

## Exploring the Mysterious Link Between Sleep and Epilepsy

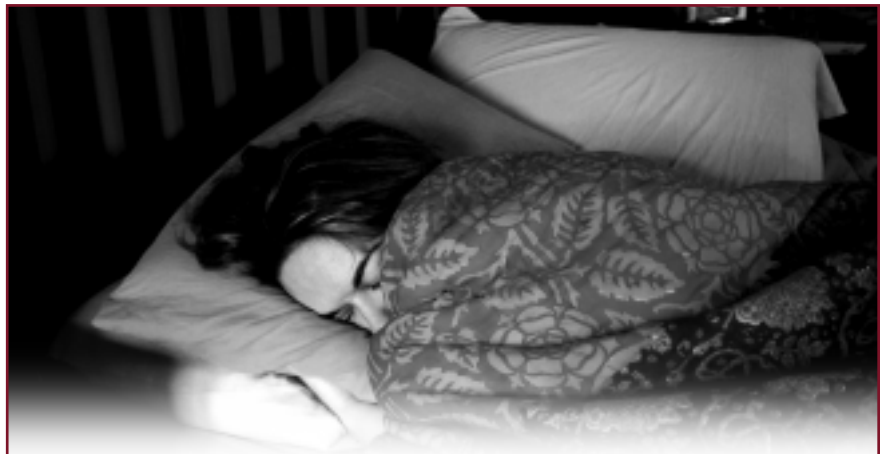
Nocturnal seizures often go unnoticed or misdiagnosed. Here's how to stay alert to their signs and symptoms.

**M**any of us spend about one third of our lives sleeping (some a little more; physicians often get less). It seems clear that sleep is essential. When we are sleep deprived, even for short periods of time, we experience troubles with memory, attention, concentration and personality changes. Doctors and nurses know the consequences of this well: sleep deprivation, when extreme, can lead to medical errors. This understanding has led to the limitation of resident work hours in certain states like New York. Although we may spend one third of our lives sleeping, we understand the phenomenon poorly.

The relationship between sleep and medical illnesses is even less well defined. However, we are starting to learn more about an intriguing connection: recent research has begun to define the link between seizures, seizure medications and sleep.

### Nocturnal Events and Nocturnal Seizures

In some epilepsy syndromes, seizures occur more often either during sleep or upon awakening. For instance, frontal lobe onset partial seizures tend to be brief, cluster and occur most often during sleep. The hallmark of idiopathic localization-related epilepsy (often called Benign Rolandic Epilepsy) is that the centrotemporal epileptiform discharges increase during sleep. The myoclonic seizures of juvenile myoclonic epilepsy tend to occur most often upon awakening. As the name would suggest, in the syndrome of grand mal seizures on awakening, GTCs occur



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shortly after waking up. Though this association is well known, the reason why the seizures have this pattern is unknown.

There are many types of nocturnal events that can be mistaken for nocturnal seizures (see Table 1). The history is critical in making the diagnosis. Of course, the person who is having the event(s) may recall little of the event itself. In these instances, the person's partner or roommate may provide essential clues. What was the description of the event? When during the night did the event occur? Was it when the person was going to sleep? Waking up? Were there complex motor movements, such as automatisms like lip smacking, picking or fumbling movements of one hand?

Some events which occur during sleep are "normal"—in other words, they do

not signal an underlying neurological problem. For instance, many people have experienced a "hypnic jerk" or "sleep myoclonus." The concern that a neurologist might have is that these are myoclonic seizures. What distinguishes hypnic jerks from seizures is that they can occur at any age, and usually consists of a sudden synchronous extension of two (or more) limbs, just as the person is falling asleep. Sleep myoclonus tends to worsen if there is overuse of stimulants during the day. Another example is "sleep drunkenness," which can be mistaken for a nocturnal complex partial seizure (CPS). Unlike CPS, which may manifest automatisms, sleep drunkenness consists of stumbling while walking and slurred speech. It occurs in children, just as they are awakening from a deep sleep. These



## Table 1. Differential Diagnosis of Nocturnal Events

### “Normal” sleep phenomena:

- Sleep myoclonus (hypnic jerks)
- Sleep drunkenness

### Non-REM Parasomnias:

- Sleep terrors
- Somnambulism (sleepwalking)
- Somniloquy (sleep talking)
- Periodic limb movements

### REM Parasomnias:

- Nightmares (which can sometimes be associated with running, punching or other complex motor movements)

events may worsen with sleep deprivation or stimulant medications.

