to develop successful spinal cord repair strategies in the laboratory that can be taken to the clinic in a timely and responsible fashion; its research areas include epidural stimulation.

University of Pittsburgh: Human Engineering Research Laboratories (HERL)
http://www.herl.pitt.edu/
VA Pittsburgh Healthcare System
6425 Penn Avenue, Suite 400
Pittsburgh, PA 15206
Phone: 412-822-3700
Email: herl@shrs.pitt.edu
HERL's mission is to continuously improve the mobility and function of people with disabilities through advanced engineering in clinical research and medical rehabilitation. HERL operates an assistive technology registry which informs people of research studies, which are open to anyone at least 18 years old who use any form of assistive technology. People do not need to live in or travel to Pittsburgh in order to participate.

Wings for Life: Making Spinal Paralysis Curable
https://www/wingsforlife.com/us/
A non-profit organization in Austria that funds research projects focusing on curing paraplegia.

Journals

Spinal Cord: The Official Journal of the International Spinal Cord Society
http://www.nature.com/sc
Spinal Cord is published monthly and deals with all aspects of spinal anatomy, physiology and lesions (injury and disease).

Topics in Spinal Cord Injury Rehabilitation

http://www.thomasland.com/about-spinalrehab.html
Quarterly peer-reviewed journal that discusses functional approaches and innovative techniques for spinal cord injury rehabilitation. Each issue focuses on research papers with the latest clinical developments as well as an in-depth review of a single key topic.

American Journal of Physical Medicine & Rehabilitation
https://journals.lww.com/ajpmr/pages/default.aspx
American Journal of Physical Medicine & Rehabilitation focuses on the practice, research and educational aspects of physical medicine and rehabilitation. This monthly publication, associated with the Association of Academic Physiatrists, focuses on the practice, research, and educational aspects of physical medicine and rehabilitation. Many articles regularly feature spinal cord injury topics and research.

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