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ScienceWorld®

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OCTOBER 27, 2014
VOL. 71 NO. 4
ISSN 1041-1410

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PHYSICS

MIND CONTROL

Can scientists use light to treat devastating brain disorders?

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PHYSICS: Light // BIOLOGY: Health

MIND CONTROL

How scientists use light to manipulate the brain—and treat illness

A mouse crouches on the floor of a small rectangular enclosure. It sniffs the air curiously. Then, a small light attached to the top of its head glows blue. The mouse begins running around the enclosure. The light turns off. The mouse stops. By flipping a switch, scientists are controlling the part of the mouse's brain that makes it run.

A breakthrough technology called optogenetics made this experiment possible back in 2007. Optogenetics lets scientists modify *neurons*, or brain cells, to make them respond to light. They shine light on the cells to activate them. Since some neurons have different roles than others, targeting a particular group of neurons lets scientists control specific behaviors. "If we wanted to, we could create a mouse that we could run like a remote control car," says Eric Turner, a neuroscientist at Seattle Children's Research Center in Washington.

But Turner and other scientists studying optogenetics have bigger ideas. They're using it to understand how the brain creates our thoughts, emotions, and behaviors—and how to treat devastating brain disorders.

BRAIN BASICS

How the brain works is largely a mystery, even to doctors and scientists. The human brain contains about 86 billion neurons. Electrical signals whiz throughout the brain along pathways that connect multiple neurons, causing every behavior from tasting to texting, and every emotion from happiness to fear. Figuring out the one network of neurons that controls each of these responses isn't easy.

Optogenetics is the first tool that could reveal these secrets. Using it, scientists may finally be able to figure out what causes psychiatric disorders like depression and anxiety and diseases like Parkinson's and epilepsy. Better therapies could then be developed to treat these illnesses.

A BRIGHT IDEA

Optogenetics all began with an unlikely source: pond scum. In

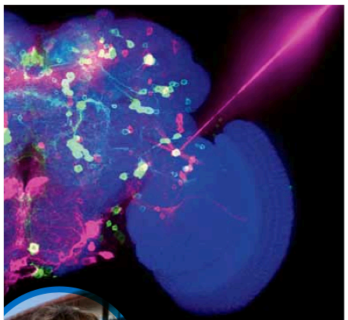
OPTOGENETICS IN ACTION: This illustration shows brain cells that are activated by light, with optogenetics.

WATCH A VIDEO ABOUT OPTOGENETICS

CLICK FOR 4 BONUS SKILLS SHEETS

LIT UP: Blue light is delivered to a mouse's brain to change its behavior.

JOHN B. CARNETT/POPULAR SCIENCE VIA GETTY IMAGES (MOUSE); HENNING DALHOFF/SCIENCE PHOTO LIBRARY/GETTY IMAGES (NEURONS)



NEURON NETWORKS: A view inside a fly's brain (*blue*) showing two networks of neurons (*green* and *pink*). Optogenetics was used to make the pink neurons light sensitive.

ELECTRODE THERAPY: For severe cases of epilepsy or depression, electrodes can be implanted in the brain to control neurons. This treatment can be effective but also zaps large parts of the brain. Treatments developed from optogenetics would be much more precise.

KARL DEISSEROTH

2004, Karl Deisseroth, a neuroscientist at Stanford University in California, became fascinated by a green algae called *Chlamydomonas*. The algae don't have brains, but they do have proteins called *opsins*. Opsins are sensitive to light: When the sun hits one, it sends a blast of electricity through the algae that signals it to move toward or away from the light. *Chlamydomonas* uses sunlight to create energy, similar to what plants do during photosynthesis. Moving toward the sun allows them to collect more energy.

Deisseroth wondered if he could use opsins to "talk" to neurons in the brain. He thought that it might be possible because both opsins and neurons use the same language: electricity. If he inserted an opsin into a neuron, he might be able to change how the neuron behaves by exposing it to light.

No scientist had tried it before because no one thought it was possible. "I thought it probably wouldn't work perfectly," Deisseroth says. "But it was worth a shot."

In 2006, Deisseroth and his team tested their idea on a mouse. They inserted the opsin's *gene*—the opsin's hereditary material—into neurons that control sleep and wakefulness. Then they put a thin fiberoptic cable into that area of the brain. The cable was connected to a very tiny laser, allowing it to shine light directly into the brain.

