

Parkinson's Disease Clinic and Research Center
University of California, San Francisco
505 Parnassus Ave., Rm. 798-M, Box 0114
San Francisco, CA 94143-0114
(415) 476-9276
<https://pdcenter.ucsf.edu>



Sleep and Parkinson's Disease

Introduction/Background

Sleep-Wake Cycle

Sleep is characterized by two alternating phases, rapid eye movement (REM) sleep and non-rapid eye movement sleep (NREM). These phases are defined by brain wave activity, muscle activity, and eye movements. As people start to fall asleep they enter into the lightest of the four stages of NREM sleep, Stage 1. As sleep continues, people descend into the deeper states of sleep down through Stages 2 and 3. Then, people move back up through these stages and enter a REM episode. When people are awakened during REM sleep, they often report having been dreaming.

Circadian Rhythms

This term refers to things that occur rhythmically roughly every 24 hours. The sleep-wake cycle is one of the most obvious of our body's circadian rhythms. Other circadian rhythms include body temperature and secretion of many hormones. These rhythms are controlled by a time-keeping mechanism (or clock) in our brains. This clock can be influenced by a variety of internal and external parameters, including aging, time-zone shifts, exercise, melatonin and the light-dark cycle. The light-dark cycle is the strongest external parameter affecting this clock.

Changes in Sleep with Aging

As people age, they experience a number of changes in their circadian rhythms, and among the most noticeable are the changes in the sleep-wake cycle. Older people tend to wake up earlier and go to bed earlier than they did when they were younger. They wake up more often during the night and have more difficulty going back to sleep than younger people. They also tend to sleep more during the daytime hours. Therefore, if one looks at total sleep time over the 24-hour day, the total time spent sleeping changes very little but the distribution of sleep may be quite different. Younger people experience a consolidated nighttime episode with little or no daytime sleep, whereas older individuals experience sleep episodes throughout the 24-hour day. Daytime sleepiness is affected by two major factors: the amount and quality of nighttime sleep, and the strength of the circadian rhythm. In addition, older people tend to have a reduced amount of N3 or deep slow wave sleep.

Sleep Disturbances in Parkinson's Disease

In general, research seems to indicate that people with Parkinson's disease have more sleep disruptions than similarly aged people without the disease. The most commonly reported sleep-related problems are the inability to sleep through the night and difficulty returning to sleep after awakening, generally referred to as maintenance insomnia. Unlike many older adults, patients

with Parkinson's disease often find that they have no trouble initiating sleep, but often wake up within a few hours and find sleeping through the rest of the night to be difficult. People with Parkinson's disease also report daytime sleepiness, nightmares, vivid dreams, nighttime vocalizations, leg movements/jerking while asleep, restless legs syndrome, inability to or difficulty turning over in bed, and awakenings to go to the bathroom.

Although all the reasons for these sleep changes are unknown, potential explanations include reactions to/side effects of medications (e.g. dopamine agonists, levodopa) and awakening due to symptoms such as pain, stiffness, urinary frequency, tremor, dyskinesia, depression and/or disease effects on the internal clock.

Insomnia

Insomnia is the inability to fall asleep or maintain sleep. The first step in treating insomnia is to initiate a "sleep hygiene program" as described below. Not all of these behaviors will be appropriate for everyone. Choose appropriate behaviors that fit your type of sleep problem: getting to sleep, staying asleep, moving in bed, or waking to go to the bathroom. Behaviors should be initiated one at a time, and their effect monitored over a week or more by using a diary (see evaluation, below).

Vivid Dreams and Nightmares

Vivid dreams or nightmares can be the result of a nighttime dose of dopamine medication. If the dreams are bothersome, the dose can be reduced or possibly eliminated. Other medications that can cause vivid dreams are hypnotics, especially triazolam. Some tricyclic antidepressants prescribed for depression or as a sleep aid can also cause nightmares. If acting-out dreams by movement or vocalization is present, REM behavior disorder (RBD) must be considered. RBD is very common in PD patients.. Evaluation may include referral for a nighttime sleep study. Treatment is considered for safety reasons and RBD can usually be controlled with medication.

