

Disrupting the brain's internal clock causes depressive-like behavior in mice

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Credit: Martha Sexton/public domain

Disruptions of daily rhythms of the body's master internal clock cause depression- and anxiety-like behaviors in mice, reports a new study in *Biological Psychiatry*. The findings provide insight into the role of the brain's internal time keeping system in the development of mood disorders, such as bipolar disorder and major depressive disorder, which have been associated with disturbed daily (circadian) rhythms.

"Our data show that perturbing circadian rhythms in otherwise totally undisturbed animals is enough to cause behaviors similar to human

depression," commented first author Dr. Dominic Landgraf of the University of California, San Diego.

Inherent circadian clocks help us function throughout the day, by telling us when to sleep, wake and eat, as well as by synchronizing our bodily processes. "It is perhaps not surprising that disruptions of our natural synchronization can have heavy impacts on our physical and mental health," Dr. Landgraf added.

However, until now researchers did not know if disturbed circadian rhythms were a cause or consequence of [mood disorders](#). In the new study, a team led by David K. Welsh has shown for the first time a causal relationship between functioning circadian clocks and mood regulation.

The researchers developed a new genetic mouse model by suppressing *Bmal1*, one of the master genes that drives circadian rhythms, in the suprachiasmatic nucleus (SCN), which serves as the brain's central clock regulator. Diminished *Bmal1* expression reduced the strength of the clock signals produced by the SCN by about 80%. Targeting this particular brain region allowed the researchers to focus on the specific effects of the SCN circadian rhythms, and to avoid alterations in other brain regions that have confounded previous studies.

In behavioral tests, mice with reduced circadian rhythms, relative to control mice, were less motivated to escape an uncomfortable situation, which is commonly interpreted as despair or hopelessness in the animal. The mice also showed increased aversion to brightly lit areas, considered to be an indicator of anxiety-like behavior.

In addition to the altered behavior, mice with reduced circadian rhythms gained more weight than normal mice, even though they consumed the same amount of food. This finding suggests that disrupted SCN

circadian rhythms could lead to metabolic abnormalities observed in many depressed patients.

Importantly, the findings show that even though the SCN does not directly regulate mood, alterations to circadian rhythms in the SCN are sufficient to cause depression- and anxiety-like behaviors in [mice](#).

"We have long known that disruptions in circadian rhythms may contribute to depression, particularly in people at risk for major depression or bipolar disorder," said Dr. John Krystal, Editor of *Biological Psychiatry*. "This new study provides additional evidence implicating the *Bmal1* gene in the relationship between these [circadian rhythms](#) and mood."

According to Dr. Landgraf, the results are an important step toward developing new depression treatments that directly target the [circadian clock](#) in humans.

More information: Dominic Landgraf et al. Genetic Disruption of Circadian Rhythms in the Suprachiasmatic Nucleus Causes Helplessness, Behavioral Despair, and Anxiety-like Behavior in Mice, *Biological Psychiatry* (2016). [DOI: 10.1016/j.biopsych.2016.03.1050](https://doi.org/10.1016/j.biopsych.2016.03.1050)

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