A Brain Implant that Uses Light

A novel optical device could ultimately be used to treat neurological disease.

By Mark Williams Pontin

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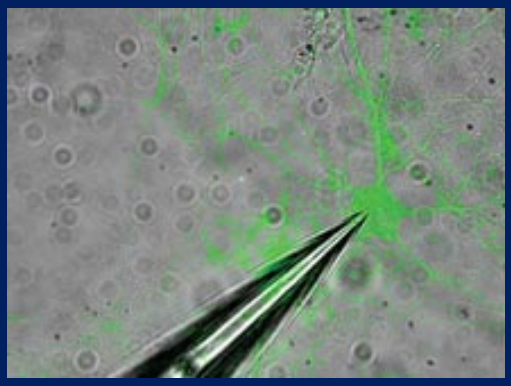
Researchers at Medtronic are developing a prototype neural implant that uses light to alter the behavior of neurons in the brain. The device is based on the emerging science of optogenetic neuromodulation, in which specific brain cells are genetically engineered to respond to light. Medtronic, the world's largest manufacturer of biomedical technologies, aims to use the device to better understand how electrical therapies, currently used to treat Parkinson's and other disorders, assuage symptoms of these diseases. Medtronic scientists say they will use the findings to improve the electrical stimulators the company already sells, but others ultimately hope to use optical therapies directly as treatments.



Light therapy: A neuron (green) engineered to express a light-sensitive protein fires in response to specific wavelengths of light. A glass electrode (lower left corner) records the neuron's electrical response. Researchers from Medtronic used this system to confirm that a new implantable stimulator can properly activate neurons with light.

Today's neural implants work by delivering measured doses of electrical stimulation via a thin electrode surgically inserted through a small hole in a patient's skull, with its tip implanted in a localized brain area. Since the U.S. Food and Drug Administration approved such "brain pacer" devices and the electrically based treatment they deliver –called Deep Brain Stimulation (DBS)–for a disorder called essential tremor in 1997, for Parkinson's disease in 2002, and for dystonia in 2003, over 75,000 people have had them installed. The electrical pulses are thought to counter the abnormal neural activity that results from different diseases, though physicians know little about how DBS works.

Despite their success, such neural prostheses have serious drawbacks. Beyond the blunt fact of their physical locations, they stimulate neurons near the electrode indiscriminately. That overactivity can trigger dizziness, tingling, and other side effects. Furthermore, they produce electrical “noise” that makes tracking quieter neural signals difficult and the simultaneous use of scanning systems like MRI practically impossible, which in turn prevents researchers from gaining any evidence about how DBS actually works.

In the last few years, scientists have developed a way to stimulate neurons using light rather than electricity. Researchers first introduce a gene for a light-sensitive molecule, called channelrhodopsin 2 (ChR2), into a specific subset of neurons. Shining blue light on these neurons then causes them to fire. One advantage of this approach is its specificity–only the neurons with the gene are activated. It also provides a way to shut neurons off–introducing a different molecule, halorhodopsin (NpHR), silences the cells in response to yellow light. “That’s the other unique thing about this approach,” says Tim Denison, senior IC engineering manager in Medtronic’s neuromodulation division. “It allows us to silence neurons’ activity, which is extraordinarily difficult with electrostimulation.”

While academic scientists are developing new tools to deliver light to the brain, Medtronic is developing an optogenetically based implant for commercial use. The module, which is approximately the size and shape of a small USB flash drive, has wireless data links, a power management unit, a microcontroller, and an optical stimulator. It uses a fiber-optic wire to direct light from a blue or green LED at target neurons in the brain. The company plans to market the device to neuroscience researchers and use it for in-house research on the effects of DBS.

Medtronic scientists emphasize the very early nature of the device. “This is research for use with animal models and not ready for any kind of human translation currently,” emphasizes Denison. Still, he continues: “What’s exciting is that therapies today remain based on these electrically based ideas from the 19th century. Now this novel, disruptive technology offers a unique interface to the nervous system.”

Today, over 500 laboratories are applying optogenetic tools to animal models of Parkinson’s, blindness, spinal injury, depression, narcolepsy, addiction, and memory. Medtronic, which has built its business by pioneering market implementation of medical research, has consulted extensively with optogenetic pioneers Karl Deisseroth of Stanford and Ed Boyden of MIT to build an implant to support this new science. (Boyden is an occasional columnist for *Technology Review*.)

In order to transform the research implant into a clinical device, Medtronic or others will need to find ways to safely deliver the necessary genes to specific neural circuits in the brain. Denison says he thinks that development of practical optogenetic-based therapies for human patients will be gradual. “Frankly, this is a technology I can see my son working on as a Medtronic employee,” he says.

MIT’s Boyden, however, envisions a more accelerated development: “I think it’s more in the three- to 10-year span,” he says. Boyden has cofounded a company, Eos, to develop gene therapies to cure blindness. (Because it targets the eye, this therapy would not require an implant.) Jerry Silver of Case-Western University has a startup, LucCell, that aims at such therapies to restore damaged spinal cord function. “Gene therapy is a maturing field,” says Silver. “There’s a virus type called AAV –adeno-associated virus–that is natural, that almost all of us already carry, that has no

symptoms, and that already has been used in many hundreds of patients without a single serious adverse event."

Overall, Boyden concludes: "In many neural or psychiatric disorders, a very small fraction of brain cells have very big alterations –Parkinson's is the death of perhaps a few thousand cells. If with optogenetics you can correct those downstream targets without altering all the 'normal neurons'–in quotes–you could solve our present problem, which is that every drug for treating brain disorders has very serious side-effects and neural implants are extremely blunt instruments. So that's the hope."

Mark Williams is a contributing editor at TR.