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Progress in RESEARCH

The Christopher & Dana Reeve Foundation was founded in 1982 by families determined to find a cure for paralysis. At the time, it was not only an act of hope, but defiance: the idea that injuries could be treated was inconceivable.

Over the next four decades, the Reeve Foundation's investment of more than $140 million in spinal cord injury research reinvigorated the field and redefined what was deemed possible. Now, labs around the world are pursuing an array of treatments to restore function and improve the health of people living with paralysis.

A glimpse at the innovative research currently underway hints at the transformative treatments to come — and the role Reeve will play in accelerating progress. In one recent study, neuroscientists at the École Polytechnique Fédérale de Lausanne successfully built a digital bridge between the brain and spinal cord that allowed a man living with paralysis to walk for the first time in more than a decade. The potentially game-changing therapy involved spinal cord stimulation technology created by ONWARD, a Netherlands-based company funded in part by the Reeve Foundation.

Increasing collaboration across the field, along with strategic investments, will be central to Reeve's efforts to advance the treatments finally within reach. In 2022, we launched the Reeve Foundation Scientific Advisory Board, comprised of leading scientists from across the country, to help identify results-driven research that will yield the greatest impact for community members. This summer, we co-hosted with Lineage Cell Therapeutics the first annual SCI Investor Symposium, linking individuals living with SCI with academics and industry peers.

It is an honor to lead the Reeve Foundation's Research Program in what I believe will be an extraordinary period of discovery in spinal cord injury research. Our portfolio brims with initiatives that offer great promise, including an upcoming study of brain and spinal interface and bladder function. If you're able, please donate to the Foundation and help us harness the momentum of this moment — and stay tuned to this space for stories of progress that forty years ago would have been considered impossible.

Dr. Marco Baptista
Chief Scientific Officer

INSIDE

CHRISTOPHER & DANA REEVE FOUNDATION
TODAY'S CARE. TOMORROW'S CURE.®

MAKING DREAMS REALITY STUDY FOR SCI PATIENTS

Spinal Implants Are Making the Impossible Possible for Spinal Cord Injury Patients

In a plot twist straight out of a science fiction novel, scientists have built a digital bridge between the brain and spinal cord, enabling a paralyzed man to walk naturally for the first time in more than a decade.

When Gert-Jan Oskam, 40, thinks, the system decodes his thoughts and translates them into movement through a brain-spinal interface (BSI). An implant in Oskam's brain tracks his intentions to move and wirelessly transfers them to a second implant in his lower spine, creating natural movement.

"After several minutes of training, he was able to walk naturally using the system," said Henri Lorach, a professor with the Ecole Polytechnique Federale de Lausanne, during a press briefing. "After using the system routinely, we observed functional recovery, including movement of the hip, knee, and ankle joints." The research findings, published in May 2023 in the journal *Nature,* represent a giant leap forward to advance solutions for patients with spinal cord injury (SCI).

Advancing Complex Technologies

For years, scientists have been using implantable nerve stimulators to help patients with SCI recover function and movement. But without direct communication between the brain and spinal cord, the resulting movements were robotic, and patients were unable to navigate different terrain.

With the BSI, researchers have created a system that bypasses injured parts of the spinal cord, opening a door for patients with SCI to adopt a more natural stride. The dual-implant system captures Oskam's thoughts and translates them into stimulation of the spinal cord to reestablish voluntary leg movement.

Gert-Jan Oskam

Oskam had tried stimulation procedures in the past, and even recovered some ability to walk, but each time, his progress plateaued. Oskam felt as if something outside of him was creating the movement. "With previous stimulators, the stimulator was controlling me," he said, during a press briefing. "Now, I'm controlling the stimulation."

The BSI provides Oskam with feedback when he moves, allowing him to traverse all kinds of terrain. He can climb stairs, pass over ramps, and decide when to stop and start walking. There's even evidence that the BSI improves functional recovery. Earlier studies show that spinal stimulation can spur the growth of new neurons, and that appears to be the case for Oskam. More than a year after getting the implant, Oskam can walk with crutches, even when the system is switched off.

The Promise of Artificial Intelligence

The success of Oskam's BSI experience relies on artificial intelligence, or AI. The research team implanted electrodes in Oskam's skull and spine, then observed which parts of the brain lit up when he tried to move various body parts.

One part of the brain lit up when Oskam tried to move his hips, another when he tried to move his knees, and still another when he wanted to move his ankles. Armed with this information, investigators used another algorithm to create a "bridge" from the brain implant to the spinal implant that spans the damaged part of the spine.

