

USING SLEEP MEDICINE TO SOLVE DIFFICULT NEUROLOGIC CASES

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Sleep Issues in Patients with Epilepsy:

Background:

Sleep provides an opportunity to examine and potentially improve epilepsy. The variety of physiological repercussions of sleep influences the electrical and pathophysiological manifestations of epilepsy. These range from promotion or inhibition of epileptic events to the theoretical effects of “kindling” in epileptic pathophysiology. In addition, epilepsy can cause further sleep disruption and changes in sleep architecture. Likewise, the treatment of epilepsy can impact sleep. These dynamic relationships lead to patients with epilepsy frequently having sleep problems.

The influence of sleep can be examined by the effect of total sleep and the effect of each stage. For centuries, patients with epilepsy have been warned to avoid sleep deprivation, and several studies show the provocative nature of sleep deprivation on epileptic events. In addition, oversleeping appears to increase the occurrence of epileptic seizures. Although no good selective sleep stage deprivation studies have been performed in humans, studies in animals suggest the selective loss of REM sleep may enhance the kindling process and cause progression in intractability of focal onset seizures. Likewise, sleep stage may influence seizure onset. Stages of NREM sleep are more likely to produce seizures, whereas REM sleep appears to be protective against seizures. Similarly, interictal discharges are more likely in NREM sleep, with the greatest increase in frequency, topography, and localization noted with the approach of deeper stages of NREM sleep. REM sleep is the state least likely to have interictal discharges, and these discharges are most restricted to near the epileptic focus; thus REM sleep offers an opportunity for better localization of epileptic foci. Although these observations are clear, the underlying reason for the difference of topography of the interictal discharges is still somewhat unclear. Most theories rest on the hypothesis that more neurons are in the resting state in NREM sleep and thus are available for recruitment into the discharge. Whereas during REM sleep, there is overall greater neuronal firing, and neurons are less available to be recruited into the interictal firing.

Some epilepsies are specifically related to sleep. Benign epilepsy of childhood with central temporal spikes is associated typically with seizures of focal spasms of the face or hand with jerking, occurring in the first third of the night. These events classically start in NREM sleep and, for many patients, the interictal discharge appears only during sleep. Similarly, autosomal dominant nocturnal frontal lobe epilepsy is also seen as a variety of brief and occasionally violent hyperkinetic events occurring from NREM sleep. This disorder is associated with an abnormality in the nicotinic receptor complex, and appears to become hypersensitive during sleep. These patients appear to respond to carbamazepine or lamotrigine, however, a portion remain intractable. Other epilepsy syndromes such as Benign childhood Epilepsy with centrottemporal spikes, Panayiotopoulos Syndrome, Landau-Kleffner Syndrome or Continuous Spike and Wave in Sleep are also associated with nocturnal events or discharges. Some primary generalized epilepsies, especially those including myoclonus, are associated with seizures soon after awakening, indicating that seizure generation is somehow more prominent during the sleep-to-wake transition period.

Epilepsy also produces changes in sleep. Seizures are noted to cause post-ictal somnolence, but also evoke more wake after sleep onset, sleep fragmentation, and REM sleep suppression during the sleep period following the seizure. This effect appears to extend beyond frank seizures. Interictal discharges also cause sleep fragmentation, potentially by disrupting signals involved in sleep circuitry thus disrupting the physiological coordination of sleep. This disruption may have some downstream effect as hypothesized that nighttime discharges may influence daytime learning. Recent studies have shown correlations between nighttime seizure activity, and complaints of nighttime disruption, and daytime symptoms. Similarly in adults, patients with frequent interictal discharges during sleep had more daytime symptoms of sleepiness, and antiepileptic drugs may help decrease the frequency of nocturnal discharges and improve daytime symptoms.

