

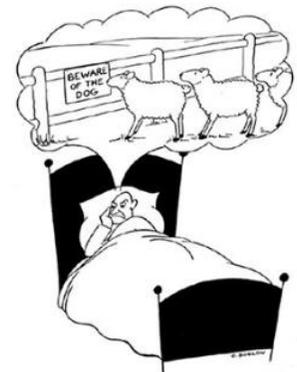
Accelerated Cure Project for MS

March 2019



The Elusive Forty Winks

According to the Irish proverb, “a good laugh and a long sleep are the two best cures for anything.” Both points certainly ring true. Regardless of one’s circumstances, maintaining a sense of humor is something to strive for. Unfortunately, a good night’s sleep can be much more fleeting. [Studies](#) show more than half of people living with MS have difficulty sleeping. This could be for a variety of reasons. Some may have to get up to use the bathroom frequently at night, while leg spasms or pain may awaken others. Some may be taking medications that cause insomnia. No matter what the cause, sleep deprivation can not only aggravate physical MS symptoms, such as balance and spasticity, but it can also worsen things like cognition and fatigue, which are harder to see, but equally disabling.



Sleep disturbance is a general term for a wide range of sleep-related symptoms and disorders. While people with MS may experience any (or multiple) of these conditions, there are several that they are more prone to. A [2014 study](#) from the University of California Davis (UC Davis) reported that 32% of people with MS experience moderate to severe insomnia. [Insomnia](#) is characterized by difficulty

initiating or maintaining sleep. Some of the most common MS symptoms, such as pain, bladder dysfunction, spasticity, overheating, stress, anxiety and depression, all have the potential to interfere with an individual’s ability to fall, or stay, asleep. Mobility issues may make it more difficult to shift positions in bed. The resulting discomfort from this can keep some people with MS awake. UC Davis researchers also found that 38% of people with MS have difficulty with [obstructive sleep apnea](#). Interestingly, overweight individuals are also more prone to this disorder. This type of [sleep-disordered breathing](#) (SDB) occurs when a person’s throat muscles relax too

much and their airway is temporarily blocked. While people with sleep apnea usually do not have trouble falling asleep, their breathing is affected once asleep, and the sudden inability to take a breath wakes them repeatedly throughout the night. There is [evidence](#) that people with progressive forms of MS and those with more severe disability are more likely to develop SDB. The above-mentioned study also showed that 37% of people with MS experience restless legs syndrome. [Restless legs syndrome](#) (RLS), also known as Willis-Ekbom Disease, is defined as a “neurologic disorder that is characterized by an overwhelming urge to move the legs when they are at rest.” According to the National Sleep Foundation, this urge is usually, but not always, accompanied by unpleasant sensations. In fact, several common MS symptoms, such as cramping, pain or spasticity, can be difficult to discern from RLS. The process underlying this condition is still poorly understood. It typically occurs in the evening or before bedtime, and is relieved by movement. Treatment involves medications, such as [Requip](#) (ropinirole). Reducing consumption of alcohol, caffeine, or nicotine can also be helpful. Other useful strategies include stretching, massaging, or applying hot (or cool) packs to the affected limb. There is evidence that [certain medications](#) can cause or worsen RLS. Other sleep disorders that are less common in people with MS include [hypersomnia](#) (difficulty with too much sleep), [narcolepsy](#) (uncontrollable lapses into sleep), or abnormal behaviors during sleep (such as acting out dreams). Individuals who think they may have a sleep disorder should consult with their healthcare team to identify any causative/contributing factors, and identify the best course of treatment.

Sleep disturbance is a known side effect of some medications commonly used to treat MS and its symptoms. For example, insomnia has been reported as a potential side effect of [Lemtrada](#) (alemtuzumab), an infusion therapy for RRMS. Insomnia and excessive daytime sleepiness are common side effects of [steroids](#) (which are frequently used to treat MS flares). Fortunately, the sleep disturbance from steroid use is temporary and usually resolves once treatment is finished. As mentioned in the article entitled “[Understanding and Living With MS Fatigue](#),” stimulant medications such as modafinil, amantadine and methylphenidate are often prescribed to treat MS-related fatigue. Stimulants can cause restlessness and disrupt sleep. Fortunately, adjusting the dosage and timing of administration can help mitigate these side effects.

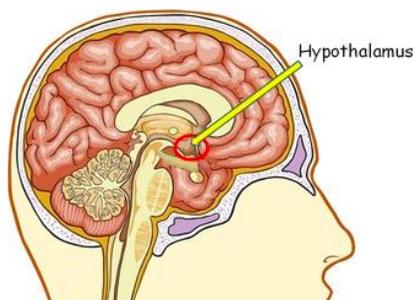


There are many tools available to help diagnose sleep disorders. It’s important to note that anyone having difficulty sleeping should have a physical examination to rule out any underlying medical causes before undergoing such an evaluation. [Sleep logs](#) (or diaries) are used to record valuable information related to an individual’s sleep habits and history. These diaries are typically completed by individuals on a daily basis over a period of several months, and include such information as estimated time to fall asleep, quality of sleep, number of awakenings, wake-up time and medication use. This information can be very useful to a diagnosing physician. A sleep study, or [polysomnogram](#) (PSG), is a test that records specific physical activities, such as brain waves, heart rate, breathing rate, eye movement, muscle activity, and blood oxygen levels during sleep. These data are then analyzed to determine a diagnosis. There are different types of sleep study. The [Multiple Sleep Latency Test](#) (MSLT), or nap study, measures the tendency to fall asleep, while your brain waves, chin-



muscle activity, and eye movements are recorded. The [Maintenance of Wakefulness Test](#) is similar to the MSLT, but measures your ability to stay awake in a non-stimulating environment. [Actigraphy](#) is the continuous measurement of activity or movement over an extended period of time with the use of a device called an actigraph. An actigraph is a small, lightweight device that is typically worn on a wrist or an ankle. Actigraphy can be performed at home, which is a benefit over PSG, which typically involves an overnight stay in a sleep clinic (or related clinical facility).

