

SLEEP AND EPILEPSY: SOMETHING ELSE WE DID NOT KNOW

Sleep Deprivation Does Not Affect Seizure Frequency During Inpatient Video-EEG Monitoring

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PURPOSE: To determine whether acute sleep deprivation facilitates seizures during inpatient monitoring in a controlled protocol.

METHODS: Eighty-four patients with medically refractory partial epilepsy undergoing inpatient monitoring were assigned in consecutive blocks to either sleep deprivation every other night or to normal sleep. In both groups, subjects were requested to stay awake during the day, from 6 AM to 10 PM. In the sleep-deprivation group, patients also stayed awake between 10 PM and 6 AM every other night beginning with day 2. Patients were removed from sleep deprivation if they had two or more secondarily generalized seizures within 24 hours. Patients were removed from the normal sleep group and were sleep deprived if they did not have a complex partial or secondarily generalized seizure by day 6 of monitoring. In these patients removed from sleep deprivation or from normal sleep, data were analyzed up to and including the day of removal from the protocol.

RESULTS: The sleep deprivation and normal sleep subjects did not differ in age, sex, seizure localization, or percentage dosage reduction in antiepileptic drugs from baseline at days 1 to 3 of monitoring. Protocol duration was 6.5 ± 2.4 days (mean \pm SD) for the sleep-deprivation group and 5.8 ± 2.0 days for the normal sleep group. Seizures per day for complex partial, secondarily generalized, and combined complex partial and secondarily generalized, calculated from admission until end of protocol, did not differ significantly between the two groups.

CONCLUSIONS: Acute sleep deprivation did not affect seizure frequency during inpatient monitoring in our patients with intractable complex partial seizures with secondary generalization.

COMMENTARY

Sleep and epilepsy interact on many levels, and in many areas, the relation is unclear. Frontal lobe seizures, for example, occur somewhat more frequently during sleep, but are no more likely to secondarily generalize than when beginning during wakefulness. With temporal lobe seizures, it is the reverse: seizures start more often while awake, but generalize more when asleep (1). Rapid-eye-movement (REM) sleep is protective against partial seizures (1,2) but paradoxically is decreased by seizures (3). Considerable controversy exists about the influences of individual anticonvulsant drugs on sleep, both positive and negative (4). One of the most well accepted phenomena (by both physicians and patients) is that sleep deprivation exacerbates most, or all, seizure types. Epilepsy monitoring units (EMUs), therefore, routinely use sleep deprivation to increase the chances that a patient will have a seizure. This article brings this nearly universal process into question.

Malow et al. used a very systematic approach to the question of whether sleep deprivation increases seizures. Patients were in a controlled setting (an EMU), and were randomized to receive every-other-night sleep deprivation (more severe than used in many EMUs), or normal sleep nightly. In both groups, anticonvulsant drugs were tapered by using the same, standard protocol. The groups were similar in age, sex, seizure type, and time in the protocol; baseline seizure frequency was higher in the sleep-deprivation group, although this was not statistically significant. They found a virtually identical seizure frequency in the two groups.

The results are highly suggestive that sleep deprivation does not increase seizure frequency in this patient group, which consisted of patients with intractable localization-related epilepsy. There are several caveats to this conclusion. First, it may be that the hospitalized setting somehow changed the influence of sleep deprivation, whether by relief from other stresses of day-to-day living, medication taper, or other factors. This seems unlikely. Second, the study was by necessity unblinded; it could be that the intervention of being in the study somehow altered the expectations of one or both groups, and therefore the seizure rate. This also seems very unlikely. Finally, the study was relatively short (average, 6 days), so more prolonged sleep deprivation could exacerbate seizures.

In some ways, this may be analogous to the belief that

psychological stress increases the incidence of seizures. This is another widespread belief among patients and physicians; however, in a single study of a stressful event (SCUD missile attacks on Israel), there was no apparent increase in the frequency of seizures (5). Again, there may be other types of stressors or other conditions in which stress increases seizures, suggesting that this also is not a simple relation.

It is well known that other epilepsy syndromes, such as juvenile myoclonic epilepsy and awakening grand mal, are exacerbated by sleep deprivation. It also may be true that individual patients with localization-related epilepsy could be sensitive to the effects of sleep deprivation, but this effect could not be seen in a series of patients.

This study is important because it suggests that the routine practice of sleep deprivation in EMUs is not helpful in reducing hospital stays. More important, it highlights the gaps in our existing knowledge about the relation between sleep and epilepsy. In addition to the effects of sleep and sleep deprivation on seizures, several other, potentially important areas exist in which questions have incomplete answers. How frequently do various sleep disorders coexist with epilepsy? How prevalent is drowsiness in the epilepsy population (6), and how much of this arises from the disease itself, from seizures, from concurrent sleep disorders, or from medication? What are the effects of individual anticonvulsants on sleep (7–13), and (perhaps more important) are these clinically significant? Further research in this area is clearly warranted, and this study is an excellent first step toward understanding one aspect of the complicated sleep/epilepsy relation.

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References

1. Herman ST, Walczak TS, Bazil CW. Distribution of partial seizures during the sleep-wake cycle: differences by seizure onset site. *Neurology* 2001;56:1453–1458.
2. Bazil CW, Walczak TS. Effects of sleep and sleep stage on epileptic and nonepileptic seizures. *Epilepsia* 1997;38:56–62.
3. Bazil CW, Castro LHM, Walczak TS. Diurnal and nocturnal seizures reduce REM in patients with temporal lobe epilepsy. *Arch Neurol* 2000;57:363–368.
4. Mendez M, Radtke RA. Interactions between sleep and epilepsy. *J Clin Neurophysiol* 2001;18:106–127.
5. Neufeld MY, Sadeh M, Cohn DF, Korczyn AD. Stress and epilepsy: the Gulf war experience. *Seizure* 1994;3:135–139.
6. Malow BA, Bowes RJ, Lin X. Predictors of sleepiness in epilepsy patients. *Sleep* 1997;20:1105–1110.
7. Salinsky MC, Oken BS, Binder LM. Assessment of drowsiness in epilepsy patients receiving chronic antiepileptic drug therapy. *Epilepsia* 1996;37:181–187.
8. Wolf P, Roder-Wanner UU, Brede M. Influence of therapeutic phenobarbital and phenytoin medication on the polygraphic sleep of patients with epilepsy. *Epilepsia* 1984;25:467–475.
9. Placidi F, Diomedei M, Scalise A, Marciani MG, Romigi A, Gigli GL. Effect of anticonvulsants on nocturnal sleep in epilepsy. *Neurology* 2000;54(suppl 1):S25–S32.
10. Yang JD, Elphick M, Sharpley AL, Cowen PJ. Effects of carbamazepine on sleep in healthy volunteers. *Biol Psychiatry* 1989;26:324–328.
11. Foldvary N, Perry M, Lee J, Dinner D, Morris HH. The effects of lamotrigine on sleep in patients with epilepsy. *Epilepsia* 2001;42:1569–1573.
12. Rao ML, Clarenbach P, Vahlensieck M, Kratzschmar S. Gabapentin augments whole blood serotonin in healthy young men. *J Neural Transm* 1988;73:129–134.
13. Mathias S, Wetter TC, Steiger A, Lancel M. The GABA uptake inhibitor tiagabine promotes slow wave sleep in normal elderly subjects. *Neurobiol Aging* 2001;22:247–253.