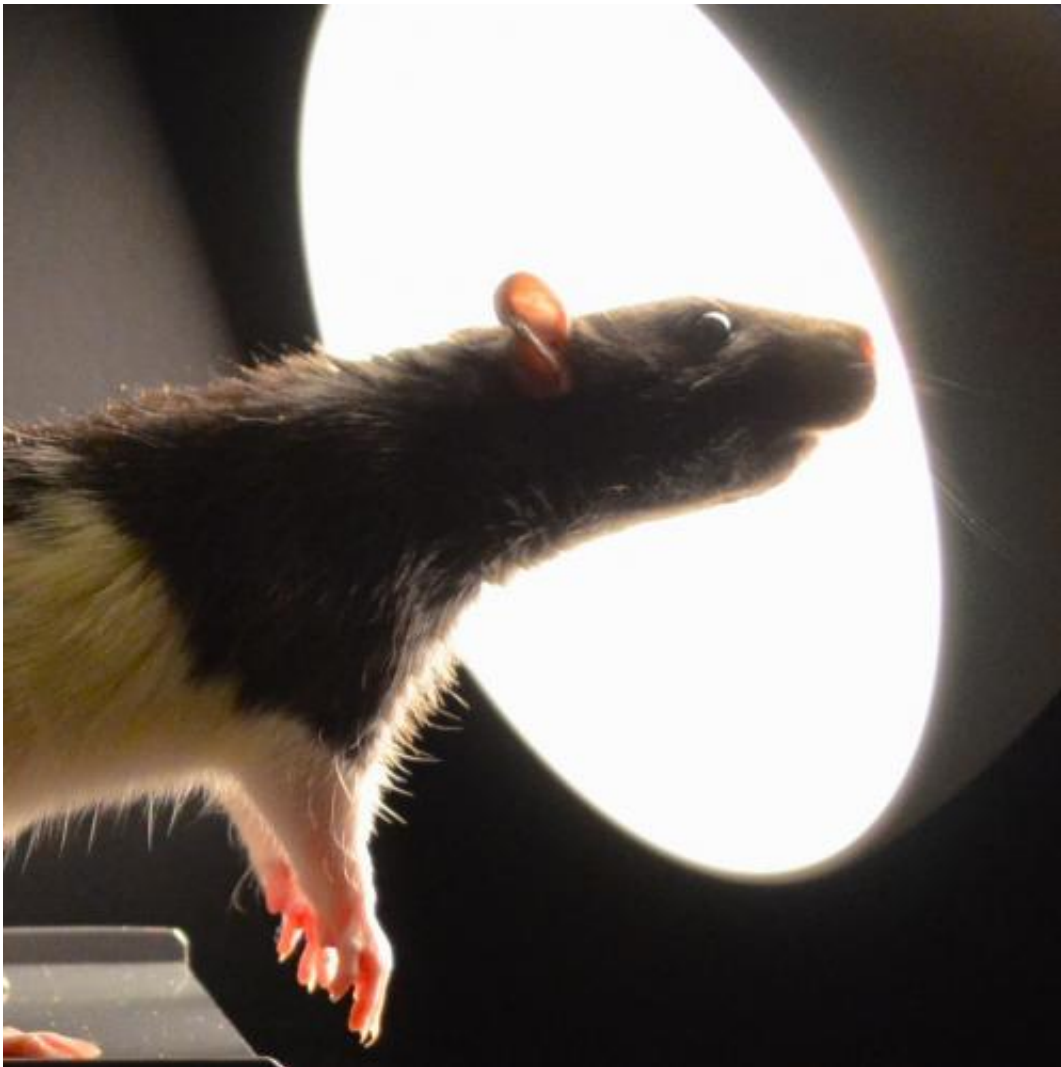


## Light switches brain signaling: Longer days bring 'winter blues' for rats

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Adult rat display more confident exploratory behavior in the open arm of the elevated plus maze following one-week exposure to short-day photoperiod. Light exposure affects dopamine expression in the hypothalamus controlling stress response. Credit: Davide Dulcis and Pouya Jamshidi

Most of us are familiar with the "winter blues," the depression-like symptoms known as "seasonal affective disorder," or SAD, that occurs when the shorter days of winter limit our exposure to natural light and make us more lethargic, irritable and anxious. But for rats it's just the opposite.

Biologists at UC San Diego have found that rats experience more [anxiety and depression](#) when the days grow longer. More importantly, they discovered that the rat's brain cells adopt a new chemical code when subjected to large changes in the day and night cycle, flipping a switch to allow an entirely different neurotransmitter to stimulate the same part of the brain.

