

Companion Guide:

The Critical Role of Healthy Sleep Habits for People with Epilepsy

INTRODUCTION

This guide was designed to assist healthcare providers in understanding the intricate relationship between sleep and epilepsy. As a companion to a video resource, it provides actionable insights to enhance patient care. The guide explores the bidirectional link between sleep and epilepsy, effective screening strategies, and evidence-based interventions to help patients adopt healthier sleep habits.

IN THIS COMPANION GUIDE:

Sleep, Interictal Epileptiform Discharges (IEDs) and Seizures	. 2
Sleep and IEDs	2
Impact of Sleep on Epilepsy	
Impact of Epilepsy on Sleep	. 2
Epilepsy and Sleep Disorders	7
Screening for Sleep Issues	4
Effective Screening Tools	
Routine Sleep Assessments	4
Sleep Hygiene Tips for Epilepsy Patients	
Managing Insomnia: Pharmacological and Behavioral Treatments	
Pharmacological Treatment	
Behavioral Treatment	7
Melatonin Use for Sleep in Patients with Epilepsy	



Sleep, Interictal Epileptiform Discharges (IEDs) and Seizures

SLEEP AND IEDS



NREM Sleep

IEDs are more frequent during non-rapid eye movement (NREM) sleep. This increased frequency is due to the synchronization of neuronal activity during these stages, which facilitates the occurrence of IEDs. [1,2]

IMPACT OF SLEEP ON EPILEPSY

Seizure Modulation by Sleep Stages

Seizures are more likely to occur during NREM sleep compared to REM sleep. Interictal epileptiform discharges (IEDs) are also more frequent during NREM sleep. [4, 5]

Circadian Rhythms

Over 90% of people with epilepsy exhibit circadian periodicity in their seizures, with many seizures occurring during sleep or transitions between sleep stages. [4]

Sleep Deprivation

Lack of sleep can exacerbate seizure frequency and severity. Sleep deprivation is a known trigger for seizures in many patients with epilepsy. [6]



REM Sleep

In contrast, rapid eye movement (REM) sleep tends to suppress IEDs, although breakthrough epileptic activity during REM sleep can help localize the seizure onset zone. [3]

IMPACT OF EPILEPSY ON SLEEP

Sleep Architecture Disruption

Epilepsy can lead to fragmented sleep, increased sleep latency, frequent awakenings, and reduced sleep efficiency. Patients with epilepsy often experience less REM sleep and more disruptions during sleep.[7]

Nocturnal Seizures

Seizures occurring during sleep can lead to awakenings and arousals, further disrupting sleep continuity and quality.[5]

Comorbid Sleep Disorders

Sleep disorders such as sleep apnea are more prevalent in patients with epilepsy and can worsen seizure control. Treatment of sleep apnea has been shown to reduce seizure frequency in some cases.[4]



EPILEPSY AND SLEEP DISORDERS

The most common sleep disturbances in patients with epilepsy include insomnia, obstructive sleep apnea (OSA), excessive daytime sleepiness (EDS), and parasomnias such as REM sleep behavior disorder (RBD) and confusional arousals.

Insomnia

Insomnia is highly prevalent among epilepsy patients, with studies indicating that it affects between 28.9% and 74.4% of adults with epilepsy. Insomnia can manifest as difficulty falling asleep, maintaining sleep, or experiencing non-restorative sleep. [4,5]

Obstructive sleep apnea (OSA)

Obstructive sleep apnea (OSA) is also common, with a higher prevalence in epilepsy patients compared to the general population. OSA is associated with increased seizure frequency and can be exacerbated by the use of multiple anti-seizure medications (ASMs) and longer duration of epilepsy. [4,6]

Excessive daytime sleepiness (EDS)

Excessive daytime sleepiness (EDS) is frequently reported, often due to poor nocturnal sleep quality, nocturnal seizures, or the sedative effects of ASMs. [7, 8]

Parasomnias

Parasomnias, including REM sleep behavior disorder (RBD) and confusional arousals, are more frequent in patients with drug-resistant epilepsy. [9]

