



Sleep Disorders in Epilepsy: Current Trends and Future Perspectives

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Abstract

Purpose of Review Sleep complaints are common in people with epilepsy (PWE). We aim to highlight the updated evidence regarding comorbid sleep disorders and epilepsy and the impact of epilepsy and its treatments on sleep.

Recent Findings Up to two thirds of PWE report sleep disturbances which may signal presence of a comorbid sleep disorder, including insomnia, arousal parasomnias, excessive daytime sleepiness, obstructive sleep apnea, or restless legs syndrome. Uncontrolled seizures contribute to poor sleep quality, while presence of epilepsy (with or without seizures) and antiepileptic drugs is associated with changes in sleep architecture. Chronic intracranial EEG monitoring with implanted devices reveals a nocturnal peak for interictal epileptiform activity. Epilepsy surgery outcomes suggest better seizure control may improve sleep architecture and quality.

Summary Screening for and treating sleep disorders may lead to improved seizure control and quality of life in PWE. Epilepsy surgery and implanted devices to treat refractory epilepsy provide new insights into the relationship between sleep and epilepsy.

Keywords Sleep disorders · Epilepsy · Sleep architecture · Parasomnias · Obstructive sleep apnea · Epilepsy surgery

Abbreviations

AEDs	Antiepileptic drugs
CAP	Cyclic alternating pattern
EEG	Electroencephalography
IED	Interictal epileptiform discharge
NREM	Non-rapid eye movement sleep
N1	NREM stage 1 sleep
N2	NREM stage 2 sleep
N3	NREM stage 3 sleep
OSA	Obstructive sleep apnea
PSG	Polysomnography

PWE	People/patients with epilepsy
REM	Rapid eye movement sleep
WASO	Wake after sleep onset

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Introduction

Epilepsy affects about 1% of the population and carries substantial global physical, social, and economic consequences, accounting for an estimated 0.5% of disease burden worldwide [1, 2]. Persons with epilepsy (PWE) tend to have poorer quality of life than the general population, with a greater degree of impairment in the presence of reported sleep disturbances [3, 4]. Sleep impairment in PWE is a multifaceted concern, owing to numerous factors including diurnal and nocturnal seizures and medication side effects as well as comorbid sleep disorders [5, 6]. One area gaining increasing attention is the presence of comorbid sleep disorders, as treatment of such underrecognized conditions may lead to improvements in seizure control and overall quality of life in PWE. This article reviews both pivotal and current research as pertains to sleep and epilepsy with an emphasis on sleep disorders.

Sleep Concerns in Epilepsy

Broad Sleep Concerns

According to the NIH Sleep Disorders Research Plan, an estimated 25–30% of the general adult population—and a comparable percentage of children and adolescents—suffer from diminution of sleep health [7]. Sleep disturbances have been reported in up to two thirds of PWE, with similar rates in people with focal and generalized onset epilepsies, and twice as often as the general population [1, 8–11]. Sleep-related concerns include insufficient sleep, increased nocturnal and early morning awakenings (sleep-maintenance insomnia), impaired initiation of sleep (sleep-onset insomnia), nonrestorative sleep, and excessive daytime sleepiness whether or not antiepileptic drugs (AEDs) are used [1, 5, 8, 10, 12, 13]. As a result, patients experience a detrimental impact on quality of life, work productivity, and overall health [1, 14]. Studies suggest comorbidities and intractable seizures are important causes of sleep disturbances [11]. Owing to the intricate relationship between sleep and epilepsy, the origins of these concerns are manifold.

Epilepsy and Sleep Architecture

Epilepsy produces changes in sleep macrostructure and microstructure. In general, patients with epilepsy experience increased wake after sleep onset (WASO) and frequency of stage shifts, prolonged sleep onset latency, increased time spent in light non-rapid eye movement (NREM) sleep (stages I (N1) and II (N2) sleep), and decreased percentage of rapid eye movement (REM) sleep [15]. Polysomnographic (PSG) findings vary slightly depending on the underlying type of epilepsy and the frequency of ictal or interictal activity. Patients with untreated nocturnal frontal lobe epilepsy showed increased WASO and slow wave sleep duration with reduced N2 sleep. They were also found to have a reduction in REM sleep (duration and percentage), prolonged REM sleep latency and increased cyclic alternating pattern (CAP) time and rate, a marker of sleep instability [16, 17]. In a population of 99 patients with Juvenile Myoclonic Epilepsy (JME), PSG showed poorer sleep quality as evidenced by decreased sleep efficiency and REM sleep, prolonged sleep latency, and increased WASO and N1 sleep compared with controls. Epileptiform discharges occurred more often during N1 and N2 sleep. These trends were observed similarly between drug-naïve and treatment groups [18]. Findings are generally similar across several recent studies [19–21]. Diurnal seizures produce postictal daytime somnolence, whereas nocturnal seizures directly disrupt sleep. In addition, the sleep period following seizure activity is characterized by increase WASO, sleep fragmentation and suppression of REM sleep, with a greater degree of impairment if seizures occur during the sleep

