

Study: Brain connections strengthen during waking hours, weaken during sleep

Most people know it from experience: After so many hours of being awake, your brain feels unable to absorb any more-and several hours of sleep will refresh it.

Now new research from the University of Wisconsin School of Medicine and Public Health clarifies this phenomenon, supporting the idea that sleep plays a critical role in the brain's ability to change in response to its environment. This ability, called plasticity, is at the heart of learning.

Reporting in the Jan. 20, 2008, online version of *Nature Neuroscience*, the UW-Madison scientists showed by several measures that synapses - nerve cell connections central to brain plasticity - were very strong when rodents had been awake and weak when they had been asleep.

The new findings reinforce the UW-Madison researchers' highly-debated hypothesis about the role of sleep. They believe that people sleep so that their synapses can downsize and prepare for a new day and the next round of learning and synaptic strengthening.

The human brain expends up to 80 percent of its energy on synaptic activity, constantly adding and strengthening connections in response to all kinds of stimulation, explains study author Chiara Cirelli, associate professor of psychiatry.

Given that each of the millions of neurons in the human brain contains thousands of synapses, this energy expenditure "is huge and can't be sustained."

"We need an off-line period, when we are not exposed to the environment, to take synapses down," Cirelli say. "We believe that's why humans and all living organisms sleep. Without sleep, the brain reaches a saturation point that taxes its energy budget, its store of supplies and its ability to learn further."

To test the theory, researchers conducted both molecular and electro-physiological studies in rats to evaluate synaptic potentiation, or strengthening, and depression, or weakening, following sleeping and waking times. In one set of experiments, they looked at brain slices to measure the number of specific receptors, or binding sites, that had moved to synapses.

"Recent research has shown that as synaptic activity increases, more of these glutamatergic receptors enter the synapse and make it bigger and stronger," explains Cirelli.

The Wisconsin group was surprised to find that rats had an almost 50 percent receptor increase after a period of wakefulness compared to rats that had been asleep.

In a second molecular experiment, the scientists examined how many of the receptors underwent phosphorylation, another indicator of synaptic potentiation. They found phosphorylation levels were much higher during waking than sleeping. The results were the same when they measured other enzymes that are typically active during synaptic potentiation.

To strengthen their case, Cirelli and colleagues also performed studies in live rats to evaluate electrical signals reflecting synaptic changes at different times. This involved stimulating one side of each rat's brain with an electrode following waking and sleeping and then measuring the "evoked response," which is similar to an EEG, on another side.

The studies again showed that, for the same levels of stimulation, responses were stronger following a long

period of waking and weaker after sleep, suggesting that synapses must have grown stronger.

"Taken together, these molecular and electro-physiological measures fit nicely with the idea that our brain circuits get progressively stronger during wakefulness and that sleep helps to recalibrate them to a sustainable baseline," says Cirelli.

The theory she and collaborator Dr. Giulio Tononi, professor of psychiatry, have developed, called the synaptic homeostasis hypothesis, runs against the grain of what many scientists currently think about how sleep affects learning. The most popular notion these days, says Cirelli, is that during sleep synapses are hard at work replaying the information acquired during the previous waking hours, consolidating that information by becoming even stronger.

"That's different from what we think," she says. "We believe that learning occurs only when we are awake, and sleep's main function is to keep our brains and all its synapses lean and efficient."

Source: University of Wisconsin-Madison

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