Nearly two thirds of patients with epilepsy note sleep complaints. These complaints translate into higher prevalence of underlying sleep issues. Polysomnographic examination of patients with epilepsy showed a high prevalence of obstructive sleep apnea (OSA), a disorder in which the upper airway collapses during sleep, often accompanied by sleep fragmentation.⁹ Diagnosis and treatment of co-morbid sleep apnea may offer an opportunity to improve seizure frequency and quality of life in patients with epilepsy. Several case series and one randomized double-blind have shown that addressing co-morbid sleep problems was associated with improvement in intractable epilepsy.

Many medications used to treat epilepsy influence sleep, yet most need further study in both patients with epilepsy and in normal controls. Traditional medications such as phenobarbital, carbamazepine, phenytoin, and valproate have a soporific effect but they also may produce significant changes in overall sleep architecture, such as decreased REM sleep or increased sleep fragmentation. Pregabalin and gabapentin both appear to have a benefit by increasing slow-wave sleep and may improve sleep and attention in patients with epilepsy and insomnia. Some medications such as felbamate, zonisamide or lamotrigine at high doses may cause insomnia. At lower doses, lamotrigine and levetiracetam appear to have little overall effect on sleep. The overall downstream influence of these medications on sleep and, possibly, on the epileptic focus during sleep, still need to be studied. Preliminary work suggests a role for chrono-pharmacology in higher levels of sedating anticonvulsant medication at night may improve seizure response and lower incidence of side effects.

Investigation:

Patients with epilepsy may present with classic sleep-related symptoms of excessive daytime sleepiness or insomnia, or they may present with increasing frequency of seizures. In any of these presentations, the clinician should be keenly aware that sleep issues may be contributing to the symptoms and approach this opportunity by obtaining information in the following categories:

1. Is the patient getting enough sleep (bedtime and wake time)
2. Is the patient's sleep disrupted (does the patient find the sleep refreshing, do they snore or move about excessively?)
3. Is the patient sleeping at a wrong time (sleep diary)
4. Does the patient have a medication that is interfering with their sleep and or ability to be awake (review of medication dosing and timing)
5. Does the patient have some other issue such as depression in the background.

The clinician should first investigate the patient's bedtime and wake time, the overall sleep quality through the night, the appearance of snoring or excessive movement at night and the bedroom environment (dark, quiet, comfortable). Many times a sleep diary may be helpful to identify sleep schedule issues. If the sleep diary is not helpful activity or feeding may be beneficial to identify true schedule. Patients with epilepsy may have decreased activity during the day and thus may not develop enough of a homeostatic sleep drive to have good sleep quality at night. Therefore suggestions to increase daytime activities may be helpful to improve sleep. To identify patients who may have obstructive sleep apnea the STOP-BANG questionnaire may be helpful and the Pittsburgh sleep quality index may identify other sleep issues. For patients with snoring, witnessed apneas or excessive movement at night should have an overnight sleep study. For patients with nocturnal events overnight polysomnogram with extended EEG recording or video EEG recording may be beneficial in identifying the etiology.

Management:

Patients with epilepsy have an opportunity to improve their overall condition by practice of good sleep hygiene. Patients who have a variable sleep schedule should be instructed to make their sleep-wake schedule more consistent focusing on the time that they wake up emphasis should be given to avoid under and over sleeping since both have been demonstrated to increase recurrent seizures. For these patients the key is first to regularize the schedule and then improve their underlying sleep hygiene. Engaging them in daily activities such as work volunteering and exercise may also be helpful. Sometimes the use of melatonin or increasing the percentage of dose of somnogenic medications in the evening while decreasing the somnogenic dose of medications in the morning may improve daytime alertness. For patients who have obstructive sleep apnea, PAP therapy has been demonstrated to improve the patient's seizure frequency and quality of life. Similarly some investigators have suggested that improvement in treatment of other sleep disorders may also improve the underlying epilepsy.

