

# Sleep and pediatric epilepsy

DUDLEY S. DINNER, MD

**T**HE very close relationship between sleep and epilepsy has been recognized since antiquity, as with Aristotle's observation that epilepsy often began during sleep. The most distinctive contribution, however, to the study of the relationship between epilepsy and the sleep-wake cycle was made by Janz in 1962.<sup>1</sup> He studied the grand mal epilepsies and divided them, on the basis of their temporal relationship, into sleep epilepsies, wake epilepsies, and diffuse epilepsies (occurring during sleep or wakefulness). The effect of sleep and circadian fluctuations in vigilance on seizures is now well accepted. Sleep also has a significant effect on interictal epileptiform activity (IEA) in terms of its morphology and frequency; on the other hand, seizures may have a profound effect on sleep and its architecture.

This paper will discuss these interrelationships between sleep and epilepsy in pediatric patients and also the role of sleep and sleep deprivation as techniques in the electroencephalographic (EEG) recordings of patients with epilepsy.

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## GENERALIZED TONIC-CLONIC (GRAND MAL) EPILEPSY

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### Effect on seizures

Gowers,<sup>2</sup> (1885) in a study of 840 patients, found seizures restricted to sleep in 21% of the group. Janz,<sup>1</sup> (1962) in a study of 2110 "grand mal" epilepsy patients, found epilepsy restricted to sleep in 45%. Pure sleep-related epilepsy was found by Billiard<sup>3</sup> in 28.5% of his cases. Gowers<sup>2</sup> found a predominance of seizures in the first two hours of sleep or at the end of sleep. This pattern has been substantiated by several investigators.

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From the Section of Epilepsy and Clinical Neurophysiology, The Cleveland Clinic Foundation.

In Janz's study<sup>1</sup> the two peaks were 9 to 11 PM and 3 to 5 AM. In a study by Montplaisier<sup>4</sup> of one patient with sleep-related grand mal seizures, all the seizures occurred in stage 2 or 3 nonrapid eye movement (nonREM) sleep. Patients with sleep-related epilepsy may continue to have their seizures only in sleep, but 20% of such patients may take on a diffuse pattern in their course with seizures during the waking as well as sleeping states.<sup>1</sup>

### Effect on IEA

Generalized IEA usually increases in nonREM sleep and decreases in REM sleep.<sup>3,4</sup> In the majority of patients, discharges are most prominent at sleep onset and during the first part of the night. In some patients, however, discharges are prominent in nonREM sleep of the last part of the night. In waking or diffuse epilepsy, epileptiform discharges may occur at any time; but in pure sleep epilepsy, discharges have been noted in REM sleep or awake in 9% of patients, and in nonREM sleep in 41%. The morphology of the interictal discharges also is affected by sleep. During nonREM sleep, generalized bursts become fragmented, polyspikes may occur, and IEA may appear as only focal or lateralized spikes.<sup>5,6</sup>

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## ABSENCE (PETIT MAL) EPILEPSY

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### Effect on seizures

Clinical absence seizures are observed only in the waking state; but in association with the burst of 3-Hz spike-and-wave complexes (SWCs) during sleep Neidermeyer has observed fluttering of the eyelids.<sup>7</sup> A few cases of "absence status" occurring in REM sleep have been detected by EEG.<sup>8,9</sup>

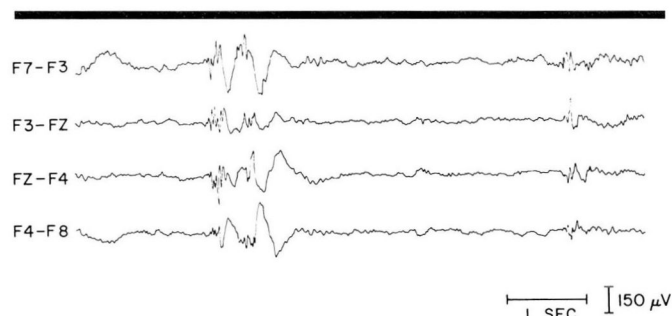


FIGURE 1. Interictal generalized polyspikes from the sleep EEG recording of a 14-year-old boy with typical absence seizures. Only the activity from the frontal regions is shown.

### Effect on IEA

IEA is activated by nonREM sleep especially during the first sleep cycle.<sup>10</sup> Some investigators have found a greater activation in stages 1 and 2 nonREM sleep<sup>10-12</sup>; others, in stages 3 and 4 nonREM sleep.<sup>10,11</sup> During stage 1 nonREM sleep, bursts of generalized SWCs became shorter with well-defined morphology. During stage 2 nonREM sleep, bursts are more irregular and less well organized and intermixed with polyspikes (Figure 1).