period [22, 23]. Zanzmera et al. documented an association between poor seizure control and sleep latency, REM sleep latency, frequency of arousals, sleep efficiency, and total sleep time [24], while Ismayilova and colleagues reported a correlation between seizure control, nocturnal seizures, and insomnia [10]. Interictal discharges may also increase sleep fragmentation, independently of seizures, by interfering with the physiologic coordination of sleep, which may in turn result in daytime somnolence and impaired learning [22, 25].

Mood Disorders and Sleep Hygiene

Maestri and colleagues did not observe a difference in daytime sleepiness (as measured by nocturnal polysomnography, visual reaction times, and Epworth Sleepiness Scale) between de novo untreated patients with epilepsy (PWE) who were without significant comorbidities or frequent seizures and the control group, leading to the suggestion that comorbid psychiatric or sleep disorders, nocturnal seizures, sleep fragmentation, and antiepileptic therapy may play a larger role than the physiologic factors related to epilepsy itself [6, 26, 27]. Several additional studies have highlighted the potential impact of depression on sleep quality in PWE. Moser et al. conducted a retrospective and prospective study in a small population of PWE ($N=32$) to find that depression scores were a strong predictor of poor sleep, independent of the number of antiepileptic medications [28]. Vendrame et al. suggested a similar correlation between depression, sleep impairment, and quality of life, whereas the work of Ismayilova et al. and Im et al. did not support this finding [6, 9, 10].

Sleep hygiene encompasses the habits, behaviors, and environment that impact the duration and quality of sleep. Optimizing sleep conditions requires maintenance of a regular sleep schedule, creation of a comfortable sleeping environment (generally dark, quiet, and of the appropriate temperature), avoidance of activities beyond sleep and sex in the bedroom (particularly use of electronic devices that emit blue light), limitation of strenuous or stimulating activity late in the day (including late evening heavy exercise, nicotine, caffeine), and elimination of alcohol prior to bed [23]. Much of our understanding of the impact of sleep hygiene on epilepsy is extrapolated from the awareness of the overall impact of sleep dysfunction on epilepsy with fewer data to support a direct relationship between sleep hygiene and seizure control [15]. Inadequate sleep hygiene is known to reduce sleep quality and duration, and as such has often been attributed to poor seizure control [8, 23, 29]. Manni et al. conducted a questionnaire-based survey of more than 200 epilepsy patients in attempt to measure sleep hygiene in this population. He evaluated habits including coffee drinking, smoking, irregular sleep-wake/sleep deprivation, upsetting activities at bedtime, evening napping, bedroom heating/humidity, bedroom brightness, bedroom noise, and alcohol intake at bedtime. He found

overall sleep hygiene was better in epilepsy patients when compared to controls in all categories but that of smoking and coffee consumption. This observation is possibly attributed to habitual avoidance of practices known to exacerbate seizures. No significant relationship between degree of sleep hygiene practice and severity of epilepsy was observed within this limited population [29]. While evidence to support the direct impact of sleep habits on epilepsy may be lacking, there are data to suggest a distinct relationship between inadequate sleep hygiene and low quality of life in PWE [30].

Sleep Deprivation in Epilepsy

The clinical relevance of sleep deprivation in epilepsy is a controversial topic. Many studies have been performed; however, multiple different methodologies and outcomes were assessed making comparison between the studies difficult. It has been long accepted that sleep deprivation facilitates neuronal excitation and thus interictal and ictal epileptiform activity [31–33]. Several animal models as well as transcranial magnetic stimulation studies have supported this principle [34–36]. Badawy et al. suggest that the result is due to an imbalance between neuronal excitation and inhibition in the setting of sleep deprivation, which has been supported by his studies using transcranial magnetic stimulation to assess cortical excitability [34]. Giorgi and colleagues published an extensive review of sleep deprivation and EEG studies and concluded that standardized methods of sleep deprivation could enhance future studies on this topic [37••]. There has been additional research suggesting that, when controlled for other variables such as emotional stress and alcohol, acute sleep deprivation alone does not increase seizure activity when compared with a normal sleep condition [38, 39].

