Alzheimer's Disease Research

ALZHEIMER'S SCIENCE NEWS

FALL 2022

IS DAYTIME NAPPING CONNECTED TO ALZHEIMER'S?

Is sleep disruption and a malfunctioning biological clock related to Alzheimer's disease? With the help of a grant from Alzheimer's Disease Research, Peng Li, PhD, of Harvard Medical School, has found that excessive daytime napping may point to a heightened risk for this disease.

Humans have an inner biological or circadian clock that regulates bodily functions like heart rate and blood supply to the brain. It also helps drive physical, mental, and behavioral changes over a 24-hour day-night cycle.

It's long been known that a diagnosis of Alzheimer's often follows years of sleep disturbance. However, it's not clear whether the disease disrupts sleep first, or if disrupted sleep contributes to the disease's development.

In a long-term study of over 1,400 people, Dr. Li and his colleagues focused on sleep patterns over the entire 24-hour cycle. Participants wore a watch-like device on their wrists for up to two weeks, which helped scientists track their activity, including day and night sleep habits.

Excessive daytime napping may signal an increased risk for Alzheimer's.

The researchers found that as people aged, they napped more often. Longer, more frequent naps increased the risk of being diagnosed with Alzheimer's, according to their study results.

Their next step will be to assess if there is a causal link between excessive daytime napping and the risk of developing Alzheimer's. If yes, it would highlight the importance of circadian health and "encourage people to maintain regular daily schedules including sleep/wake in order to reduce Alzheimer's risk," said Dr. Li.

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PRESIDENT'S CORNER

Alzheimer's is a devastating disease. But we're making exciting progress against it—and we have you to thank for that.

With your support, scientists we fund are tackling this mind-stealing disease on multiple fronts. They're identifying new warning signs, testing potential therapies, and investigating ways to prevent this disease.

You play a critical role in making research like this possible. Without help from friends like you, many promising studies might never get off the ground—delaying urgently needed advances by years or even decades.

With your partnership, we will continue to press forward with vital research until we one day find a cure for this heartbreaking disease. Thank you for your commitment to our mind-saving work.

Stacy Pagos Haller

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RESEARCHER SPOTLIGHT: SHANNON MACAULEY, PHD

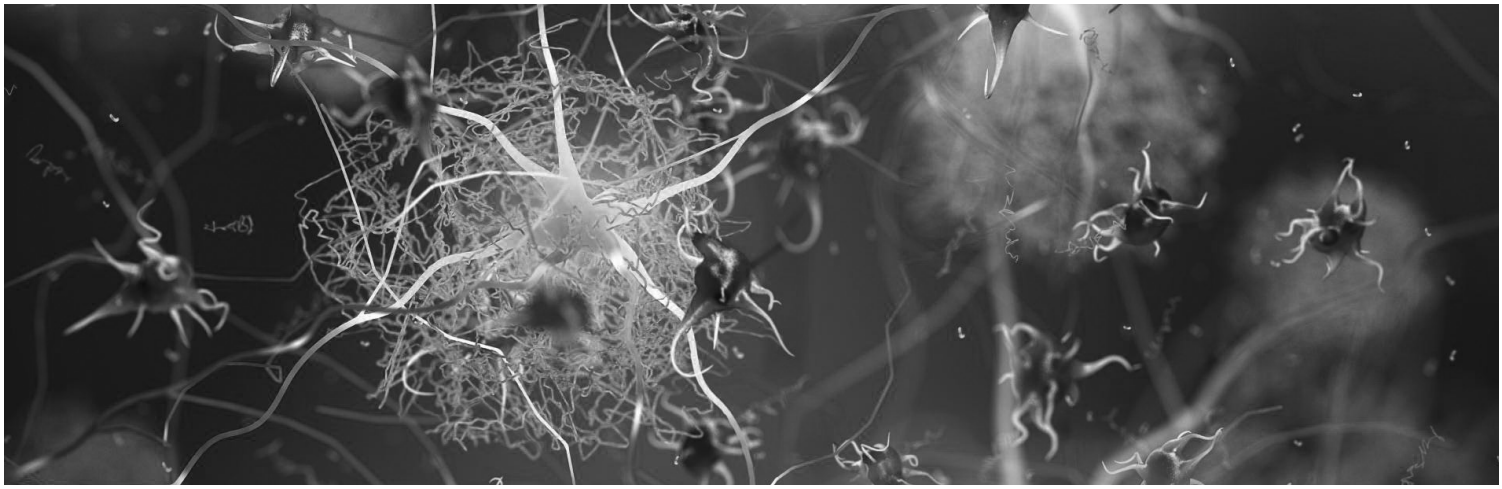
Shannon Macauley, PhD

Brain hyperexcitability is a defining feature of Alzheimer's. It also represents a promising treatment target. That's why Alzheimer's Disease Research grant recipient Shannon Macauley, PhD, of Wake Forest University, is exploring ways to dampen overactive neurons in the brain and decrease Alzheimer's pathology.

