MedicalXpress

Interrupted sleep impairs memory in mice

July 25 2011

With the novel use of a technique that uses light to control brain cells, Stanford University researchers have shown that fragmented sleep causes memory impairment in mice.

Until recently scientists have been unable to tease out the effects on the brain of different yet intertwined features of sleep. But these investigators were able to overcome that problem and come to their findings by using the novel method, known as optogenetics, to manipulate brain cells to affect just one aspect of sleep.

The study shows that "regardless of the total amount of sleep, a minimal unit of uninterrupted sleep is crucial for memory consolidation," the authors write in the study that will be published online July 25 in the Proceedings of the National Academy of Sciences.

The study was co-led by Luis de Lecea, PhD, associate professor of psychiatry and behavioral sciences, whose work focuses on the neural circuitry underlying wakefulness, and H. Craig Heller, PhD, professor of biology.

Experts have long hypothesized that sleep is important for memory, but this has been a difficult area to study — in part because of the sleep-deprivation techniques used in research. Gentle handling is one way to keep animal subjects from sleeping but, as de Lecea explained, "Rodents are very sensitive to physical awakenings. If you wake an animal up it's going to be up for awhile, and it will experience stress." And stress itself has been shown to affect memory.

In addition, any kind of sleep manipulation affects all features of the sleep — not only duration, but also quality, continuity and composition (percentage of rapid eye movement and non-REM sleep). It hasn't been possible to distinguish the role of a specific characteristic of sleep, such as sleep continuity, on memory.

The Stanford team, as well as other scientists, assumed that memory would become impaired with a lack of sleep continuity. Memory deficits are often seen in people with certain neurological and psychiatric conditions, such as alcoholism and sleep apnea, during which sleep continuity — though perhaps not total sleep time or type of sleep — is affected. (Patients with apnea can stop breathing and experience so-called "micro-arousals" as many as hundreds of times a night.)

The challenge for the Stanford researchers was this: How could they fragment sleep into shorter episodes without affecting sleep intensity or duration and without invoking a stress response, so they could see its effects on memory?

Knowing the traditional methods of sleep deprivation wouldn't allow them to do what they needed, the team turned to optogenetics, a technique in which specific cells can be genetically engineered to be controlled by pulses of visible light. The researchers used the method on the type of neurons that play a key role in switching between sleep and wake, and they found that by stimulating these cells with 10-second bursts of light, they could fragment the animals' sleep without affecting total sleep time or quality and composition of sleep.

The technique, de Lecea said, represented "a very fine, very subtle way of sleep fragmentation."

After manipulating the mice's sleep, the researchers had the animals undergo a task during which they were placed in a box with two objects:

one to which they had previously been exposed, and another that was new to them. Rodents' natural tendency is to explore novel objects, so if they spent more time with the new object, it would indicate that they remembered the other, now familiar object. In this case, the researchers found that the mice with fragmented sleep didn't explore the novel object longer than the familiar one — as the control mice did — showing that their memory was affected.

The findings, Heller explained, "point to a specific characteristic of sleep — continuity — as being critical for memory."

While the study does not reach any conclusions about the amount of sleep needed to avoid memory impairment in humans, it does suggest that memory difficulties in people with apnea and other sleep disorders are likely connected to the compromised continuity of sleep caused by such conditions.

Noting that this is just "the first step in looking at one aspect of sleep," first author and postdoctoral scholar Asya Rolls, PhD, said she and her colleagues are planning to further study the sleep mechanisms used to preserve memory. The team expects other research groups to use the method in animals to manipulate and study different features of sleep. (The optogenetic technique cannot be used in humans at this time as it requires still-experimental genetic modifications to brain cells.)

Provided by Stanford University Medical Center

provided for information purposes only.