Sleep Disorders in Epilepsy

Arousal Parasomnias

Arousal parasomnias (somnambulism, sleep terrors, and confusional arousals) are common in patients with epilepsy [40, 41] and may manifest with behaviors similar to those observed in sleep-related frontal and temporal lobe seizures [42]. Tassanari et al. suggest that activation of central pattern generators in the brainstem may be responsible for the similar behavioral manifestations in nocturnal frontal lobe epilepsy and arousal parasomnias [43]. Provini and colleagues found arousal parasomnias commonly occur in patients with nocturnal frontal lobe epilepsy, or as it is now referred to, sleep-related hypermotor epilepsy, and their family members ($N=34$ and $39/100$, respectively) in a case-controlled family study [41]. Another case-controlled family study in patients with sleep-related hypermotor epilepsy and their families

reported significantly greater lifetime prevalence of somnambulism compared to healthy controls [40]. This increased comorbid prevalence in patients and their family members suggests that genetic factors may influence the manifestation of these disorders.

Distinguishing between sleep-related hypermotor epilepsy and arousal parasomnias can be a diagnostic dilemma and lead to misdiagnoses. Benbir et al. reported CAP increases in arousal parasomnias and frontal and temporal lobe epilepsies compared to healthy controls. Different CAP features were observed in patients with NREM parasomnias compared to those with epilepsy [44]. Although scalp Video EEG may be normal during these seizures if associated with a deeper ictal focus, prolonged Video EEG or PSG should be considered to record hypermotor seizures or interictal epileptiform discharges (IEDs) to confirm sleep-related hypermotor epilepsy according to the diagnostic criteria outlined by Tinuper et al. [45•].

Insomnia

Insomnia and poor sleep are common in patients with epilepsy (PWE) and may adversely impact seizure control and quality of life. Prevalence of insomnia in PWE has been reported from 28.9 to 74.4%, based on different inclusion criteria and methodology between studies [46], and are more common than prevalence of insomnia in the generalized US population, which has been reported to range from 10 to 15% [47]. In one study by Vendrame et al., 51% of PWE surveyed had insomnia based on the Insomnia Severity Index and 72% were poor sleepers based on the Pittsburgh Sleep Quality Index; these factors significantly correlated with the number of anti-epileptic medications, scores of depressive symptoms, and were significant predictors of lower quality of life on the Quality of Life in Epilepsy Inventory-31 [6]. A recent study by Im and colleagues found sleep disturbances were more common in PWE vs. healthy controls (53 vs. 25.5%, $p<0.001$). Poor sleep quality, excessive daytime sleepiness, and insomnia were significantly associated with epilepsy; however, PWE who were seizure-free over the past year had lower rates of insomnia [9]. Another recent study by Quigg et al. confirmed findings that insomnia in PWE was associated with short-term poor seizure control and worse quality of life [48]. Although further studies are needed to determine the relationship between insomnia and seizure frequency, these findings suggest that the presence of insomnia may influence the manifestation of seizures.

Hypersomnia and Narcolepsy

Excessive daytime sleepiness is a common complaint in patients with epilepsy (PWE). Evidence suggests that uncontrolled seizures, comorbid sleep disorders, and mood disorders

are major contributing factors [11, 14, 28, 49]. There are conflicting studies regarding the impact of AEDs on daytime sleepiness. A recent study by Maestri et al. demonstrated that newly diagnosed PWE not on AEDs had no difference from controls on Multiple Sleep Latency tests, reaction times, or Epworth Sleepiness Scale scores [26]. Another study demonstrated 11.1% of PWE had excessive daytime sleepiness, more frequently in the presence of obstructive sleep apnea and depression [49]. Although excessive daytime sleepiness is frequently reported, comorbid narcolepsy and epilepsy has been infrequently documented with only a few recent case series published [50, 51].

