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Researchers identify brain cells responsible for keeping us awake

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Bright light arouses us. Bright light makes it easier to stay awake. Very bright light not only arouses us but is known to have antidepressant effects. Conversely, dark rooms can make us sleepy. It's the reason some people use masks to make sure light doesn't wake them while they sleep.

Now researchers at UCLA have identified the group of neurons that mediates whether light arouses us — or not. Jerome Siegel, a professor of psychiatry at the Semel Institute for Neuroscience and Human Behavior at UCLA, and colleagues report in the current online edition of the *Journal of Neuroscience* that the cells necessary for a light-induced arousal response are located in the hypothalamus, an area at the base of the brain responsible for, among other things, control of the autonomic nervous system, body temperature, hunger, thirst, fatigue — and sleep.

These cells release a neurotransmitter called hypocretin, Siegel said. The researchers compared mice with and without hypocretin and found that those who didn't have it were unable to stay awake in the light, while those who had it showed intense activation of these cells in the light but not while they were awake in the dark.

This same UCLA research group earlier determined that the loss of hypocretin was responsible for narcolepsy and the sleepiness associated with Parkinson's disease. But the neurotransmitter's role in normal behavior was, until now, unclear.

"This current finding explains prior work in humans that found that

narcoleptics lack the arousing response to light, unlike other equally sleepy individuals, and that both narcoleptics and Parkinson's patients have an increased tendency to be depressed compared to others with chronic illnesses," said Siegel, who is also a member of the UCLA Brain Research Institute and chief of neurobiology research at the Sepulveda Veterans Affairs Medical Center in Mission Hills, Calif.

Prior studies of the behavioral role of hypocretin in rodents had examined the neurotransmitter's function during only light phases (normal sleep time for mice) or dark phases (their normal wake time), but not both. And the studies only examined the rodents when they were performing a single task.

In the current study, researchers examined the behavioral capabilities of mice that had their hypocretin genetically "knocked-out" (KO mice) and compared them with the activities of normal, wild-type mice (WT) that still had their hypocretin neurons. The researchers tested the two groups while they performed a variety of tasks during both light and dark phases.

Surprisingly, they found that the KO mice were only deficient at working for positive rewards during the light phase. During the dark phase, however, these mice learned at the same rate as their WT littermates and were completely unimpaired in working for the same rewards.

Consistent with the data in the KO mice, the activity of hypocretin neurons in their WT littermates was maximized when working for positive rewards during the light phase, but the cells were not activated when performing the same tasks in the dark phase.

"The findings suggest that administering hypocretin and boosting the function of hypocretin cells will increase the light-induced arousal

response," Siegel said. "Conversely, blocking their function by administering hypocretin receptor blockers will reduce this response and thereby induce sleep."

Further, Siegel noted, "The administration of hypocretin may also have antidepressant properties, and blocking it may increase tendencies toward depression. So we feel this work has implications for treating sleep disorders as well as depression."

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