Stress transmitter wakes your brain more than 100 times a night—and it is perfectly normal

July 14 2022

Credit: Unsplash/CC0 Public Domain

You wake up. The alarm clock says 02:56.

"Oh no, it is not time to wake up yet," you think, fearing that you will need lots of coffee to stay awake the following day.

Most people believe that a good night's sleep should be uninterrupted. That is why it can be extremely annoying to wake up in the middle of the night when all you want to do is sleep.

New research from the University of Copenhagen shows that the stress transmitter noradrenaline causes you to wake up many times a night. But do not worry. It is all part of a normal, good night's sleep and can even mean that you have slept well.

Noradrenaline

Noradrenaline is a stress hormone and transmitter substance, which is associated with the body's fight or flight response. It is related to adrenaline, and levels may increase during stress, but it also helps you stay focused.

"You may think that sleep is a constant state that you are in, and then you wake up. But there is a lot more to sleep than meets the eye. We have learned that noradrenaline causes you to wake up more than 100 times a night. And that is during perfectly normal sleep," says Assistant Professor Celia Kjærby from the Center for Translational Neuromedicine, who is one of the first authors of the study.

Even though noradrenaline technically causes the brain to wake up more than 100 times a night, we do not think of it as waking up.

"Neurologically, you do wake up, because your brain activity during these very brief moments is the same as when you are awake. But the moment is so brief that the sleeper will not notice," explains Ph.D. Student Mie Andersen, who is the second first author of the study.

Even though the researchers have studied mice, their findings can in all probability be translated to humans, because they have focussed on basic

biological mechanisms—that is, mechanisms shared by all mammals.

The stress transmitter noradrenaline affects the sleep waves

Professor Maiken Nedergaard, who has led the study, sees the new finding as an important piece of the puzzle to understand what happens in the brain when we sleep.

"We have found the essence for the part of sleep that makes us wake up rested and which enables us to remember what we learned the day before. We have found that the refreshing part of sleep is driven by waves of noradrenaline. The very short awakenings are created by waves of norepinephrine, which are also so important for memory," says Maiken Nedergaard. "You could say that the short awakenings reset the brain so that it is ready to store memory when you dive back into sleep."

We will return to the subject of memory shortly.

What the researchers did

Microscopic optical fibers made of glass and genetically manipulated "light receptors" were inserted into the brains of the test mice. The optical fibers were attached to cables, including an LED light source.

Subsequently, the researchers measured the here and now levels of noradrenaline while the animals slept and compared it to the electrical activity in their brains. This was where they spotted the high levels of noradrenaline.

The researchers then conducted memory tests by using the implanted equipment to increase the amplitude of the noradrenaline waves,

improving the animals' memory.

Previous research has suggested that noradrenaline, which is associated with stress, is inactive during sleep. Therefore, the researchers were surprised to see how active noradrenaline really is during sleep.

The new study shows that when we sleep the level of noradrenaline in the body is constantly increasing and decreasing in a wavelike pattern. High levels of noradrenaline mean that the brain is briefly awake, while low levels of noradrenaline mean that you are asleep. That is, your noradrenaline levels and degree of "awakeness" are connected and constantly changing.

"Approximately 30 seconds pass from one 'top' to the next, which means that your noradrenaline levels are constantly changing. At the same time, we could tell that the deeper the 'valley', i.e. the better the sleep, the higher the subsequent top, and the higher degree of awakening," says Mie Andersen.

"This shows that perhaps you do not need worry if you wake up at night. Of course, it is not good to be sleepless for extended periods, but our study suggests that short-term awakenings are a natural part of sleep phases related to memory. It may even mean that you have slept really well," Kjærby adds.

The mice developed 'super memory'

It is a well-known fact that sleep is good for us—in a number of ways. It removes waste products, prevents Alzheimer's and improves our memory.

The latter was also a focus in this study, and the findings suggest that the mice with the highest number of deep noradrenaline valleys were also

the ones with the best memory.

"The mice developed 'super memory'. They had less trouble remembering things they had learned the previous day. Of course, this suggests that the noradrenaline dynamic strengthens the sleep processes which affect our memory," says Kjærby.

First, the mice were allowed to sniff at two identical objects. They were then put to sleep, and once awake they were returned to the objects. However, one of the two objects had now been replaced by a new one. The mice who had seen the highest number of noradrenaline valleys were more inclined to study the new object, which suggests that they remembered having seen a different object last time.

New perspectives on the use of noradrenaline in antidepressants

Besides increasing our knowledge of the engine room of sleep, the new study provides food for thought when it comes to antidepressants.

"Some forms of antidepressants increase the level of noradrenaline in the body, which increases the risk that you will see fewer deep sleep valleys. Our study shows that this is likely to affect your memory," Kjærby says and adds that "that is why we need to focus attention on how different types of medication regulating the level of noradrenaline in the body affect our sleep. In the future, we should seek to develop drugs that do not affect the noradrenaline waves during sleep."

The research was published in *Nature Neuroscience*.

More information: Celia Kjaerby et al, Memory-enhancing properties of sleep depend on the oscillatory amplitude of norepinephrine, *Nature*

Neuroscience (2022). DOI: 10.1038/s41593-022-01102-9