

## The brain may actively forget during dream sleep

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A team of Japanese and U.S. NIH-funded researchers studied how the activity of neurons found deep inside the mouse brain may control forgetting during REM sleep. Credit: Yamanaka lab, Nagoya University, Japan.

Rapid eye movement, or REM, sleep is a fascinating period when most



of our dreams are made. Now, in a study of mice, a team of Japanese and U.S. researchers show that it may also be a time when the brain actively forgets. Their results suggest that forgetting during sleep may be controlled by neurons found deep inside the brain that were previously known for making an appetite stimulating hormone. The study was funded by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health.

"Ever wonder why we forget many of our dreams?" said Thomas Kilduff, Ph.D., director of the Center for Neuroscience at SRI International, Menlo Park, California, and a senior author of the study published in *Science*. "Our results suggest that the firing of a particular group of neurons during REM sleep controls whether the brain remembers new information after a good night's sleep."

REM is one of several sleep stages the body cycles through every night. It first occurs about 90 minutes after falling asleep and is characterized by darting eyes, raised heart rates, paralyzed limbs, awakened brain waves and dreaming.

For more than a century, scientists have explored the role of sleep in storing memories. While many have shown that sleep helps the brain store <u>new memories</u>, others, including Francis Crick, the co-discoverer of the DNA double helix, have raised the possibility that sleep—in particular REM sleep—may be a time when the brain actively eliminates or forgets excess information. Moreover, recent studies in <u>mice</u> have shown that during sleep—including REM sleep—the brain selectively prunes synaptic connections made between neurons involved in certain types of learning. However, until this study, no one had shown how this might happen.

"Understanding the role of sleep in forgetting may help researchers better understand a wide range of <u>memory</u>-related diseases like <u>post-</u>



traumatic stress disorder and Alzheimer's," said Janet He, Ph.D., program director, at NINDS. "This study provides the most direct evidence that REM sleep may play a role in how the brain decides which memories to store."

Dr. Kilduff's lab and that of his collaborator, Akihiro Yamanaka, Ph.D., at Nagoya University in Japan, have spent years examining the role of a hormone called hypocretin/orexin in controlling sleep and narcolepsy. Narcolepsy is a disorder that makes people feel excessively sleepy during the day and sometimes experience changes reminiscent of REM sleep, like loss of muscle tone in the limbs and hallucinations. Their labs and others have helped to show how narcolepsy may be linked to the loss of hypocretin/orexin-making neurons in the hypothalamus, a peanutsized area found deep inside the brain.

In this study, Dr. Kilduff worked with Dr. Yamanaka's lab and Akira Terao's, D.V.M., Ph.D., lab at Hokkaido University, Sapporo, Japan, to look at neighboring <u>cells</u> that produce melanin concentrating hormone (MCH), a molecule known to be involved in the control of both sleep and appetite. In agreement with previous studies, the researchers found that a majority (52.8%) of hypothalamic MCH cells fired when mice underwent REM sleep whereas about 35% fired only when the mice were awake and about 12% fired at both times.





Brain state-dependent inhibition of melanin concentrating hormone (MCH)-producing neurons using optogenetics revealed that memory was improved if MCH neurons were inhibited during REM sleep. Credit: Akihiro Yamanaka, RIEM, Nagoya University



They also uncovered clues suggesting that these cells may play a role in learning and memory. Electrical recordings and tracing experiments showed that many of the hypothalamic MCH cells sent inhibitory messages, via long stringy axons, to the hippocampus, the brain's memory center.

"From previous studies done in other labs, we already knew that MCH cells were active during REM sleep. After discovering this new circuit, we thought these cells might help the brain store memories," said Dr. Kilduff.

To test this idea, the researchers used a variety of genetic tools to turn on and off MCH neurons in mice during memory tests. Specifically, they examined the role that MCH cells played in retention, the period after learning something new but before the new knowledge is stored, or consolidated, into long term memory. The scientists used several memory tests including one that assessed the ability of mice to distinguish between new and familiar objects.

To their surprise, they found that "turning on" MCH cells during retention worsened memory whereas turning the cells off improved memories. For instance, activating the cells reduced the time mice spent sniffing around new objects compared to familiar ones, but turning the cells off had the opposite effect.

Further experiments suggested that MCH neurons exclusively played this role during REM sleep. Mice performed better on memory tests when MCH neurons were turned off during REM sleep. In contrast, turning off the neurons while the mice were awake or in other sleep states had no effect on memory.

"These results suggest that MCH <u>neurons</u> help the <u>brain</u> actively forget new, possibly, unimportant information," said Dr. Kilduff. "Since



dreams are thought to primarily occur during REM sleep, the sleep stage when the MCH cells turn on, activation of these cells may prevent the content of a dream from being stored in the hippocampus—consequently, the dream is quickly forgotten."

In the future, the researchers plan to explore whether this new circuit plays a role in <u>sleep</u> and memory disorders.

**More information:** S. Izawa el al., "REM sleep–active MCH neurons are involved in forgetting hippocampusdependent memories," *Science* (2019). <u>science.sciencemag.org/cgi/doi ... 1126/science.aax9238</u>

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