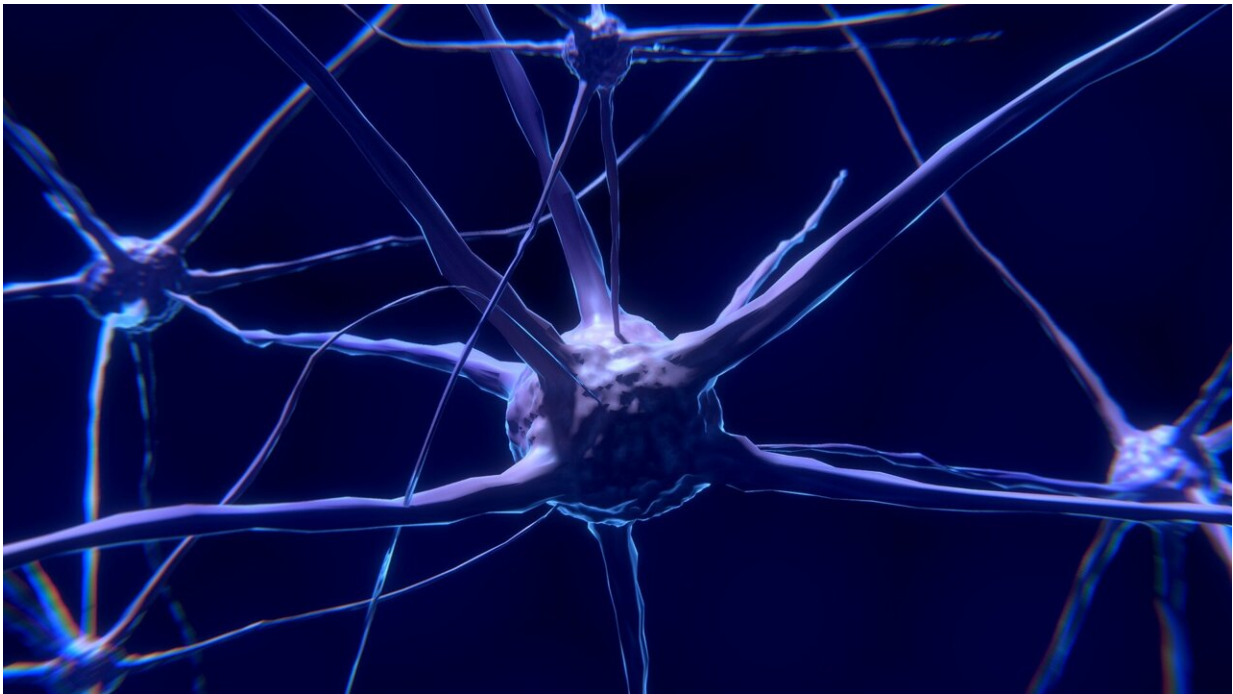


# Loss of neurons, not lack of sleep, makes Alzheimer's patients drowsy

April 4 2022

---



Credit: Pixabay/CC0 Public Domain

The lethargy that many Alzheimer's patients experience is caused not by a lack of sleep, but rather by the degeneration of a type of neuron that keeps us awake, according to a study that also confirms the tau protein is behind that neurodegeneration.

The study's findings contradict the common notion that Alzheimer's

patients [sleep](#) during the day to make up for a bad night of sleep and point toward potential therapies to help these patients feel more awake.

The data came from study participants who were patients at UC San Francisco's Memory and Aging Center and volunteered to have their sleep monitored with electroencephalogram (EEG) and donate their brains after they died.

Being able to compare sleep data with microscopic views of their post-mortem brain tissue was the key to answering a question that scientists have been pondering for years.

"We were able to prove what our previous research had been pointing to—that in Alzheimer's patients who need to nap all the time, the disease has damaged the neurons that keep them awake," said Grinberg, a neuropathologist who, along with psychiatrist Thomas Neylan, MD, is a senior author on the study, which appears in the April 4, 2022 issue of *JAMA Neurology*.