Focal spikes may be seen in the frontal regions. Discharges may also occur in a semiperiodic fashion. In stages 3 and 4 nonREM sleep, one notes a further decline in rhythmicity and more single spikes or polyspikes. In addition, the repetition rate of generalized SWCs decreases to 0.5 to 2 Hz. In REM sleep, bursts of generalized 3-Hz SWCs are similar to those in the awake pattern, but their frequency and duration are decreased.<sup>10,11</sup>

### JUVENILE MYOCLONIC EPILEPSY

#### Effect on seizures

In this syndrome, both myoclonic and generalized tonic-clonic seizures occur characteristically in the morning after awakening. That these may also occur on awakening after a nap at other times in the day was shown by Janz.<sup>13</sup>

#### Effect on IEA

The typical IEA is polyspikes. Discharges increase markedly at sleep onset and upon awakening but are virtually absent in nonREM and REM sleep.

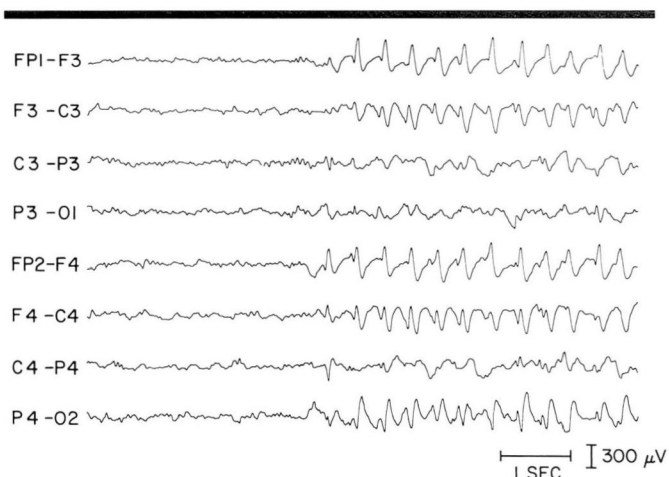


FIGURE 2. Interictal generalized slow SWCs from the sleep EEG recording of a 5-year-old boy with Lennox-Gastaut syndrome. Only the activity from the parasagittal regions is shown.

### LENNOX-GASTAUT SYNDROME

This syndrome refers to patients with intractable generalized seizures, mental retardation, and generalized slow SWCs.

#### Effect on seizures

The seizure disorder in Lennox-Gastaut syndrome is intractable and consists of tonic, atonic, atypical absence, myoclonic and generalized tonic-clonic seizures. There is no information on the effect of sleep on the occurrence of these seizures in this syndrome.

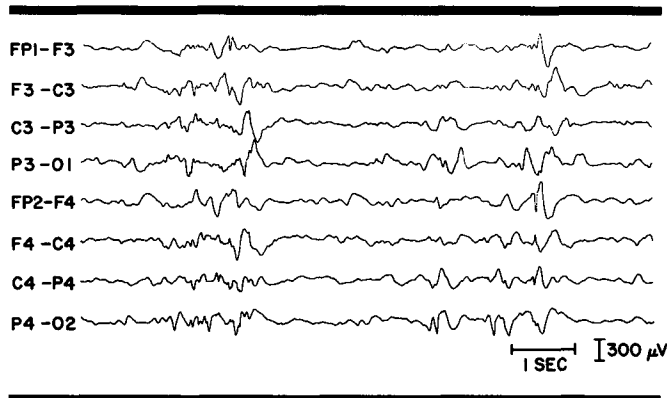
#### Effect on IEA

Typical interictal epileptiform discharges consist of generalized slow SWCs at a frequency of 2.5 Hz or less. The quantity of these bursts increases in nonREM sleep (Figure 2).

Their morphology may also be altered, with polyspikes becoming more prominent. There may be runs of generalized polyspikes and rhythmic 10- to 20-Hz activity. Bursts of electrodecremental activity may occur. If such bursts alternate with bursts of polyspikes, a burst-suppression-like pattern may appear.

### INFANTILE SPASMS (WEST SYNDROME)

This syndrome describes the triad of infantile spasms, psychomotor retardation, and hypsarrhythmia.



**FIGURE 3.** Interictal sleep EEG recording from a 15-month-old boy with infantile spasms, with IEA appearing in a semi-periodic fashion, giving a burst-suppression-like pattern. Only the activity from the parasagittal regions is shown.

#### Effect on seizures

Infantile spasms occur much less frequently in sleep.<sup>14,15</sup> Only 2% to 5% of such spasms occurred during sleep, for instance, in the series of Kellaway et al<sup>14</sup>; and they are most likely to occur prior to going to sleep or after waking from sleep.<sup>15</sup>

#### Effect on IEA

The EEG abnormalities may be increased in non-REM sleep, and the hypsarrhythmia pattern may become more apparent. Occasionally, the hypsarrhythmia pattern may be seen only during sleep.<sup>16</sup> Bursts of spikes and slow waves may tend to alternate with periods of generalized suppression of EEG activity in a semiperiodic fashion, giving rise to a burst-suppression-like pattern<sup>17</sup> (Figure 3).