Medications used to treat hypersomnia and narcolepsy may lower seizure threshold; however, modafinil and sodium oxybate may not increase risk of seizures. Ozsoay et al. demonstrated a dose-dependent decrease in seizure frequency and duration with administration of modafinil in rats with pentylenetetrazol-induced convulsive epilepsy [52]. Although this benefit has not been reported in human studies, retrospective studies suggest modafinil does not exacerbate seizures [53, 54]. One case series of patients with Video EEG proven idiopathic generalized epilepsy and comorbid narcolepsy Type I demonstrated no increased seizure frequency after sodium oxybate was added to antiepileptic medications [51].

Restless Legs Syndrome

Restless Legs Syndrome is a common disorder (5–15% US population) that manifests with an uncomfortable sensation in the limbs in the evenings at rest associated with an urge to move that improves with movement. It can be associated with iron deficiency, insomnia, and potentially, daytime impairment. Although primary Restless Legs Syndrome has been reported in 5.8% of an unselected Turkish epilepsy population [55] and 11% in a Nigerian epilepsy population [56], Geyer et al. found that 42% of patients with right temporal lobe epilepsy had primary Restless Legs Syndrome, 4.6 more likely than patients with left temporal lobe epilepsy, and some of those patients had Restless Legs Syndrome symptoms as a prodromal sign of seizures [57]. Further studies into targeted epilepsy populations may lead to a better understanding about the relationship between epilepsy and Restless Legs Syndrome.

Sleep Apnea and Epilepsy

The prevalence of obstructive sleep apnea in patients with epilepsy (PWE) exceeds that of the general population and is associated with increased daytime somnolence, worsening quality of life, refractoriness of seizures, and potentially the risk of sudden unexpected death in epilepsy syndrome [23, 58–64]. Malow et al., in a study of 39 patients with refractory

partial epilepsy, diagnosed obstructive sleep apnea (OSA; respiratory distress index > 5) in 33% of the population, with 13% having moderate to severe OSA (respiratory disturbance index > 10) [59]. More recently, Foldvary-Schaefer et al. demonstrated a similar prevalence of OSA in a retrospective study involving a population of 130 adults with epilepsy, 30% of whom had mild OSA and 16% of whom had more severe disease. The prevalence has been quoted as low as 9–10%, only slightly higher than the general population [58, 65], and as high as 80% [66], with variability depending on the population surveyed. The most consistent predictors of sleep apnea in PWE mirror risk factors for development of sleep apnea in the general population, including increasing age [58–60] and male gender [58, 59, 66]. There was less consistent data regarding association with higher body mass index [58, 67], neck circumference [67], increased seizure frequency [24, 58–60, 66, 68], nocturnal seizures [58, 59, 66], and dental problems [60].

While the reasons for increased prevalence of OSA among PWE are not fully elucidated, Foldvary-Schaefer et al. proposed one cause to be impairment of upper airway control related to extensive interictal discharges or seizures occurring from sleep [69]. Epilepsy treatments may also have an impact on the prevalence of sleep-disordered breathing. For instance, barbiturates and benzodiazepines may increase airway collapsibility, whereas valproic acid and carbamazepine may cause weight gain further increasing risk of obstructive apnea [33]. Vagus nerve stimulation is also known to worsen sleep-disordered breathing, including both obstructive and central sleep apneas, likely attributed to peripheral effects on upper airway musculature innervated by the Vagus nerve, alteration of central mechanisms responsible for airway patency and respiratory drive as well as increased vagal tone [33, 70, 71]. These deleterious effects may be reduced by decreasing Vagus nerve stimulation intensities and/or increasing signal off time as well as using continuous positive airway pressure therapy. These findings support the importance of screening patients for sleep apnea both before and after Vagus nerve stimulator implantation [72, 73].

Several studies have suggested worsening seizure control in patients with concomitant epilepsy and sleep apnea, suggesting a bi-directional relationship between OSA and epileptic seizures. This observation may be explained by chronic sleep deprivation, reduced sleep quality (i.e., fragmentation, frequent stage shifts, arousals, and sleep deprivation), acute and chronic paroxysmal hypoxia, and hypoxemia as well as sympathetic activation on epileptogenic brain regions [24, 33, 68, 74–76]. This conclusion is further reinforced by the numerous studies showing improvement in seizure control and reduction in interictal spike frequency with treatment of sleep apnea [61, 66, 77–80], highlighting the importance of diagnosis and treatment of sleep apnea in PWE as well as the need for

further investigation into the potential pathogenic mechanisms.

