



Sleep and Multiple Sclerosis

Waking up to sleep problems and their consequences in multiple sclerosis.

By Tiffany J. Braley, MD, MS



Although sleep disturbances have become increasingly recognized for their contributions to adverse health, cognitive, and occupational consequences in the general population, the potential effects of pathologic sleep on the disease course, response to treatment, and function of persons with multiple sclerosis (MS) have yet to be fully realized. Sleep disturbances affect up to 60% of people with MS, and recent research suggests that common sleep disorders including obstructive sleep apnea (OSA), chronic insomnia, and restless legs syndrome (RLS) contribute to substantial morbidity in this population. Because sleep disorders are often treatable, a keen knowledge of their causes, consequences, presentations, and management are critical to providing optimal MS care.

Common Sleep Disorders

OSA

OSA is a chronic sleep disorder characterized by repeated episodes of upper airway obstruction and hypoxia during sleep. Although OSA affects up to 20% of people in the US,^{1,2} recent estimates suggest 20% to 50% of people with MS are at risk for OSA.^{3,4} The biologic basis for this increased association is still unknown. Although persons with MS are susceptible to the same OSA risk factors as the general population, additional risk factors associated with MS, including impairment of brainstem networks that control airway patency and respiratory drive, may increase the risk or severity of OSA in this population.^{5,6} Increased disability level and use of centrally-acting medications may also confer additional risk.⁷

In addition to cardiovascular disease, depression, and metabolic syndrome (which may independently contribute to MS disability),^{2,8-10} OSA is associated with several of the most impactful chronic MS symptoms, including cognitive dysfunction and fatigue. OSA severity, as well as nocturnal arousals and reduced sleep time are significantly associated with diminished memory, executive function, attention, and processing speed in people with MS.¹¹ Additional research is under way to determine whether positive airway pressure therapy (PAP) therapy, the guideline-standard treatment for OSA, improves cognitive function in people with MS who have OSA.^a If a

causal pathway between OSA and cognitive impairment exists, sleep-based interventions such as PAP could provide new opportunities to alleviate this challenging MS symptom.

In addition to excessive daytime sleepiness—a more commonly recognized consequence of sleep problems—a growing body of work also suggests OSA contributes to fatigue, which is among the most common and disabling symptoms of MS. Although fatigue may have several causes within an individual, sleep disorders, including sleep apnea, have been linked to fatigue in multiple prior studies.^{3,4,12} Furthermore, previous work suggests that PAP use effectively reduces sleepiness¹³ and may improve fatigue in people with MS.¹⁴ Large-scale clinical trials are still needed to demonstrate the effects of PAP on fatigue and other MS-related symptoms.

Insomnia

Insomnia is characterized by difficulty initiating or maintaining sleep and can exist as a symptom or a formal sleep disorder. Insomnia is classified as a sleep disorder only when it is associated with some form of distress about poor sleep; leads to impaired social, academic, or vocational functioning; and occurs despite adequate opportunities for sleep.¹⁵ As a symptom, insomnia may affect up to 40% of people with MS.³

Interestingly, many salient features of daytime impairment that characterize insomnia disorder overlap with some of the most common chronic MS symptoms. Fatigue, mood disturbances, cognitive dysfunction, and vocational difficulties, which are considered core features of insomnia disorder are common in MS and highlight the importance of screening for insomnia in those who experience these symptoms.

Potential causes of insomnia in people with MS include psychophysiologic factors, medical causes, or symptoms related to MS. Some common MS symptoms, including chronic pain, neurogenic bladder, spasticity, anxiety, and depression, all have the potential to interfere with sleep initiation, sleep maintenance, or sleep perception^{3,16} and should be viewed as potential exacerbating factors for insomnia. Concomitant sleep disorders such as OSA, RLS, or circadian rhythm disorders can also contribute to difficulty falling or staying asleep and should be considered during the workup. Nocturnal patterns of insomnia may vary by cause. For example,



sleep-onset insomnia, or difficulty falling asleep, is commonly associated with states of hyperarousal (including psychophysiologic insomnia), RLS, or chronic pain, whereas sleep-maintenance insomnia may be more likely to arise from OSA or neurogenic bladder.¹⁶ Identification of underlying causes can aid in management.

