Simple 'Learning' in Cell Culture

In the search for the molecular basis of learning and memory, scientists have steadily moved from the complexities of the mammalian brain to simpler nerve cell connections in less complex animals. Now Eric Kandel of Columbia University in New York City reports that his research team is examining perhaps the simplest component of a learning system: just two types of nerve cells taken from snails and allowed to establish connections on a laboratory plate.

"We are beginning to get a system where long-term memory can be explored in cellular detail," Kandel told a symposium at the new Fidia-Georgetown Institute for the Neurosciences at Georgetown University in Washington, D.C. In their recent experiments, Kandel, Samuel Schacher and their colleagues provided isolated cells with conditions that mimic a simple learning experience in the intact snail. The isolated cells responded with the same changes that underlie forms of both short-term and long-term memory in an animal.

The learning process under study is called sensitization. It can cause an animal to pay attention to an innocuous stimulus, because that stimulus has previously accompanied a painful stimulus.

The marine snail *Aplysia* demonstrates sensitization in the reflex that withdraws its gill and siphon, a small fleshy spout above the gill, when the siphon is touched. The neural circuit underlying this reflex (SN: 1/22/83, p. 58) includes a sensory nerve cell, a motor nerve cell and a few other nerve cells. When a touch to the siphon has been accompanied by an electric shock to the tail, the signal that directs the gill withdrawal response is enhanced. The enhanced response to a siphon touch lasts for a few minutes. But if the noxious shock is repeated several times, this sensitization can last weeks.

In previous work, Kandel and his colleagues determined the steps underlying sensitization. Some nerve cells of the reflex release neurotransmitters, one of which is called serotonin, that activate receptors on the sensory nerve cell. These receptors trigger a cascade of biochemical events that eventually increases the amount of neurotransmitter the sensory cell releases, enhancing its signal to the motor nerve cell.

Earlier experiments analyzed the effect of serotonin on the cell body, rather than on the thin extension, the axon, where the cell makes its contacts. More recent work indicates that serotonin also increases the nerve cell signal in growth cones, the developmental precursors to mature axons. Because this enhancement occurs even when growth cones have been separated from the cell body (the site of protein syn-

thesis), no new protein is required.

Long-term sensitization appears to involve a more extensive change. When viewing nerve cell connections with an electron microscope, scientists can see active zones, sites where neurotransmitter is released. Long-term sensitization increases both the number and size of active zones in the sensory nerve cells.

The molecular basis of long-term sensitization is now being examined in sensory and motor cells maintained in laboratory culture. The scientists mimic a sensitizing stimulus by applying serotonin directly to the cells. The sensory cells respond with an enhanced signal. To produce long-term sensitization, the scien-

tists apply serotonin to the cells five times at 15-minute intervals. A day or more later, the cells still show an enhanced signal.

Long-term sensitization appears to involve new protein production. During the repeated exposures to serotonin, the scientists have treated the cells with chemicals that block protein synthesis. These chemicals do not interfere with short-term sensitization, but they do block long-term enhancement. One of these drugs inhibits an early step in gene expression.

"This indicates that long-term memory involves an alteration in gene expression," Kandel says. "Now two questions remain: What is the signal and what are the genes involved?"

— J.A. Miller

German-run shuttle mission successful

The 22nd space shuttle mission, first ever to have almost its entire payload under the control of a foreign government, landed Nov. 6 from its week-long flight with West German officials dubbing the results "near perfect." The Spacelab D-1(D for Deutschland) mission carried 76 experiments — of which 75 "achieved... or went beyond their goals" — ranging from materials processing tests to space sickness studies aboard an electrically powered "sled" that ran down the lab's aisle.

The shuttlecraft Challenger's eightmember crew was the largest ever flown in space, including two German and one Dutch "mission specialists" as well as five U.S. participants. Together they kept Spacelab running 24 hours a day, managed by the West German space agency not through NASA in Houston but through the German Space Operations Center (where 140 scientists also provided support) in Oberpfaffenhofen near Munich.

The flight's only major non-Spacelab activity was the successful deployment of a test satellite to relay messages for a proposed Defense Department system. Deployed by a spring from one of NASA's "Getaway Special" canisters, it recouped an attempt that had failed due to battery problems last April.

Another shuttle makeup operation proved itself just two days before the Spacelab launching, when ground controllers radioed up commands that successfully ignited a formerly malfunctioning rocket motor to raise the altitude of the already orbiting Syncom 3 communications satellite. Spacewalking astronauts had repaired the satellite in August (SN: 9/7/85, p. 150), but the proof of the pudding—the firing order—had to wait until the satellite reached its proper position.

The Spacelab D-1 mission's final accomplishment before Challenger rolled to

a stop at California's Edwards Air Force Base was a test of a computerized steering system for the shuttle's nosewheel, designed to remedy brake damage and excess tire wear last suffered during an April landing at Kennedy Space Center in Florida. Landings since then have been restricted to the more "forgiving" West Coast strip, but last week's test initially appeared successful and should help repave the way for East Coast homecomings.

The next mission will be aboard the shuttle Atlantis, which lacks the new nosewheel system and will land in California. Set for launch on Nov. 26, it will feature a structural-assembly test in which spacewalking astronauts will construct a 45-foot-high tower from the payload bay.

— J. Eberhart

HHS chief nominated

A former Indiana governor and smalltown doctor was nominated by President Reagan last week to head the Department of Health and Human Services. If the Senate confirms the appointment of Otis R. Bowen, 67, he will administer a \$316 billion budget and about 130,000 employees. The federal department includes Social Security, Medicare, Medicaid, the Public Health Service, the National Institutes of Health and the Food and Drug Administration. Currently an Indiana University School of Medicine professor, Bowen has served on a number of federal advisory committees. In that capacity he recommended an increase in federal alcohol and tobacco taxes to bolster Medicare. If appointed, Bowen would replace Margaret M. Heckler, whom Reagan has nominated to be ambassador to Ireland.

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