S
leep is vital to the health and well-being of all people but takes on new meaning for patients with epilepsy. People with epilepsy are commonly referred to a sleep laboratory because of disrupted sleep. Daytime sleepiness and insomnia are frequent symptoms experienced by patients with epilepsy. Other reported symptoms include poor cognitive performance, memory dysfunction and sleep related breathing issues. Frequently, these symptoms are attributed to medications or the underlying seizure disorder; an underlying sleep disorder is often missed.

An increase in health problems occurs as a result of untreated sleep disorders across all people, but people with epilepsy can experience additional devastating effects. There is a clear connection between seizures and sleep. Disruption of sleep can increase seizure frequency and severity, particularly in the case of sleep-disordered breathing. Many medications used to treat seizure disorders have adverse effects on sleep, which is further intensified when a sleep disorder exists and is untreated. All of these effects may lead to uncontrolled epilepsy and severe disability. It is important to note that most of the sleep disorders occurring in conjunction with epilepsy are treatable.

ABOUT EPILEPSY & SEIZURES

Approximately three million people in the U.S. have epilepsy, and 200,000 new cases of epilepsy are diagnosed each year, according to the National Epilepsy Foundation. A seizure is defined as “an electrical brainstorm” or abnormal electrical activity in the brain with an underlying cause, which elicits some change in activity or behavior. Epilepsy is defined as a disorder in which a person has a predisposition to having seizures. Rather than being considered a disease, epilepsy is mainly viewed as a symptom of a disease. Although there are numerous causes of epilepsy such as a tumor, trauma, infection, and a genetic disorder, the cause of many cases of epilepsy is unknown. There are many types of epilepsy syndromes, which have specific seizure types as well as associated symptoms.

SLEEP & SEIZURE RHYTHMS

As early as the late 1800s, studies demonstrated the strong correlation between sleep and seizures. Epileptiform activity follows a cyclical pattern, and in certain conditions it may be predominately nocturnal. The human circadian rhythm also has a cyclical pattern and oscillates between wake and sleep, and sleep oscillates between non-rapid eye movement (NREM) sleep and REM sleep. Epileptic activity is influenced by sleep stages. In some idiopathic epilepsies, NREM sleep physiologic oscillations and epileptic seizures are generated by the same cerebral circuitry. Epileptiform activity is facilitated during NREM sleep, and partially inhibited during REM sleep. Certain epileptic syndromes produce seizures almost exclusively during sleep (e.g., frontal lobe epilepsy), and some produce seizures almost exclusively upon awakening (e.g., juvenile myoclonic epilepsy). Sleep architecture is likewise influenced by epileptic activity. Effects can include an increase in sleep latency, increase in number and duration of awakenings, decrease in sleep efficiency, and reduction or fragmentation of REM sleep.

SEIZURE TYPES

Seizures are primarily classified by the area of the brain involved. Many factors are involved in determining the causes of seizures; causes may vary depending on age, gender and related medical conditions. It is important to identify the seizure type, primarily because it may affect the treatment options.

Seizures are typically classified in two primary groups: partial and generalized. Partial seizures affect only a part of the brain at onset. Generalized seizures are widespread and involve both cerebral hemispheres simultaneously. Partial seizures may spread to become generalized, just as a single spark can light a fire. Partial seizures are further broken into categories of simple and complex; simple seizures do not alter alertness, whereas complex seizures do have an impact on consciousness. The following list is a classification of seizure disorders.