Epilepsy Treatments and Sleep

Antiepileptic Drugs

AEDs have been reported to directly affect sleep architecture and indirectly contribute to various sleep disorders. An older review by Vaughn et al. reported drowsiness, increased sleep fragmentation, and reduced REM sleep with older AEDs including carbamazepine, phenobarbital, phenytoin and valproate, and increased slow wave sleep with pregabalin and gabapentin. Insomnia can be observed with felbamate, zonisamide, and high-dose lamotrigine [8]. A recent review by Jain and Glauser evaluated and rated the published evidence regarding the effects of AEDs on sleep architecture. Excessive daytime sleepiness was worsened with higher dosage levetiracetam, phenobarbital, and valproic acid but not with zonisamide or topiramate. Improved sleep efficiency and/or reduced sleep onset latency was observed with clobazam, carbamazepine, gabapentin, pregabalin, and tiagabine [27]. Studies on chronopharmacology, adjusting AED amount and timing, show promise regarding strategies to tailor therapy and potentially improve seizure control in individuals, but further randomized studies are needed to determine which patients are likely to benefit [81].

Epilepsy Surgery

Sleep stage has been shown to correlate with the expression of epilepsy with the most restricted fields manifesting during REM sleep. Okanari and colleagues demonstrated that children with generalized interictal epileptiform discharges (IEDs) on scalp Video EEG monitoring and normal/subtle changes on magnetic resonance imaging who underwent intracranial Video EEG for epilepsy surgery evaluation demonstrated both generalized and focal IEDs on intracranial Video EEG. Generalized IEDs occurred the least often during REM sleep (37%) and were more frequent during NREM sleep (67%, $p < 0.001$), and wakefulness (54%, $p = 0.003$). Lateralized IEDs were more frequent during REM sleep than NREM sleep. The hemisphere with lateralized IEDs during wakefulness, NREM, and REM sleep corresponded with the surgical side in 16 of 17 children. Multilobar resection was performed in 16 of 17 children, and 13 children were seizure-free after a mean 3.3 years postoperatively [82]. These findings suggest that IEDs recorded during REM sleep on intracranial Video EEG may help lateralize the epileptogenic zone in children with generalized IEDs and normal/subtle changes on magnetic resonance imaging.

Uncontrolled seizures have been reported to be a major cause of disrupted sleep in patients with epilepsy (PWE). Zanzner and colleagues prospectively evaluated the effects of epilepsy surgery on subjective and objective measures of sleep in 17 PWE. Twelve (70.6%) patients had good surgical outcome (reduced seizure frequency), and these patients demonstrated improved subjective daytime sleepiness and objective arousal index and total sleep time suggesting improved sleep consolidation and sleep efficiency while three (25%) of these patients also demonstrated resolution of obstructive sleep apnea (apnea-hypopnea index improved from > 5 to < 5) [83]. Serafini et al. evaluated the frequency of IEDs and effects on sleep macrostructure in 11 patients with refractory mesial temporal lobe epilepsy who became seizure-free for at least 2 years following epilepsy surgery. Reduction in IEDs was observed in all patients. A significant increase in total sleep time and REM sleep ($p = 0.006$) was observed after 1 year ($p = 0.032$ and 0.006 , respectively) and REM sleep further increased after 2 years ($p = 0.028$) [84]. These findings suggest that only those patients with good postoperative seizure control (Engle classes I and II), but not those with persistent uncontrolled seizures, may show improvements in subjective and objective measures of sleep.

Deep Brain Stimulation

Deep brain stimulation of the bilateral anterior nuclei of the thalamus has been shown to improve seizure control in a large trial of people with refractory focal epilepsy [85]. Due to the importance of thalamic control of sleep-wake mechanisms, further understanding of the impact of thalamic deep brain stimulation on sleep is warranted. A recent study found that deep brain stimulation of the anterior nuclei of the thalamus was associated with sleep disruption. Increased arousals were observed during periods of stimulation appeared to be voltage-dependent [86]. Further studies are needed to characterize the impact of deep brain stimulation on sleep in patients with epilepsy.

Vagus Nerve Stimulation

As noted above, vagus nerve stimulation can worsen or induce sleep apnea at higher stimulus intensities. Additionally, vagus nerve stimulation is reported to have a voltage-dependent effect on daytime sleepiness and vigilance in patients with epilepsy (PWE) with lower stimulus intensities demonstrating improvements in subjective and objective sleep measures compared to pre-implantation, including in subjects without reductions in seizure frequency [87]. Lower stimulus intensities have been shown to improve daytime vigilance and quality of life in PWE as well [88]. Another study in children with vagus nerve stimulation for refractory epilepsy demonstrated decreased sleep latency and N1 sleep along with increased

slow wave sleep during PSG. Increased arousals were observed, especially prior to stimulation; however, most children had reduced seizures, interictal epileptiform discharges, and improved quality of life [89].

