Dopamine fends off zzzz’s
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The chemical keeps sleep-deprived people going

A reward chemical in the brain is a real eye-opener.

Dopamine, a feel-good brain chemical, helps keep sleep-deprived people awake, researchers from the National Institute on Drug Abuse show in the August 20 *Journal of Neuroscience*. Dopamine is also required for activity of a drug that treats narcolepsy, Japanese and Chinese scientists report in the same issue of the journal.

“Dopamine has been a forgotten neurotransmitter for sleep regulation,” says Emmanuel Mignot, a sleep researcher and Howard Hughes Medical Institute investigator at Stanford University. Increasing evidence is pointing toward dopamine as an important ingredient in the brain’s recipe for promoting wakefulness.

The new findings suggest dopamine may naturally increase when a person is sleep-deprived, as a way to counteract a revved-up drive to sleep, says David Dinges of the University of Pennsylvania School of Medicine. Dinges was not involved in the two new studies, but he has studied the effect of sleep deprivation on people.

Sleep deprivation affects some people profoundly, impairing their ability to pay attention and lengthening their reaction times, Dinges says. Other people function nearly as well when mildly sleep-deprived as they do when well-rested. The extent to which dopamine rises in the brain after sleep loss may help explain some of the variability in people’s abilities to cope with sleep deprivation, Dinges says.

Dopamine has gotten an undeserved bad reputation, says Mignot, who was not involved in the studies. “People think dopamine equals addiction,” Mignot says. But the chemical plays an important role in many brain functions.

Nora Volkow of the National Institute on Drug Abuse led a team at the National Institutes of Health in Bethesda, Md., and the Brookhaven National Laboratory in Upton, N.Y. The researchers recruited 15 healthy volunteers and tested each person’s memory and ability to pay attention to visual cues after a good night’s sleep and after being kept awake all night. A brain scan called positron emission tomography (PET) indirectly measured dopamine levels in the volunteers’ brains.

Sleep deprivation increased dopamine in the striatum, a part of the brain that registers motivation and reward. Dopamine also went up in the thalamus, a brain region that helps control alertness, when the volunteers were sleep-deprived. Increases in the brain chemical kept the volunteers awake, but those same increases also correlated with the volunteers reporting that they felt tired.

Although increased levels of the neurotransmitter help keep the brain aroused after a sleepless night, higher levels of dopamine don’t fend off the thinking and learning problems associated with sleep deprivation, says Volkow, a clinical neuroscientist and director of NIDA.

Some stimulants, such as amphetamines, also increase dopamine in the brain. Previous studies have shown that medical students taking stimulants thought they were more alert and performed better on tests. Despite the students’ perceptions, their actual performance was worse on the drug.
"A little bit of dopamine is good," says Paul Shaw, a sleep researcher at Washington University in St. Louis. "More is bad. Less is bad too. You've got to be in the sweet spot," to think, respond and learn correctly.

He speculates that learning and memory may require precise levels of dopamine to work well, but that arousal is controlled by a more robust circuit that is not as sensitive to minor changes in dopamine concentration. "This simply reinforces the idea that sleep loss alters the vulnerability of specific circuits but not the entire brain, at least initially," Shaw says.

Researchers said the finding fits with Shaw's recent study in fruit flies (SN: 8/30/08). Restoring dopamine activity in the flies helped them overcome the learning deficits caused by sleep deprivation, but these flies started with suboptimal dopamine levels. Sleep deprivation pushed the people in the new study past the prime levels of dopamine.

Staying awake and alert is a problem for people with the sleeping disorder narcolepsy. The drug modafinil is used to treat the condition, but no one is entirely sure how it works. Previous research has suggested that the drug acts on a wide variety of brain chemicals including serotonin, glutamate, orexin and histamine. But the second new study, by researchers at the Osaka Bioscience Institute in Japan and at the Fudan University in Shanghai, China, shows that two proteins sensitive to dopamine's action are essential for the arousal effect of modafinil.

The research is the most direct evidence that dopamine plays a role in the drug's action, Dinges says. Dopamine could be the drug’s direct target, but there is not enough data to rule out the possibility that dopamine may just be a key link in a cascade set off by other excitatory molecules.

Other molecules are almost certainly involved in the brain's response to sleep loss, Volkow says. "Sleep is so important that it would be over-simplistic to say that sleep deprivation is only going to change the dopamine system."