INSIDE SCIENCE NEWS SERVICE

Sending Light Through The Skull To Influence Brain Activity

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Genetically engineered protein responds remotely to red light.

Originally published: Jul 18 2014 - 3:15pm

By: Peter Gwynne, Contributor

(Inside Science) -- A team of biological engineers has developed a light-sensitive protein that permits scientists to control activity inside the brains of mice from outside the rodents' skulls.

The protein, called Jaws, promises to expand scientists' ability to study brain activity in experimental animals and -- eventually -- humans. Ultimately, it holds the prospect of facilitating treatment of human conditions such as epilepsy.

Researchers are also using the protein to treat eye disease in experimental animals. Here, an immediate goal is therapy for certain eye ailments in humans.

Scientists use optogenetics, as the technology is known, to study the behavior and pathology of experimental animals' brains by shining light on proteins known as opsins. Introduced into the brain aboard viruses, the opsins respond to the light by suppressing or stimulating electrical signals in brain cells.

The opsins normally used in brain studies are sensitive to blue, green, or yellow light. Because bodily tissue absorbs those colors easily, the sources of such light must lie inside the brain. Typically, the light is delivered through an optical fiber implanted in an experimental animal's brain.

The newly developed Jaws protein responds to red light, which penetrates living tissue so effectively that it can influence the protein from outside the animal's head.

A team led by Ed Boyden, associate professor of biological engineering and brain and cognitive sciences at the Massachusetts Institute of Technology, in Cambridge, reporting in Nature Neuroscience, demonstrated that red light shone from outside a mouse's head can influence the Jaws protein up to three millimeters deep inside the brain. In fact, Boyden said, "we think the light goes further into the brain." A mouse's brain is only about four millimeters thick.

"This [research] is a huge advance, in that it allows for much deeper penetration of effective light," said David Lyon, an associate professor of anatomy and neurobiology at the University of California, Irvine School of Medicine. Lyon was not involved in the research on Jaws.

Optogenetics' advantage over alternative approaches to brain research stems from the directionality and speed of light.

"Electricity travels in all directions, but light allows you to focus on just one region," Boyden explained. "And drugs are really slow to act, taking seconds to minutes to hours. Optogenetics allows you to target specific brain cells within milliseconds."

It's also a much more practical approach for studying the brains of growing animals, especially over the long term.

"Inserting optical fibers into the brain just doesn't work for developing brains," Boyden explained. "As the brain grows, they could cause damage." Similarly, the non-invasive approach enables long-term studies of the brain.

"And, if you want to silence a large region of the brain, the non-invasive approach works well." Boyden added.

His team has used optogenetics with implanted light sources to study mice with symptoms of anxiety, fear, memory loss and post-traumatic stress disorder. Scientists examine the effects on those conditions of stimulating specific groups of neurons. Other research teams have taken a similar approach to studies of grooming behavior in mice and the neural pathways through which cocaine flows

in the brain.

The Jaws protein will permit more extensive studies of that type. "Advances like Jaws certainly help with non-invasive treatment strategies," Lyon agreed.

However, he noted that implanted light sources will retain some use. "Probably the most likely scenario will be to use them to activate opsins in deeper brain structures."

Applying the new technology to human subjects is not practical at present, as it would require gene therapy to introduce the opsin into individuals' brains.

"Gene therapy is not approved in the United States," Boyden said.

But if that changes, non-invasive optogenetic technology facilitated by the Jaws protein has significant healing potential. "The ability to turn off brain activity might allow you to stop overactive regions of the brain -- during epileptic seizures, for example," Boyden said.

The advance also shows promise for treating certain types of blindness, a possibility explored by Botond Rosko and Volker Busskamp of the Freidrich Miescher Institute for Biomedical Research in Basel, Switzerland, in their research on color vision.

When he heard about Jaws, Rosko surmised that it could surpass the performance of a similar protein he had already used to restore cones' sensitivity to light. Tests on the retinas of mice, reported in the same Nature Neuroscience paper, showed that Jaws more closely resembles retinal cones' natural opsins and offers a greater range of light sensitivity.

Rosko and colleagues have begun studies of the Jaws protein in mice and non-human primates. They started a company that aims to use the optogenetic approach to combat retinitis pigmentosa, a degenerative condition of the retina that causes partial or total blindness in humans.

"Whenever you have blindness and there are remaining cones, this treatment is possible," Rosko said. "We expect that optogenetics will be able to restore some objective vision in blind patients suffering retinitis pigmentosa."

After working to identify opsins that produced electrical current in response to red light, Boyden's graduate student Amy Chuong developed Jaws. Tests confirmed that the protein's response to red light beamed at it from outside a mouse's brain was sufficient to shut down the electrical activity of neurons in the brain. Jaws, the tests showed, responds just as effectively to light beamed from outside the brain as traditional opsins to light from inside.

Continued progress in the research should provide better insights into the brain and bring closer the prospect for treatment of brain conditions.

"We want to understand the basic science of the brain," Boyden said, "and how to fix the brain."

A former science editor of Newsweek, Peter Gwynne is a freelance science writer based in Sandwich, Massachusetts.

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