During REM sleep, there is marked attenuation or disappearance of the hypsarrhythmia pattern.<sup>16</sup>

#### LOCALIZATION-RELATED EPILEPSY WITH SIMPLE PARTIAL SEIZURES

##### Effect on seizures

In Billiard's 29 cases, only 6.2% of the patients presented with pure sleep-related epilepsy; another 6.2% had seizures during both sleep and waking.<sup>3</sup>

##### Effect on IEA

Most studies of patients with this condition have found activation of interictal epileptiform discharges at sleep onset and in nonREM sleep.<sup>4</sup>

#### LOCALIZATION-RELATED EPILEPSY WITH COMPLEX PARTIAL SEIZURES

##### Effect on seizures

In Billiard's study of 127 patients, 9.4% had pure sleep-related seizures and an additional 29% had seizures during sleep and waking.<sup>3</sup> In 1975, Passouant et al<sup>17</sup> postulated that complex partial seizures (CPSs) were selectively activated in REM sleep. In 1982, Cadilhac<sup>18</sup> described the time of occurrence of sleep-related CPSs in 50 patients; 32 had seizures in nonREM sleep, eight during REM, and 10 in both states. Montplaisier,<sup>4</sup> however, recording in patients with mesial temporal foci, found none of ten patients to have seizures in REM sleep; studying patients with neocortical foci, he found only two seizures recorded in REM sleep.

##### Effect on IEA

Most studies have found an increase in interictal epileptiform discharges in nonREM sleep with a decrease in REM sleep; but some studies have shown an increase in REM sleep. Thus, there is some controversy about what occurs during REM sleep in patients of this type.

#### BENIGN CHILDHOOD EPILEPSY WITH CENTROTEMPORAL SPIKES

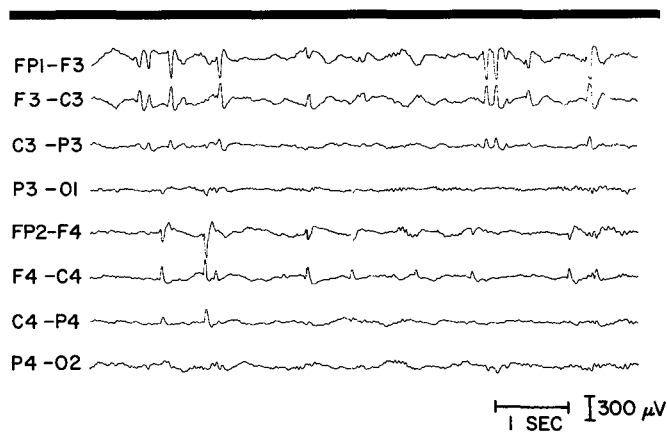
In benign childhood epilepsy with centrotemporal spikes, the seizures tend to occur during sleep or shortly after awakening. Such seizures have been reported to occur only in sleep in 51% to 80% of the cases studied.<sup>19</sup>

##### Effect on IEA

Marked activation of the sharp waves in sleep has been observed (Figure 4). Sharp waves have been reported to appear only in sleep in 2.5% of patients, with a range of up to 35% of patients reported in various studies.<sup>19</sup>

#### EFFECT OF EPILEPSY ON SLEEP

Sleep patterns in patients with epilepsy have varied from normal to markedly disturbed.<sup>17,20–23</sup> An increase in sleep latency, stages 1 and 2 nonREM (light) sleep, wake time after sleep onset, and shifting between sleep stages have been observed as has a decrease in stages 3 and 4 nonREM (deep) sleep and total sleep time. These



**FIGURE 4.** Interictal sleep EEG recording of an 8-year-old boy with benign focal epilepsy of childhood, demonstrating marked activation of the typical IEA bifocal and independent in the left and right fronto-central regions.

features are also seen in other conditions which may disturb sleep, such as the obstructive sleep apnea syndrome or sleep-related myoclonus; thus, they are probably only nonspecific features of the disturbed sleep architecture. Besset found that in primary and secondary generalized epilepsy, total sleep time was decreased by approximately one hour, compared to that in a nonepileptic control group.<sup>24</sup> He also found that wake time after sleep onset was increased by 44% in primary and by 6% in secondary generalized epilepsy. NonREM stage 2 sleep was decreased by 50% in patients with primary grand mal seizures and by 41% in patients with secondary generalized seizures.

