

SCI Research



There are no definitive treatments yet for spinal cord injury. However, ongoing research to test new therapies is progressing rapidly. Drugs to limit injury progression, decompression surgery, nerve cell transplantation and nerve regeneration, as well as nerve rejuvenation therapies, are being examined as potential ways to minimize the effects of spinal cord injury. The biology of the injured spinal cord is enormously complex but clinical trials are underway with more coming; hope for restoring function after paralysis continues to rise, and for good reason.

Still, paralysis from disease, stroke or trauma is considered one of the toughest of medical problems. In fact, just over a generation ago, any damage to the brain and spinal cord that severely limited motor and/or sensory function was thought to be untreatable. In recent years, though, the word “cure” in this context has not only entered the vocabulary of the science community but also that of clinicians. Restorative neuroscience is bubbling with energy and expectation. To be sure, scientific progress is a slow but steady march. One day in the not-too-distant future there will be a host of some procedures or treatments to mitigate the effects of paralysis. But it is not reasonable to expect a one-size-fits-all “magic bullet” for restoring function. It is almost a certainty that these coming treatments will involve combinations of therapies, given at various time points in the injury process, including a significant rehab component.

Here is a snapshot of work being done in several research areas.

Nerve protection: As in the case of brain trauma or stroke, the initial damage to spinal cord cells is followed by a series of biochemical events that often knock out other nerve cells in the area of the injury. This secondary process can be modified, thus saving many cells from damage. The steroid drug methylprednisolone (MP) was FDA-approved in 1990 as a treatment

for acute SCI; it is still the only approved acute treatment. MP is believed to reduce inflammation if people get the drug within eight hours of injury. The medical community is not entirely sold on the effectiveness of MP; many neurosurgeons won't recommend it and suggest the steroid dosage actually causes more damage. Meanwhile, research is underway in many labs around the world to find a better acute treatment. Several drugs look promising, including Riluzole (protects nerves from further damage from excess glutamate), Cethrin (reduces inhibitors to growth), a molecule called anti-Nogo (tested in Europe, promotes spinal cord cell growth by blocking inhibition), and a magnesium chloride compound in polyethylene glycol (PEG) called AC105 (in animal studies, AC105 was neuroprotective and improved motor function in SCI and cognitive function in TBI when initiated within four hours of injury). Cooling of the spinal cord is another possible acute therapy; hypothermia appears to reduce cell loss. Protocols for cooling (how cold, how long) have not been fully determined. Stem cells have also been considered as an acute therapy: The biotech firm Geron began (then abandoned) human safety trials using human embryonic stem cells to treat acute spinal cord injuries (see more on this trial below).

Well more than one hundred years ago, Spanish scientist Santiago Ramón y Cajal noted that the ends of axons broken by trauma become swollen into what he called “dystrophic endballs” and are no longer capable of regeneration. This remained a central issue in recovery of function—there seems to be some sort of barrier or scar that traps the nerve tips in place. Recent studies in several labs have revealed that these dystrophic growth cones can get unstuck using a molecule that breaks down the sugar chains forming the scar (chondroitinase, nicknamed chase). There has been much work published about the potential for chase; it has helped restore function in paralyzed animals. There have been no human trials yet; effective delivery of chondroitinase to the injury site has not been fully worked out.

Bridging: The idea of a bridge is conceptually easy—transplanted cells or perhaps a type of miniature scaffold, fill the damaged area of the cord (often a scar-lined cyst), and thus allow nerves of the spinal cord to cross through otherwise inhospitable terrain. In 1981, Canadian scientist Albert Aguayo showed that spinal cord axons could grow long distances using a bridge made of peripheral nerve, proving without doubt that axons will grow if they have the right environment. A variety of techniques has evolved through experiments to create a growth enhancing environment, including the use of stem cells, nerve cells called olfactory ensheathing glia (OEG) that come from the upper nose, and Schwann cells (support cells of peripheral nerves that have been shown to help spinal cord and brain cells).

