Roots of memory impairment, resulting from sleep deprivation, identified

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(Medical Xpress) -- From high-school students to surgeons, anyone who has pulled an all-nighter knows there is a price to be paid the next day: trouble focusing, a fuzzy memory and other cognitive impairments. Now, researchers at Penn have found the part of the brain and the neurochemical basis for sleep deprivation's effects on memory.

Ted Abel, a professor of biology in Penn's School of Arts and Sciences and director of the University's interdisciplinary Biological Basis of Behavior program, led the research team. His partners included Cédrick Florian, a postdoctoral fellow in biology, and Christopher Vecsey, a neuroscience graduate student, as well as researchers from the Massachusetts Institute of Technology and Tufts University.

Their research was published in The Journal of Neuroscience.

Abel's group aimed to better understand the role of the nucleoside adenosine in the hippocampus, the part of the brain associated with memory function.

"For a long time, researchers have known that sleep deprivation results in increased levels of adenosine in the brain, and has this effect from fruit flies to mice to humans." Abel said. "There is accumulating evidence that this adenosine is really the source of a number of the deficits and impact of sleep deprivation, including memory loss and attention deficits. One thing that underscores that evidence is that caffeine is a drug that blocks the effects of adenosine, so we sometimes

refer to this as ‘the Starbucks experiment.’”

Abel’s research actually involved two parallel experiments on sleep-deprived mice, designed to test adenosine’s involvement in memory impairment in different ways.

One experiment involved genetically engineered mice. These mice were missing a gene involved in the production of glial transmitters, chemicals signals that originate from glia, the brain cells that support the function of neurons. Without these gliatransmitters, the engineered mice could not produce the adenosine the researchers believed might cause the cognitive effects associated sleep deprivation.

The other experiment involved a pharmacological approach. The researchers grafted a pump into the brains of mice that hadn’t been genetically engineered; the pump delivered a drug that blocked a particular adenosine receptor in the hippocampus. If the receptor was indeed involved in memory impairment, sleep-deprived mice would behave as if the additional adenosine in their brains was not there.

To see whether these mice showed the effects of sleep deprivation, the researchers used an object recognition test. On the first day, mice were placed in a box with two objects and were allowed to explore them while being videotaped. That night, the researchers woke some of the mice halfway through their normal 12-hour sleep schedule.

On the second day, the mice were placed back in the box, where one of the two objects had been moved, and were once again videotaped as they explored to see how they reacted to the change.

“Mice would normally explore that moved object more than other objects, but, with sleep deprivation, they don’t,” Abel said. “They literally don’t know where things are around them.”

Both sets of treated mice explored the moved object as if they had received a full night's sleep.

"These mice don't realize they're sleep-deprived," Abel said.

Abel and his colleagues also examined the hippocampi of the mice, using electrical current to measure their synaptic plasticity, or how strong and resilient their memory-forming synapses were. The pharmacologically and genetically protected mice showed greater synaptic plasticity after being sleep deprived than the untreated group.

Combined, the two experiments cover both halves of the chemical pathway involved in sleep deprivation. The genetic engineering experiment shows where the adenosine comes from: glia's release of adenosine triphosphate, or ATP, the chemical by which cells transfer energy to one another. And the pharmacological experiment shows where the adenosine goes: the A1 receptor in the hippocampus.

The knowledge that interrupting the pathway at either end results in mice that show no memory impairments is a major step forward in understanding how to manage those impairments in humans.

"To be able to reverse a particular aspect of sleep-deprivation, such as its effect on memory storage, we really want to understand the molecular pathways and targets," Abel said. "Here, we've identified the molecule, the cellular circuit and the brain region by which sleep deprivation affects memory storage."

Such treatments would be especially enticing, given how sensitive the brain is to sleep deprivation's effects.

"Our sleep deprivation experiments are the equivalent of losing half of a night sleep for a single night," Abel said. "Most of us would think that's

pretty minor, but it shows just how critical the need for sleep is for things like cognition."

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