Scientists Discover 'Reset' Button For Brain's Biological Clock

04/02/2015

Researchers at Vanderbilt University have discovered a "reset" button for this biological clock, which could pave the way for more effective treatments for seasonal affective disorder (SAD), jet lag and some of the negative health effects of shift work.

The biological clock is located in the brain's suprachiasmatic nucleus (SCN) -- a tiny region within the hypothalamus, a section of the brain that controls hormone production. The SCN maintains a 24-hour cycle of rest and activity that helps us figure out when we should be eating and sleeping. The cycle is also linked to biological activities like hormone regulation, brain wave activity and cell regeneration. And while these rhythms are regulated in the brain, they're affected by external cues like light and temperature.

In their research, the Vanderbilt scientists found that they were able to artificially stimulate mice's brains with a specific technique to change when the mice naturally woke up and went to sleep, without needing to change the light. They did this by stimulating or suppressing neurons in the SCN, effectively "resetting" the biological clock.

To complete the study, the team genetically engineered two strains of mice. (They chose the animal because mice have a biological clock that's nearly identical to the ones humans have, except that mice are nocturnal.) In one strain, the neurons in the mice's brains contained a light-sensitive protein that triggers neuron activity when exposed to light. In the second strain of mice, the neurons had a similar protein that *suppressed* neural activity when exposed to light. In

other words, one of the strains of mice was wired to be nocturnal, while the other was wired to be diurnal, or awake in the day.

Then, the researchers stimulated neurons in the biological clocks of both strains of mice using a laser and an optical fiber, through a technique called optogenetics -- a method that allows researchers to stimulate or suppress neurons with just a beam of light. First, light-sensitive genes are inserted into the neurons in order to make those neurons "turn on" when stimulated with the laser. By assessing how the neurons responded to the light, the researchers were able to both measure and control the rate at which neurons fired in the SCN.

By altering the firing of neurons in the SCN, the researchers could actually *"reset" the mice's circadian rhythms* -- shifting their internal schedules for sleeping and waking.

Jeff Jones, a researcher who worked on the study, told The Huffington Post that the team was able to use optogenetics "to directly activate the SCN in the absence of light," resetting the clock without changing anything external about the mice's environment.

According to Michael Tackenberg, a doctoral student who also worked on the study, scientists have been able to measure how quickly neurons fire within the biological clock, but they've never been able to control and alter the neural activity that happens there. Now, the optogenetic technique has given them the ability to do that.

While this approach isn't yet ready for human use, the Vanderbilt team and other researchers are making progress towards the eventual creation of targeted pharmaceuticals that could turn on and off neurons that are implicated in circadian-related health problems.

"These kinds of advances let the field investigate the system for drug targets more effectively," Tackenberg said. "If it were to be implemented, the type of stimulation that we used would theoretically be plausible in patients."

The findings were published in the February 2 issue of the journal Nature Neuroscience.