Researchers identify potential new treatment for those who act out their dreams while sleeping

May 25 2023

Credit: Unsplash/CC0 Public Domain

Mount Sinai researchers have published what they say is the first study to identify a new form of treatment for rapid eye movement (REM)

sleep behavior disorder. This condition affects more than 3 million Americans, mostly adults over the age of 50, who often unknowingly physically act out their dreams with vocal sounds or sudden, violent arm and leg movements during slumber, leading to significant injury to themselves or bed partners.

The new study, published in the *Journal of Neuroscience*, outlines a novel model to better characterize how REM sleep behavior disorder develops due to neurodegeneration—when brain cells lose function over time—which is associated with the accumulation of tau protein. This model provides an early-life biomarker of impending deterioration of the brain, which could guide future prevention and treatment.

The paper also demonstrates for the first time that sleep medications known as dual orexin receptor antagonists—commonly used to treat insomnia, or difficulty falling and remaining asleep—can significantly reduce REM sleep behavior disorder. Current therapeutic options for this disorder are primarily limited to melatonin and clonazepam, also known as Klonopin, so these findings suggest a promising new treatment with potentially fewer side effects.

"We were interested in understanding all of the ways in which sleep quality breaks down as neurodegeneration progresses and whether there were any ways to mitigate such changes," said corresponding author Andrew W. Varga, MD, Ph.D., Associate Professor of Medicine (Pulmonary, Critical Care and Sleep Medicine) at the Icahn School of Medicine at Mount Sinai.

"We identify a novel model in which REM sleep behavior disorder can develop, due to neurodegeneration associated with accumulation of tau protein, and a novel therapy that could minimize REM sleep behavior disorder."

Mount Sinai researchers used a mouse model to study neurodegenerative disorders by examining the brain following abnormal deposits of tau, a protein that normally helps stabilize the internal skeleton of nerve cells in the brain. They analyzed behavioral states including wakefulness, phases of REM (sleep with dreams), phases of non-REM (sleep without dreams), length of sleep, transitions from waking to sleep, and how some factors are related to age.

Nearly a third of the older subjects exhibited dream enactment behaviors reminiscent of REM sleep behavior disorder, including chewing and limb extension. After administering a dual orexin receptor antagonist twice during a 24-hour period, to evaluate sleep in light and dark phases, the researchers observed that the medication not only reduced the time it took to fall asleep and increased both the quality and duration of sleep but also reduced levels of dream enactment.

Researchers hope their findings will encourage future trials of dual orexin receptor antagonists to treat REM sleep behavior disorder in humans, given that the medication is already FDA approved and available to treat people with insomnia.

"We anticipated finding breakdown of sleep quality with progressive neurodegeneration related to tau accumulation, but the observation of dream enactment was a surprise," said lead author Korey Kam, Ph.D., Assistant Professor of Medicine (Pulmonary, Critical Care and Sleep Medicine) at Icahn Mount Sinai. "It was even more surprising and exciting to observe that a dual orexin receptor antagonist could significantly minimize the dream enactment behaviors."

More information: Korey Kam et al, Effect of aging and a dual orexin receptor antagonist on sleep architecture and NREM oscillations including a REM Behavior Disorder phenotype in the PS19 mouse model of tauopathy, *Journal of Neuroscience* (2023). DOI:

10.1523/JNEUROSCI.1828-22.2023

Provided by The Mount Sinai Hospital