Adult neurogenesis essential for sleep-induced memory consolidation in mice

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Adult neurogenesis, in which new neurons are generated within the hippocampus in the fully developed adult brain, occurs in mice—but how new neurons are functionally integrated into existing brain circuitry

has remained largely unknown. A study publishing June 4 in the journal *Neuron* shows an important new role for neurons generated during adulthood in consolidating memories during sleep in mice.

Previous studies have tied the presence of adult-born neurons (ABNs) to memories and synaptic plasticity, making them logical candidates to take part in memory consolidation during sleep, when hippocampal neurons often repeat activity patterns present when the animal learns a new task. But ABNs' function during sleep has been unknown.

Now, lead author Masanori Sakaguchi, associate professor at the International Institute for Integrative Sleep Medicine at University of Tsukuba, Japan, has found that ABNs are essential for synaptic structural remodeling and memory consolidation during rapid eye movement (REM) sleep in mice.

"Our study is the first to show any ABN activity and function during sleep in animals," he says. "Our results pave the way to revealing mechanistic insights into how ABNs tie into known memory functions during sleep."

The researchers were able to detect ABN activity by using new techniques to visualize neuronal activity over the duration of four hours in naturally sleeping mice. Because a single REM episode usually lasts less than a minute in mice, the researchers precisely manipulated ABN activity during these episodes through optogenetics—genetically engineering neurons to allow scientists to stimulate them with light.

Sakaguchi and colleagues were initially surprised to see that young ABNs showed little activity during sleep. They then saw that a small population of ABNs activated while the mice were learning a fear memory—receiving a mild foot shock—and became reactivated in subsequent REM sleep.

"Although ABN activity levels actually decreased during REM sleep once the animals had successfully learned the memory, a memory-consolidation process during REM sleep reactivated the ABNs that had been activated when the mice were learning," Sakaguchi says. Therefore, when ABN activity was silenced, the animals' overall memory consolidation was impaired. Optogenetic manipulation that both increased and decreased ABN activity during REM sleep resulted in memory impairment, suggesting that there are highly coordinated ABN activities playing critical roles for memory consolidation during REM sleep.

The next steps involve exploring how the reactivation of ABNs during REM sleep consolidates memory. Does the reactivation represent memory replay? What coordinates ABN activity during REM sleep? How do ABNs enforce memory consolidation downstream?

"We believe that these mechanisms are critical for new neurons to functionally integrate into existing neuronal circuitry," Sakaguchi says. He hopes that "collectively, these studies will contribute to developing new therapeutic strategies to regenerate the damaged brain."

More information: *Neuron*, Kumar et al.: "Sparse activity of hippocampal adult-born neurons during REM sleep is necessary for memory consolidation" www.cell.com/neuron/fulltext/S0896-6273(20)30354-8 , DOI: 10.1016/j.neuron.2020.05.008

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