The team tried the experiment on a sleeping mouse. When they turned on the laser, the mouse began to move. The light inside its head was activating the neurons that tell the mouse, "Wake up!" The experiment was a success.

MIND MAPPING

Optogenetics is now one of the fastest-developing fields in science. By inserting the opsin gene into different neurons and flipping on light to see what the mice do, scientists can figure out what different neural pathways are controlling. "You name it—any behavior, any cognition—you can study it with optogenetics," says Deisseroth.

CORE QUESTION

How could optogenetics help treat brain disorders?

By gradually working through the brain one neural pathway at a time, scientists hope to create the first finely detailed map of the human brain. It could show us how emotions, behaviors, and brain disorders come to be.

HEALING WITH LIGHT

One disorder that could benefit from optogenetics is *epilepsy*—an incurable condition that can cause seizures (uncontrollable shaking of muscles). Epileptic seizures happen when neurons go haywire, firing their electrical signals out of control.

To regulate some severe cases of epilepsy, doctors implant electrodes in the part of the brain that's malfunctioning. The electrodes emit pulses of electricity that stop the neurons from firing wildly. But electrodes aren't precise—they can zap healthy neurons along with misfiring ones. With optogenetics, doctors could treat only the neurons that are malfunctioning.

People who suffer from anxiety could also benefit. Current medicines expose the entire brain to a treatment, which can lead to undesirable side effects like sleepiness or confusion. So Deisseroth's lab decided to try to locate the exact neurons involved in anxiety. They put the opsin gene into a circuit of neurons in a mouse's *amygdala*, a part of the brain associated with fear and anxiety. Then they implanted a cable into the amygdala and watched what happened when they flipped the light on (*see illustration, right*).

Mice are fearful of open spaces, where they can't hide from predators. When Deisseroth's team placed the mouse in a maze, it spent most of its time in an area protected by high walls, occasionally poking its nose out to explore. But when they switched on the light, the mouse suddenly ventured out, exploring the open spaces without concern.

The results suggest that the team located an anxiety circuit in the brain. Someday, doctors could help people with anxiety disorders by treating that circuit with more precise medication.

TOO MUCH CONTROL?

Optogenetics could help millions of people. But is manipulating the brain ethical? Some people worry that if scientists can control the brains of mice with light, what's to stop someone from controlling people's brains against their will?

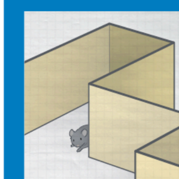
Deisseroth says current optogenetic technology isn't nearly sophisticated enough to make this a remote possibility. Plus, he says, the benefits far outweigh any concerns.

The potential rewards are great: Optogenetics may be the key to the first sophisticated treatments for devastating brain disorders. It could also help answer one of the biggest questions of all: how our brains make us who we are.

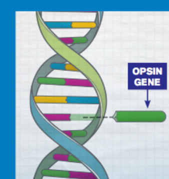
—*Stephanie Warren Drimmer*

HOW TO CONTROL A MOUSE'S MIND

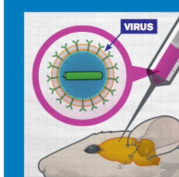
Deisseroth's lab used optogenetics to shut off neurons in a mouse's brain that cause anxiety. Mice are afraid of open spaces, but optogenetics can make them get over that fear. The process below shows how it works. Steps 2 through 4 show the basics of all optogenetics experiments.



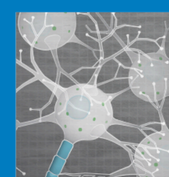
1 An untreated mouse lingers in the corner of the maze, too scared to explore beyond the sheltered walls.



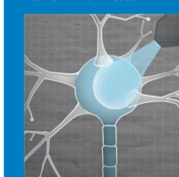
2 The opsin gene (the opsin's hereditary material) is removed from light-sensitive algae.



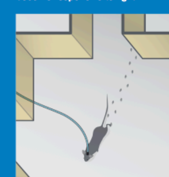
3 The opsin gene is inserted into a harmless virus and injected into the brain of a mouse.



4 Neurons, in this case related to a mouse's fear response, become responsive to light.



5 Scientists shine light into the mouse's brain through a cable. The neurons respond to light, stopping the mouse's fear response.



6 The mouse, no longer afraid of open spaces, bravely explores the maze. The animal does not experience anxiety.