Her preliminary research suggests that sulfonylureas, a group of medications used in treating type 2 diabetes, can act on blood vessels to reduce brain hyperexcitability and amyloid plaque formation. Since brain hyperexcitability can also drive the development of neurofibrillary tangles, she is testing whether these FDA-approved drugs can be repurposed to reduce tau pathology and preserve healthy brain function.

Dr. Macauley is using cutting-edge imaging techniques to assess neuronal structure and network function. If tests are successful, this could open the door to new therapies that target neurovascular function as a way to decrease Alzheimer's pathology.

RARE APOE VARIANT REDUCES PLAQUES LINKED TO ALZHEIMER'S



A rare genetic variant called APOE3-Jac has been shown to prevent amyloid plaques.

There are three variations of the apolipoprotein E (APOE) gene: APOE2, APOE3, and APOE4. The APOE4 version increases a person's risk for developing Alzheimer's, while APOE2 decreases the risk. Until recently, the most common type, APOE3, was thought to be neutral.

Now, however, an Alzheimer's Disease Research–funded scientist, Chia-Chen (Jenny) Liu, PhD, of Mayo Clinic Jacksonville, has shown that a rare APOE3 genetic variant called APOE3-Jacksonville, or APOE3-Jac, also protects against the disease.

APOE's job is to carry cholesterol and lipids in the blood throughout the body and brain. APOE4 is expressed at higher levels than other APOE proteins, which contributes to the formation of amyloid beta plaques, a hallmark of Alzheimer's.

Dr. Liu and her colleagues confirmed that people with the APOE3-Jac variant had fewer plaques than those with regular APOE3. They then showed that the APOE3-Jac gene reduces clumping of APOE proteins—including APOE4—and is better able to bind beneficial lipids that the brain needs to function properly. Finally, using a mouse model of Alzheimer's, they showed that mice with APOE3-Jac had fewer amyloid beta plaques and associated brain toxicity.

Since people with greater plaque buildup are more likely to have Alzheimer's, learning more about APOE's protective role against plaque formation may pave the way for new treatments.

WHAT IS "HEALTHY SLEEP" AND WHY IS IT IMPORTANT?

Research shows that regularly getting a good night's sleep helps the brain flush out waste material and prevents buildup of amyloid plaques linked to Alzheimer's. By contrast, chronic sleep disruption can impact overall health and damage the brain.

Brendan Lucey, MD, a sleep specialist at Washington University in St. Louis and former Alzheimer's Disease Research grantee, says it's important to allow enough time to sleep; have a quiet, dark bedroom; treat any medical problems that disturb nighttime sleep; and avoid sleeping too much during the day.

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HELP FIGHT ALZHEIMER'S THROUGH A DONOR ADVISED FUND

Would you like to gain the most favorable tax benefits while flexibly and easily supporting our mind-saving work? If so, consider giving through a donor advised fund (DAF).

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To learn more about DAFs, contact Charlie Thomas, our Planned Giving Manager, at 301-556-9362 or plannedgiving@brightfocus.org.

DAFs help simplify your charitable giving and offer immediate tax benefits.

Alzheimer's Disease Research

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WHAT IS "HEALTHY SLEEP" ... CONTINUED FROM PAGE 3

There are many reasons why older adults can have disturbed sleep at night and nap more during the day. For instance, apnea is more common as people age. Medication, such as diuretics for heart problems, can cause people to wake up at night to urinate. Sleep disturbances can lead to poor attention, which makes it harder to remember things.

Fortunately, there are steps you can take to get enough rest: Allow adequate time to sleep; maintain a regular sleep schedule at night; avoid light exposure at night; and have a consistent bedtime routine.

Although there are many unanswered questions about the relationship between sleep and Alzheimer's, maintaining good sleep habits is beneficial for your brain and overall health.

IS NAPPING BAD?

A short daytime nap is normal for older adults, especially during illness. If you get seven to eight hours of sleep a night and can do all of your daily activities without feeling drowsy, it's likely that you don't have a problem. However, if you nap throughout the day, experience drowsiness that impairs function, or have fragmented night sleep, it could be a sign of issues you should discuss with your doctor.

Please share this newsletter with someone you know who might be interested in learning about some of the latest advancements in research to diagnose, prevent, treat, and cure Alzheimer's disease.

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