If bursts of generalized SWCs in the EEG are frequent, sleep spindles and vertex sharp transients may be reduced or obscured. Thus, usual sleep activity may be disrupted, making it difficult to differentiate the various stages of sleep.<sup>23,24</sup> It may even be difficult to score REM sleep in some patients.<sup>17,23</sup>

In a study of patients with CPS, it was only those with multiple nocturnal seizures who demonstrated a significantly reduced amount of REM sleep.<sup>25</sup> If patients had a single CPS, no significant change in sleep architecture was observed.

#### ELECTRICAL STATUS EPILEPTICUS IN SLEEP (ESES)

In 1971 Patry et al described six children with EEG status epilepticus, which occurred with the onset of sleep and persisted throughout nonREM sleep.<sup>9</sup> The

term “continuous” was used to define the presence of the EEG pattern for at least 85% of nonREM sleep. The EEG pattern consisted of generalized 2 to 2.5 Hz SWCs. During REM sleep, the electrical status disappeared, and there were only rare bursts of generalized SWCs or focal spikes, predominantly in the frontal region. The awake EEGs also showed a dramatic improvement with intermittent bursts of generalized SWCs.<sup>26</sup> During nonREM sleep, the continuous SWCs resulted in the obscuring of sleep spindles and vertex sharp transients of sleep so that it was difficult to differentiate the various stages of nonREM sleep. NonREM and REM sleep, however, could be distinguished, the proportion being 80% and 20% respectively.

This condition occurred almost always in patients with a prior history of epilepsy. The onset of ESES was associated with a severe decrease in IQ. After ESES resolved, performance and behavior improved markedly. Recovery, however, was slow, and returned to normal in only two of 11 children who were previously of normal development in Tassinari's series.<sup>26</sup> In his group of children with prior abnormal psychomotor development, when ESES stopped, the level of mental activity was not very different from that during ESES, but there was marked improvement in their psychiatric condition.

#### SLEEP AND EEG IN THE EVALUATION OF EPILEPSY

Sleep is an important activating technique used during routine EEG. It should be utilized in routine EEGs in the evaluation of epilepsy especially when IEA is not defined in the awake recording. Sleep was shown to activate IEA by Gibbs and Gibbs; 19% of 174 patients demonstrated discharges awake, while 63% demonstrated discharges in the sleep EEG recordings.<sup>27</sup> Subsequent studies found sleep necessary to define IEA in one third of 667 patients,<sup>28</sup> in 23 of 36 patients,<sup>29</sup> in 30 of 89 patients,<sup>30</sup> and in 23 of 73 patients.<sup>31</sup> In our study of 30 patients with CPS, in the first EEG, sharp waves were present in 16 during the awake recording and increased in amount in 14 of the 16 during sleep; in an additional eight patients, sharp waves appeared only during sleep.<sup>32</sup>

Medication is frequently employed to induce sleep in the EEG laboratory, but barbiturates and benzodiazepines may enhance beta activity and make the interpretation of the EEG more difficult. Chloral hydrate has less tendency to increase beta activity and has a low potential for any side effects; thus, it is an ideal



alternative as an hypnotic.

Sleep deprivation enhances the possibility of obtaining sleep during the routine EEG and thus activating IEA. In addition, sleep deprivation may increase the possibility of recording sharp waves in the waking EEG record. Two studies have shown this technique to yield epileptiform discharges in a second awake EEG compared to a normal first EEG in 47 of 114 patients<sup>33</sup> and in 31 of 42 patients.<sup>34</sup> It should be noted, however, that such an increase in the rate of abnormalities may be due in part to the increase in recording time.

All-night sleep recordings may be of value in patients who present with only nocturnal (sleep-related) seizures and who have normal daytime awake and sleep EEGs. The yield of epileptiform discharges may be increased because of the recording of sleep and the additional prolonged recording that is obtained. This technique is certainly used in epilepsy monitoring units evaluating patients for possible surgery of an intractable epilepsy.

#### SUMMARY

Characteristic of the intimate relationship between sleep and epilepsy are an increase in IEA in nonREM

sleep and a decrease in REM sleep, in both generalized and partial epilepsies. The morphology of epileptiform discharges may also be affected by sleep, with a change or breakdown of the generalized pattern in generalized epilepsy, but a better definition of sharp waves in partial epilepsy, during nonREM sleep. One notes a predilection for certain types of epilepsy to occur in sleep, such as benign focal epilepsy of childhood, or to occur shortly after awakening (juvenile myoclonic epilepsy). Epilepsy may disrupt the sleep architecture with an increase in light sleep and a decrease in deep sleep, and an increase in awake time after sleep onset.

Sleep is an important activator of IEA and is of value both in the routine EEG evaluation of epilepsy as well as in more prolonged studies used in epilepsy monitoring units.

DUDLEY S. DINNER, MD

Section of Epilepsy and Clinical Neurophysiology  
The Cleveland Clinic Foundation  
One Clinic Center  
9500 Euclid Avenue  
Cleveland, Ohio 44195

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