Pulsing light quiets overactive neurons

Anne Trafton
News Office

Scientists at the MIT Media Lab have invented a way to reversibly silence brain cells using pulses of yellow light, offering the prospect of controlling the haywire neuron activity that occurs in diseases such as epilepsy and Parkinson's disease.

Such diseases often must be treated by removing neurons that fire incorrectly. The new MIT research could lead to the development of optical brain prosthetics to control neurons, eliminating the need for irreversible surgery.

"In the future, controlling the activity patterns of neurons may enable very specific treatments for neurological and psychiatric diseases, with few or no side effects," said Edward Boyden, assistant professor in the Program in Media Arts and Sciences and leader of the Media Lab's new Neuroengineering and Neuromedia Group.

Boyden and Media Lab research affiliate Xue Han published their results in the March 21 issue of the online journal PLOS One.

The work takes advantage of a gene called halorhodopsin found in a bacterium that grows in extremely salty water, such as the Great Salt Lake in Utah. In the bacterium, Natronomas pharaonis, the gene codes for a protein that serves as a light-activated chloride pump, which helps the bacterium make energy.

When neurons are engineered to express the halorhodopsin gene, the researchers can inhibit their activity by shining yellow light on them. Light activates the chloride pumps, which drive chloride ions into the neurons, lowering their voltage and silencing their firing.

That inhibitory effect may be extremely useful in dealing with diseases caused by out-of-control neuron firing, said Boyden. "In such diseases, inhibition is more direct than excitation, because you can shut down neural circuits that are behaving erratically," he said.

Many epilepsy patients have implanted electrodes that periodically give their brains an electric jolt, acting as a defibrillator to shut down overactive neurons. This new research opens up the possibility of an optical implant that could do the same thing, using light instead of electricity. The Media Lab neuroengineering group plans to start studying such devices in transgenic mice this year.

The group also plans to use the new method to study neural circuits. Last year, Boyden devised a technique to stimulate neurons by shining blue light on them, so with blue and yellow light the researchers can now exert exquisite control over the stimulation and inhibition of individual neurons.

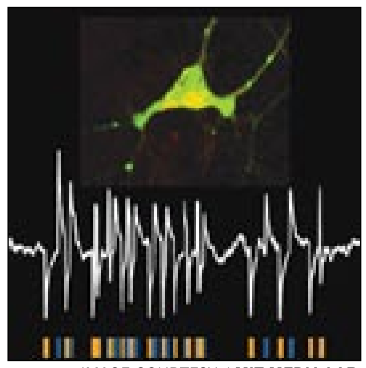

IMAGE COURTESY / **MIT MEDIA LAB**

This voltage trace of a single neuron shows pulses of blue light stimulating the neuron, yellow light inhibits it.

Learning more about the neural circuits involved in epilepsy could help scientists develop devices that can predict when a seizure is about to occur, allowing treatment (either shock or light) to be administered only when necessary, Boyden said.

The technique also offers a way to study other brain diseases, as well as normal brain circuitry, offering insight into which brain regions and neurons contribute to specific behaviors or pathological states, Boyden said.

The halorhodopsin gene was originally discovered in the 1980s, but Boyden didn't think its full potential had been explored. The protein expressed by the gene turned out to have exactly the right characteristics to make it useful in neuron inhibition.

"Often if you are patient and think carefully about what you want to do, you can find a molecule that is very close to what you want, and with a little bit of luck it will turn out to work," Boyden said.

The halorhodopsin work is one of the first projects from the Media Lab Neuroengineering and Neuromedia Group, which was formed about six months ago to enhance the Media Lab's study of the brain-body relationship.

"The Media Lab has always been interested in studying the interface between people and the world," Boyden said, "but now people are getting interested in the interface between bodies and brains in the world."

The research was funded by an anonymous donor, the MIT Media Lab and the Helen Hay Whitney Foundation.

