



Maiken Nedergaard M.D., co-director of the University of Rochester's Center for Translational Neuromedicine, is a rock star in the world of sleep research. Writer Donna Jackel caught up with her this summer to discuss her latest findings, including a groundbreaking link between sleep and neurodegenerative disease.

By Donna Jackel

How much sleep do we really need?

The amount of sleep you require varies depending on your age and your individual needs.

10

The National Institutes of Health recommends school-age children get at least 10 hours of sleep daily; teens nine to 10 1/2 hours, and adults seven to eight hours.

30%

Many of us fall far short of these goals. According to the National Health Interview Survey, nearly 30 percent of adults reported an average of six or fewer hours of sleep per day in 2005 to 2007.

3%

In 2009, only 3 percent of high school students reported getting at least eight hours of sleep on an average school night.

Why do we sleep? And why do we require so much of it—an average of seven to nine hours a night?

It's a mystery scientists have been trying to solve for centuries.

A University of Rochester lab has identified a key piece of the puzzle: Using mice, researchers showed that during sleep the brain flushes out proteins, including potential toxins that build up during waking hours. Maiken Nedergaard M.D., D.M.Sc., co-director of the University of Rochester's Center for Translational Neuromedicine, calls the brain's "dishwashing" machinery that carries out this process the glymphatic system.*

By tracking the movement of red and green dye, Nedergaard's team could observe that when mice were asleep, the brain's cellular volume shrank, allowing cerebrospinal fluid (CSF) to enter the brain and flush all the metabolic waste into the bloodstream. From there, the waste is carried to the liver for detoxification. When the mice were asleep or anesthetized, the dye flowed rapidly; when the mice were awake, the dye barely flowed.

"It's like opening and closing a faucet," Nedergaard says.

In the second phase of the experiment, the UR team injected beta amyloid—a protein that accumulates in the brains of patients with Alzheimer's disease—into the brains of sleeping mice and awake mice. They found that during sleep, the CSF cleared the proteins away twice as quickly. To explain just how essential brain cleaning is, Nedergaard likens it to a dirty fish tank.

"If there is no filter in the fish tank, the fish die," she says. Scientists already knew that sleep was important for storing memories. But Nedergaard strongly believed that there had to be a more basic reason for sleep.

"I thought, 'There was no way we were spending all that time sleeping (just) for memory because sleep is so dangerous,'" she says. When animals sleep in the wild, they are vulnerable to predators.

The waste removal system helps explain why a good night's sleep is crucial to our health.

"They have known for 50 years that all neurodegenerative diseases, such as ALS (Amyotrophic lateral sclerosis), Parkinson's

(disease) and dementia, are linked to the accumulation of protein amyloids and are associated with sleep disturbances," says Nedergaard.

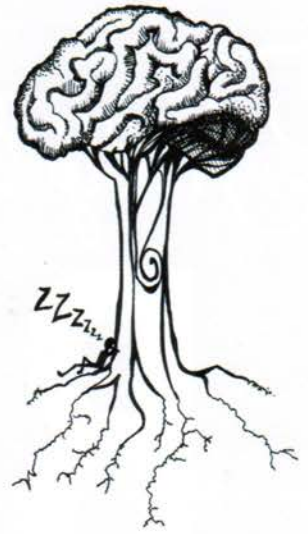
This summer, in a collaboration with anesthesiologist Helene Benveniste at Stony Brook University, Nedergaard hopes to continue this research on human brains using MRI. Experts say Nedergaard's discovery could have broad implications in the treatment of a range of disorders. Sigrid Veasey M.D., a scientist at the University of Pennsylvania's Center for Sleep and Circadian Neurobiology, finds the most compelling aspect of Nedergaard's study is the slowness with which amyloid proteins are cleared during prolonged wakefulness.

This finding directly relates to Veasey's work: She has been researching the differences between short-term sleep loss, like pulling an all-nighter for an exam, and constant sleep deprivation, like what shift workers experience.

"While our brains can recover quickly from short-term sleep loss, chronic, prolonged wakefulness and sleep disruption stresses the brain's metabolism," Veasey says. "This leads to a buildup of free radicals in the brain, which damage the proteins and mitochondria, ultimately leading to cell death. This type of damage could accelerate the aging of the brain." She adds: "If someone was going to get Parkinson's at 80, they may be getting it at 60 instead. We are just starting to look at this in humans."

The two researchers' work supports one another, says the UPenn associate professor. "Maiken's work shows that sleep serves to take out trash—the interstitial fluid. My work shows that inadequate sleep means that the neurons become injured ... and you are putting more trash out on the street, so it's harder to pick up."

For all of us night owls, workaholics and insomniacs, these findings offer powerful evidence as to why regularly getting a good night's sleep should top the to-do list. But Veasey warns: "Sleep-deprived individuals are poor judges of how impaired they are."



How Sleep Deprivation Hurts U

- Increases the risk of feeling sleepy or actually nodding off while driving, particularly on longer drives
- Increases appetite, raising the risk of obesity
- Increases risk of diabetes and heart problems
- Increases risk for psychiatric conditions, including depression and substance abuse
- Decreases ability to pay attention, react to signals or remember new information

Source: National Sleep Foundation

Ways to Get Better Sleep

- Go to bed and rise at the same times, even on weekends
- Stick to a bedtime routine you find relaxing, such as soaking in a hot bath or listening to soothing music.
- At bedtime, keep your bedroom dark, quiet, comfortable and cool
- Sleep on a comfortable mattress and pillow
- Use your bedroom only for sleep and sex
- Finish eating at least two to three hours before bedtime
- Exercise regularly
- Avoid caffeine and alcohol close to bedtime and give up smoking
- Schedule sleep like any other daily activity, by putting it on your to-do list.

Source: National Sleep Foundation