"It's not that these patients are tired during the day because they didn't sleep at night," noted Grinberg. "It's that the system in their brain that would keep them awake is gone."

The opposite phenomenon occurs in patients with other neurodegenerative conditions, such as [progressive supranuclear palsy](#) (PSP), who were also included in the study. Those patients have damage to the neurons that make them feel tired, so they are unable to sleep and become sleep deprived.

Grinberg's team developed the hypothesis that Alzheimer's patients were having trouble staying awake, after [discovering a set of neurons that keep us awake and that are affected in Alzheimer's](#) from the onset of the disease.

"You can think of this system as a switch with wake-promoting neurons and sleep-promoting neurons, each tied to neurons controlling [circadian rhythms](#)," said Joseph Oh, a medical student and one of the lead authors. "Finally, with this post-mortem tissue, we've been able to confirm that this switch, which is known to exist in model animals, also exists in humans and governs our sleep and awake cycles."

## **"Extremely Smart Neurons" Disrupted by Tau Proteins**

Oh describes these neurons as "extremely smart" because they can produce an array of neurotransmitters and can excite, inhibit, and modulate other [nerve cells](#).

"It's a small number of neurons but their computational capabilities are incredible," Oh said. "When these cells are affected by disease, it can have a huge effect on sleep."

To determine what's contributing to the degradation of these neurons in Alzheimer's, the researchers looked at the brains of 33 patients with Alzheimer's, 20 with PSP, and 32 volunteers who'd had healthy brains through the end of life.

The team measured the amounts of two proteins often associated with the neurodegenerative process—beta amyloid and tau. Which of the two is more involved in disrupting sleep has been a long-disputed question, with most researchers crediting the sleep problems to beta-amyloid accumulation.

During sleep, the brain clears out the beta amyloid that accumulates during the day. When we can't sleep, it builds up. So, Neylan said, since the PSP patients never sleep, she expected to see lots of the protein in

their brains.

"But it turns out that they have none," he said. "These findings confirm with direct evidence that tau is a critical driver of sleep disturbances."

In patients with PSP, said Grinberg, this understanding turned the treatment paradigm on its head.

"We see that these patients can't sleep because there is nothing telling the "awake" neurons to shut down," she said. "Now, rather than trying to induce these people to sleep, the idea is to shut down the system that's keeping them awake."

## **Clinical Trial is Giving Patients Hope**

That idea is currently being tested in a clinical trial of patients with PSP, using a treatment that specifically targets the overactive 'awake' system that keeps these patients from sleeping. This approach contrasts with the traditional trial-and-error treatment with sleep medications.

At the helm of that trial is Christine Walsh, Ph.D., the study's other lead author, who has also worked on the study for a decade. Noting that PSP and Alzheimer's are at opposite ends of the sleep-disturbance spectrum, she said she expects the research to lead to new ways of treating sleep disturbances driven by neurodegeneration. Treatments for Alzheimer's could be adjusted depending on the patient's needs, bumping up the "awake" system while tamping down the "sleep" system, said Walsh, who along with Grinberg, is a member of the UCSF Weill Institute for Neurosciences.

The PSP trial is still underway, and Walsh is highly optimistic that this new approach will have better results than current medications for people with either condition. Based on the findings of the study

published today, she said, "We're even more hopeful that we can actually make a difference in the lives of these [patients](#)."

**More information:** *JAMA Neurology* (2022).  
[jamanetwork.com/journals/jaman ... jamaneurol.2022.0429](https://jamanetwork.com/journals/jaman...jamaneurol.2022.0429)

Provided by University of California, San Francisco

Citation: Loss of neurons, not lack of sleep, makes Alzheimer's patients drowsy (2022, April 4)  
retrieved 27 April 2024 from  
<https://medicalxpress.com/news/2022-04-loss-neurons-lack-alzheimer-patients.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.