RLS

RLS is a neurologic disorder characterized by restlessness or an uncomfortable sensation of the lower extremities that is exacerbated by rest and inactivity, tends to occur in the evening or before bedtime, and is relieved with movement.^{17,18}

RLS is classified as idiopathic (primary) if no other cause is identified, or secondary if associated with another comorbid medical or neurologic condition known to increase vulnerability, such as MS.¹⁵ For primary RLS, a genetic etiology is favored,¹⁹⁻²¹ and dysfunction of brain circuits that require the neurotransmitter dopamine have been implicated in the pathogenesis.²² Although reasons for the association between MS and RLS are still not fully understood, damage to downstream dopaminergic pathways that project to the spinal cord has been postulated as a potential cause.²³ Via dopaminergic transmission, these pathways are responsible for the suppression of sensory inputs and motor excitability and are susceptible to damage from diseases that affect the spinal cord.²⁴⁻²⁶ Specific MS features that reflect disease severity, including progressive MS subtype, increased disability level, and cervical cord damage have been linked to RLS within people with MS.^{26,27} Certain medications, including antiemetics, antipsychotic dopamine antagonists, antidepressants, and antihistamines²⁸ can also cause or worsen RLS.²⁹⁻³¹

RLS is characterized by 4 essential criteria: 1) presence of a restlessness or uncomfortable sensation in the lower extremities or, less commonly, the upper extremities; 2) exacerbation with rest and inactivity; 3) presence in the evening or before bedtime (ie, a circadian component); and 4) amelioration with movement.¹⁷ In addition, the International Classification of Sleep Disorders-3 criteria require that the symptoms are not better accounted for by another medical or behavioral condition and that symptoms cause some form of concern, distress, sleep disturbance, or daytime impairment for the individual. Many descriptors can be used to describe the restless sensation, including creeping, crawling, burning, tightening, or tingling—symptoms that can be conflated with common symptoms of MS, such as nocturnal spasticity. Some people will describe this sensation as painful.³²

Untreated RLS is associated with adverse health consequences, positioning it as an important yet often under-recognized comorbidity. Prior work suggests RLS contributes to both sleep-onset insomnia and excessive daytime sleepiness.^{33,34} For those with MS, specifically, RLS has also been associated with fatigue and reduced quality of life,^{35,36} making

recognition and treatment of this condition an essential component of symptom management.

Diagnostic Considerations

Some of the most consequential and yet treatable sleep disorders among persons with MS include chronic insomnia, OSA, and RLS. Because these disorders are significantly under-recognized in people with MS,^{3,4} clinicians who treat people with MS should maintain a low threshold to screen for sleep disturbances and initiate diagnostic workups if clinically indicated. Symptoms of daytime dysfunction—as opposed to reported problems with sleep—may be the chief complaint and may be perceived as worsening of MS without careful questioning. A systematic approach that accounts for clinical features of MS will enhance recognition of sleep disorders and facilitate appropriate treatment. Sleep specialty referrals should be considered for conditions that require polysomnography (PSG) for diagnosis and complex cases that present a diagnostic or therapeutic challenge.

Brief screening questionnaires may be useful to determine who is most likely to benefit from more extensive sleep evaluation. The Insomnia Severity Index (ISI) is a useful instrument, consisting of 7 questions designed to assess the nature, severity, and impact of insomnia in adults.³⁷ This tool does not allow assessment of opportunity and circumstances for sleep, however, and these factors must be assessed separately to ensure that such habits and environment are not contributing to the sleep disturbance. Elevated ISI scores should prompt a more comprehensive sleep history with assessment of MS-specific symptoms and medications that can interfere with sleep.

