A Gripping Tale of Strength

More hand strength and dexterity is a dream shared by most people who live with quadriplegia. Over the years, many research efforts have arrived at solutions—but all have either involved invasive techniques with long wait times for results, or cumbersome devices such as exoskeleton gloves. Recently, researchers at UCLA unveiled a breakthrough approach.

The jury has been in for some time. In numerous surveys and consultations over the past couple of decades, people with quadriplegia have made it clear: priority one is regaining the ability to use their hands. Nothing, they've collectively said, would restore greater independence.

Many researchers have heard these pleas, and a number of solutions have been developed. But few have enjoyed widespread acceptance. Surgical techniques to transfer tendon and nerve function have been successful, but the cost and invasive nature, along with the length of time required for healing and results to appear, have tempered enthusiasm for these procedures. Meanwhile, many devices have been developed to allow people with quadriplegia to exercise hand function, but these offer only modest gains. Many bionic gloves have also been developed, but lack of practicality and high cost have limited their commercial success.

In April, researchers at the University of California (UCLA) unveiled a possible game-changer—a revolutionary new, non-invasive therapy that appears to restore hand function for people with quadriplegia. They described the therapy and how they tested it in the April issue of the journal *Neurotrauma*.

While more research is clearly needed, the experimental therapy must be considered a breakthrough—it appears to be inexpensive, easily administered over a short period of time (perhaps even at home) without surgery, and, above all, overwhelmingly successful—even for people who were injured years ago.

The UCLA lab behind the therapy is that of Dr. Reggie Edgerton, a leading expert in neuromodulation—interventions that involve the activation of the spinal networks after SCI using electrical stimulation applied epidurally (surgically implanted electrodes under the skin) or transcutaneously (electrodes placed on the surface of the skin).

You might recall that, in our Winter 2014 issue, we told you about the Edgerton lab's success with neuromodulation to improve bladder function. Parag Gad, a research assistant in Edgerton's lab, led that project, and he's also the lead author of this latest study on hand function.

"One of our earlier studies showed that the cervical spinal cord could be neuromodulated using epidural (invasive) spinal stimulation," says Gad. "Based on these ideas, our team wanted to test the efficacy of using the non-invasive spinal stimulation to enable hand function."

Gad explains that the therapy has two components. The first is transcutaneous enabling motor control, or tEmc, which involves the use of a small, portable pulse generator connected to electrodes. Once the electrodes are placed on the skin above the spinal cord at the C3-C4 and C6-C7 vertebral levels, electrical pulses are delivered at varying frequencies and intensities. This stimulates and awakens the dormant circuitry of the spinal cord that's responsible for delivering instructions from the brain to the hands. The second component is manual rehabilitation exercise during the delivery of the stimulation—in simple terms, repetitive squeezing of an exercise device.

"The spinal stimulation works on two principles," says Gad. "First, it increases the level of baseline excitation in the neural networks that control upper extremity (arm and hand) function. Second,

Pioneers of neurostimulation therapies: Dr. Reggie Edgerton (left) and Parag Gad

it acts as a 'hearing aid' to amplify descending commands that the brain sends down via the spinal cord to the various muscles of the upper extremity."

In other words, subjecting the nerve pathways to a series of electrical stimuli "awakens" them so that the brain's instructions to the hand are able to get through much more easily. In turn, repetitively exercising the target muscles during stimulation leads to gains that persist months (and perhaps even permanently) after the therapy sessions have ended.

The researchers began by recruiting eight participants with quadriplegia, of whom six would ultimately finish the training sessions. Their time since injury ranged from one to 21 years. Prior to the study, none of the participants could turn a doorknob with one hand or twist a cap off a plastic water bottle. All had great difficulty operating a mobile phone. And three of the participants had complete injuries and couldn't move their fingers at all.

Each participant took part in eight 90-minute training sessions—two per week over four weeks. During these sessions, participants were provided with electrical stimulation while simultaneously squeezing a small gripping device 18 times with each hand, with each squeeze lasting three seconds. The gripping device measured the amount of force they were able to generate.

The results were quite remarkable.

"Within two or three sessions, everyone started showing significant improvements, and kept improving from there," says Gad.

After four weeks of training, participants' hand grip force increased on average by 325 percent in the presence of stimulation and 225 percent without stimulation. These improvements were witnessed in both left and right hands, regardless of which hand was dominant.

