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## Brain Circuit May Permit Scientists to Eavesdrop on Memory Formation

Howard Hughes Medical Institute researchers have identified a circuit in the brain that appears crucial in converting short-term memories into long-term memories. The circuit links the major learning-related area of the brain to another region that governs the brain's higher functions.

The studies open the way for eavesdropping on one of the central processes in learning and memory, says HHMI investigator Erin M. Schuman. She and graduate student Miguel Remondes of the California Institute of Technology published their findings in the October 7, 2004, issue of the journal *Nature*.

According to Schuman, the finding sheds light on a central question in learning and memory research that concerns the roles of two brain structures, the hippocampus, which is involved in memory formation, and the neocortex, which is associated with higher brain functions.

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"There are two key findings required to understand the present work," said Schuman. "First, lesions of the hippocampus prior to training can prevent the formation of some kinds of short-term memory. Second, if one delays the hippocampal lesion to days after training, one can observe that as the delay increases, the memory deficit decreases. These data suggest that the importance of the neocortex as a memory storage site increases with the lifetime of the memory. In addition, there is a clear need for the hippocampus and cortex to talk to one another."

One candidate for the communication conduit is the temporoammonic (TA) projection, "a pathway that we have been chipping away at understanding for years," said Schuman. "We and others had studied the physiology of this very direct connection between the two areas, but no one had directly studied this

pathway's importance in learning.”

For the experiments, Remondes perfected a technique to make precise electrical lesions of the TA projection in the brains of rats. In the first set of experiments, he created the lesions in animals and then tested their ability to learn to navigate a tank full of opaque water to find a submerged platform. When the researchers tested the rats the day after the electrical lesions were made, they still recalled the platform's location. But they lost that memory four weeks after training.

“There were two possible explanations for this result,” said Schuman. “Either we had selectively impaired the process of converting short-term memories into long-term memories. Or, short-term and long-term memories are on parallel pathways, and the lesion had selectively affected the long-term memory pathway.”

So, in a second set of experiments, the researchers created the TA lesions in animals 24 hours after they had learned the position of the platform. These animals still retained short-term memory; but four weeks later they lost that memory as well. Since the lesion was made after learning, this experiment suggested that the animals had problems converting their short-term memory into a long-term memory—a process also called consolidation.”

“If this really was a process of memory consolidation, it implies that there's a window of vulnerability that will close,” said Schuman. “Thus, in the last experiment, we waited three weeks for the memory to consolidate and then made the lesion. When tested a week later, a majority of the animals remembered the platform location even though they had just received the lesion; that is, it appeared that they had already adequately consolidated the memory in the three weeks post-training prior to the lesion.

“These experiments tell us that the TA projection is an important part of the dialog between the hippocampus and the cortex that occurs after learning,” said Schuman. “Now, what is needed is an exploration of the specific firing patterns of neurons that make up the TA projection during learning and the consolidation period. It's interesting that a lot of the important activity likely takes place off-line, when the animal is removed from the direct behavioral experience.”

Future studies could give insight into whether sleep plays a role in memory consolidation, a theory that has been proposed by many researchers, said Schuman. Studies by other researchers have shown that there is distinctive coordinated brain activity between the hippocampus and neocortex during sleep, she said.