For OSA, the STOP-BANG questionnaire is an 8-item screening test, forming the acronym STOP-BANG.³⁸ A recent validation study showed reasonably high sensitivity for moderate-to-severe OSA in people with MS and good negative predictive

The STOP-BANG Checklist for Obstructive Sleep Apnea

- ☐ **S** Snoring heard by others
- ☐ **T** Tired, fatigued or sleepy in daytime
- ☐ **O** Observation of gasping/choking/loss of breath during sleep
- ☐ **P** Pressure (hypertension)
- ☐ **B** Body mass index >35
- ☐ **A** Age >50
- ☐ **N** Neck size >16 inches
- ☐ **G** Gender (men's risk>women's)



value for OSA in the context of MS.³⁹ Scores of 3 or more should prompt consideration of PSG for diagnostic evaluation. Because the STOP-BANG does not account for potential MS-specific OSA risk factors (eg, brainstem pathology), however, a low score should not supersede clinical suspicion.

Considering potential overlap between RLS features and chronic MS symptoms (eg, cramping, clonus, spasticity, or neuropathic pain)⁴⁰ the Restless Legs Syndrome Diagnostic Index (RLS-DI) may be a useful tool to rule out false-positive diagnoses. The RLS-DI is a 10-item questionnaire designed to improve diagnostic decision making in suspected cases of RLS.⁴¹ This instrument incorporates essential RLS diagnostic criteria with additional supportive criteria that can be useful to rule out RLS mimics (eg, nocturnal spasticity). Asking whether the nocturnal movements seem voluntary (suggesting RLS) or involuntary (suggesting spasticity or clonus) can be helpful. Overnight PSG is not required to diagnose RLS.

Treatment Considerations

Amelioration of precipitating causes of insomnia is a cardinal step in management of the condition. Medications or substances that may contribute to insomnia should be reduced or discontinued, if possible. If stimulants are needed, earlier administration should be discussed. Comorbid nocturnal symptoms (eg, spasticity, pain, neurogenic bladder) should be addressed. If comorbid symptoms are not significant contributors, or if insomnia persists despite adequately addressing these issues, behavioral therapies can be considered. Adherence to healthy sleep hygiene should be prioritized. If a more formalized regimen is necessary, cognitive behavioral therapy for insomnia (CBT-I) is suggested. CBT-I promotes healthy sleep habits and strategies to correct psychologic processes and cognitive distortions that can perpetuate insomnia. Multiple randomized controlled trials have demonstrated the effectiveness of CBT-I among those with and without MS.^{42,43} Pharmacologic therapies (benzodiazepine agonists, melatonin receptor agonists, orexin receptor antagonists) can be considered if more conservative strategies have been exhausted or are not fully effective.

Positive airway pressure (PAP) therapy remains the criterion-standard treatment for OSA in people with MS. Selection of a mask interface should take into account MS-specific symptoms or limitations (eg, trigeminal neuralgia or dexterity issues). Although surgical approaches for OSA including newer hypoglossal nerve stimulators are also available, the potential for neurologic progression among people with MS makes surgery less attractive as a permanent solution. Certain MRI procedures may also be contraindicated with hypoglossal nerve stimulators, which may be a factor for the majority of people with MS who

require MRI for disease surveillance. Careful consideration of potential postsurgical risks in the setting of immunosuppressive therapy is also necessary and should involve consultation with an MS specialist.

Treatment for RLS begins with minimizing exacerbating factors (eg, dopamine antagonists, lithium, selective serotonin/norepinephrine reuptake inhibitors (SS/NRIs), antihistamines, tricyclics, alcohol, tobacco, or caffeine). Iron supplementation should be implemented in the context of low ferritin levels. As in those without MS, pharmacologic treatment should be individualized based on symptom frequency and severity. Although dopamine agonists may be considered, the alpha-2-delta ligands gabapentin and pregabalin may be more ideal choices for those with concomitant neuropathic pain or seizures, or for anyone who has experienced side effects or augmentation from dopaminergic agents.

Although successful treatment of sleep disturbances may improve symptoms exacerbated by underlying sleep disorders, chronic MS symptoms, and fatigue in particular, may require additional management especially if fatigue is multifactorial. Existing interventions include behavioral and pharmacologic strategies. In a recent double-blind, placebo-controlled cross-over study of modafinil, amantadine, and methylphenidate—the most commonly used agents to treat fatigue in people with MS—none were shown to be superior to placebo, leading the authors to conclude indiscriminate use could not be supported. Study limitations included lack of adjustment for concomitant sleep disorders or activity level, fixed medication dosing schedules, short treatment intervals, and submaximal dosing of modafinil and methylphenidate.⁴⁴ Nonetheless, given these findings and other trials to date, widespread use of these medications is not recommended, but can be considered on a case-by-case basis in the context of the overall clinical picture.

