White Coat Notes
News from the Boston-area medical community

MASS GENERAL , HARVARD UNIVERSITY , MIT

Boston scientists use light to control behavior in monkeys

E-mail | Print | Comments (0)07/26/2012 12:37 PM

By Carolyn Y. Johnson, Globe Staff

A team of Boston scientists has for the first time altered the brain activity and behavior of monkeys with what sounds like science fiction -- blue flashes of light that directly activate brain cells.

The technique, called optogenetics, has already transformed basic neuroscience research on addiction and memory conducted in mice and simpler animals. But the new work shows it can be used to explore and probe complex brains capable of human-like tasks and vulnerable to similar illnesses. The feat lays the foundation for the possible development of the technology, co-invented by an MIT neuroengineer, into a therapy for neurological or psychiatric diseases.

In the new experiment, a team led by a researcher from Massachusetts General Hospital found that two rhesus monkeys responded more quickly to a visual prompt by shifting their gaze when their brains were activated by light. The change was subtle, but scientists said it shows the power of optogenetics to study brain circuits involved in sophisticated behaviors or cognitive abilities that go awry in humans, such as attention.

“There are all sorts of experiments in science and ideas for medicine that in theory sound good, but showing you can do it in a complex brain that has more similarities to the human brain ... allows people’s imagination to reach reality,” said Edward Boyden, a neuroengineer at the Massachusetts Institute of Technology and a coauthor of the new work, published online Thursday in the journal Current Biology. Boyden, with Stanford University psychiatrist Dr. Karl Deisseroth, invented optogenetics in 2004.

Though the technology is less than a decade old, many scientists say it is already revolutionary. It has rapidly moved from an engineering demonstration into a widespread tool in hundreds of laboratories. Earlier this year, a team of MIT scientists reported they could use light to activate a fear memory in mice. Stanford researchers last year reported the discovery of an anti-anxiety circuit in the brain, which when activated by light made the mice calmer and more willing to take risks. Researchers from the University of North Carolina at Chapel Hill last year described using the technology to begin to unpack the neural circuitry involved in addiction, using light to manipulate reward-seeking behavior in mice.

As the name suggests, the technology is a fusion of optics and genetics. Scientists use viruses to carry genes transplanted from algae into brain cells. There, the genes produce light-sensitive proteins that act like on-off switches when exposed to light. Scientists implant thin optical fibers to shine light on specific brain circuits they want to stimulate or inhibit, to trigger behaviors and figure out which cells or circuits are involved.

A now iconic video shows how dramatic the light control of the brain can be: a mouse with a fiber optic cable implanted in its head wanders around its cage, but when a blue light is flicked on, it begins to run in a counter-clockwise circle.

Several previous papers had shown that it was possible to insert the algae genes into monkey brain cells and to activate them with light, but in those cases it had no visible effect on the monkey’s behavior.

“This study is proving to others that with monkey research, you can use it and do stuff you won’t be able to do with other methods,” said Wim Vanduffel, an assistant professor of radiology at Harvard Medical School and Mass. General who led the research.

In the new paper, the researchers first used brain imaging to map the precise areas of the brain involved with an eye movement task. Then, they injected viruses carrying the algae gene to make all the cells in those regions sensitive to light activation. Two implanted optical fibers were used to illuminate the brain region. The rhesus monkeys were trained to perform a specific visual task in response to a visual cue -- when a dot in their peripheral vision dimmed, they looked toward a green target to receive a reward. Monkeys performed the task both with the light on and the light off, and the researchers found their performance was boosted by about 20 milliseconds when the light was on.

“No one has been able to use these tools to modify behavior [in primates], and in many cases that’s the key opportunity with optogenetics,” said Karel Svoboda, a group leader at Janelia Farm Research Campus in Ashburn, Va. who uses optogenetics in mice and was not involved in the new work. “It is a big step to get this to work in primates.”

But he added that the most exciting research would be in the future, as scientists refined their efforts in primates and used the technique to turn on specific subsets of cells, revealing which cells underlie complex behaviors. He compared a behavior to a symphony and said optogenetics gives scientists a way to understand how each brain cell -- each player in the orchestra -- contributes to the whole.

Krishna Shenoy, who heads the Neural Prosthetic Systems Laboratory at Stanford and who was not involved in the work said that it is an important paper, and that his own laboratory will this fall present similar results from working in a different part of the monkey brain involved in arm movement.

What is important, he said, is the fact that it opens up the technique to be adapted to explore more complicated behaviors and tasks. While it will likely be many years before such techniques could be adapted to human therapy, if they ever are, diseases like Parkinson’s disease already benefit from using electrical stimulation in the brain, and scientists are dreaming big. Finer control of neural circuits could be used, for example, to turn off a seizure in patients with epilepsy, to restore vision to blind patients, or to treat spinal cord injury.

“Monkeys are capable of much higher cognitive tasks” and provide a more accurate model of neurological diseases, Shenoy said. “We might finally be able to tease apart what’s really going in on in these diseases, because we really don’t know.”

Carolyn Y. Johnson can be reached at cjohnson@globe.com. Follow her on Twitter@carolynyjohnson.