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Even in fruit flies, enriched learning drives need for sleep

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Just like human teenagers, fruit flies that spend a day buzzing around the "fly mall" with their companions need more sleep. That's because the environment makes their brain circuits grow dense new synapses and they need sleep to dial back the energy needs of their stimulated brains, according to a new study by UW- Madison sleep researchers.

Researchers saw this increase in the number of synapses -- the junctions between nerve cells where electrical or chemical signals pass to the next cell -- in three neuronal circuits they studied. The richer "wake experience" resulted in both larger synaptic growth and greater sleep need.

The study, published today in the journal *Science*, provides structural evidence for the theory that "synaptic homeostasis" is one of the key reasons all animals need sleep. Researchers Dr. Daniel Bushey, Dr. Giulio Tononi and Dr. Chiara Cirelli of the Wisconsin Center for Sleep and Consciousness also looked at the role the gene implicated in Fragile X syndrome plays in re-normalizing the brain during sleep.

In one experiment, researchers took young fruit flies that spent the first days of their lives alone in single tubes too small to allow flying. Then they released them in groups into a large lighted chamber that allowed them to fly around together for their 12-hour day.

All the flies grew more synapses while they were awake for several hours, the research showed. But this was especially true for the flies in

the enriched environment, which grew new branches with many new synapses. After their mall visit, the flies were put back into the single tubes and slept much longer for at least one day. Their synapses returned to normal size after sleep.

Those flies that visited the mall, but were deprived of sleep, continued to have synapses that were larger and denser.

"Sleep prunes back the new synapses; you have to create space for synapses to grow again or you can't learn again the next day," says Cirelli, associate professor of psychiatry at the School of Medicine and Public Health. "Even more importantly, the pruning saves energy, and for the brain, energy is everything. Learning without sleep is unsustainable from an energy point of view."

In earlier work, the lab also showed that the strengthened synapses had higher levels of proteins that build up during a day of learning, and that sleep also dials down protein levels.

In the current study, UW researchers also looked at the role of the gene Fmr1, which, when it isn't expressed in humans, results in Fragile X Syndrome, a cause of autism and mental disabilities. People with Fragile X also have difficulty sleeping.

In this study, the sleep researchers looked at what happens when Fmr1 is over-expressed; that is, when more Fmr1 protein is present in the brain. Previous work had shown that Fmr1 probably facilitates the pruning of synapses. Bushey and colleagues found that when Fmr1 is over-expressed, the increase in synapse number during wake does not occur, and the need for sleep declines.

"This suggests that if the synapses are already down regulated, there is less need for sleep," Cirelli says. "It is more evidence for the theory that

sleep is driven by the need to reduce the brain's energy needs."

Provided by University of Wisconsin-Madison