Closed Loop Device May Alleviate Treatment-Resistant Depression

A patient with treatment-resistant depression experienced rapid and sustained improvements with personalized brain mapping and a closed loop deep brain sensing and stimulation device. Results from the proof-of-concept trial appeared in *Nature Medicine*.

The patient was a 36-year-old woman with childhood-onset severe major depressive disorder that was resistant to multiple antidepressant combinations and electroconvulsive therapy. Before placing the device, researchers at the University of California San Francisco (UCSF) used intracranial electrophysiology and electrical stimulation to identify brain activity coinciding with her high-symptom states and to pinpoint a location where stimulation improved her depression symptoms.

With that knowledge, they surgically implanted the NeuroPace RNS System—a device approved for treatment-resistant epilepsy—in the patient’s previously identified brain locations. Once closed loop therapy was deployed, the device automatically provided a 6-second burst of electricity in the right ventral capsule—ventral striatum whenever it detected brain activity patterns in the amygdala associated with depressive symptoms.

The patient’s symptom severity scores improved quickly, beginning the morning after brain stimulation began. Within several months, Montgomery–Åsberg Depression Rating Scale scores indicated that her condition was in remission.

“In the early few months, the lessening of the depression was so abrupt, and I wasn’t sure if it would last,” the patient said in a UCSF news story. The improvements have been maintained for 15 months.

According to the study’s authors, the response is unusual in treatment-resistant depression, “where the 1-year remission rate for ‘treatment as usual’ is approximately 3.5% and symptom relief from [deep brain stimulation] can take months to emerge.” To see if the results may be generalizable, they’ve enrolled 2 other patients in the early trial and plan to add 9 more. They cautioned that a larger, double-blind randomized clinical trial will be needed to establish closed loop neuromodulation’s effectiveness for major depressive disorder.

Guided Ultrasound Opens Blood-Brain Barrier to Cancer Drugs

In a first-in-human trial, physicians used magnetic resonance–guided focused ultrasound (MRgFUS) to temporarily open the blood-brain barrier (BBB) and enhance medication uptake in brain tumors.

The trial involved 4 patients in Canada with breast cancer that was positive for human epidermal growth factor receptor 2 (formerly HER2/neu) and brain metastases. The patients had progressive intracranial disease and stable systemic disease and were treated with the monoclonal antibody trastuzumab. Physicians used intracranial MRgFUS to target specific brain lesions while patients received intravenous trastuzumab over 20 outpatient sessions.

No treatment-related serious adverse events occurred and the novel technique improved drug delivery to the brain, the researchers reported in *Science Translational Medicine*. Imaging revealed enhanced drug uptake in MRgFUS-treated lesions compared with nontreated control lesions. The procedure decreased targeted tumor sizes, but larger studies will be needed to confirm improvements in radiographic response. Magnetic resonance imaging showed that BBB permeability was reconstituted within 24 hours of the procedures.

The noninvasive technique has the potential to precisely deliver large molecules like antibody-based targeted therapies and immunotherapies to brain lesions in cancer and other neurological diseases. Antibody therapies previously ruled out for the brain due to low penetration now may be repurposed there, according to the authors. The study also demonstrated that MRgFUS can be used to increase drug uptake in brain regions where radiation and surgery may be limited, including the brainstem.

The data “are critical to establishing the utility of low-intensity MRgFUS in brain cancer and set the stage for a new means of delivering a wide array of large therapeutic molecules to the brain that otherwise cannot breach the BBB,” the authors wrote.

Augmented Cane Could Help People With Visual Impairments

Despite the invaluable assistance they provide for many people with visual impairments, white canes can’t detect obstacles beyond their length. Meanwhile, guide dogs are expensive to train, putting them out of reach for many.

Now, scientists at Stanford University have designed a prototype, low-cost, augmented cane to help people with visual impairment navigate faster and more easily. Described in *Science Robotics*, the device is a white cane outfitted with a microcontroller that receives information from mounted sensors including a camera, GPS (global positioning system), 2-dimensional light detection and ranging, and a measurement unit that estimates orientation.

Based on the sensor data, the controller plans navigation, provides audio instructions, and physically guides the user with a motorized wheel at the end of the cane. The wheel applies torque to the ground to steer the user left or right, an approach called grounded haptic feedback. But ultimately the human is still in control—they can overpower the haptic feedback or turn it off. They also select their own forward walking speed.

In a series of blindfolded navigation challenges, people with varying levels of visual impairment walked 18% faster with the augmented cane than with a white cane. The open-source design still requires “substantial engineering improvements,” according to its developers. One needed change: the cane weighs almost 3 lb, and study participants said that’s too heavy. ~Jennifer Abbasi

**Note:** Source references are available through embedded hyperlinks in the article text online.