Memories may be formed throughout the day, not just while sleeping

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Scientists have long thought that processes occurring during sleep were responsible for cementing the salient experiences of the day into long-term memories. Now, however, a study of scampering rats suggests that the mechanisms at work during sleep are also active while the animals are awake -- and that they encode events more accurately.

The finding has significant implications for understanding the way the brain learns and remembers, the researchers say. Among other things, it could offer insights into, and possible strategies for combating, post traumatic stress disorder.

The study is reported in the June 14 online edition of the July 2009 issue of "*Nature Neuroscience*."

As people - and rats - go about their daily lives, they receive a ceaseless stream of sensory stimuli that is taken up by neurons, or nerve cells, in the eyes, ears, nose, taste buds and skin. This information is encoded in the neurons and transmitted along neural pathways into various processing centers in the brain that assess the information and decide what to do with it.

The current study focused on the neural activity in a region of the brain known as the hippocampus, a horseshoe-shaped structure responsible for encoding all spatial and event memories of daily life. It is thought that the hippocampus rapidly encodes all experiences in highly plastic, or flexible, neural circuits within it and then, later, reactivates those neural

representations of the experience that are deemed significant, allowing their patterns to be engrained in less-plastic hippocampal-neocortical circuits where they are stored as long-term memory.

"The accepted dogma has been that one learns something while awake - the process of rapid encoding -- and that later, while asleep, one replays the memory over and over again until it is cemented, or consolidated, in circuits throughout the brain," says the senior author of the study, Loren M. Frank, PhD, assistant professor of physiology and member of the W.M. Keck Center for Integrative Neuroscience at UCSF.

But this theory has not explained what happens if one does not sleep right after an experience, Frank notes. "We've known the memory doesn't necessarily go away but we haven't known what supported memory formation in such cases."

Scientists have known that rats, during brief pauses in movement as they scurry about their day, replay their immediate experience. This allows them to learn the experience in the short term and to integrate knowledge about it with past experiences in order to make decisions about next steps. The process may even prompt changes in synaptic connections between neurons that begin the process of laying down long-term memories.

However, until now, scientists have thought that awake replay of events was limited to the immediate past.

In the current study, Frank and first author Mattias P. Karlsson, PhD, a graduate student in Frank's lab, studied rats' neural replay in several settings - while they sniffed and explored two different places, one familiar, one novel -- and while they dozed in a rest box. In each case, the scientists recorded the activity of individual neurons in the hippocampus as they fired, one after the other, as the hippocampus

"reflected" back on their experience in each place.

The first surprise was that in both awake settings there was a near constant replay of events that had taken place in the past - some 20 to 30 minutes earlier. These replay events were seen in peppered bursts of activity present during the brief pauses the animals made repeatedly during their exploration.

"These past experiences were popping up over and over again - every couple of seconds," says Frank.

More surprisingly, the awake replay often involved events that had occurred in a different setting than the ones the animals were in during replay. In fact, 40 to 50 percent of the replays of past experience the animals had as they moved through the familiar place involved events they had experienced in the novel place.

"These findings suggest that elements of past experience are constantly being reactivated as we go about our daily lives, independent of incoming sensory information," says Frank.

Provocatively, the neural replay of past experiences detected in the animals while they slumbered was significantly less accurate than when they were awake. One possible explanation, says Frank, is that the replay during a sleep-like state may not be intended to be a perfect reenactment of what occurred. Evidence suggests that sleep is a time for making connections. "Maybe during sleep the brain is sort of relaxing, saying 'I'm not going to be completely true to the experience I just had. I'm going to wander around and explore and make new connections.'"

The team's next step is to determine if awake replay of past experiences is essential for learning, a question they plan to explore by electrically interrupting, or "turning off," discrete segments of the replay process as

the animals scurry about their day. The question we will ask, says Frank, is "can we stop the learning?"

More broadly, the team wants to see if the awake replay of past experiences seen in the hippocampus is driving memory processes across the brain. "We should be able to see neural signatures of past experience come up in the prefrontal cortex -- another region of memory storage -- when these signatures come up in the hippocampus," he says.

Ultimately, says Frank, "We'd like to explore whether we can control these replay processes in a subtle way. Can we, for example, pick out certain kinds of neural patterns that we allow to happen and not others. Could we prevent or enhance the creation of some memories and not of others?"

This possibility poses the question of whether it would be possible to prevent the traumatic memories associated with post traumatic stress syndrome or to stop them. "The question for me has always been-- why do these experiences have such a lasting impact? This is the first time I've found something that might make sense of all of that," Frank adds.

Source: University of California - San Francisco