Another type of bridge, or perhaps more like a bypass, stitches a piece of peripheral nerve above and below the area of spinal cord lesion. This type of surgery is not used clinically in the United States. In experiments, however, a nerve bypass restored some diaphragm function and breathing in animals with high cervical injuries, and some bladder control in animals with lower injuries. The research team is hopeful this can one day benefit people.

Cell replacement: While it may be tantalizing to think broken or lost spinal cord nerve cells can be replaced by new ones, this has not been done; cell replacement is not yet a source of spare parts. Stem cells from one's own body or from other sources (including embryonic cell lines), OEG cells, fetal tissue, and umbilical cord blood cells have been used experimentally to restore function after paralysis; results have been encouraging but not because the new cells

take on the identity of the lost or damaged ones. Replacements seem to offer support and help nurture surviving cells.

A stem cell is a cell from the embryo, fetus, or adult that, under certain conditions, has the ability to reproduce itself for long periods or, in the case of adult stem cells, throughout the life of the organism. A stem cell can give rise to specialized cells that make up the tissues and organs of the body. Be mindful that stem cell therapy is considered a drug by the FDA; the only approved use in the United States is bone marrow transplantation.

The first-ever embryonic stem cell trial (halted midstream in 2011 by its sponsor, Geron, citing financial priorities) hoped to use transplanted stem cells to rejuvenate existing cells in the area of an acute spinal cord injury, thereby restoring the myelin wrapping necessary for signal transmission. Five people were enrolled in the Phase I trial, looking mainly at safety; there were no adverse effects reported, but no functional gains either. The Geron cells may get a reprise; two former Geron executives acquired the rights to the cell line and formed a new company, BioTime, intending to run more trials. See www.biotimeinc.com

In an ongoing clinical trial in Switzerland, a California biotech, StemCells, Inc., is testing human stem cells from a fetal source in people injured three months to a year. These cells, too, are believed to restore myelin. The first trial is showing the cells are safe; early data shows some return of sensory function, too. The science behind the StemCells, Inc. trial comes from the labs of husband-and-wife team Brian Cummings and Aileen Anderson at the University of California, Irvine. Anderson is a member of the Reeve International Research Consortium on Spinal Cord Injury (see www.ChristopherReeve.org, click on “research”). StemCells, Inc. has begun preclinical animal studies of the company’s cells as a potential treatment for long-term cervical spinal cord injury. www.stemcellsinc.com

A third SCI stem cell clinical trial, underway from a company called Neuralstem, is testing human neural cells in a chronic SCI model, one-to two-years post-injury. The transplanted cells are derived from stem cells native to the brain and spinal cord. The company found a way to produce them in large quantity for direct injection to the spinal cord; the same cell line has been in clinical trials for several years for ALS.

In preclinical studies using Neuralstem’s human cells in animals, researchers suggest the replacement cells integrate with spinal nerves and form new relay circuits—the animals showed significantly improved function. Why do the cells seem to grow and form connections so well? This preliminary success with animals might have to do with the delivery system, using a fibrin matrix as a scaffold, plus the addition of a cocktail of growth factors. The first human trials, however, won’t test the combination of matrix or factors. See www.neuralstem.com

Clinical trials in several countries have tested the safety and efficacy of OEG cells transplanted into the lesion area of the spinal cord; results have been promising. Meanwhile, the Miami Project has begun a clinical trial for transplanted Schwann cells, support cells of peripheral nerves that have been shown to encourage the regrowth of axons after spinal cord injury. Combining Schwann cells with other growth molecules may ultimately be more useful than transplants of Schwann cells alone. For example, a team at the Miami Project found that Schwann cells alone activated nerves to grow into a bridge but they stopped short of crossing the gap in the injured spinal cord. By adding OEG cells to the Schwann cells, the axons crossed the bridge and entered the spinal cord on the other side of the lesion. See www.themiamiproject.org

