

Electrically stimulating the brain may restore movement after stroke

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Micrograph showing cortical pseudolaminar necrosis, a finding seen in strokes on medical imaging and at autopsy. H&E-LFB stain. Credit: Nephron/Wikipedia

UC San Francisco scientists have improved mobility in rats that had experienced debilitating strokes by using electrical stimulation to restore a distinctive pattern of brain cell activity associated with efficient movement. The researchers say they plan to use the new findings to help develop brain implants that might one day restore motor function in

human stroke patients.

After a [stroke](#), roughly one-third of [patients](#) recover fully, one-third have significant lingering [movement](#) problems, and one-third remain virtually paralyzed, said senior author Karunesh Ganguly, MD, Ph.D., associate professor of neurology and a member of the UCSF Weill Institute for Neurosciences. Even patients who experience partial recovery often continue to struggle with "goal-directed" movements of the arms and hands, such as reaching and manipulating objects, which can be crucial in the workplace and in daily living.

"Our main impetus was to understand how we can develop implantable neurotechnology to help stroke patients," said Ganguly, who conducts research at the San Francisco VA Health Care System. "There's an enormous field growing around the idea of neural implants that can help neural circuits recover and improve function. We were interested in trying to understand the circuit properties of an injured brain relative to a healthy brain and to use this information to tailor neural implants to improve [motor function](#) after stroke."

Over the past 20 years, neuroscientists have presented evidence that coordinated patterns of neural activity known as oscillations are important for efficient brain function. More recently, low-frequency oscillations (LFOs)—which were first identified in studies of sleep—have been specifically found to help organize the firing of neurons in the brain's primary motor cortex. The motor cortex controls voluntary movement, and LFOs chunk the cells' activity together to ensure that goal-directed movements are smooth and efficient.

In the new study, published in the June 18, 2018 issue of *Nature Medicine*, the researchers first measured neural activity in rats while the animals reached out to grab a small food pellet, a task designed to emulate human goal-directed movements. They detected LFOs

immediately before and during the action, which inspired the researchers to investigate how these activity patterns might change after stroke and during recovery.

To explore these questions, they caused a stroke in the rats that impaired the animals' movement ability, and found that LFOs diminished. In rats that were able to recover, gradually making faster and more precise movements, the LFOs also returned. There was a strong correlation between recovery of function and the reemergence of LFOs. Animals that fully recovered had stronger low-frequency activity than those that partially recovered, and those that didn't recover had virtually no low-frequency activity.

To try to boost recovery, the researchers used electrodes to both record activity and deliver a mild electrical current to the rats' brains, stimulating the area immediately surrounding the center of the [stroke damage](#). This stimulation consistently enhanced LFOs in the damaged area and appeared to improve motor function: when the researchers delivered a burst of electricity right before a rat made a movement, the rat was up to 60 percent more accurate at reaching and grasping for a food pellet.

"Interestingly, we observed this augmentation of LFOs only on the trials where stimulation was applied," said Tanuj Gulati, Ph.D., a postdoctoral researcher in the Ganguly lab who is co-first author of the study, along with Dhakshin Ramanathan, MD, Ph.D., now assistant professor of psychiatry at UC San Diego, and Ling Guo, a neuroscience graduate student at UCSF.

"We are not creating a new frequency, we are amplifying the existing frequency," added Ganguly. "By amplifying the weak low-frequency oscillations, we are able to help organize the task-related [neural activity](#). When we delivered the electrical current in step with their intended

actions, motor control actually got better."

The researchers wanted to know whether their findings might also apply to humans, so they analyzed recordings made from the surface of the brain of an epilepsy patient who had suffered a stroke that had impaired the patient's arm and hand movements. The recordings revealed significantly fewer LFOs than recordings made in two epilepsy patients who hadn't had a stroke. These findings suggest that, just as in rats, the stroke had caused a loss of low-frequency [activity](#) that impaired the patient's movement.

Physical therapy is the only treatment currently available to aid stroke patients in their recovery. It can help people who are able to recover neurologically get back to being fully functional more quickly, but not those whose stroke damage is too extensive. Ganguly hopes that electrical brain stimulation can offer a much-needed alternative for these latter patients, helping their brain circuits to gain better control of motor neurons that are still functional. Electrical [brain](#) stimulation is already widely used to help patients with Parkinson's disease and epilepsy, and Ganguly believes stroke patients may be the next to benefit.

More information: Low-frequency cortical activity is a neuromodulatory target that tracks recovery after stroke, *Nature Medicine* (2018). www.nature.com/articles/s41591-018-0058-y

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