massachusetts institute of technology

MITnews

Silencing the brain with light

MIT neuroengineers find a new way to quickly and reversibly shut off neurons with multiple colors of light, which could lead to new treatments for epilepsy and chronic pain.

Anne Trafton, MIT News Office

January 7, 2010

email comment

print share

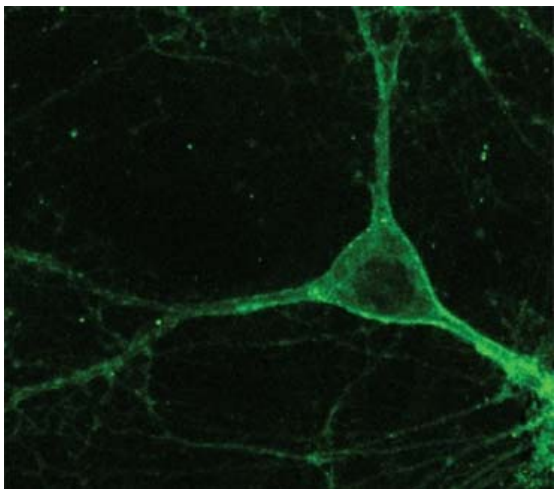
today's news

Next exit: MIT

This 1951 map shows a proposed highway cutting through MIT.
Image courtesy of the MIT archives

Traffic vs. Tech in the 1960s: how a highway could have split the Institute's campus

Straining forward
January 6, 2010



Mouse neuron expressing Arch gene
Image courtesy of Brian Chow, Xue Han and Ed Boyden/MIT

Giving epilepsy patients an electric jolt to shut off out-of-control neuron firing during seizures is being explored as a way to treat the chronic brain disorder. New research from MIT now raises the possibility of silencing those seizures with light instead of electricity.

A team led by neuroengineer Edward Boyden has found a class of proteins that, when inserted into neurons, allow them to be turned off with rays of yellow-green light. The silencing is near instantaneous and easily reversible.

This kind of selective brain silencing, reported in the Jan. 7 issue of *Nature*, could not only help treat brain disorders but also allow researchers to investigate the role of different types of neurons in normal brain circuits and how those circuits can go wrong.

“We hope to enable a broad platform of molecular tools for controlling brain activity, thus enabling new general therapeutic tools, and new ways of studying brain function,” says Boyden, the Benesse Career Development Professor in the MIT Media Lab and an associate member of the McGovern Institute for Brain Research at MIT.

‘Clean and digital’

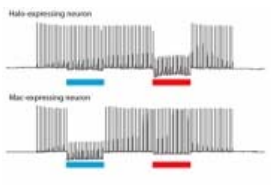
Boyden first demonstrated the use of light to reduce brain activity in 2007. However, the feat was performed in cells, not living animals, and the silencing was not as precise. In the new study, the researchers used a different protein — one that inhibits neurons more strongly, silences more brain tissue and can be repeatedly activated because it returns to its original state within milliseconds of light activation.

With the new protein, called Arch, brain silencing is “extremely clean and digital,” says Boyden. “The other one was more like a volume knob turning up and down.”

Boyden and his colleagues combined genetic and optical techniques to control neuron activity, a strategy that has come to be called “optogenetic.” First, they engineered brain cells of living mice to express the gene for the Arch protein, which functions as a proton pump, moving protons across the cell membrane to alter the cell’s voltage. The proton pumps are light-sensitive, so they pump protons out of cells when activated by yellow-green light. That lowers voltage inside the cells, silencing their firing.

In their previous work, the researchers used a light-sensitive chloride pump called

multimedia



Halorhodopsin-expressing neurons are selectively silenced by red light, but not by blue light. The opposite is true for neurons expressing the gene Mac.
Image courtesy of Brian Chow, Xue Han and Ed Boyden/MIT

related

Synthetic Neurobiology Group

McGovern Institute for Brain Research at MIT

Media Lab

ARCHIVE: "MIT neuroengineers' pulsing light silences overactive neurons"

Work could lead to new treatments for epilepsy, Parkinson's

PRESS RELEASE: "Neuroengineers silence brain cells with multiple colors of light"

tags

Biology, bioengineering and biotech

Genetics

Health sciences and technology

Media Lab / media arts

halorhodopsin, which changes neurons' voltage by pumping chloride ions into the cell. However, they weren't satisfied with it and started looking for a better chloride pump, examining proteins from a range of bacteria, plants and fungi. They couldn't find a chloride pump that offered the kind of control they were seeking, but discovered the new Arch proton pump in a strain of archaebacteria called Halorubrum sodomense that lives in the Dead Sea.

"This is the result of mining the wealth of the natural world — genomic diversity and ecological variation — to discover new tools that can empower scientists to study complex systems like the brain," says Boyden. "We're using natural tools isolated from the wild to help us understand how neural circuits work." This strategy has long been used in molecular and cellular biology, resulting in tools like restriction enzymes, PCR and GFP, but with Boyden's work only recently has been applied to tackle complex systems-level biological problems.

One major advantage of the new pumps is that they can be used over and over again: They recover their ability to be light-activated within seconds, rather than the minutes required for the old tool, halorhodopsin, to reprime itself.. That is critical to neuroscientists who want to study the role of particular cell types in different tasks, says Edward Callaway, professor of systems neurobiology at the Salk Institute, who was not involved in the research.

"If you have to wait a long time to get recovery, you just can't compare different conditions quickly," says Callaway, who studies vision-processing circuits in the brain. The new channels offer a "much more practical" way to use optogenetics for animal studies such as testing which neurons are involved in different visual tasks, he says.

To achieve brain silencing in mice, the researchers implanted an externally controllable light source inside the mice's brains. While the current device requires mice to be wired up to an external control, the researchers are designing a fully wireless system.

Boyden's group, working with the Desimone lab at the McGovern Institute at MIT, is now performing pre-clinical testing of this approach in non-human primates, to assess its safety as a potential therapy for epilepsy, chronic pain and post-traumatic stress disorder. The team has also developed, in collaboration with other groups at MIT, hardware for optical neural stimulation, which could be valuable for neural prosthetic purposes

The MIT researchers have also discovered other proton pumps activated by different colors of light, which, combined with previously discovered tools, allow them to selectively silence different brain regions using red and blue light. "One beautiful thing about this is we can inactivate different projections in the same brain," says Boyden.

In future studies, the researchers plan to use their neuron-silencing tools to examine the neural circuits of cognition and emotion, and to determine whether the new pumps are safe and effective in monkeys — a critical step towards potentially using optical control to treat human diseases.

Comments

Log in to write comments

and sciences

Neuroscience