Sleep issues in Patients with Headache:

Background:

Headaches, similar to epileptic seizures, share a complex bidirectional relationship with sleep. Although both headaches and sleep issues may be common and occur in the same patient, the relationship of sleep to headache appears to be more than coincidental. Sleep disruption can predispose, provoke, and perpetuate headache issues, whereas sleep may also improve headaches. In general, sleep deprivation and excessive sleep increase headaches in both children and adults. For patients predisposed to headaches, the link to sleep is even greater. Nearly 86% of episodic migraine patients note poor sleep quality and poor sleep was associated with increasing headache frequency and headache related disability. Likewise, poor sleep hygiene was noted as a frequent perpetuating agent in transformed migraine, and the improvement of sleep practices reverted the transformed migraine back to episodic migraine.

This relationship between headaches and sleep extends to those with primary sleep disorders. Patients with insomnia have a 50% greater likelihood of having headaches and more severe headaches. Similarly, bedpartners of habitual snorers are also more likely to have headaches, suggesting the environmental disturbance of sleep makes headaches more likely. Also, 15-60% of patients with obstructive sleep apnea complain of headaches, and these individuals are more likely to develop morning headache, migraine, chronic headache, and tension type headaches. Yet, treatment of sleep apnea with CPAP appears to improve headache frequency and intensity. Some headache types emerge from specific stages of sleep, indicating sleep may set the neurochemical stage to initiate the headache. Cluster headaches typically emerge during REM sleep. Migraine headaches that awaken a patient from sleep are more likely to be associated with vivid dreaming, suggesting they may arise during REM sleep, however further studies are needed. Hypnic headaches (sometimes called "alarm clock" headaches) abruptly awaken patients after one to three hours of sleep, and may respond to caffeine or if frequent, treatment with lithium. Chronic paroxysmal hemicranias also may awaken patients suddenly from sleep with abrupt clawing pain, and these events respond well to indomethacin. Despite our lack of understanding, both the mechanisms for sleep and headache generation share some of the same hypothalamic and brainstem circuitry, and improvement in sleep offers a unique pathway to improve headache care.

Investigation:

For patients with increasing headaches the investigation approach showed first identify the underlying sleep habits. This is especially true for patients who have transformed their headaches from intermittent headaches to chronic daily headaches. These patients may have several maladaptive behaviors that impact their overall sleep and contribute to the transformation of their headaches to be more severe. Investigation of the underlying sleep hygiene would include the review of their daily schedule including bedtime and wake time, the use of a sleep diary or the application of an actinic graffiti recording for 1-2 weeks. In addition tracking caffeine use, and intake of herbs and supplement and other underlying foods may be crucial in identifying key contributors to identifying mechanisms that disrupt their sleep-wake cycle. Similarly the use of light admitting devices in the evening may play a role in sleep disruption. Patients should also be questioned as for symptoms of snoring or pauses in their breathing or excessive movement at nighttime. Patients with these symptoms should undergo an in laboratory sleep study. Some patients with chronic headaches exclusively in the morning may be identified as having elevated carbon dioxide levels and may require carbon dioxide measurements during sleep. The finding of hypoventilation is more common in patients with obesity or neuromuscular disorders. Additionally medications may play a role disrupting sleep. Many patients find that caffeine can help for acute migraine headaches however this may cause disruption of sleep after the headache. Similarly other medications that may be used to abort migraines may actually also be alerting and disrupt sleep.

Management:

For patients with frequent headaches, increasing headaches or chronic daily headache the management approach be first to improve the sleep-wake cycle. This can be done by first attempting to have a set up a specific wake up time. Then the patient should be instructed to optimize the use of bright light exercise and social interactions during the day as well as regularly timed meals. These features will accentuate the circadian rhythm to alertness and the absence of these will improve sleep at night. Similarly cognitive behavioral therapy especially stimulus control therapy may be beneficial in the promoting the appropriate clues in the evening to go to sleep. Some patients will need weaned from caffeine and other alerting substances and including these on a diary with

headaches may make it easier to identify potential triggers as well as note the improvement as the sleep hygiene is also improved. As with other neurological disorders if the patient is found to have sleep apnea appropriate therapy including PAP therapy.

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