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A Light Switch for the Brain

Scientists have developed a light-triggered switch to control brain cells, which could aid in the development of therapies for epilepsy and other diseases--and shed light on the neural code.

By Emily Singer

Scientists can now turn on and off specific parts of the brain with a simple flash of light. The new molecular tool, developed by scientists at MIT and Stanford, allows unprecedented control over the brain and could lead to more-effective treatments for epilepsy, Parkinson's, and other diseases. It could also help neuroscientists crack the language of the brain: the information encoded in the electrical activity of neurons, which forms our memories and directs our every move.

"In many ways, I think it's going to revolutionize the field," says Michael Hausser, a neuroscientist at University College London who wrote a commentary accompanying the research, published today in *Nature* and last month in *Public Library of Science One*. "It could replace the stimulating electrode, which has been the main tool for neurophysiologists for the last 100 years. It could also improve clinical applications where implanted electrodes have been shown to be useful by targeting excitation or inhibition to specific cells."

Neurons encode information with a series of electrical pulses transmitted between cells. Neuroscientists have traditionally studied the function of brain cells by sending jolts of electricity delivered by an electrode, which sparks activity in neurons. However, it's difficult to target that activity to a specific type of cell, and there is no corresponding treatment to turn off cells.

Last year, Karl Deisseroth, a bioengineer and physician at Stanford, and Ed Boyden, a bioengineer at MIT, co-opted a light-sensitive channel from jellyfish to create a genetic "on" switch. The channel sits on the cell membrane and opens when exposed to light, allowing positive charge to flow into the cell. Shining light on neurons that are genetically engineered to carry the channel triggers electrical activity within the cell that then spreads to the next neuron in the circuit. (Scientists use optical fibers to shine light into the brain.)

Deisseroth and Boyden have now independently created an "off" switch that works by a similar mechanism. This time the scientists used a gene that codes for a protein pump: when hit with yellow light, it pumps negative charge into the cell, blocking that neuron from firing. Both switches can be used in the same cell, effectively giving neuroscientists a light switch that can be used to turn on and off neural activity.

This newfound ability to precisely control neurons could finally bring answers to major questions about the brain. It might help scientists find the specific cells or neural activity patterns that are involved in cognitive processes, such as attention, or in particular diseases, such as epilepsy.

Both epilepsy and Parkinson's disease can be treated with electrodes implanted into the brain. But the electricity delivered by the electrode stimulates all nearby cells rather than just the diseased ones, increasing side effects and potentially decreasing the effectiveness of the treatment. "It's been the source of incredible frustration," says Deisseroth, a practicing psychiatrist who is testing electrical stimulation as a treatment for severe depression. "We know we can get treatment benefits by sticking electrodes in the brain, but we don't really know what the target cell type is."

Deisseroth and Boyden are now using the light switches to study animal models of these diseases in order to find out exactly which cells need to be turned on or off. Their findings could be used to develop new drugs targeted to only those cells or, one day, to replace electrodes with more-precise light-activated implants.

The switch could also help decode the language of the brain by helping neuroscientists determine how different patterns of neural activity give rise to complex thoughts and actions. For example, recent research has suggested that rhythmic electrical patterns in our brain are important to our ability to pay attention. Scientists could use the switch to disrupt these patterns in animals and see if it wipes out their capacity to pay attention. Or they could try to induce these patterns and see if this improves the animals' focus. "This has been a dream of neuroscientists for a long time," says Hausser. "To be able to manipulate the spatiotemporal pattern of activity in a network and find the code that is linked to a particular kind of behavior."

In addition, scientists can manipulate the specific units of the neural code--the pulses, or spikes, of electrical activity that are transmitted between cells. "We've shown we can push spikes around, block them, delay them," says Boyden. "We can really alter neural coding at a millisecond time scale." That should allow scientists to determine which aspect of the code--the spikes' timing or the spikes' rate--encodes information in the brain, a debate that has raged for decades.