The technology reads Oskam's intentions, which are detectable as electrical signals in his brain, and matches them to muscle movements. So, it's his thoughts that prompt physical movement. And since the messages between the brain and spine are sent every 300 milliseconds, Oskam was able to quickly adjust his thoughts to achieve the desired movement.

After the motorcycle accident 11 years ago that left him unable to move from the hips down, Oskam's wish was to walk again, and he believed it was possible. As it turns out, he was right.

Scientists Learn to Share Data — A Giant Step Forward in Advancing SCI Research

Scientists in the spinal cord injury (SCI) space are clear on one thing: Every injury and every individual are unique. The same holds true for datasets and scientists. But with data sharing, the possibilities for combining efforts to affect change grow exponentially.

"We know that no single intervention is going to solve spinal cord injury," says Karim Fouad, Ph.D., co-director and editor of the Open Data Commons (ODC)-SCI and professor and Canada research chair at the University of Alberta. "So, communication between basic researchers, clinicians, and people living with SCI through open data sharing is the only way to really move the field forward."

It makes sense then that funding agencies and publishers are increasingly demanding that researchers make their datasets accessible through some sort of open data sharing platform. A transparent data culture not only enables scientists to evaluate and replicate other investigators' findings, but it also acts as a springboard to develop novel research questions.

Sharing is Caring

Dating back early days of science in India and the U.K., professionals came together to discuss their work daily or weekly, often over whiskey. Then scientists began publishing their findings in journal articles. "They shared exciting results. That's what we still do in published papers. But the rest of the data gets lost," says Fouad. "That produces a research bias."

With open data sharing, the goal is to recover all of that lost data — to publish and share everything across the board. So, when researchers have a hypothesis about a particular treatment, they can go into the ODC-SCI and review experiments that have already been completed — and that helps conserve resources.

"By making all of the data available, investigators can improve how they design trials by taking into account previous research findings," Fouad says. "Once we have the whole picture, with every detail, we'll be able to use machine learning algorithms to extract information that our brains can't even conceptualize yet."

Capturing that information saves time and money. It also allows an opportunity for independent replication, which is such a central tenant of science. Uploading data to the ODC-SCI makes it a citable data set with a digital objective identifier (DOI) — and that helps researchers comply with funding mandates. That infrastructure already exists within the SCI space. Unfortunately, the idea of entering new and old data is overwhelming for most scientists.

The Challenges of Data Sharing

Data sharing is a daunting concept for many researchers. They're trained in science, not data entry, and it's not uncommon for them to feel creatively stifled by the process of entering and uploading data. To complicate matters, many investigators don't feel like they have the time, knowledge, or bandwidth to take the steps necessary to share their data, particularly "old data."

To date, the ODC-SCI has effectively checked submitted datasets for compliance with ODC standards. Unfortunately, there's no comprehensive systematic assistance for recovering data from already published studies, and equally important, studies that were never published.

"Researchers are reluctant to dig out data from the past and reformat it to ODC-SCI, create data dictionaries and complete the required metadata to make the information shareable," says Marco Baptista, Ph.D., chief scientific officer of the Christopher & Dana Reeve Foundation. Plus, learning to enter data correctly and in a standardized format requires time and training.

There are different levels of understanding about how to format and upload research data into the ODC-SCI — and many scientists don't feel equipped to share data in a FAIR manner, meaning that it's Findable, Accessible, Interoperable, and Reusable. And some data might be trickier than others to put into an open data sharing platform.

"Conceptually, researchers are on board, but there's no personal incentive to enter data, especially old data," says Marco Baptista, Ph.D., chief scientific officer of the Christopher & Dana Reeve Foundation. "Our goal is to add those incentives while also reducing the risks involved with data sharing."

Working Toward a Sharing Culture

The complexity inherent in SCI requires myriad treatment approaches used alone and in combination. And while experts in the field agree that no single therapy will cure SCI, sharing data openly and in a standardized way poses big challenges.

To help investigators get up to speed with data sharing, The Christopher & Dana Reeve Foundation and The University of Alberta are partnering with investigators — not just to fund these efforts, but also to provide specialized training and guidance so open data sharing protocols becomes standard operating procedure.

With funds from the Open Data Sharing Grant, the University of Alberta will be hiring a "data retrieval specialist," who will not only help investigators uncover and enter old data for open data sharing but also train them to capture new data and upload it according to ODC-SCI standards.

UNIVERSITY OF ALBERTA

"It's really a two-pronged approach," explains Baptista. "The first prong relies on the ODC Grant to hire a data retrieval specialist and the second prong is to incentivize researchers to analyze shared data so new hypotheses can emerge." While the process of integrated data collection, management and sharing can be cumbersome, particularly in the early stages, the effectiveness of this approach is easily measured by how many datasets get moved into the ODC-SCI with a DOI.