Periodic Leg Movements of Sleep (PLMS) and Restless Legs Syndrome (RLS)

Leg movements are common in the elderly and even more so in people with Parkinson's disease. RLS typically occurs while at rest, and typically consists of an uncomfortable sensation in the legs that is relieved with movement. PLMS are jerking movements of the legs during sleep that are not uncomfortable but can result in nighttime awakenings. PLMS often do not bother an individual but can rarely be associated with sleep disruption. The movements are often reported by a bed partner. Both PLMS and RLS can result from medication side effects or medical conditions other than Parkinson's disease. After medical evaluation, treatment can include continuous release levodopa, dopamine agonists, and clonazepam.

Sleep Apnea

Although not necessarily more common in people with Parkinson's disease, sleep apnea is common in older adults. Obstructive sleep apnea (period of time with no or little breathing) is usually associated with snoring and complaints of excessive daytime sleepiness. Evaluation for apnea is by a nighttime sleep study and treatment is implemented by a sleep specialist.

Excessive Daytime Sleepiness and Unintended Sleep Episodes

For people with Parkinson's disease, daytime sleepiness may be caused by the many problems that interfere with nighttime sleep, resulting in sleep deprivation, or from the sedating effects of

antiparkinsonian medications. People with excessive daytime sleepiness tend to fall asleep during the day, and depending on the situation, can pose a safety hazard to themselves and others. Often the sleep episode is very short, and the person is unaware of having fallen asleep. Unintended sleep episodes have been attributed to dopamine agonist medication. However, research has shown that these episodes are not unique to the use of these medications. The unintended sleep episodes can be seen with any of the dopamine medications, including levodopa, and typically are evident with high doses.

Treatment for excessive daytime sleepiness should be discussed the individual's physician. A thorough evaluation of all medications, their side effects, and interactions must be considered. Sleep apnea, PLMS, and RLS need to be treated if present. PD medications can be changed or doses adjusted. For a significant minority of patients with Parkinson's disease, daytime fatigue is related to the disease process itself and even when other causes are excluded and medications are adjusted, they may still feel tired or fatigued during the daytime. Scheduled naps prior to 3pm and/or alerting medications such as modafinil and methylphenidate can be considered and are sometimes helpful. Caffeine may be an appropriate treatment, if not taken too late in the day.

Steps to Better Sleep Hygiene: Behavioral Changes

Getting to sleep

Regular risetime and bedtime—by doing this every day, you can help your internal clock by providing regular cues, thereby improving your sleep-wake cycle. This should help in getting to sleep faster and reduce the number of nighttime awakenings.

Get plenty of bright natural light exposure, preferably in the morning along with exercise. This will give your internal clock a strong cue to run on time.

Avoid stimulants, such as caffeine and nicotine. Avoid caffeine-containing drugs, drinks, and foods for eight hours before bedtime. Avoid tobacco in the evening. This will help with getting to sleep and staying asleep.

Avoid thoughts or discussions about topics that cause anxiety, anger, and frustration before bedtime. This will help with getting to sleep.

Institute and maintain a definite bedtime routine that is relaxing to help signal the body that sleep is to occur soon. Examples might include: a bath, brushing teeth, a small glass of warm milk (4-6 oz.), or a light snack. This will help with getting to sleep and will reduce the need to awaken due to hunger.

Reserve the bedroom and especially the bed for sleeping. Avoid activities like reading and watching television in bed. Your body needs cues to associate the bed with sleeping and not other activities.

If you nap, try to do so at the same time every day and for no more than 1 hour, and ending by 3pm.

Don't spend more than 15 minutes trying to sleep—if you cannot sleep after 15 minutes get out of bed and engage in a quiet activity. Ideally, the activity should be in low light and sedentary, for example, listening to soft relaxing music or meditating, not reading with a bright light or watching television. Return to bed only when you are sleepy.

Staying asleep

Minimize light and noise at bedtime and throughout the night. This will reduce stimulation and promote normal function of the body's melatonin rhythm that helps to promote and maintain sleep. Ear plugs may be helpful if the environment is noisy. Avoid alcohol within 4-6 hours of bedtime. When taken at bedtime, alcohol may help induce sleep but disrupts sleep later in the night.