Among nonpharmacologic options, cognitive behavioral therapy (CBT) is considered first-line therapy for MS fatigue. CBT promotes self-management skills, including adaptive thought processes and behaviors, goal-setting, and behavioral activation strategies to manage symptoms. Indeed, CBT has been shown to ameliorate MS fatigue in clinical trials and can be effectively delivered virtually.⁴⁵⁻⁵⁰ Despite success of combination behavioral/pharmacologic strategies for the treatment of other chronic symptoms (eg, depression and insomnia), use of multimodal strategies for MS fatigue has received insufficient attention. Additional research to determine if medications combined with behavioral approaches, such as CBT, could provide additional benefit and offer a more pragmatic approach to fatigue treatment in people with MS. A pragmatic trial to study the effects of modafinil and CBT combination therapy on MS fatigue, in the context of important effect modifiers including sleep disorders, is under way.⁵¹



A growing body of research also highlights exercise as a promising intervention for MS fatigue, associated with significant, moderate reductions on fatigue severity. Variability in exercise interventions and fatigue measures in prior trials, however, preclude formal recommendations regarding specific exercise regimens for MS fatigue to date.⁵²

Conclusion

Sleep disorders are prevalent yet under-recognized contributors to morbidity in people with MS. Recognition and prompt treatment of these consequential conditions offer an important opportunity to optimize health and quality of life. ■