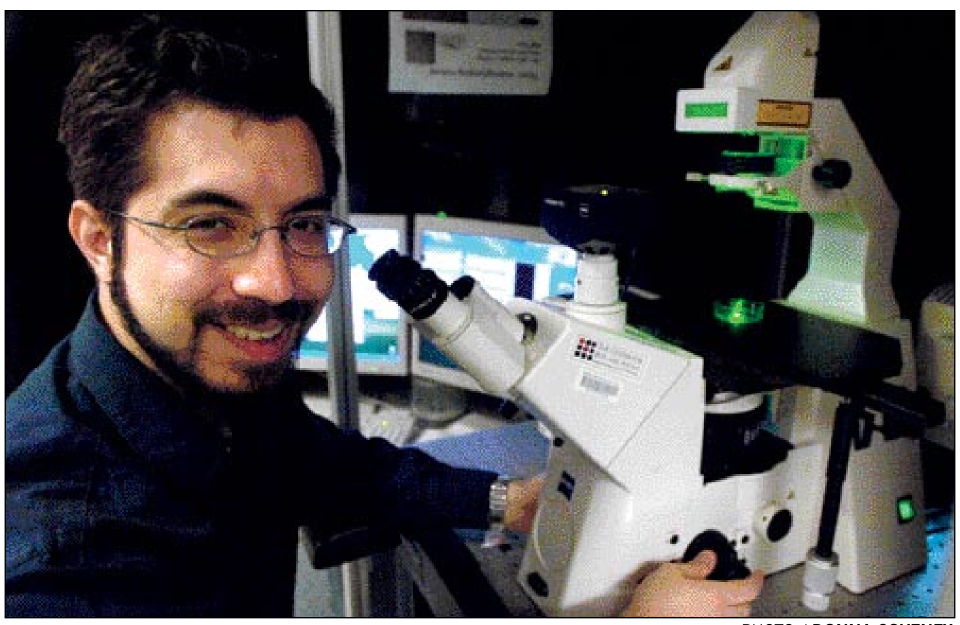

PHOTO / **DONNA COVENEY**

Edward Boyden, assistant professor in the MIT Media Lab, uses light to silence brain cells, which could block abnormal neuron activity in diseases like epilepsy and Parkinson's.

Child's play shows cause and effect

Deborah Halber
News Office Correspondent

It's not child's play to Laura E. Schulz, assistant professor of brain and cognitive sciences at MIT, to figure out what child's play is all about.

Schulz spoke March 21 at an MIT Museum Soap Box event, "Twisting the Lion's Tail: Exploratory Play and Children's Causal Learning."

Soap Box is a series of salon-style, early-evening conversations with scientists and engineers in the news, a public forum for debate about ideas and issues in science and technology.

The theory of cause and effect is fundamental to our understanding of the world. However, despite almost universal agreement that children learn about cause and effect through exploratory play, little is known about how children's play might support accurate causal learning, Schulz said.

"One of the deep mysteries of cognitive science is how we predict the future and how we explain the past and intervene in the present," she said. Causal reasoning even pervades our emotional lives when we speculate about why someone has a certain expression on her face or why a friend or colleague said what he did.

Causation in a nutshell: If you change this, all else being equal, something else changes. From earliest infancy and across all species, action and effect are correlated. Anyone who owns a pet knows that an animal quickly learns that opening a certain food container means dinner is on the way.

Statistical evidence is one factor that contributes to our rich beliefs about the universe. Our prior experiences and beliefs

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Infectious diseases to be first focus of Singapore-MIT Alliance for Research and Technology (SMART)

Elizabeth Thomson
News Office

Infectious diseases will be the focus of the first research group through the proposed Singapore-MIT Alliance for Research and Technology (SMART) Center, as announced by the Singaporean National Research Foundation (NRF), which will sponsor the center.

This research group "aims to develop an integrated, cutting-edge research program to study pathogen-host interactions of infectious diseases," as described in a fact sheet released by Singapore's Research, Innovation and Enterprise Council.

"It will focus on infectious diseases of importance to Singapore, Asia and the world. These diseases are respiratory syncytial virus, influenza, tuberculosis and malaria."

MIT Professor Jianzhu Chen of the Department of Biology will lead the group, which will comprise eight MIT faculty members and 17 researchers from universities, industry and institutes in Singapore.

"This research activity, along with the future programs of SMART, will strengthen and expand ongoing educational and research collaborations between MIT and Singapore," said Subra Suresh, Ford Professor of Engineering at MIT and MIT team leader for SMART.

SMART will serve as an intellectual hub for interactions between MIT and global researchers in Singapore at the frontiers of science and technology. SMART is the first of several world-class centers planned by the NRF in the international Campus for Research Excellence and Technological Enterprise.

MIT has worked with Singapore for eight years through the Singapore-MIT Alliance. Plans for MIT and Singapore to formalize SMART are expected to be completed in the next several months.

