Q&A: Researcher explains the relationship between Parkinson's disease and sleep, treatment options

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Trying to get a full night's rest while living with Parkinson's disease is often easier said than done. Patients often face frequent interruptions

and irregular sleep due to a number of issues, such as poor nap patterns, abnormal movements during sleep, medication side effects, and difficulties surrounding sleep-improving exercise.

Amy Amara, MD, Ph.D., Professor of Neurology and Movement Disorders Section Head at the University of Colorado School of Medicine, helps patients navigate the challenges. Amara became interested in sleep medicine after seeing how her patients with Parkinson's struggle with sleep.

"It's really rewarding to make somebody feel better by helping to improve their sleep," she said. "Especially seeing how their life turns around while improving how they function during the daytime."

Below, Amara details the current state of research in the relationship between Parkinson's and sleep and the vital importance of exercise in treatment.

How are Parkinson's disease and sleep disorders related?

Parkinson's patients commonly have rapid eye movement (REM) sleep behavior disorder (RBD), which can occur many years before Parkinson's is diagnosed—even 15 to 30 years before people develop the tremor, walking problems or other signs of Parkinson's. For people who act out their dreams (abnormal movement during sleep), up to 80 to 90% of those people later develop Parkinson's or some type of atypical Parkinsonism.

There are other causes of acting out dreams that likely aren't associated with increased risk of Parkinson's, such as narcolepsy, a sleep disorder called arousal parasomnia that can occur when sleep apnea wakes you

during dreams, or trauma-related sleep disorder. Acting out dreams not associated with those other conditions is associated with higher Parkinson's risk.

There's also a big intersection in the relationship between cognition and sleep. That's true for healthy aging and for people with Alzheimer's, Parkinson's and other neurodegenerative conditions. As sleep gets worse, cognition can also get worse, and there are changes in the different aspects of sleep. There can be reductions in the deepest stage of sleep, non-REM stage 3, which is also called slow-wave sleep—which is very important for cognition.

Are there other diagnostic tests to help detect Parkinson's with regards to sleep?

Interestingly, there's a newly developed or identified biomarker of Parkinson's. It's called the synuclein seeding assay. Synuclein is a protein that's abnormally clumped together in Parkinson's. There are ways now to detect that in the spinal fluid, and this will be available for the blood as well. This biomarker can be found in people with REM sleep behavior disorder, too, who don't yet have the diagnosis of Parkinson's. The biomarker can't detect timing or severity of disease, however; it's only a positive or negative. It doesn't quantify how much abnormality there is.

Additionally, sleep spindles are a pattern of brain waves and another non-REM related sleep feature that we can look for and seem to be very important for memory consolidation and for cognitive function. We found that having fewer numbers of sleep spindles predicts later development of cognitive problems, and people with RBD have fewer sleep spindles than Parkinson's patients who don't have RBD.

What are the connections between losing sleep and

Parkinson's?

It's hard to know for sure which change happens first. It may be that the sleep is abnormal because people at risk for cognitive problems are already undergoing the brain changes that are associated with the underlying disorder. Alternatively, the sleep changes may lead to cognitive trouble.

What we do know: Sleep is very important. It is clear that if people who have Parkinson's or other movement disorders or other neurodegenerative disorders have a night of poor sleep, the next day will be worse. Their cognition performance will be worse. Their movements will be worse.

New research shows that there is actually lymphatic drainage from the brain. For a long time, it was thought that the brain didn't have any lymphatic system, but there's a fairly newly described glial lymphatic or glymphatic system that has been associated with clearing neurotoxins from the brain. That clearance seems to be increased during that deep stage of sleep, that slow-wave sleep. Not having as much slow-wave sleep could be reducing that clearance of neurotoxins from the brain, which then can be detrimental for that protein buildup that causes all the neurodegenerative disorders like Parkinson's.

Could you talk a little bit about the patient experience and some of the complaints that you hear? Is it waking during deep REM periods that causes some of the symptoms that patients are vocal about and some of the stuff that's happening physiologically?

One thing to note is the tremor of Parkinson's goes away during sleep:

When people act out their dreams during sleep, the Parkinson's symptoms don't seem to show up as much. It seems like the motor pathway that's allowing people to act out their dreams is definitely different from what they're doing during their waking movements and speech.

The biggest complaint, however, is sleep fragmentation and disruptions. People without a sleep disorder or Parkinson's, for instance, might wake up, have a three-second arousal, not even realize it and just go back to sleep. Parkinson's patients, however, can have a tremor in that arousal window, waking them up further.

Parkinson's causes people to be bradykinetic, or slow-moving, but also very rigid or stiff. If you're sleeping in some position and you become uncomfortable, you just roll over and go back to sleep. But if you have to have your bed partner assist you to be able to roll over, or have to work hard to change position, then that leads to being much more awake.

Patients with Parkinson's also have autonomic dysfunction. They might have night sweats, or they have to get up to pee at night, disrupting their sleep.

What does treatment look like? Is it entirely on a case-by-case basis?

There are some things that we fall back on, but it is very personalized.

For example, if people are complaining of waking up a lot, we tend to do a sleep study to make sure there's no sleep apnea or other sleep disorders. It's an increased risk as people get older, and Parkinson's is also a disorder of aging.

Then we try to optimize treatment around sleep:

- REM sleep behavior disorder itself can be treated with medications. Melatonin can suppress the behaviors, and so can clonazepam.
- For insomnia, a lot of times the approach is related to behavioral changes. Making sure people are using the right types of sleep habits: not using electronics in bed, not staying in bed if they can't sleep—as long as they're safe to get up from the balance standpoint. Cognitive behavioral therapy often works for insomnia, too—usually better than medications.
- For daytime sleepiness we try to schedule naps—usually around when medications are taken. We try to limit naps to 20 minutes and not after 2 p.m. in order to avoid nighttime sleep disruption.
- Exercise is great for sleep. We found that exercise can increase sleep spindles and improve sleep efficiency, or the percentage of time you spend in bed that you are actually sleeping.

What specific types of exercise are you recommending to patients?

The most beneficial one that has the most evidence is probably the high intensity exercise—getting the heart rate up. Parkinson's patients sometimes do have balance trouble, so mitigating that with a stationary bike or water exercise can be helpful.

Ultimately, what I often tell patients is that the most important type of exercise is the exercise that you'll keep doing. We tell patients, "Try and view it as a prescription like your other medications."

Our prior research has shown that exercise does improve sleep efficiency and it increases slow wave sleep, that deepest stage of sleep,

which is important for cognition and thinking. We have an ongoing study where we are using mostly weightlifting or resistance training as an intervention.

Where are you hoping to take your research at CU Anschutz over the next few years, and where do you hope the field is headed?

There are a couple areas we're investigating:

- Exercise intervention: We're trying to understand more about the mechanisms of why exercise affects sleep and why that's important for cognition. We're looking at things like sleep spindles and the different EEG signatures during sleep.
- The disconnect between patient feeling and data: We're doing comprehensive sleep assessments because in Parkinson's, there's often a disconnect between what patients report about how they're sleeping and what we see on the sleep study.
- Inflammation: This is a big area of research. There are definitely increased pro-inflammatory factors in Parkinson's that aren't present in healthy aging, and not sleeping well or sleep apnea increases inflammation.
- Efficacy of different therapies: Deep brain stimulation is an excellent therapy for the movement symptoms of Parkinson's, and it seems to also improve sleep. So we're looking into those mechanisms and seeing if we can influence sleep at night.

Our ultimate goal is to cure Parkinson's or to slow down progression. In the absence of that, trying to improve the symptoms and quality of life is crucial.