Researchers use laser light to remote control flies

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Yale University School of Medicine researchers have found a way to exercise a little mind control over fruit flies, making the flies jump, beat their wings, and fly on command by triggering genetic "remote controls" that the scientists designed and installed in the insects' central nervous systems, according to a new report in the 8 April issue of the journal Cell.

Susana Lima and Gero Miesenbock hope that the remote control system will provide a valuable way to study how nerve-cell activity and connections are related to specific behaviors, from simple movements to more complex behaviors like learning, aggression, and even abstract thought.

The ability to control specific groups of neurons without implanting electrodes in the brain or using similarly invasive techniques "would represent a significant step in moving neuroscience from passive observation…to active and predictive manipulation of behavior," the Cell authors write.

Miesenbцck also says "one could use this method to restore neural signals that have been lost" due to injury or disease, such as in spinal cord trauma, although he notes that the possibility is "far-fetched" at the moment.

The remote control is based on the idea that specific nerve cells could be equipped with molecular "receivers" that allow them to recognize an

outside signal like a laser light pulse and translate that signal into the electrical signals characteristic of nerve-cell activity.

To accomplish this, Miesenbцck and Lima devised a triggered molecular lock and key system, where the "lock" was the receiver genetically encoded to be expressed in the target neurons, the "key" was the molecule that would bind to and activate the lock, and laser light was the trigger that brought the key to the lock.

For the lock, the researchers used an ion channel, or a pore-forming protein that allows charged particles to pass through a cell membrane. The small molecule ATP activates the ion channel chosen by the researchers, so ATP became the key. To keep the ATP from binding to the ion channel and jump-starting the nerve cell's activity before the proper moment, Lima and Miesenbцck caged the ATP with other chemical compounds that could be removed by the laser light.

Miesenbцck says one of the most difficult parts of the experiment was deciding which particular nerve cells to target with the remote control system. "To ascertain that the system actually worked, it wasn't clear how we could measure activation in the neurons in moving, freely behaving organisms," he explains.

The breakthrough, he says, came when they decided to target a small set of nerve cells in the fly called the giant fiber system. The giant fiber system controls very specific, stereotypical movements such as escape movements, jumping, and the beginnings of flight. If the flies engaged in these behaviors after the giant fiber neurons had been outfitted and "operated" with the remote control, Miesenbцck and Lima reasoned, they could be sure that their system was working.

After genetically engineering the flies to express the ion channel in the giant fiber system cells and using the tiniest of injections to place the

caged ATP inside the flies, the researchers shone a ultraviolet-wavelength laser in brief, millisecond pulses at the flies trapped inside a glass-domed arena. On command, the flies began a series of escape movements--extending their legs, jumping, and opening and rapidly flapping their wings.

The laser-triggered remote controls in the giant fiber system worked about 63 percent of the time, while remote controls placed in other nerve cells that were targets of the giant fiber system worked 82 percent of the time, the researchers concluded. Lima and Misenbцck also equipped another set of nerve cells called dopaminergic neurons with the remote controls, boosting the flies' activity levels and changing their flight paths.

Misenbцck says the triggered behaviors can last seconds or continue for minutes, depending on whether the neural circuit activated by the remote control has feedback loops that keep the circuit. "In the case of the flight circuits," he says, "it is like pushing a swing. One initial kick and it keeps swinging back and forth for a while."

Source: Cell Press