"About midway through the sessions, I could open my bedroom door with my left hand for the first time since my injury, and could open new water bottles, when previously someone else had to do this for me," says Cecilia Villarruel, a participant from California who was injured in a car accident 13 years ago. "Most people with an SCI say they just want to go to the bathroom like a normal person again. Small accomplishments like opening jars, bottles and doors enable a level of independence and self-reliance that is quite satisfying, and have a profound effect on people's lives."

Surprisingly, some participants also experienced other benefits beyond improved grip strength and finger dexterity, including improvements in blood pressure, bladder function, cardiovascular function, and trunk control.

The results were so positive that even the researchers admit to being surprised.

"After just eight sessions, they could do things they haven't been able to do for years," says Edgerton, adding that

Cecilia Villarruel, a research participant from California, regained the ability to open bottles and doors.

this is the largest reported recovery of the use of hands that has been reported in patients with such severe SCI.

"We were initially not expecting the results to be as effective as they were, especially in the autonomic functions and trunk function," says Gad. "The entire team was super-excited to see and hear what the patients reported back to us."

As for permanence of the benefits, results are again promising, as two of the six returned to Edgerton's laboratory 60 days after the training ended and clearly still had their grip strength intact—they could still turn a doorknob or use a fork with one hand, and twist off a bottle cap. But Gad concedes that the permanence won't be known for some time.

"We're still exploring this aspect," he says, adding that there were no adverse events or side-effects experienced by any of the participants.

While exciting, the study can't really be considered conclusive because of the small size and the lack of a control group to compare with those receiving the treatment. Gad says the immediate priority is confirming the benefits with more people, via controlled, blinded studies (studies in which participants are randomly selected to either receive the therapy, or a sham therapy, with no one, including the researchers knowing who is in which group).

"Studies are being planned by us and some of our collaborators around the world to test this in a larger cohort of subjects over a longer period of time," he says. He wouldn't put a timetable on this, but confirms that, because the technology is relatively inexpensive and the treatment so easily carried out, a larger trial could happen as early as next year.

Meanwhile, the prototype stimulation device used for the treatment, which was developed in Edgerton's lab specifically for this purpose, has already been spun off into NeuroRecovery Technologies, a medical technology company Edgerton co-founded. Currently, the company is seeking FDA approval for the device so it can be used by rehabilitation clinics and others. Approval could happen quickly if the company can make its case that the stimulator is a Class II non-significant risk device.

Many readers will end up here wondering, "OK, great, but when can I get my four weeks of training, and can I get it locally, ideally in my own home?"

"Best case scenario, it could take two to four years," says Gad. "We hope that this device can be used by as many people as possible, at home, in the doctor's office, in the rehab centres. We see this as an effective and inexpensive solution that could help thousands of patients in the near future."

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Research Suggests Neuromodulation Can Restore Sexual Function

While Dr. Reggie Edgerton's UCLA laboratory is ground zero for most research in neuromodulation in SCI, there are many other complementary projects taking place around the world.

In April, University of Minnesota researchers reported that neuromodulation, delivered through an implanted (epidural) device, appeared to restore some degree of voluntary movement, bladder and bowel control in two women with paraplegia. Not only that, one of them also regained orgasmic function.

The research was led by Dr. David Darrow, a fifth-year resident in neurosurgery. He believes that perhaps the most significant benefit of the therapy for the two women, both in their 40s, is the increased ability to support their bodies, leading to greater independence.

"These are big benefits to patients," Darrow says.

The findings are first results of the Epidural Stimulation After Neurologic Damage (E-STAND) study, which were recently presented at the American Association of Neurological Surgeons (AANS) 2018 Annual Meeting.

"It's been about 10 years since the serendipitous discovery that if you apply spinal cord stimulation below their lesion, patients with thoracic paraplegia can regain some ability to control their legs, despite not having moved them in up to four years," Darrow says. "This changed the paradigm of how we think about complete spinal cord injury…and opened up the opportunity to look at the narrative of spinal cord injury from the perspective of neuromodulation."

As with the UCLA work to restore hand function, the stimulation is not directed to the actual site of the lesion, but instead delivered within a segment of the cord where there are intact neural connections that pass through the lesion.