"For open data sharing to be effective, we have to change the culture," Fouad says. "But once scientists begin using old data to come up with new conclusions that move the field forward, the culture will shift. It's not going to happen overnight, but we're coming at it from all angles, including incentives, training, and ongoing assistance."

REEVE FOUNDATION'S SCIENTIFIC ADVISORY BOARD: **CHET MORITZ, PH.D.**

From the time Chet Moritz was a young boy, he was drawn to helping people with physical limitations. He attended a school in Seattle, WA, that accommodated children with disabilities.

"Starting in about 3rd grade, I had a lot of exposure to kids who used wheelchairs for various reasons," says Dr. Moritz, Ph.D. Hwang Endowed Professor, University of Washington Departments of Electrical & Computer Engineering, Rehabilitation Medicine, and Physiology & Biophysics. "I'd always felt this desire to help them in some way — not to walk again, but rather a sort of kinship that fed my interest in health sciences."

At first, Dr. Moritz thought he wanted to be a physical therapist. But he got bitten by the research bug as an undergraduate when he began studying how large insects control the muscles used to flap their wings. "Once I got into the lab and started sticking electrodes in the muscles of these tiny insects, I was hooked," Dr. Moritz says.

Becoming a Lab Rat

Trained as a biologist, Dr. Moritz's initial interest focused on understanding the engineering aspects of movement control—how the brain and spinal cord coordinate movement over rocky versus slick terrain, for example—transcutaneous stimulation on upper extremity. To that end, during his first post-doc, Dr. Moritz—whose Ph.D. is in integrative biology—focused on analyzing how individual neurons innervating muscles are controlled—meaning how they stimulate muscles into action. With his second post-doc, he wanted to "fix the system," to begin building technologies that could help people move again.

Dr. Moritz and his colleagues started conducting studies on brain computer interfaces (devices), trying to figure out how to extract information from the brain about how animals intended to move. "We came up with this idea that maybe we could record neural messages from intact areas of the brain and reroute the signals below the spinal cord injury to stimulate paralyzed muscles electrically in real time," Dr. Moritz says.

The approach worked and with that simple detour, scientists were able to hot-wire damaged nerves in animals and restore voluntary movement to paralyzed limbs. The logical next step: building neural prostheses, or neural prosthetic devices for humans with spinal cord injuries (SCIs).

From Bench to Bedside

Historically, young scientists shied away from SCI research. They had the sense that there was no forward movement in the field and, as a result, SCI-related research projects wouldn't get funded.

"But dating back 40 years ago, Dr. Reggie Edgerton, a researcher and neurobiologist at UCLA, showed that if you stimulate the spinal cord below the level of injury, animals with no connection between their brain and their lower body could make stepping movements on a treadmill," Dr. Moritz says. "That early research is now beginning to bear fruit and there have been tremendous breakthroughs in SCI research over the past 10 to 12 years."

DONATE TO SUPPORT
STANDARDIZED TESTING RESEARCH IN VIVO ENDEAVOR (STRIVE)

What is STRIVE? One of the persistent challenges in SCI research is the lack of a standardized SCI preclinical model with consistent study outcome measures, both of which require skilled surgeons and behaviorists. This standardized model is a prerequisite to engaging more and larger researcher organizations and investors in SCI science.

The Reeve Foundation's STRIVE initiative seeks to implement a standardized injury preclinical model that labs may use for a fee so that there is always a consistent, positive "control" for studies. Such an established model will benefit both academic and industry researchers, making the science less expensive to conduct and result in faster assessments of potential therapeutics. STRIVE will also help support the early assessment of combinatorial approaches.

How will Reeve implement STRIVE? The Reeve Foundation is raising funds to identify, train and validate the most widely used translational injury model(s) and outcome measures via an established and competitive contract research organization (CRO). The STRIVE model will be assessed against other widely used technologies commonly utilized in preclinical labs and in clinical trials. After the initial model is validated, we will expand with models of injury level, length of injury (e.g., acute vs chronic) and various outcome assessments.

What other collaborators are involved? This initiative is being developed with input from a range of SCI stakeholders, including SCI scientists and government representatives at the National Institute of Neurological Disorders and Stroke and the Department of Defense. The Foundation will also be seeking potential partners and identifying a steering committee to further inform the approach as it seeks CRO bids.

What will STRIVE cost? STRIVE is a $1 million investment by the Foundation over three years.

To learn more about how to support STRIVE, please contact Colleen Coppla at **ccoppla@christopherreeve.org**