- Peppard PE, Young T, Barnett JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiol*. 2013;177(9):1006-1014.
- Gottlieb DJ, Yenokyan G, Newman AB, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the sleep heart health study. *Circulation*. 2010;122(4):352-360.
- Braley TJ, Segal BM, Chervin RD. Obstructive sleep apnea and fatigue in patients with multiple sclerosis. *J Clin Sleep Med*. 2014;10(2):155-162.
- Brass SD, Li CS, Auerbach S. The underdiagnosis of sleep disorders in patients with multiple sclerosis. *J Clin Sleep Med*. 2014;10(9):1025-1031.
- Braley TJ, Segal BM, Chervin RD. Sleep-disordered breathing in multiple sclerosis. *Neurology*. 2012;79(9):929-936.
- Levit E, Bouley A, Baber U, Djonicic L, Sloane JA. Brainstem lesions are associated with sleep apnea in multiple sclerosis. *Mult Scler J Exp Transl Clin*. 2020;6(4):2055217320967955.
- Braley TJ, Chervin RD. A practical approach to the diagnosis and management of sleep disorders in patients with multiple sclerosis. *Ther Adv Neurol Disord*. 2015;8(6):294-310.
- Redline S, Yenokyan G, Gottlieb DJ, et al. Obstructive sleep apnea-hypopnea and incident stroke: the sleep heart health study. *Am J Respir Crit Care Med*. 2010;182(2):269-277.
- Acker J, Richter K, Pielh A, Herold J, Ficker JH, Niklewski G. Obstructive sleep apnea (OSA) and clinical depression-prevalence in a sleep center. *Sleep Breath*. 2017;21(2):311-318.
- Fitzgerald KC, Damian A, Conway D, Mowry EM. Vascular comorbidity is associated with lower brain volumes and lower neuroperformance in a large multiple sclerosis cohort. *Mult Scler*. 2021;1352458520984746.
- Braley TJ, Kratz AL, Kaplish N, Chervin RD. Sleep and cognitive function in multiple sclerosis. *Sleep*. 2016;39(8):1525-1533.
- Veauthier C, Blau A, Paul F. 'Obstructive sleep apnea is associated with fatigue in multiple sclerosis' by Kaminska et al. *Mult Scler*. 2013;19(3):372-373.
- Chotinaiwattarakul W, O'Brien LM, Fan L, Chervin RD. Fatigue, tiredness, and lack of energy improve with treatment for OSA. *J Clin Sleep Med*. 2009;5(3):222-227.
- Cote I, Trojan DA, Kaminska M, et al. Impact of sleep disorder treatment on fatigue in multiple sclerosis. *Mult Scler*. 2013;19(4):480-489.
- International Classification of Sleep Disorders (ICSD-3): Diagnostic and Coding Manual. In. 3rd ed. Darien, IL2014.
- Stanton BR, Barnes F, Silber E. Sleep and fatigue in multiple sclerosis. *Mult Scler*. 2006;12(4):481-486.
- Allen RP, Picchietti D, Henning WA, et al. Restless legs syndrome: diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med*. 2003;4(2):101-119.
- Henning W, Allen RP, Tenzer P, Winkelman JW. Restless legs syndrome: demographics, presentation, and differential diagnosis. *Geriatrics*. 2007;62(9):26-29.
- Pichler I, Hicks AA, Pramstaller PP. Restless legs syndrome: an update on genetics and future perspectives. *Clin Genet*. 2008;73(4):297-305.
- Winkelmann J, Polo O, Provini F, et al. Genetics of restless legs syndrome (RLS): State-of-the-art and future directions. *Mov Disord*. 2007;22 Suppl 18:S449-458.
- Winkelmann J, Schormair B, Lichtner P, et al. Genome-wide association study of restless legs syndrome identifies common variants in three genomic regions. *Nat Genet*. 2007;39(8):1000-1006.
- Cervenka S, Palhagen SE, Comley RA, et al. Support for dopaminergic hypoactivity in restless legs syndrome: a PET study on D2-receptor binding. *Brain*. 2006;129(Pt 8):2017-2028.
- Frauscher B, Loscher W, Hogg B, Poewe W, Kofler M. Auditory startle reaction is disinhibited in idiopathic restless legs syndrome. *Sleep*. 2007;30(4):489-493.
- Telles SC, Alves RC, Chadi G. Periodic limb movements during sleep and restless legs syndrome in patients with ASIA A spinal cord injury. *J Neurol Sci*. 2011;303(1-2):119-123.
- Manconi M, Fabbini M, Bonanni E, et al. High prevalence of restless legs syndrome in multiple sclerosis. *Eur J Neurol*. 2007;14(5):534-539.
- Manconi M, Rocca MA, Ferini-Strambi L, et al. Restless legs syndrome is a common finding in multiple sclerosis and correlates with cervical cord damage. *Mult Scler*. 2008;14(1):86-93.
- Italian RSG, Manconi M, Ferini-Strambi L, et al. Multicenter case-control study on restless legs syndrome in multiple sclerosis: the REMS study. *Sleep*. 2008;31(7):944-952.
- Braley TJ, Segal BM, Chervin RD. Hypnotic use and fatigue in multiple sclerosis. *Sleep Med*. 2015;16(1):131-137.
- Hoque R, Chesson AL, Jr. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: literature review, qualitative scoring, and comparative analysis. *J Clin Sleep Med*. 2010;6(1):79-83.
- Lutz EG. Restless legs, anxiety and caffeineism. *J Clin Psychiatry*. 1978;39(9):693-698.
- Pigeon WR, Yurcheshen M. Behavioral sleep medicine interventions for restless legs syndrome and periodic limb move-