These sleep disturbances significantly impact seizure control and overall sleep health. Poor sleep quality and sleep disorders can exacerbate seizure frequency and severity. For instance, insomnia and OSA are linked to increased seizure activity, and effective management of these sleep disorders can lead to better seizure control.[1,3,7] Additionally, disrupted sleep architecture, such as decreased REM sleep and increased wake after sleep onset, can impair cognitive function and quality of life in epilepsy patients. [7,11]

Addressing sleep disturbances through appropriate interventions, such as cognitive behavioral therapy for insomnia, continuous positive airway pressure (CPAP) for OSA, and optimizing ASM regimens, is crucial for improving both sleep health and seizure control in patients with epilepsy. [6,10]



Screening for Sleep Issues

EFFECTIVE SCREENING TOOLS

Ask this auestion:

"Are you feeling refreshed with your sleep?"

Use validated tools like the <u>Epworth Sleepiness Scale</u> and <u>STOP-BANG Questionnaire</u> for quick assessment.

ROUTINE SLEEP ASSESSMENTS

- Incorporate sleep evaluations into regular epilepsy care visits.
- Encourage patients to maintain a sleep diary to identify patterns of sleep disturbances and triggers.

Sleep Hygiene Tips for Epilepsy Patients

QUICK REFERENCE:

Consistency

Maintain regular sleep and wake times, even on weekends.

Light Exposure

Maximize natural light during the day and minimize bright light in the evening.

Sleep Goals

Aim for 7–9 hours of sleep. Avoid excessive time in bed or late-afternoon naps.

Limit Stimulants

No caffeine after 12:00 PM, including sodas and chocolate.

Bed Use

Use the bed only for sleep and intimacy. Avoid screens or other activities in bed.

Calming Routine

Establish a relaxing bedtime routine, such as reading or light stretching, and avoid vigorous exercise within two hours of sleep.

FREE RESOURCES FOR SCREENING SLEEP

Epworth Sleepiness Scale



STOP-BANG Questionnaire



VA Sleep Diary





Managing Insomnia: Pharmacological and Behavioral Treatments

PHARMACOLOGICAL TREATMENT

Medications should be carefully chosen to avoid adverse effects on seizure control and address comorbid conditions.

SEDATING ANTI-SEIZURE MEDICATIONS (ASMS)

Selecting an ASM with sedative properties can help address both seizure control and insomnia:

Anti-Seizure Medication	Mechanism of Action	Sedation Risk	Comments
Phenobarbital	Enhances GABA-mediated inhibition	High	Significant sedative effects; may impair cognition and coordination.
Clobazam	Benzodiazepine, enhances GABA action	Moderate to High	Sedation common; dose- dependent and may lessen with tolerance over time.
Clonazepam	Benzodiazepine, enhances GABA action	High	Strong sedative effects, often used for acute seizure management.
Gabapentin	Modulates calcium channels	Moderate	Sedation, dizziness, and fatigue are common, especially at higher doses.
Pregabalin	Modulates calcium channels	Moderate	Sedation frequently reported; may also cause dizziness and weight gain.
Topiramate	Blocks sodium channels, enhances GABA	Moderate	Sedation, cognitive slowing, and fatigue are common.



SEDATING ANTI-SEIZURE MEDICATIONS (ASMS) CONTINUED

Anti-Seizure Medication	Mechanism of Action	Sedation Risk	Comments
Tiagabine	Inhibits GABA reuptake	Moderate	Sedation and dizziness often reported; may also cause confusion.
Valproate (Valproic Acid)	Enhances GABA, blocks sodium channels	Moderate	Sedation more prominent at higher doses; can also cause tremors.
Zonisamide	Blocks sodium and calcium channels	Moderate	Sedation is dose-dependent; may cause dizziness and fatigue.
Lacosamide	Enhances slow sodium channel inactivation	Moderate	Sedation, dizziness, and diplopia are common side effects.
Levetiracetam	Modulates synaptic vesicle protein SV2A	Low to Moderate	Sedation can occur, particularly at treatment initiation.
Epidiolex (Cannabidiol)	Modulates endocannabinoid and other neuronal signaling pathways	Low to Moderate	Sedation can occur, particularly in combination with clobazam; also associated with fatigue and diarrhea.