PARTIAL (FOCAL OR LOCAL) SEIZURES

Simple Partial Seizures
These seizures do not impair consciousness and often begin in the temporal or frontal lobe. Simple partial seizures are classified according to the following characteristics:

- Motor signs, including postural, versive and phonatory (vocalization or arrest of speech)
- Somatosensory or special sensory signs, including simple hallucinations such as tingling, buzzing sounds and flashes of light
- Autonomic signs or symptoms, including sweating, flushing and papillary dilation
- Psychic symptoms, including déjà vu; cognitive and affective impairments, such as time distortion, fear, and anger; and structured hallucinations, such as music and scenes
Complex Partial Seizures

These seizures impair consciousness and often begin in the temporal or frontal lobe. They also may begin as simple partial seizures (the aura) and evolve to complex partial seizures. Complex partial seizures are classified according to these signs and symptoms:

- Impairment of consciousness upon seizure onset
- Simple partial seizure onset with evolvement to complex partial seizure. Symptoms include those of simple partial seizures as listed above, followed by impairment of consciousness. Symptoms also may include automatisms (involuntary and purposeless movements), followed by impairment of consciousness

Partial Seizures Evolving into Secondarily Generalized Seizures

These seizures occur in three forms, with symptoms described above. The onset can be a simple partial or complex partial seizure that evolves to a generalized seizure. Or, onset may be a simple partial seizure evolving to a complex partial seizure, and finally evolving to a generalized seizure.

GENERALIZED SEIZURES

Absence Seizures

Typical absence seizures begin and end abruptly, typically lasting from five to 20 seconds and rarely longer than one to two minutes. Children older than four years of age are primarily affected; however, seizures rarely persist into adulthood. Absence seizures impair consciousness and may occur many times a day. They can occur alone, or may include automatisms, atonic symptoms, clonic symptoms, and/or autonomic symptoms. Often the patient will stare blankly, and eye fluttering or eyes rolling upward may be observed. Posture is often maintained. Typically the person will have no recollection of the event. NREM sleep and hyperventilation are facilitators of absence seizures. Often school-aged children with absence seizures are misdiagnosed with attention and behavioral problems.

Myoclonic Seizures

Myoclonic seizures are characterized by rapid, involuntary muscle contraction. Muscle involvement may be local or generalized. Myoclonic seizures may be related to specific epileptic syndromes or may result from degenerative central nervous system diseases, such as encephalitis, renal failure and postanoxic states.

Tonic, Clonic and Tonic-clonic Seizures

Tonic seizures involve flexion or stiffening of muscles. Clonic seizures involve rhythmic flexor spasms usually affecting the entire body. Spasms are brief and violent. Incontinence and apnea may occur. Tonic-clonic seizures combine the characteristics of clonic and tonic seizures. Initially a tonic seizure will occur, typically involving extended legs and semiflexed arms. The tonic phase lasts about 10 to 20 seconds and transforms into a clonic seizure with its rhythmic jerking. The entire seizure lasts from one to three minutes. A period of confusion or deep sleep may follow a tonic-clonic seizure. These seizures are common during sleep in certain epileptic syndromes and occur only during NREM sleep.

Atonic or Akinetic Seizures

A “drop attack” is the term often used to describe an atonic seizure, because the event involves a fall without warning. These seizures last less than 15 seconds and involve the sudden loss of muscle tone. Manifestations may include facial drooping, dropping objects and falling. Patients who suffer from these episodes often require helmets or other protection to prevent injury.

SLEEP-WAKE CYCLE

Seizures occur most frequently during stage 2 sleep, but they also occur during drowsiness and slow wave sleep; they rarely occur during REM sleep. Many studies have demonstrated that sleep deprivation causes an increase in seizure frequency. Sleep continuity is disrupted, and daytime sleepiness with increased seizures may occur when nocturnal seizures are more frequent. It is also noted that people with epilepsy have a higher incidence of parasomnias, nighttime awakenings, longer sleep latency, daytime sleepiness and altered sleep habits.

