MedicalXpress

Study of marine snail leads to new insights into long-term memory

June 19 2008

UCLA cellular neuroscientists are providing new insights into the mechanisms that underlie long-term memory — research with the potential to treat long-term memory disorders.

"The more we know about how long-term memory is induced in the brain and how our memories are maintained in the brain, the more we are going to be able to treat long-term memory loss," said David Glanzman, UCLA professor of physiological science and neurobiology, whose new research appears June 19 in the early online edition of the journal *Current Biology*.

For 25 years, Glanzman has studied learning and memory in the marine snail Aplysia, which is substantially larger than its garden-variety counterpart and has approximately 20,000 neurons in its central nervous system; humans have approximately 1 trillion.

"All the things that we find in the snail, we eventually find in the mammalian brain," said Glanzman, who is helping to unravel the brain's mysteries. "Knowledge about learning and memory in Aplysia will inform us about the kinds of changes that take place in our brains when we learn."

During long-term memory, in the snail and in our brains, synaptic connections become stronger.

Scientists had thought that during learning in snails, the neurotransmitter

serotonin binds to receptors on the presynaptic axon and, through a complicated process, causes the growth of new presynaptic axons. In Current Biology, Glanzman and his UCLA colleagues report that "the process is not actually initiated in the presynaptic axon, but that this presynaptic change is actually initiated in the postsynaptic neuron."

"Surprisingly, we're seeing that there is a specific presynaptic protein whose synthesis is actually regulated by postsynaptic calcium," Glanzman said. "What we think happens is when serotonin binds to receptors on the postsynaptic neuron, it causes an elevation of calcium within the postsynaptic neuron, and somehow this elevation of postsynaptic calcium causes synthesis of presynaptic proteins. In other words, the information is going backwards. We don't know yet how that happens.

"The more I understand about the nature of synaptic change during learning," he said, "the more amazed I am by how complicated it gets. Why does it have to be so complicated? Why can't serotonin just cause the presynaptic change all by itself? Why does it need this postsynaptic signal? There's a complicated dance taking place between the postsynaptic cell and the presynaptic cell."

This complex process may be the brain's way of preventing mistaken learning, according to Glanzman.

"Nature seems not to want your synapses to change very easily," he said. "To learn something, you have to produce fairly detailed cellular changes. It looks like you can't just change one side of the synapse if you want to have a long-term memory. You don't want long-term changes at synapses that are important for learning to occur easily. This is a way to minimize mistaken learning; it keeps synapses from changing for unimportant reasons. It's better than a lock-and-key relationship; you can put the key in, but you also have to have a code to get the key to turn to

lock something in long-term memory."

For memories that last for weeks or longer, the presynaptic and postsynaptic cell have to talk to each other, Glanzman said, and "we're beginning to understand the chemical signals of the conversation."

It will take time, because memory is such a complicated phenomenon, but the research is progressing rapidly.

"Every day," he said, "we learn new, unexpected things."

Glanzman's research to understand learning and memory on a fundamental level has the potential to help with human brain disorders. His research may lead to such applications as developing interventions for people with memory-related disorders and reducing age-related memory loss.

"As far as I can tell, the main reason why snails don't learn Shakespeare and do algebra is they just don't have the computational power, because they have only 20,000 neurons," Glanzman said. "However, in terms of learning, all the cellular and molecular processes seem to be very, very similar. The fundamental mechanisms of learning and memory are identical, as far as we can tell."
Synaptic change requires an interaction between the two sides of the synapse, Glanzman said.

"The synthesis of presynaptic proteins depends on postsynaptic calcium," he said. "Now the question for us to understand is what are the signals that are activated by postsynaptic calcium that travel across the synapse or somehow affect the presynaptic cell to trigger the synthesis of these proteins."

Glanzman and his co-authors — Diancai Cai and Shanping Chen, UCLA

research associates in Glanzman's laboratory — believe they are the first scientists ever to see the synthesis of a specific presynaptic protein that is mediated by postsynaptic calcium during a learning-related synaptic change.

The marine snail processes information about its environment and is capable of learning when an environment is safe and when it is not, learning to escape from predators, and learning to identify food. The marine snail is native to California, living in tidal waters off the coast.

Glanzman is also studying learning at the synaptic level in the zebra fish.

As a graduate student at Stanford University, Glanzman began studying cognitive psychology and psycholinguistics but "kept getting more and more reductionistic" in his thinking.

"I wanted to understand how the brain actually works," he said. "In the Aplysia, one understands what the physiological and behavioral functions of individual neurons are. You can look at a neuron in the Aplysia and say, 'That's a motor neuron, that's a sensory neuron.' We know that the activity of those neurons has a significant role in behavior. When looking at a change in a synaptic connection between a pair of neurons in the Aplysia nervous system, we know, for some of the neurons, what effect that will have on behavior."

Source: University of California - Los Angeles