Sleep problems, Alzheimer's disease are linked, but which comes first?

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A new article explores the pathophysiological factors that link sleep disturbances and Alzheimer's disease. Better understanding of this connection may lead to potential diagnostics and therapeutics for Alzheimer's disease and other neurodegenerative diseases and dementia. The article is published ahead of print in the *Journal of Neurophysiology*.

Alzheimer's research has largely focused on the presence of two proteins—amyloid beta and tau—in the brain. Amyloid beta is thought to be involved with learning and the ability of the brain to change and adapt, and tau helps regulate normal signaling between neuronal cells. People with Alzheimer's disease have been found to have both hallmarks: a buildup of amyloid beta and tau tangles in the brain.

Previous studies in healthy animals and humans have reported higher levels of amyloid beta after a single night of sleep deprivation. This is consistent with normal fluctuation patterns of the protein that occur before sleeping and upon waking. These findings suggest that sleep helps the body eliminate excess amyloid beta before too much accumulates in the brain. Research has also shown that disruption of slow-wave sleep—a deep sleep phase—causes amyloid beta levels to rise as much as 30 percent. "This evidence demonstrates the significance of sleep in clearing metabolic waste and sleep disruption as a significant mediator in the development of [Alzheimer's disease]," Shen Ning and Mehdi Jorfi, Ph.D., the authors of the article, wrote.

The presence of tau—the protein that is found tangled in the brain of people with Alzheimer's disease—in the fluid that surrounds the brain and spinal cord (cerebrospinal fluid) is a marker of injury to the nerve cells, the authors explained. Sleep deprivation for as little as one night has been found to increase tau levels by as much as 50 percent in cerebrospinal fluid.

The research suggests that increased production of amyloid beta and tau and reduced elimination of these proteins is the primary contributing factor to Alzheimer's disease. While quality sleep seems to be able to help the body clear excess proteins, "the question remains whether sleep disruption aggravates [Alzheimer's disease] symptoms and augments disease progression, or if sleep disruption actually initiates the cascade of [Alzheimer's disease] development," the researchers wrote.

Continuing study of the relationship between sleep and Alzheimer's disease "holds great promise in bridging the molecular and cellular biology of sleep in context of the development of [Alzheimer's disease]. It may even provide helpful therapeutic benefits in preventing not only [Alzheimer's disease], but also in improving diagnosis and treatments for psychiatric and metabolic diseases," the researchers wrote.

More information: Shen Ning et al. Beyond the sleep-amyloid interactions in Alzheimer's disease pathogenesis, *Journal of Neurophysiology* (2019).

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