- ment Disorder. *Sleep Med Clin*. 2009;4(4):487-494.
- Bassetti CL, Mauerhofer D, Gugger M, Mathis J, Hess CW. Restless legs syndrome: a clinical study of 55 patients. *Eur Neurol*. 2001;45(2):67-74.
- Fulda S, Wetter TC. Is daytime sleepiness a neglected problem in patients with restless legs syndrome? *Mov Disord*. 2007;22 Suppl 18:S409-413.
- Allen RP, Picchietti DL, Garcia-Borreguero D, et al. Restless legs syndrome/Willis-Ekbom disease diagnostic criteria: updated International Restless Legs Syndrome Study Group (IRLSSG) consensus criteria—history, rationale, description, and significance. *Sleep Med*. 2014;15(8):860-873.
- Cederberg KL, Jeng B, Sasaki JE, Braley TJ, Walters AS, Motl RW. Restless legs syndrome and health-related quality of life in adults with multiple sclerosis. *J Sleep Res*. 2020;29(3):e12880.
- Giannaki CD, Aristotelous P, Stefanakis M, et al. Restless legs syndrome in Multiple Sclerosis patients: a contributing factor for fatigue, impaired functional capacity, and diminished health-related quality of life. *Neural Res*. 2018;40(7):586-592.
- Morin CM, Belleville G, Belanger L, Ivers H. The Insomnia Severity Index: psychometric indicators to detect insomnia cases and evaluate treatment response. *Sleep*. 2011;34(5):601-608.
- Chung F, Subramanyam R, Liao P, Sasaki E, Shapiro C, Sun Y. High STOP-Bang score indicates a high probability of obstructive sleep apnea. *Br J Anaesth*. 2012;108(5):768-775.
- Singh M, Gavidia R, Dunietz GL, et al. Validation of an obstructive sleep apnea symptom inventory in persons with multiple sclerosis. *Mult Scler J*. (in press) doi: 10.1177/13524585211013014
- Henning WA, Allen RP, Washburn M, Lesage SR, Earley CJ. The four diagnostic criteria for restless legs syndrome are unable to exclude confounding conditions ("mimics"). *Sleep Med*. 2009;10(9):976-981.
- Benes H, Kohnen R. Validation of an algorithm for the diagnosis of Restless Legs Syndrome: The Restless Legs Syndrome-Diagnostic Index (RLS-DI). *Sleep Med*. 2009;10(5):515-523.
- Edinger JD, Means MK. Cognitive-behavioral therapy for primary insomnia. *Clin Psychol Rev*. 2005;25(5):539-558.
- Edinger JD, Wohlgemuth WK, Radtke RA, Marsh GR, Quillian RE. Cognitive behavioral therapy for treatment of chronic primary insomnia: a randomized controlled trial. *JAMA*. 2001;285(14):1856-1864.
- Nourbakhsh B, Revirajan N, Morris B, et al. Safety and efficacy of amantadine, modafinil, and methylphenidate for fatigue in multiple sclerosis: a randomised, placebo-controlled, crossover, double-blind trial. *Lancet Neurol*. 2021;20(1):38-48.
- Asano M, Berg E, Johnson K, Turpin M, Finlayson ML. A scoping review of rehabilitation interventions that reduce fatigue among adults with multiple sclerosis. *Disabil Rehabil*. 2015;37(9):729-738.
- Asano M, Finlayson ML. Meta-analysis of three different types of fatigue management interventions for people with multiple sclerosis: exercise, education, and medication. *Mult Scler Int*. 2014;2014:798285.
- Beckerman H, Blikman LJ, Heine M, et al. The effectiveness of aerobic training, cognitive behavioural therapy, and energy conservation management in treating MS-related fatigue: the design of the TREFAMS-ACE programme. *Trials*. 2013;14:250.
- van den Akker LE, Beckerman H, Collette EH, Eijssen IC, Dekker J, de Groot V. Effectiveness of cognitive behavioral therapy for the treatment of fatigue in patients with multiple sclerosis: a systematic review and meta-analysis. *J Psychosom Res*. 2016;90:33-42.
- van den Akker LE, Beckerman H, Collette EH, et al. Cognitive behavioral therapy positively affects fatigue in patients with multiple sclerosis: results of a randomized controlled trial. *Mult Scler*. 2017;23(11):1542-1553.
- Ehde DM, Elzei JL, Verrall AM, Gibbons LE, Smith AE, Amtmann D. Efficacy of a Telephone-Delivered Self-Management Intervention for Persons With Multiple Sclerosis: A Randomized Controlled Trial With a One-Year Follow-Up. *Arch Phys Med Rehabil*. 2015;96(11):1945-1958 e1942.
- Kratz AL, Alschuler KN, Ehde DM, et al. A randomized pragmatic trial of telephone-delivered cognitive behavioral-therapy, modafinil, and combination therapy of both for fatigue in multiple sclerosis: the design of the "COMBO-MS" trial. *Contemp Clin Trials*. 2019;84:105821.
- Heine M, van de Port I, Rietberg MB, van Wegen EE, Kwakkel G. Exercise therapy for fatigue in multiple sclerosis. *Cochrane Database Syst Rev*. 2015(9):CD009956.

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