Health

Sleeping pills disrupt the brain

A common sleep medication seems to slow down the brain's waste disposal system

Grace Wade

SLEEPING pills might help you doze off, but the sleep you get may not be as restorative. When mice were given zolpidem, a medication commonly found in sleeping pills such as Ambien, it prevented their brains from effectively clearing waste during sleep.

Sleep is critical for removing waste from the brain. At night, a clear liquid called cerebrospinal fluid circulates around brain tissues, flushing out toxins through a series of thin tubes known as the glymphatic system.

Think of it like a dishwasher that the brain turns on when asleep, says Maiken Nedergaard at the University of Rochester Medical Center in New York. However, the mechanism that pushes fluid through this network wasn't well understood – until now.

Nedergaard and her colleagues implanted optical fibres in the brains of seven mice. By illuminating chemical compounds in the brain, the fibres let them track the flow of blood and cerebrospinal fluid during sleep.

They found that as levels of a molecule called norepinephrine (also called noradrenaline) rise, blood vessels in the brain constrict, decreasing the volume of blood and letting cerebrospinal fluid rush into the brain. When norepinephrine levels fall, blood vessels expand, pushing cerebrospinal fluid back out.

"Think of the brain's waste removal system like a dishwasher that it turns on when asleep"

In this way, fluctuations in norepinephrine during non-rapid eye movement (NREM) sleep stimulate blood vessels to act like a pump for the glymphatic system, says Nedergaard.

This finding reveals that norepinephrine plays a crucial role in cleaning waste out of the brain. Previous research has shown that, as we sleep, our brains release this chemical in a slow, oscillating pattern. These norepinephrine waves occur during NREM, which is a crucial sleep stage for memory, learning and other cognitive functions.

Next, the team treated six mice with zolpidem, a sleep medication commonly sold under the brand names Ambien and Zolpimist. While the mice fell asleep faster than those treated with a placebo, the flow of cerebrospinal fluid in their brains dropped by roughly 30 per cent, on average (*Cell*, doi.org/g8x4gd). In other words, "their brain doesn't get cleaned very well", says Nedergaard.

Although the experiment tested zolpidem, nearly all sleeping pills inhibit the production of norepinephrine. This suggests they may interfere with the brain's ability to flush out toxins.

It is too soon to tell whether these results will translate to humans. "Human sleep architecture is still fairly different than a mouse, but we do have the same brain circuit that was studied here," says Laura Lewis at the Massachusetts Institute of Technology. "Some of these fundamental mechanisms are likely to apply to us as well."

If sleeping pills do interfere with the brain's ability to remove toxins during sleep, that means we must develop new sleep medications, says Nedergaard. Otherwise, we risk exacerbating sleep problems, potentially worsening brain health in the process. ▮

MYVIEWPOINT/ALAMY