Avoid heavy exercise within 6 hours of bedtime. Exercise increases the body temperature. Sleep onset normally occurs as the core body temperature is decreasing. Artificially increasing body temperature can therefore give the wrong cue to the brain and contribute to sleep disruption.

Avoid heavy late night meals. They can interfere with the ability to fall and stay asleep. A light snack at bedtime, however, may promote sleep. Good bedtime snacks include dairy products and carbohydrates.

Assure the bedroom environment is right for sleep: comfortable bed, dark, quiet, and a cool temperature for sleeping.

Avoid looking at the bedroom clock if you awaken. If necessary, face the clock to the wall.

Moving in bed

Use of satin sheets on the bed or pajamas to help with moving in bed can minimize the effects of stiffness or pain. (Also, see antiparkinsonian medications, below)

Waking to go to the bathroom

Decrease evening fluids (3-4 hours before bedtime) to lessen the chance of waking up to go to the bathroom. Make sure that you drink plenty of fluids in the morning hours. If you often get dizzy when you stand, sit on the side of the bed for a moment or two while flexing your leg muscles before you stand up.

Go to the bathroom immediately before retiring.

A commode placed at the bedside will minimize the activity and necessary light needed for nighttime toileting.

Evaluation of Sleep Hygiene Program: Sleep Diary

Monitoring the effectiveness of behavior changes is best done by keeping a diary. The table below depicts a sample diary that could be kept by the bedside and filled out upon arising by the patient or caregiver. If daytime sleepiness and napping are problems, items can be added to

record the number, time, and duration of napping episode. The diary can be carried with the patient.

Date	February 17	February 18	February 19
Treatment	No alcohol	No alcohol	No alcohol
What time did you turn the lights off ?	10:00pm		
How long did it take you to fall asleep?	15 minutes		
How many times did you wake up?	5		
What time did you wake up this morning?	6:15am		
When time did you get out of bed?	6:30am		
How many hours did you sleep last night?	8		
How well did you sleep?	7		
(Scale 1, poor, 10=excellent)			

Medications for Sleep

Sleeping pills

Historically, medications known as benzodiazepines have been widely used for insomnia in all ages. These medications are classified as short-, intermediate-, or long-acting. Short-acting benzodiazepines (e.g., triazolam) are useful when getting to sleep is the primary concern. However, their side effects include confusion, agitation, impaired motor performance, and amnesia. Intermediate-acting benzodiazepines (e.g., temazepam) are useful when sleep maintenance and/or early morning awakening are the primary symptoms. Long-acting benzodiazepines (e.g., flurazepam) are useful for getting to sleep and sleep maintenance, and when insomnia occurs with daytime anxiety. However, these drugs are often associated with daytime sleepiness and confusion. Newer, nonbenzodiazepine drugs, zolpidem (Ambien®), zolpidem CR (Ambien CR®), zaleplon (Sonata®) and ezopiclone (Lunesta®) have recently become available. These newer drugs seem to have a better safety profile, fewer complications with long-term use, and produce fewer daytime symptoms than the older sleeping medications.

Antidepressants

Tricyclic antidepressants and trazadone are frequently prescribed for sleep disturbances. Since depression is a common cause of sleep disturbances in patients with Parkinson's disease, these drugs can help treat both problems. The more sedating tricyclics (e.g., amitriptyline) are used to assist in sleep initiation and maintenance. These drugs must be monitored carefully as they have a high incidence of side effects such as constipation and dry mouth.

Antiparkinsonian medications

All of the antiparkinsonian medications can either help or hinder sleep depending on the problem. If symptoms of Parkinson's disease are causing the sleeping problem, the longer acting

levodopa formula at bedtime may help. Adding an agonist or COMT inhibitor may also maximize levodopa activity to prevent breakthrough symptoms during the hours of sleep. Levodopa can also have an alerting effect, and may need to be reduced at bedtime. Selegiline is also known to cause insomnia.

Bladder medications

To reduce the frequency of urination, medications such as oxybutynin and tolterodine are often used. These prescription medications work by relaxing the bladder.

Other insomnia interventions

In addition to a sleep hygiene program, other interventions may also be useful. These include sleep restriction programs, chronotherapy, bright light therapy, relaxation training, meditation, biofeedback, and cognitive therapy.

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