ATTENTION

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Brain signals related to the knowledge we have acquired about the world are called top-down. Signals related to incoming sensory information are called bottom-up.

"Loud, flashy things like fire alarms automatically grab our attention," Miller said. "By contrast, we choose to pay attention to certain things we think are important. We found two different modes of brain operation related to each, and they seem to originate in different parts of the brain. Further, automatic versus willful modes of attention seem to rely on two different frequency channels in the brain, suggesting that the brain might communicate in different frequency bands to take advantage of the type of internal network best suited for the task at hand."

ADD involves being overly sensitive to the automatic attention-grabbers and less able to willfully sustain attention. "Our work suggests that we should target different parts of the brain to try to fix different types of attention deficits," Miller said.

To address the fact that neural activity from the prefrontal and sensory cortices had never been directly compared, Miller and co-author Timothy J. Buschman, an MIT graduate student in the Department of Brain and Cognitive Sciences, conducted a series of experiments in which monkeys were engaged in different kinds of tasks. The researchers looked at activity in two areas of the brains simultaneously—the prefrontal cortex, also called the brain's executive because it is in charge of voluntary behavior, and the sensory cortex, which integrates sensory information coming from various parts of the body.

The monkeys had to pick out rectangles of certain colors and orientations on a video screen. Some of the rectangles popped out at them like the anaconda in the forest; others they had to search for.

The results support the idea that when something pops out at us, the visual part of our brain directs our eyes toward the stimulus. When we look for something, the prefrontal cortex is doing the driving.

"Taken together, these data suggest two modes of operation: When a stimulus pops out, a bottom-up, fast target selection occurs first in the posterior visual cortex; while in search mode, a top-down, longer latency target selection is reflected first in the prefrontal cortex," Miller said. "To our knowledge, these are the first direct demonstrations that these areas may have different contributions to these different modes of attention."

This work is supported by the RIKEN-MIT Neuroscience Research Center and the National Institute of Neurological Disorders and Stroke.

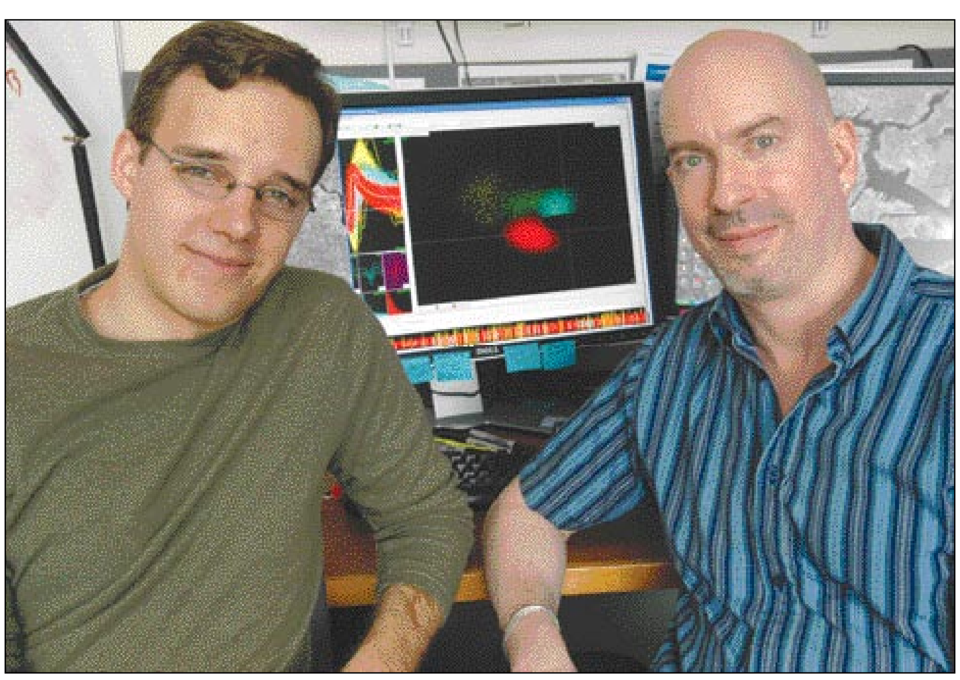

PHOTO / **DONNA COVENEY**

MIT graduate student Timothy J. Buschman, left, and Professor Earl Miller of the Department of Brain and Cognitive Sciences have found concrete evidence that two radically different brain regions play different roles in the different modes of attention.