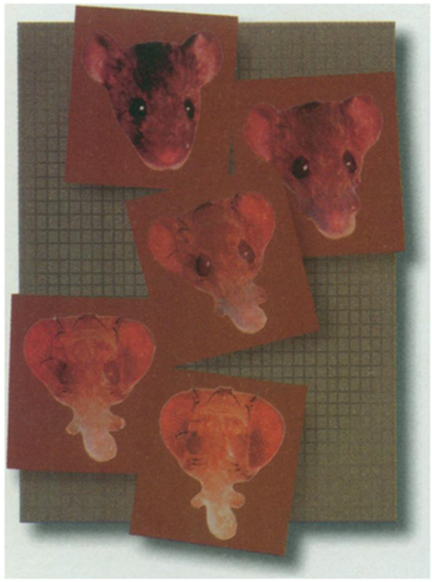
Mice, Flies Share Memory Molecule



Concept: Margot Bennett/ Illustration, James Egan

Ever wonder why cramming for a test can result in a passing grade but no recollection 6 months later of the material you studied?

Just ask Tim Tully, a fruit fly geneticist at the Cold Spring Harbor (N.Y.) Laboratory. Two reports by his group in the Oct. 7 CELL indicate that permanent recall results only when learning occurs with rests between training — or study — sessions. The reports also reveal distinct memory types and describe a molecule essential to long-term memory storage.

And as dissimilar as insects are to humans, Tully's data may also apply to people. A third report in this issue of CELL shows that the same molecule, a protein called CREB, seems key to mouse memory. "Undoubtedly, CREB plays the very same role in humans," says Alcino J. Silva, also at Cold Spring Harbor.

In contrast to short-term memory, permanent recall involves the production of new proteins, a process requiring gene activation. CREB stands for cyclic AMP response element (CRE) binding protein. It attaches to CRE sites on genes. The Cold Spring Harbor researchers think CREB initiates recall by revving up genes whose protein products then turn on other genes.

Eric Kandel of Columbia University's College of Physicians and Surgeons in New York City already had implicated CREB in the permanent retention of a learned response. While other molecules can activate CREB, cyclic AMP appears vital to memory storage, he now reports in the same issue of CELL.

For their work, Tully and his colleagues first teach fruit flies to associate a particular odor with an electric shock. When given a choice, these insects later avoid that odor 9 out of 10 times. However, "cramming" — exposing a fruit fly to the conditioning odor for a minute every other minute for 20 minutes total — yields no long-term memory, while training the fly with 15-minute rests between each exposure does, Tully says. Flies given the rest avoided the odor even after a week, while those that crammed did so for only 3 days.

Other tests demonstrate that, like people, the insects possess anesthesia-resistant memory, which doesn't kick in until a few minutes after learning and then slowly diminishes. This type of memory does not involve the creation of new proteins, Tully finds. When Tully, molecular biologist Jerry C.P. Yin, and their coworkers disrupted CREB function in one type of mutant, the flies retained short-term and anesthesia-resistant memory but not long-term recall. "There are distinct memory phases," Tully concludes. "They are functionally distinct, and they are genetically distinct."

Meanwhile, Silva's group studied normal mice and mice genetically altered to lack CREB. In one task, all the mice learned to associate a shock with a particular sound or cage, but mice without CREB forgot more quickly than normal mice to associate fear with either the cage or the tone, Silva reports.

In another test, mice learned to navigate to a slightly submerged platform while swimming in a small pool of murky water. In contrast to normal mice, altered mice never remembered their swim from one day to the next when trained just once a day for a week, Silva says. Only after the scientists intensified the training to 12 swims a day did these mice begin to learn the platform's position.

On the molecular level, Kandel's team finds it can block memory storage by adding chemicals that inhibit cyclic AMP or CREB's activating enzyme to slices of hippocampus, commonly regarded as the brain's memory storage center. "[CREB] functions as the molecular switch," Tully concludes.

"These data raise the exciting and interesting possibility that [CREB] participates in long-term memory storage, but it wouldn't be *the* molecular switch, it would be part of a concert of molecular switches," comments Daniel L. Alkon, a neuroscientist at the National Institute of Neurological Disorders and Stroke in Bethesda, Md.

Other undetected processes may go on in these animals or in tissue removed from the hippocampus, he says, emphasizing the complex nature of brain chemistry and the multiple linkages between CREB, cyclic AMP, protein synthesis, and gene regulation. The researchers should do additional studies to verify that the experimental conditions are not altering cell function or protein synthesis in unexpected ways, Alkon suggests. — *E. Pennisi*

Pacific Ocean quake stumps scientists

The huge earthquake that struck near the sparsely populated Kuril Islands northeast of Japan on Oct. 4 has geoscientists shaking their heads.

Some data gathered during and shortly after the magnitude 8.2 event suggest that the rock ruptured at the boundary where the Pacific plate sinks below another continental plate. Other evidence hints that it took place within the Pacific plate.

If the quake occurred on the boundary, it delivers another blow to the seismic gap theory, says Larry J. Ruff of the University of Michigan in Ann Arbor. This theory holds that large quakes strike the segments along plate boundaries every 100 to 200 years or so; one should not have hit the site of the Oct. 4 event for many decades. Recent earthquakes elsewhere have challenged the gap theory, Ruff notes (SN: 2/29/92, p.136).

The quake's size suggests that it was a plate boundary, or underthrusting, quake, seismologists say. Tremors within a plate rarely reach that size, adds Hiroo Kanamori of the California Institute of Technology in Pasadena. The tsunami waves resulting from the quake had the character and height of a plate boundary event, researchers agree.

However, the tremor occurred 40 to 50 kilometers below sea level and lasted only 50 seconds, making it deeper and quicker than other underthrusting quakes, Kanamori notes. Also, the Pacific plate slipped laterally during the event, which is not characteristic of plate boundary quakes.

Researchers disagree on how much the quake's energetic aftershocks resemble those of a plate boundary event.

All this preliminary evidence suggests to Kanamori that the quake wasn't "really on the boundary." Other scientists want to await more data before casting a vote. — *T. Adler*