

Can deep sleep help devastating brain disorders? Scientists studying Parkinson's want to find out

January 27 2022, by Delthia Ricks



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Sleep may be one of the most potent medicines for the brain, scientists are discovering, as they explore the inner labyrinths of the three-pound



organ during deep sleep and dream cycles in both health and disease.

Among the most active areas of sleep research are those riveted on <u>brain disorders</u> in which insomnia and other abnormal sleep patterns play a role. Parkinson's and Alzheimer's are among the major neurodegenerative conditions affected by <u>poor sleep patterns</u>, and scientists say in the not-too-distant future those conditions—and possibly others—may benefit from newly emerging studies in <u>sleep research</u>.

In Switzerland, Dr. Marta Morawska, a neuroscientist at University Hospital of Zurich, is attempting to peel away some of the mysteries underlying disturbed sleep patterns and the progressive decline of Parkinson's disease.

"Sleep disturbances have been shown to occur and to contribute to several neurodegenerative diseases, including Parkinson's disease," Morawska wrote in Science Translational Medicine. "In particular, slowwave sleep alterations show correlation with Parkinson's disease symptoms and progression."

Slow wave sleep is the period of non-<u>rapid eye movement</u>, NREM sleep, which is characterized by high amplitude, low-frequency brain waves. During NREM, also known as Phase 3 sleep, delta waves dominate when patients undergo electroencephalography, or EEG. Slow-wave sleep is the deepest, most restful stage of sleep and is believed to be the period when memory consolidation occurs.

Morawska and colleagues hypothesize that restoring healthy deep sleep may limit the accumulation of a toxic protein in the brain, and slow the progression of Parkinson's disease. The notion of slowing a devastating condition by increasing the amount of NREM sleep may seem an unusually simple solution. But an increasing number of scientists—the Swiss team included—say sleep is potent medicine and its full power has



yet to be fully harnessed.

For decades, a large body of research had long established that sleep is essential for the healthy brain, improving concentration and mood while awake. During the four stages of the sleep cycle, the body reboots and replenishes. Immune forces are bolstered, hormones are released that repair cells and control the metabolic rate. Blood pressure rises and falls as cardiovascular health is fine-tuned.

Yet, while it's well known that sleep aids the healthy brain, only now are scientists gaining more insight into sleep—and the lack of it—in serious neurodegenerative disorders.

Parkinson's disease is a progressive nervous system disorder that affects movement and gait. More than 10 million people worldwide are living with the condition, according to the Parkinson's Foundation, based in Miami, Florida.

The disorder is characterized by tremor, muscular rigidity and slow movement, its incidence increasing as people age. Within the brain itself, the disorder is marked by the degeneration of the basal ganglia and a deficiency of the neurotransmitter dopamine.

Sleep deprivation, a major problem in Parkinson's disease, can increase deposits of alpha-synuclein, say Morawska and her Zurich collaborators, referring to aggregates of a toxic protein associated with Parkinson's disease and other neurodegenerative disorders.

Although alpha-synuclein plays a critical role in the healthy brain by actively inhibiting neurotransmitters when they are overexpressed, in Parkinson's, aggregates of the protein collect in the brain. These large deposits of alpha-synuclein are known as Lewy bodies, which are hallmarks not only of Parkinson's disease but also of another disorder,



Lewy body dementia. In late-stage Parkinson's disease, dementia can occur.

To test their basic hypothesis—that increasing the amount of slow-wave sleep may have a beneficial impact on the Parkinson's brain—Morawska and her team turned to two mouse models. The team examined sleep deprivation and its impact on the accumulation of the neurotoxic aggregates. The researchers also investigated a way to increase slowwave sleep in their animal models.

"Sleep deprivation increased brain alpha-synuclein aggregates," Morawska asserted. "Enhancing slow-wave sleep with sodium oxybate reduced the alpha-synuclein burden, possibly by increasing glymphatic function and modulating protein homeostasis."

Glymphatic function, known interchangeably as the glymphatic system and the glial-dependent waste clearance pathway, refers to the brain's ability to eliminate toxic proteins and other debris during sleep. Soluble waste proteins are eliminated during the NREM phase of sleep, which may explain why the Zurich team hypothesizes that extending deep sleep may slow down Parkinson's progression.

The new Swiss research joins studies from elsewhere in Europe as well as the United States that are investigating the role of irregular sleep patterns on the other neurodegenerative disorders. An active area of research is focusing on disrupted sleep patterns and Alzheimer's disease.

In the *International Journal of Science* two years ago, researchers in Spain posed an intriguing scientific question: Is disruptive sleep a cause or consequence of Alzheimer's? The research emphasized an important point: "Affected brain structures in people with disturbed sleep coincide with vulnerable areas in Alzehimer's disease."



Another critical area of research involves sleep disturbances common in chronic traumatic encephalopathy, or CTE. The condition is linked with repeated head injuries, such as trauma sustained in boxing, football and other aggressive sports. People with CTE have sleep-related problems that cause them to move their limbs and shout during the dream phase of the sleep cycle.

As with Parkinson's disease, people with CTE are at increased risk for alpha-synuclein aggregates in the <u>brain</u>. CTE patients are also at increased risk for Lewy body dementia.

Morawska and her collaborators, meanwhile, suggest their laboratory research may lead to clinical studies involving Parkinson's patients. "The results suggest that sleep plays an important role in Parkinson's disease pathophysiology and that manipulating <u>slow-wave sleep</u> might be therapeutic in patients with Parkinson's."

More information: Marta M. Morawska, et al, Slow-wave sleep affects synucleinopathy and regulates proteostatic processes in mouse models of Parkinson's disease, *Science Translational Medicine*, (2021) DOI: 10.1126/scitranslmed.abe7099

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