TIMING

Administer sedating ASMs at night to minimize daytime drowsiness

WHEN TO REFER

Refer patients to a sleep specialist or psychiatrist if:

	Persistent insomnia occurs despite optimized therapy and interventions.
	Suspected comorbid conditions such as sleep apnea or severe anxiety are suspected
	Complex treatment is needed that requires multidisciplinary oversight.



ADDITIONAL PHARMACOLOGICAL OPTIONS

Category	Medication	Key Points
Low-Dose Antidepressants	Doxepine (up to 6 mg) Mirtazapine Trazodone Amitriptyline Nortriptyline	Doxepin is FDA-approved for insomnia. Mirtazapine, trazodone, amitriptyline, and nortriptyline are used off-label. Trazodone may cause orthostatic effects, while amitriptyline and nortriptyline can help with comorbid migraines. These low-dependency medications may also ease anxiety.
Orexin Antagonists	Suvorexant, Lemborexant, Daridorexant	Effective for sleep maintenance; little data in epilepsy patients, but currently considered safe
Z-Drugs	Zolpidem, Zaleplon, Eszopiclone	Useful for short-term sleep initiation; eszopiclone can be used for longer term. Caution; sleep walking/complex sleep behaviors, esp. with zolpidem

BEHAVIORAL TREATMENT

Cognitive Behavioral Therapy for Insomnia (CBTi) includes [12]:

Sleep Restriction Therapy

Limits time in bed to match actual sleep time, strengthening sleep drive.

Stimulus Control

Reinforces the association between the bed and sleep.

Relaxation Training

Reduces autonomic arousal, muscle tension, and intrusive thoughts.

Cognitive Therapy

Addresses unhelpful beliefs and worries about sleep.

Sleep Hygiene Education

Covers caffeine avoidance and regular sleep schedules.

SPECIAL CONSIDERATIONS FOR EPILEPSY PATIENTS [13, 14]

- Sleep Restriction Therapy may need modification, as sleep deprivation can trigger seizures. Careful monitoring is necessary.
- Medication Timing: Adjusting ASM timing can improve sleep quality.
- Comorbid Sleep Disorders: Addressing conditions like obstructive sleep apnea (OSA) is crucial. CPAP therapy may help.



MELATONIN USE FOR SLEEP IN PATIENTS WITH EPILEPSY

Improving sleep quality in patients with epilepsy should begin with reinforcing sleep hygiene strategies. These include maintaining a consistent sleep-wake schedule, creating an optimal sleep environment, and limiting screen use and stimulants (e.g. caffeine) in the hours before bedtime.

When non-pharmacological interventions are insufficient, melatonin can be considered as an adjunctive option.

CURRENT EVIDENCE AND SAFETY CONSIDERATIONS

- There are no formal, epilepsy-specific guidelines for melatonin use; however, emerging evidence suggests it is generally safe for patients with epilepsy.
- Multiple studies indicate that melatonin does not increase seizure frequency. Some studies even suggest potential neuroprotective and anticonvulsant properties, although data remain mixed. [15,16,17]
- Rare case reports have described pro-convulsant effects, particularly in neurologically complex pediatric populations, emphasizing the need for cautious monitoring. [17]

CLINICAL CONSIDERATIONS FOR PROVIDERS

- Assess individual factors such as seizure type, age, and concomitant medications.
- Be aware of potential drug interactions, particularly given melatonin's influence on hepatic enzyme activity and possible effects on ASM metabolism.
- Start with the lowest effective dose and titrate cautiously.
- Monitor for changes in seizure frequency, severity, and sleep quality after initiation.

FOLLOW-UP

- Close follow-up is recommended to assess both efficacy and tolerability.
- Consider reassessment of dosing and continued need at regular intervals.

CONCLUSION

Healthy sleep habits and tailored interventions are essential for effective epilepsy management. By incorporating sleep assessments and pharmacological or behavioral treatments, healthcare providers can significantly improve patient outcomes and quality of life.



