

# New research sheds light on fly sleep circuit

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In a novel study appearing this week in *Neuron*, Brandeis researchers identify for the first time a specific set of wake-promoting neurons in fruit flies that are analogous to cells in the much more complex sleep circuit in humans. The study demonstrates that in flies, as in mammals, the sleep circuit is intimately linked to the circadian clock and that the brain's strategies to govern sleep are evolutionarily ancient.

In the study, researchers quieted ventral lateral neurons (LNvs) and induced sleep in the flies by essentially altering the excitability of these cells with GABA, a major inhibitory neurotransmitter. GABA controls sleep onset and duration by opposing arousal. The same mechanism governs sleep in humans, explained Katherine Parisky, a post-doctoral researcher who coauthored the study led by Brandeis biologist Leslie Griffith's laboratory.

When it is time to wake up, the LNvs are believed to release a neuropeptide known as PDF, rousing the cells, and in turn, the flies. The cycle starts over again when GABA kicks in to quiet these neurons and give the flies a good night's sleep. The study found that mutant flies without PDF or its receptor were hypersomnolent.

The researchers' findings have implications for how sleep-promoting drugs are tested and developed. Currently, drugs that target GABA receptors are among the most widely-used sleep-promoting agents.

"Normally, to treat insomnia in humans, you use global drugs that suppress GABA throughout the brain," explained Griffith. "But it would

be ideal to suppress only cells that are part of the sleep circuit."

Sleep problems, from insomnia to narcolepsy, affect millions of people and are extremely costly in both economic and human health terms. The next stage of research will involve researching how PDF controls wakefulness, said Parisky.

"We're taking apart the circuit bit by bit to see how it affects sleep," she said. "We already know that in humans, some people have problems falling asleep, while others can't stay asleep, and there are probably two different mechanisms for these behaviors in flies, as well," Parisky explained.

Fruit flies offer an excellent model organism in which to study sleep because their sleep circuit is relatively simple yet seemingly very similar to the sleep circuit in humans. A greater understanding of how the sleep circuit works in flies could help scientists to design and develop drugs that strategically target different sleep problems.

Source: Brandeis University

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