Regeneration: This is perhaps the toughest of the treatment possibilities. To restore a major degree of sensation and motor control after spinal cord injury, long axons must grow again and connect over long distances—as much as two feet—to precise targets. These axons cannot regenerate unless their path is cleared of poisons, enriched with vitamins, and paved with an attractive roadbed. By blocking inhibitory factors (proteins that stop axon growth in its tracks), adding nutrients, and supplying a matrix to grow on, researchers have indeed grown spinal nerves over long distances. One group of scientists at several labs used a molecular switch to turn on nerve cell growth after trauma. PTEN is a tumor suppressor gene that was discovered by cancer researchers fifteen years ago. This gene regulates cell proliferation and it turns out to be a molecular switch for axon growth. When scientists deleted PTEN in a complete spinal cord injury model, cortical spinal axons—the ones needed for major movement function—regenerated at unprecedented rates. PTEN is complicated; you can't just get rid of it because it is the brake needed to stop certain kinds of cellular overgrowth (cancer). But there are ways to release it. Much work remains to make this relevant to human spinal cord injuries but many more labs have joined in, exploring the PTEN gene and many others related to regrowth of nerve cells.

Rehabilitation: Almost any treatment to restore function after paralysis will require a physical component to rebuild muscle, build bone, and reactivate patterns of movement. Some form of rehab will be needed after function comes back. Moreover, it appears that activity itself affects recovery: In 2002, seven years after his supposedly complete C2 injury, Christopher Reeve showed that he had regained limited function and sensation. His doctor credited his use of functional electrical stimulation, which may have kick-started the repair process, and a program of passive electrical stimulation, aqua therapy, and passive standing.

To a limited extent, Reeve also used treadmill training, a type of physical therapy that forces the legs to move in a pattern of walking as the body is suspended in a harness above a moving treadmill. The theory is that the spinal cord can interpret incoming sensory signals; the cord itself is smart. It can carry out movement commands without brain input. Locomotion is managed by a system called a central pattern generator (CPG), which activates the pattern of stepping. Stepping during treadmill training sends sensory information to the CPG, reminding the spinal cord how to step. Scientists describe the reactivation due to stepping as plasticity—the nervous system is not “hard wired” and appears to have the ability to adapt itself to new stimulation. Researchers are learning much more about the CPG and how to activate it. Rehabilitation techniques have evolved to the point that exercise and physical activity are an essential component of recovery. For the person with a spinal cord injury, it's best to stay active and always strive for the maximum outcome.

Sources: American Association of Neurological Surgeons, Craig Hospital, Christopher & Dana Reeve Foundation's Paralysis Resource Guide 2013, The National Institute of Neurological Disorders and Stroke.

Websites

<https://www.christopherreeve.org/research/international-research-consortium-on-spinal-cord-injury/discoveries-by-consortium-laboratories>

Christopher & Dana Reeve Foundation International Research Consortium on Spinal Cord Injury

636 Morris Turnpike, Suite 3A

Short Hills, NJ 07078

Phone: 973-467-8270

The mission of the Reeve Foundation International Research Consortium on Spinal Cord Injury is to promote structural repair and functional recovery in the acutely and chronically injured spinal cord.

www.ChristopherReeve.org/Research

Christopher & Dana Reeve Foundation: Research

This page has information on research into treatments and cures for spinal cord injury. The site offers free research newsletters and access to the Foundation's Progress in Research newsletters. There is also information on epidural stimulation of the spine.

<https://www.acl.gov/programs/research-and-development>

Administration for Community Living (ACL): National Institute on Disability and Rehabilitation Research (NIDILRR)'s Research Program

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.

<http://csro.com/>

Canadian/American Spinal Research Organization

90 Eglinton Ave. East, Suite 601

Toronto, ON M4P2Y3 Canada

and

1623 Military Rd

Niagara Falls, NY 14304

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.

<http://www.chnfoundation.org/>

<http://chnfoundation.org/what-we-fund/>

Craig H. Neilsen Foundation

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.