Responsive Neurostimulation

For patients with refractory epilepsy with two epileptogenic foci or a focus that overlaps eloquent cortex, implantation of a responsive neurostimulation device can detect and record seizure activity and then deliver therapeutic electrical stimulation to disrupt seizure activity. These devices provide ongoing electrocorticographical snapshots of short and long bursts of interictal epileptiform activity as well as seizures in the implanted brain areas. In some patients, the long bursts of interictal activity (i.e., long episodes) correlate with the individual patient's electrographic and/or clinical seizures and can be used as a marker for ictal activity. Analysis of these long-term intracranial recordings is providing insights into circadian and ultradian patterns of focal seizure activity.

Previous studies utilizing scalp and intracranial Video EEG have demonstrated a nocturnal peak of interictal epileptiform discharges (IEDs) for most types of epilepsy and varying circadian patterns of seizures based on epileptogenic brain region [90–93] and also by age [91]. A recent study by Spencer and colleagues demonstrated that in people with a responsive neurostimulator implanted for refractory focal epilepsy, IEDs had a nocturnal peak frequency regardless of brain region while electrographic seizures had a circadian pattern that varied based on epileptogenic brain region. Neocortical seizures peaked during night and early morning hours while mesial temporal seizures had more complex, diurnal patterns [94•]. These findings confirm previously reported scalp and intracranial Video EEG studies and encourage further responsive neurostimulation studies to help characterize insights into the circadian and ultradian patterns of ictal and interictal epileptiform activity.

Conclusion

Sleep disturbances can affect a majority of patients with epilepsy (PWE) and often signal the presence of a comorbid sleep disorder, including excessive daytime sleepiness, insomnia, arousal parasomnias, obstructive sleep apnea, and restless legs syndrome. Thus, screening for and treating sleep disorders may lead to improved seizure control and quality of life in PWE. Antiepileptic drugs can alter sleep architecture and can be associated with daytime sleepiness, although further studies are needed to determine how amounts and timing of antiepileptic drugs affect sleep. Uncontrolled seizures contribute to poor sleep quality in PWE on subjective and objective sleep measures. The interictal expression of epilepsy is

triggered by sleep with multiple scalp and intracranial EEG studies showing a nocturnal peak interictal epileptiform discharge frequency. The interictal epileptiform discharges observed during REM sleep may have lateralizing value in patients with intractable epilepsy undergoing epilepsy surgery evaluation. Epilepsy surgery outcomes suggest that improved seizure control is associated with improved sleep architecture. Although case reports suggest that epilepsy surgery may improve obstructive sleep apnea, further studies are needed to further define this association. Specific take-home points include the following:

Take-Home Points

- Uncontrolled seizures and mood disorders contribute to poor quality sleep
- Polysomnography data demonstrate poor sleep quality in patients with epilepsy (PWE), with prolonged latency of sleep onset and REM onset, reduced amounts of REM and slow wave sleep, and increased Non-REM stage 1 sleep and wake after sleep onset
- Arousal parasomnias and epilepsy are common comorbidities and may share common central pattern generators and genetic factors
- Video EEG or Polysomnography may help distinguish between arousal parasomnias and focal frontal and temporal lobe epilepsies
- Insomnia is very common in PWE and is associated with uncontrolled seizures and poor quality of life
- Obstructive sleep apnea occurs more frequently in PWE and can worsen seizure control if left untreated; treating OSA can improve seizure control
- Restless legs syndrome may be more common in people with right temporal lobe epilepsy
- Vagus nerve stimulation in PWE can induce/worsen obstructive and central sleep apnea; thus, consider polysomnographic evaluation and then vagus nerve stimulator adjustment and/or continuous positive airway pressure therapy if needed to mitigate these effects
- Interictal epileptiform discharges during REM sleep may help lateralize the seizure onset zone in children with intractable epilepsy
- Successful epilepsy surgery may improve objective sleep macrostructure, subjective sleepiness, and possibly obstructive sleep apnea

Compliance with Ethical Standards

Conflict of Interest Leslie P. Grayson declares no conflicts of interest. Jennifer L. DeWolfe reports grants from Marinus Pharmaceuticals, outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance

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