Non-REM parasomnias may also be mistaken for complex partial seizures. Night terrors occur in children and resolve by adolescence. During these, a sleeping child will suddenly sit up and scream. They are usually inconsolable. They do not remember the event. Somnambulism (sleepwalking) or somniloquy (sleep talking) also occurs in children, with the incidence peaking at about 12 years of age. However, it can occur in up to 2.5 percent of adults.

Five percent of children and up to 44 percent of adults may experience periodic limb movements during sleep. What distinguishes these movements from those which occur in partial or generalized seizures is that they preferentially involve the legs (less often, they involve the arms). Further, periodic limb movements are not clonic. Finally, neither

automatisms nor tongue biting occur with night terrors, somnambulism or periodic limb movements: these symptoms would suggest the diagnosis of seizures.

Up to 20 percent of Americans report excessive daytime sleepiness at least a few days each week. One percent said that they had an automobile accident because they fell asleep at the wheel. In many of these cases, sleep apnea is the cause of the daytime sleepiness. Although sleep apnea is not usually mistaken for seizures, it has been known to cause seizures during sleep. In fact, some people will only experience a nocturnal seizure due to their apnea. The exact cause of this is unclear, but some have proposed that the seizure occur due to prolonged hypoxia.

### Sleep, AEDs, and Epilepsy

For many centuries, physicians have observed that sleep deprivation might provoke seizures. In fact, Galen (2nd century AD) and Aristotle (4th century BC) both noted this association. Recent research by Herman et al. has shown that certain stages of sleep suppress seizures.<sup>1</sup> Dr. Herman recorded 613 seizures in 133 people with partial epilepsy. She found that seizure rarely occurred during REM sleep. In short, the association between sleep and seizures is complex and incompletely understood.

Although lack of sleep provokes seizures, it has become clear that the occurrence of seizures affects the quality of sleep. This observation is not limited to seizures that occur during sleep. In other words, seizures that occur during wakefulness will affect the quality of sleep that night.<sup>2</sup> For instance, seizures decrease total sleep time. In addition, they decrease the amount of REM sleep, and prolong the time it takes to reach REM sleep.<sup>2</sup>

The relationship between sleep and

seizures is only just beginning to be defined; similarly, little is known about the effect that seizure medications have on sleep. It is clear that sleepiness is a common side effect of many of the AEDs. However, some AEDs have been reported to have the opposite effect: felbamate, lamotrigine and zonisamide have been associated with insomnia.<sup>2</sup> In other words, the effect that a specific AED will have in a given individual is unpredictable. More recent studies have suggested that certain AEDs like gabapentin may help to increase deep stages of sleep and REM sleep. If we tie this information in with the findings of Dr. Herman, it seems logical to conclude that one of the mechanisms of action of gabapentin is mediated through its direct effect on sleep patterns. However, this is by no means clear.

### Conclusions

There is a strong link between seizures and sleep. First, seizures may occur more often during sleep (or shortly after awakening) in certain epilepsy syndromes. These must be distinguished from nocturnal events which look like seizures. Second, sleep may have a variable effect on seizures: sleep deprivation may worsen seizures, while certain stages of sleep (REM) may suppress seizures. Third, seizures during sleep reduce the quality of sleep. Daytime seizures have a long-lasting effect on the brain, and reduce the quality of sleep the following evening. Finally, AEDs have a variable effect on sleep, often causing daytime sleepiness. As we learn more about sleep, it's certain we will clarify the complex relationship between seizure, AEDs, and sleep. **PN**

1. Herman ST, Walczak TS, Bazil CW. Distribution of Partial Seizures During the Sleep-Wake Cycle: Differences by Seizure Onset Site. *Neurology* 2001;56:1453-1459.

2. Vaughn BV, D'Cruz OF. Sleep and epilepsy. *Semin Neurol*. 2004 Sep;24(3):301-13.