REFERENCES

- **1.**Méndez M, Radtke RA. Interactions between sleep and epilepsy. J Clin Neurophysiol. 2001;18(2):106-127. doi:10.1097/00004691-200103000-00003.
- **2.** Minecan D, Natarajan A, Marzec M, Malow B. Relationship of epileptic seizures to sleep stage and sleep depth. Sleep. 2002;25(8):899-904.
- **3.** Ho A, Hannan S, Thomas J, et al. Rapid eye movement sleep affects interictal epileptic activity differently in mesiotemporal and neocortical areas. Epilepsia. 2023;64(11):3036-3048. doi:10.1111/epi.17763.
- **4.** Ismayilova V, Demir AU, Tezer FI. Subjective sleep disturbance in epilepsy patients at an outpatient clinic: A questionnaire-based study on prevalence. Epilepsy Res. 2015;115:119-125. doi:10.1016/j.eplepsyres.2015.06.009.
- **5.** Macêdo PJOM, Oliveira PS, Foldvary-Schaefer N, Gomes MDM. Insomnia in people with epilepsy: A review of insomnia prevalence, risk factors and associations with epilepsy-related factors. Epilepsy Res. 2017;135:158-167. doi:10.1016/j.eplepsyres.2017.05.014.
- **6.**Peng W, Ding J, Wang X. The management and alternative therapies for comorbid sleep disorders in epilepsy. Curr Neuropharmacol. 2021;19(8):1264-1272. doi:10.2174/1570159X19666201230142716.
- **7.** Garg D, Charlesworth L, Shukla G. Sleep and temporal lobe epilepsy Associations, mechanisms and treatment implications. Front Hum Neurosci. 2022;16:849899. doi:10.3389/fnhum.2022.849899.
- **8.** Safarpour Lima B, Zokaei A, Assarzadegan F, Hesami O, Zareh Shahamati S. Prevalence of sleep disorders in patients with epilepsy: A questionnaire-based cross-sectional study. Epilepsy Behav. 2021;114(Pt A):107635. doi:10.1016/j.yebeh.2020.107635.
- **9.** Bergmann M, Prieschl M, Stefani A, et al. A prospective controlled study about sleep disorders in drugresistant epilepsy. Sleep Med. 2020;75:434-440. doi:10.1016/j.sleep.2020.09.001.
- **10.** Bonilla-Jaime H, Zeleke H, Rojas A, Espinosa-Garcia C. Sleep disruption worsens seizures: Neuroinflammation as a potential mechanistic link. Int J Mol Sci. 2021;22(22):12531. doi:10.3390/ijms222212531.
- **11.** Latreille V, St Louis EK, Pavlova M. Co-morbid sleep disorders and epilepsy: A narrative review and case examples. Epilepsy Res. 2018;145:185-197. doi:10.1016/j.eplepsyres.2018.07.005.
- **12.** Morin CM, Buysse DJ. Management of insomnia. N Engl J Med. 2024;391(3):247-258. doi:10.1056/NEJMcp2305655.
- **13.** Edinger JD, Arnedt JT, Bertisch SM, et al. Behavioral and psychological treatments for chronic insomnia disorder in adults: An American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2021;17(2):255-262. doi:10.5664/jcsm.8986.
- **14.** Mysliwiec V, Martin JL, Ulmer CS, et al. The management of chronic insomnia disorder and obstructive sleep apnea: Synopsis of the 2019 U.S. Department of Veterans Affairs and U.S. Department of Defense clinical practice guidelines. Ann Intern Med. 2020;172(5):325-336. doi:10.7326/M19-3575.
- **15.** Bazil CW, Short D, Crispin D, Zheng W. Patients with intractable epilepsy have low melatonin, which increases following seizures. Neurology. 2000;55:1746–1748. doi: 10.1212/wnl.55.11.1746.
- **16.** Peled N, Shorer Z, Peled E, Pillar G. Melatonin effect on seizures in children with severe neurologic deficit disorders. Epilepsia. 2001;42:1208–1210. doi: 10.1046/j.1528-1157.2001.28100.x.
- **17.** Sheldon SH. Pro-convulsant effects of oral melatonin in neurologically disabled children. Lancet. 1998;351:1254. doi: 10.1016/S0140-6736(05)79321-1.