<http://www.miamiproject.miami.edu>

Miami Project to Cure Paralysis

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.

<https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Hope-Through-Research/Spinal-Cord-Injury-Hope-Through-Research>

National Institute of Neurological Disorders and Stroke: Spinal Cord Injury – Hope Through Research

This page has information on spinal cord injury, including treatment, rehabilitation and research.

<http://www.ncddr.org/>

National Center for the Dissemination of Disability Research (NCDDR)

SEDL

4700 Mueller Boulevard

Austin, TX 78723

Phone: 512-476-6861, 800-266-1832 (Toll-free)

E-mail: NCDDR@sedl.org

The long-term goal of the NCDDR is to expand production, access, dissemination, and use of disability and rehabilitation research evidence among National Institute on Disability and Rehabilitation Research (NIDRR) management and grantees, people with disabilities and their families, and disability-oriented professionals, practitioners and service providers.

www.pva.org

<http://www.pva.org/research-foundation>

Paralyzed Veterans of America Research Foundation

Cheryl Vines, M.S., Director of Research and Education

Phone: 800-424-8200

E-mail: cherylv@pva.org

The PVA Research Foundation supports innovative research and fellowships that improve the lives of those with spinal cord injury and disease.

<http://www.reeve.uci.edu>

Reeve-Irvine Research Center

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.

<http://keck.rutgers.edu/>

Rutgers University: W.M. Keck Center for Collaborative Neuroscience

The Spinal Cord Injury Project

604 Allison Road, D-251
Piscataway, NJ 08854
Phone: 848-445-2061 or 848-445-9553
E-mail: SCIProject@biology.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.

<http://www.uab.edu/medicine/sci/research/research-for-cure>

Spinal Cord Injury Information Network: Research for a Cure in Spinal Cord Injury (2005)

This page has general information on research (what it is, how it's done, how to interpret results) as well as information on SCI-related research and strategies are pursuing to find a cure.

<http://www.scireproject.com/>

Spinal Cord Injury Rehabilitation Evidence (SCIRE) SCIRE is a Canadian project that synthesizes research on SCI rehabilitation for health care professionals, scientists, policy-makers and consumers.

<http://www.kentuckyonehealth.org/human-locomotion-research-center>

University of Louisville Human Locomotion Research Center

Frazier Rehab Institute
220 Abraham Flexner Way, Suite 1506
Louisville, KY 40202
Phone: 800-334-8635

The University of Louisville's Frazier Rehab Institute offers Reeve-funded programs such as an NRN site, epidural stimulation research, and a community fitness and wellness program.

<http://www.herl.pitt.edu/>

University of Pittsburgh: Human Engineering Research Laboratories (HERL)

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. The registry is open to all people at least 18 years of age who use any form of assistive technology. People do not need to be located in or travel to Pittsburgh in order to participate.

<http://www.wingsforlife.com/en-us/>

Wings for Life: Making Spinal Paralysis Curable

A non-profit organization in Austria that funds research projects focusing on curing paraplegia.

Journals

<http://www.nature.com/sc>

Spinal Cord: The Official Journal of the International Spinal Cord Society

Spinal Cord is published monthly and deals with all aspects of spinal anatomy, physiology and lesions (injury and disease).

<http://sci.washington.edu/info/newsletters/update.asp>

Spinal Cord Injury Update

This newsletter, published three times a year, covers topics related to spinal cord injury for consumers and health care providers.

<http://www.thomasland.com/about-spinalrehab.html>

Topics in Spinal Cord Injury Rehabilitation

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.

The information contained in this message is presented for the purpose of educating and informing you about paralysis and its effects. Nothing contained in this message should be construed nor is intended to be used for medical diagnosis or treatment. It should not be used in place of the advice of your physician or other qualified health care provider. Should you have any health care related questions, please call or see your physician or other qualified health care provider promptly. Always consult with your physician or other qualified health care provider before embarking on a new treatment, diet or fitness program. You should never disregard medical advice or delay in seeking it because of something you have read in this message.

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