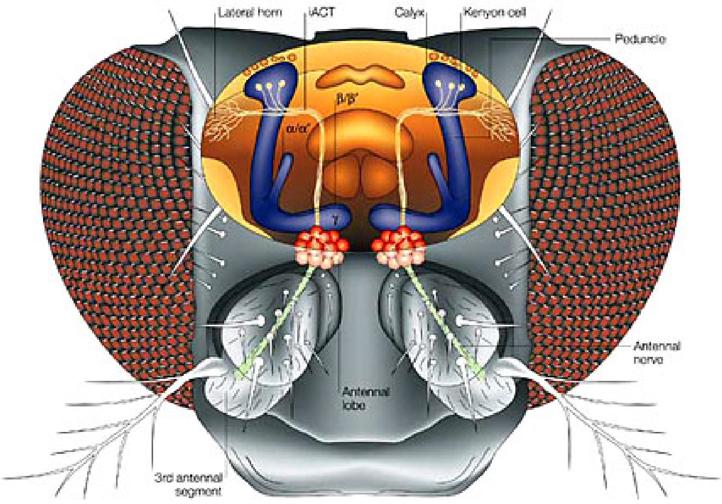
Researchers create artificial memories in the brain of a fruitfly

Nicholas Wade



Small Minds - Using genetic manipulation and light beams scientists created a memory in a fly's brain that made a tennis shoe smell something to avoid.

As part of a project to understand how the brain learns, biologists have written memories into the cells of a fruitfly's brain, making it think it had a terrible experience.

The memory trace was written by shining light into the fly's brain and activating a special class of cells involved in learning how to avoid an electric shock.

The goal of the research is not to give flies nightmares but rather to understand how learning in general works, from flies to people. "In the case of the fly, where we have a numerically rather simple nervous system that does something rather complex, I think we have a chance to break open the black box and understand it," said Gero Miesenböck of the University of Oxford, leader of the team that has developed the new technique.

Psychologists study learning by running rats through mazes, but biologists want to learn the actual mechanics of how a memory trace is laid down in a nerve cell or neuron. So they need an organism whose genes can be easily manipulated.

In the early days of molecular biology, when others were working on DNA, the biologist Seymour Benzer decided to dissect behavior by studying the fruitfly. His student Chip Quinn discovered in the early 1970s that fruitflies, surprisingly, could learn. If exposed to a chemical odor and at the same time given an electric jolt big enough to kill a person, the fruitflies associated the two and would in the future avoid the odor.

Of the two chemicals that Mr. Quinn picked, one smelled like licorice and the other "a lot like tennis shoes in July," according to Jonathan Weiner, author of "Time, Love, Memory," an entrancing history of Benzer's work. Biologists ever since have used the same system to train fruitflies. With the aid of the licorice and tennis shoe odors, Dr. Miesenböck's team has now managed to peer deep inside the black box of the fly's learning system.

His goal is to dissect the neural circuitry through which the fly associates a particular odor with electric shocks, so he began by looking at a class of neurons that generate the chemical messenger known as dopamine.

In the human brain, dopamine signals pleasure and reward but in flies it does the exact opposite: it is the messenger of fear and aversion. The fly has some 200 dopamine-producing neurons, and these must be involved to help the fly associate fragrance of tennis shoe with a really bad scene.

Dr. Miesenböck's team was able to distinguish, by their genetics, different classes of the dopamine-making neurons. By tagging each class of neurons with a gene that makes a fluorescent protein, they could make the dopamine neurons light up and they could trace their circuitry. Only one class, consisting of just 12 neurons, made the right connections in the fly's brain to function in learning shock avoidance, they report in the current issue of Cell.

These 12 neurons, which were receiving news of electric shocks and generating dopamine, converge on another group of neurons called Kenyon cells to which they seem to be passing on news of the shock, via dopamine. Since the Kenyon cells also receive messages about odors from receptors on the fly's antennae, they seemed to be the place where the memory of the experience was laid down.

To test their understanding of the system, Dr. Miesenböck and his colleagues activated the Kenyon cells themselves instead of having the fly experience an electric shock. They genetically engineered a strain of flies whose Kenyon cells would respond to flashes of light. The light releases an injected chemical to which the cells have been made sensitive.

Instead of exposing the flies to an odor and an electric shock, the researchers applied the odor and a flash of light to activate the Kenyon cells. The light was just as good as the shock: by activating the Kenyon cells at the same time as the aroma was sensed, it wrote a message in the fly's brain that eau de tennis shoe was something to eschew.

With this handle on the learning mechanism, Dr. Miesenböck hopes to trace the rest of the circuitry. He thinks the Kenyon cells may project onto others that control the fly's movement. So when the fly senses the tennis shoe odor, the Kenyon cells will all send their messages to the motion cells, acting like voters in a ballot to influence the fly's movement. The stronger the aversive connotation of the odor, the greater the number of Kenyon cells voting to leave in a hurry.

The learning system must also have some method for estimating how well the lesson has been learned, Dr. Miesenböck said in an interview. Once the association between odor and shock has been established, the fly's model of the world is 100 percent correct and there is no need for further changes to the memory trace; it is not clear, however, how this is accomplished.

When the entire learning circuitry is mapped, will the fly, and other creatures with learning neurons, seem just like biological machines? "If one really sees what interacts with the gears and how the neural clockwork runs, that would be the level of explanation that satisfies me," Dr. Miesenböck said.

Ralph Greenspan, an expert on fruitfly behavior at the Neurosciences Institute in San Diego, said, "This paper begins to pin down the detailed circuitry that underlies this associative condition pathway in the fruitfly."

Asked if the technique might help to trace the whole nervous pathway from sensing the odor to flying away, Dr. Greenspan replied, "It would be a miracle at this point because the notion of where this process produces a motor output is as undefined as it could be," meaning that the neural circuits that drive the fly's motion are still unknown. The black box of the fruitfly's brain still holds many dark corners.

New York Times, New York, Oct. 16th 2009, Science, online.