Their surprising discovery, detailed in the April 26 issue of *Science*, demonstrates that the adult [mammalian brain](#) is much more malleable than was once thought by neurobiologists. Because rat brains are very similar to [human brains](#), their finding also provides a greater insight into the [behavioral changes](#) in our brain linked to light reception. And it opens the door for new ways to treat [brain disorders](#) such as Parkinson's, caused by the death of dopamine-generating cells in the brain.

The neuroscientists discovered that rats exposed for one week to 19 hours of darkness and five hours of light every day had more [nerve cells](#) making dopamine, which made them less stressed and anxious when measured using standardized behavioral tests. Meanwhile, rats exposed for a week with the reverse—19 hours of light and five hours of darkness—had more neurons synthesizing the neurotransmitter [somatostatin](#), making them more stressed and anxious.

"We're diurnal and rats are nocturnal," said Nicholas Spitzer, a professor of biology at UC San Diego and director of the Kavli Institute for Brain

and Mind. "So for a rat, it's the longer days that produce stress, while for us it's the longer nights that create stress."

Because rats explore and search for food at night, while humans evolved as creatures who hunt and forage during the daylight hours, such differences in brain chemistry and behavior make sense. Evolutionary changes presumably favored humans who were more active gatherers of food during the longer days of summer and saved their energy during the shorter days of winter.

"Light is what wakes us up and if we feel depressed we go for a walk outside," said Davide Dulcis, a research scientist in Spitzer's laboratory and the first author of the study. "When it's spring, I feel more motivation to do the things I like to do because the days are longer. But for the rat, it's just the opposite. Because rats are nocturnal, they're less stressed at night, which is good because that's when they can spend more time foraging or eating."

But how did our brains change when humans evolved millions of years ago from small nocturnal rodents to diurnal creatures to accommodate those behavioral changes?

"We think that somewhere in the brain there's been a change," said Spitzer. "Sometime in the evolution from rat to human there's been an evolutionary adjustment of circuitry to allow switching of neurotransmitters in the opposite direction in response to the same exposure to a balance of light and dark."

A study published earlier this month in the *American Journal of Preventive Medicine* found some correlation to the light-dark cycle in rats and stress in humans, at least when it comes to people searching on the internet for information in the winter versus the summer about mental illness. Using Google's search data from 2006 to 2010, a team of

researchers led by John Ayers of San Diego State University found that mental health searches on Google were, in general, 14 percent higher in the winter in the United States and 11 percent higher in the Australian winter.

"Now that we know that day length can switch transmitters and change behavior, there may be a connection," said Spitzer.

In their rat experiments, the UC San Diego neuroscientists found that the switch in transmitter synthesis in the rat's [brain cells](#) from dopamine to somatostatin or back again was not due to the growth of new neurons, but to the ability of the same neurons there to produce different neurotransmitters.

Rats exposed to 19 hours of darkness every 24 hours during the week showed higher numbers of dopamine neurons within their brains and were more likely, the researchers found, to explore the open end of an elevated maze, a behavioral test showing they were less anxious. These rats were also more willing to swim, another laboratory test that showed they were less stressed.

"Because rats are nocturnal animals, they like to explore during the night and dopamine is a key part of our and their reward system," said Spitzer. "It's part of what allows them to be confident and reduce anxiety."

The researchers said they don't know precisely how this neurotransmitter switch works. Nor do they know what proportion of light and darkness or stress triggers this switch in brain chemistry. "Is it 50-50? Or 80 percent light versus dark and 20 percent stress? We don't know," added Spitzer. "If we just stressed the animal and didn't change their photoperiod, would that lead to changes in transmitter identity? We don't know, but those are all doable experiments."

But as they learn more about this trigger mechanism, they said one promising avenue for human application might be to use this neurotransmitter switch to deliver dopamine effectively to parts of the brain that no longer receive dopamine in Parkinson's patients.

"We could switch to a parallel pathway to put dopamine where it's needed with fewer side effects than pharmacological agents," said Dulcis.

Spitzer, Dulcis and the other researchers involved in the study are now working with biomedical scientists at the UC San Diego medical school to track the brains of individual [rats](#) with positron emission tomography after long and short days of light to determine how stable the neurotransmitter switches are and how quickly the [rat brains](#) change after being exposed to different periods of light.

**More information:** "Neurotransmitter Switching in the Adult Brain Regulates Behavior," by D. Dulcis, *Science*, 2013.

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