COMORBID SLEEP DISORDERS

Many people with epilepsy are concurrently affected by sleep disorders. The relationship between epilepsy and sleep disorders is often misunderstood and may lead to inadequate treatment or misdiagnosis if not carefully investigated. Whether they occur at night or during the day, seizures cause sleep disturbances. Many studies show increases in sleep complaints from people with epilepsy. Disruptions of the parts of the brain involved in regulating sleep and how the person is able to recognize and differentiate their related sleep and/or wake symptoms may be responsible for some of the increase in sleep complaints by persons with epilepsy. The hypnogram of patients with seizures typically reveals fragmented sleep. Sleep deprivation resulting from sleep disorders increases the occurrence of seizures in patients with seizure disorders and may cause deterioration of seizure control.

When sleep disorders are properly diagnosed and treated in patients with epilepsy, increased seizure control is usually achieved, and quality of life is significantly improved. In a study of 63 epilepsy patients with sleep disorders, 78 percent were referred for obstructive sleep apnea with 71 percent achieving a positive diagnosis. In this study, diagnoses of narcolepsy, insufficient sleep syndrome, and nocturnal seizures also were found. In addition, five of nine patients with obstructive sleep apnea achieved increased seizure control by the use of continuous positive airway pressure (CPAP) therapy and antiepileptic drugs. Other studies have confirmed that the frequency of seizures decrease in patients with sleep-related breathing disorders once the sleep disorders are successfully treated.

DRUG THERAPY

Drugs used to treat epilepsy commonly disrupt sleep (see Table 1), and a comorbid sleep disorder may worsen sleep fragmentation. Some antiepileptic drugs are commonly used to treat certain sleep disorders, such as in restless legs syndrome, REM sleep behavior disorder and periodic limb movements of sleep. Sedation is one of the most common side effects of older antiepileptic drugs, with reports of sedation as high as 70 percent with Phenobarbital, 42 percent with carbamazepine and valproate, and 33 percent with phenytoin and primidone. Among newer antiepileptic drugs, sedation rates of 5 percent to 15 percent have been reported.

For new studies and additional information, please refer to the latest research publications.
percent have been reported for gabapentin, lamotrigine, levetiracetam, vigabatrin and zonisamide, and 15 percent to 27 percent for topiramate in placebo-controlled studies. No significant reports of sedation occurred with tiagabine in placebo-controlled studies, but 25 percent reported sedation in open-label, long-term studies. Felbamate studies revealed reports of sedation and insomnia.

CONCLUSION
Recognizing sleep disorders in people with epilepsy is a vital step in guiding treatment, and physicians and technologists must be aware of the sleep effects of antiepileptic medications, as well as the sleep effects from seizures. In patients with comorbid sleep disorders and epilepsy, treatment of the seizure disorder alone may not significantly improve the patient’s overall health. The person’s sleep may be further worsened, precipitating other health issues. Raising awareness of sleep disorders affecting people with epilepsy helps ensure the best possible treatments, helps decrease disability from seizures and increases quality of life.

REFERENCES

DRUG/CLASS | U.S. TRADE NAME | EVENTS THAT IMPACT QUALITY OF SLEEP (FDA DRUG SHEETS)
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Barbiturates | e.g., Phenobarbital | Somnolence
Benzodiazepines | Klonopin | Insomnia, sleep disturbances, nightmares, vivid dreams
Benzodiazepines | Valium | Somnolence, fatigue, insomnia, sleep disturbances, nightmares
Carbamazepine | Tegretol | Somnolence
Phenytoin | Dilantin | Insomnia
Primidone | Mysoline | Fatigue, somnolence
Valproic acid | Depakene | Somnolence
Felbamate | Felbatol | Insomnia, somnolence
Fosphenytoin | Cerebyx | Somnolence
Gabapentin | Neurontin | Somnolence
Lamotrigine | Lamictal | Somnolence
Levetiracetam | Keppra | Somnolence
Tiagabine | Gabitril | Somnolence
Topiramate | Topamax | Somnolence
Zonisamide | Zonegran | Somnolence

TABLE 1. ANTIEPILEPTIC DRUGS. COMMONLY OBSERVED, ADVERSE EVENTS IMPACTING SLEEP ASSOCIATED WITH USE.