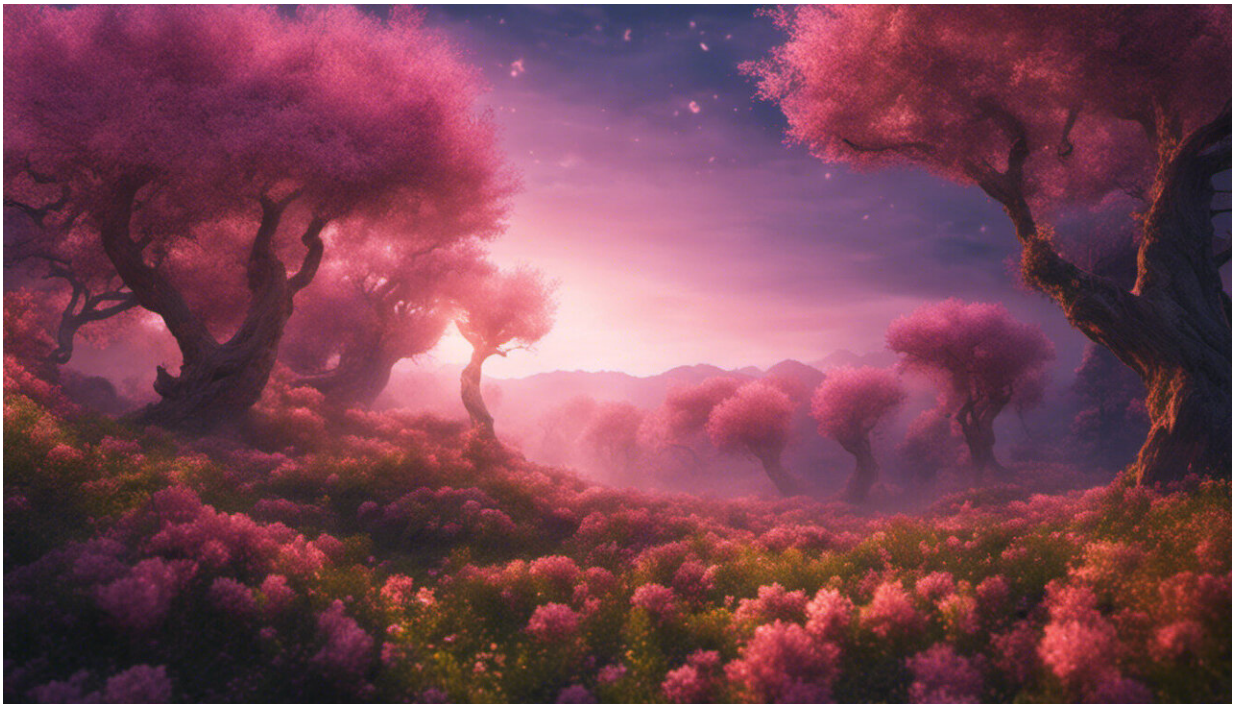


# Disrupted circadian regulation of cognition in Alzheimer's disease

November 19 2021, by Emily Caldwell

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Credit: AI-generated image ([disclaimer](#))

Circadian dysfunction linked to Alzheimer's disease is known to disrupt sleep and daily activity patterns. New research in a mouse model of the disease suggests beta-amyloid buildup in the brain, one of the hallmarks of Alzheimer's disease, could also contribute to deficits in circadian regulation of learning and memory early in the disease process.

Researchers tested cognitive behaviors in a mouse model of Alzheimer's [disease](#) that accelerates beta-amyloid accumulation in the brain to assess short-, intermediate- and long-term [memory](#) at early and late points in the disease. The nocturnal animals are typically more active and alert at night and therefore more cognitively functional at that time—as dictated by their circadian clock.

"In [normal mice](#), there was a time-of-day difference in memory retrieval. In the Alzheimer's disease mouse model, there was not—the time-of-day differences in memory were blunted, meaning that their clock is dysfunctional," said study author Anisha Kalidindi, a doctoral student in the Molecular, Cellular and Developmental Biology graduate program at The Ohio State University. "Taken together, looking at their behaviors as a whole, we see these deficits in circadian gating of cognition occur early in the disease process and may be related to dysregulation in the clock."

Kalidindi presented the work Nov. 11 in a virtual poster session at the Society for Neuroscience annual meeting.

Our ability to think clearly, and effectively, changes over the course of the day, as cellular functions in specific regions of the brain that affect memory and learning are regulated by our [circadian clock](#). The same is true in animals.

In the test of intermediate-term memory, for example, mice spent time exploring two objects in an arena. They were removed and returned 30 minutes later to the same arena, where one object had been moved. Their standard behavior would be to spend more time exploring the novelty of the moved object—a sign that they recognize the change. Normal mice in the study were significantly more likely to recognize the moved object at night than during the day, but in the Alzheimer's model mice, this time-of-day difference in novel object location orientation

was lost.

"This study gives us an unusually comprehensive understanding of circadian cognition in this model," Kalidindi said. "We have really nice data on this set of behaviors that we can use to make interesting hypotheses and find new directions from there. We're trying to take apart the disease piece by piece to see how these different factors drive dysfunction."

Additional molecular studies would be needed to confirm that circadian biology is behind the cognitive changes seen in the report, but Kalidindi said the findings create a good argument for more attention to the benefits of circadian health.

"Sleep is one circadian-regulated behavior, but even eating to optimize metabolism throughout the day and getting exposure to light—those are also important to circadian health. I'm hopeful the impact of this research could lead to a better understanding by the public of how important circadian biology is to health generally, and learning and memory specifically."

Provided by The Ohio State University

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