Researchers are working to better understand the causes of sleep disturbance in MS. A number of possible mechanisms are being investigated, including damage to key areas of the brain that are involved in sleep. The [hypothalamus](#) is a region of the brain responsible for many of the body's essential hormones and physiological processes. A [recent study](#) suggests that lesions in this area of the brain may cause hypersomnia and narcolepsy. The [suprachiasmatic nucleus](#) is a region of the hypothalamus responsible for maintaining our 24-hour body clock. Nerve damage to this area can make it difficult to maintain a consistent [sleep-wake cycle](#). The [brain stem](#) is, as the name implies, the "stem-like" part of the base of the brain that is connected to the spinal cord. It plays a key role in regulating breathing and other autonomic (involuntary) nervous system functions during sleep. [Research](#) shows lesions or damage to this area can result in sleep apnea. Damage to the hypothalamus can also disrupt key



neurotransmitters involved in sleep. For example, [hypocretin](#) (also known as orexin) is an important molecule produced by the hypothalamus that helps to regulate sleep and arousal states. Abnormally low levels of hypocretin can result in narcolepsy. The hormone [melatonin](#) plays an important role in regulating sleep-wake cycles. Melatonin is produced by the [pineal gland](#) (which is regulated by the hypothalamus). Lower levels of melatonin have been associated with poor sleep quality. A [recent study](#) linked vitamin D deficiency with a higher risk of sleep disorders in the general population.

Given that people with MS are more prone to vitamin D deficiency, additional research is needed to assess the relationship between vitamin D and sleep in MS.

Treating sleep disorders in MS can be quite challenging due to their many potential causes. In instances where the disturbance is secondary to a particular MS symptom (for example, urinary dysfunction or RLS), effective treatment of the sleep disorder may be obtained by remedying the underlying cause. [Sedative medications](#) may also be prescribed for short-term treatment of insomnia. Unfortunately, these drugs are often ineffective, are associated with a number of side effects, and are not recommended for long-term use. [Tricyclic antidepressants](#) are sometimes used to treat sleep disorders because they are sedating.

Many people find melatonin supplements to be helpful. If used occasionally, antihistamines like [Benadryl](#) (diphenhydramine hydrochloride) can be taken for their sedating side effects. Medical equipment may also be used to treat sleep disorders. [Continuous Positive Airway Pressure](#) (CPAP) therapy is frequently used to help those struggling with sleep apnea. CPAP machines usually consist of a nosepiece or facemask connected to an air pump that delivers consistent oxygen flow to keep the airway open during sleep. A [CPAP titration study](#) is frequently done in combination



with PSG to measure airflow through the nose and mouth during sleep in order to determine the appropriate therapy for each individual. [Bright light therapy](#) can be effective for treating individuals whose sleep-wake cycles are disrupted. This type of therapy is used to expose an individual's eyes to intense, but safe, amounts of light for a specific and regular length of time. It may be delivered via a [light box](#) or [light therapy glasses](#). Of note, it's important to consult a physician when considering bright light therapy, as it is contraindicated in some medical conditions (such as, diabetes) and for those on certain medications (for example, melatonin or certain antibiotics).

In some cases, sleep problems can be solved without medication. [Cognitive Behavioral Therapy](#) (CBT) focuses on identifying and replacing unhelpful thoughts and behaviors with more beneficial strategies. CBT for insomnia (CBT-I) is a type of CBT that specifically focuses on identifying and changing unhelpful thoughts and behaviors that interfere with sleep. Key components of CBT-I include keeping a weekly sleep diary, using the bed only for sleep and intimacy, practicing good [sleep hygiene](#), and using relaxation, meditation or mindfulness strategies. To cope with fatigue, people with MS often feel the need to sleep during the day. Limiting the duration of naps and taking care not to take them too close to bedtime may help one sleep more soundly at night. Many people with MS find fatigue and physical disability often lead to decreased physical activity, however, exercise is important for regulating sleep (and it doesn't have to be rigorous to provide benefits). According to the National Sleep Foundation, if sleep still isn't possible after 20 minutes in bed, one should not lie awake in the middle of the night and watch the clock. This can create an unhealthy link between the sleep environment and the inability to sleep. Moving to another space to do a relaxing activity, such as reading or listening to music, before returning to bed may be more helpful.



Awareness and treatment of sleep disorders is vital for improving the health and quality of life for people living with MS. Sleep deprivation is common in people with MS, and many find their symptoms are worsened as a result. Fortunately, there are many options to help in this regard, including both behavioral and pharmaceutical remedies. Just as each individual's journey with MS is unique, so are the solutions to any problems they may face along the way (including any sleep disorder they may be struggling with). It is very important for people with MS to discuss any concerns about the amount or quality of sleep they are getting with their healthcare team (among other things) and work with them toward the best solution.

