Nocturnal Epilepsy

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Epidemiology of Epilepsy and Gomorbidities in Sleep Disorders

- **About 1 % to 2% of the population has epilepsy, and 1 out of 10 people will have a seizure during their lifetime.**

- **Approximately 20% of patients with epilepsy will have seizures solely while asleep.**

Epidemiology of Epilepsy and Comorbidities in Sleep Disorders

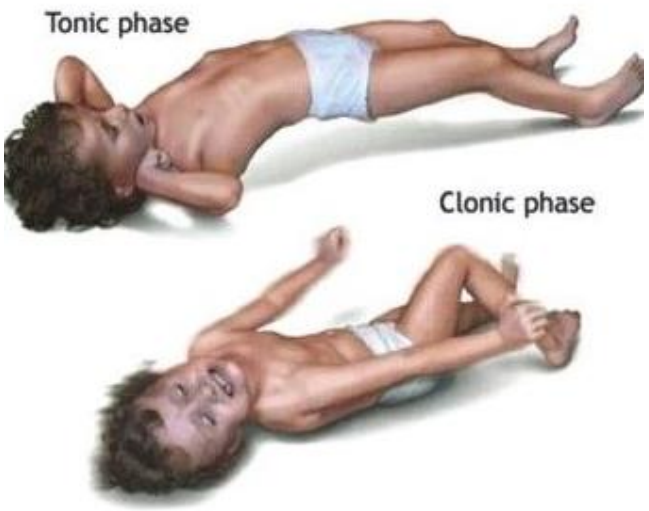
- **seizures are related to circadian rhythms and sleep**
- **different types of seizures occur more in sleep than in wakefulness**
- **Occipital and parietal epilepsy have a lower incidence of seizure during sleep, whereas frontal lobe and, to a lesser extent, temporal lobe epilepsy have a higher occurrence during sleep.**

Epidemiology of Epilepsy and Comorbidities in Sleep Disorders

- **Temporal neocortical seizures have been more related to sleep than have those of mesial origin.**
- **A particular form of benign focal epilepsy of childhood (benign Rolandic epilepsy) is clearly related to sleep.**

Epidemiology of Epilepsy and Comorbidities in Sleep Disorders

- **In idiopathic generalized epilepsy, myoclonic and tonic-clonic seizures may arise on awakening or during sleep and may randomly occur throughout the day.**



Epidemiology of Epilepsy and Comorbidities in Sleep Disorders

- **Nocturnal seizures should be distinguished from other nocturnal events such as parasomnias .**
- **The most difficult problem is to distinguish between frontal lobe seizures and parasomnias .**
- **Sleep disorders such as sleep deprivation and sleep apnea may exacerbate seizures .**
- **Conversely, seizures may affect sleep, as many of the current anti epileptic drugs produce undesirable side effects to sleep architecture and may predispose the patient to primary sleep disorders.**

Sleep State as a Facilitator of Epilepsy

➢ REM sleep

- ✓ **The increased brainstem cholinergic input, which occurs during REM sleep, induces a state of cortical activation.**

➢ NREM sleep

- ✓ **NREM sleep is a physiologic state of relative neuronal synchronization and predisposes to neuronal hyper polarization .**

Sleep State as a Facilitator of Epilepsy

NERM SLEEP

Seizure Promotor

- ✓ Synchrony of thalamocortical synaptic activity
- ✓ Greater tendency for propagation of epileptiform discharges

REM SLEEP

Seizure Protector

- ✓ Increased cholinergic tone
- ✓ Desynchronized neuronal discharge patterns
- ✓ Relative resistance to propagation of EEG potentials
- ✓ Skeletal muscle paralysis

SYNCHRONIZED SLEEP

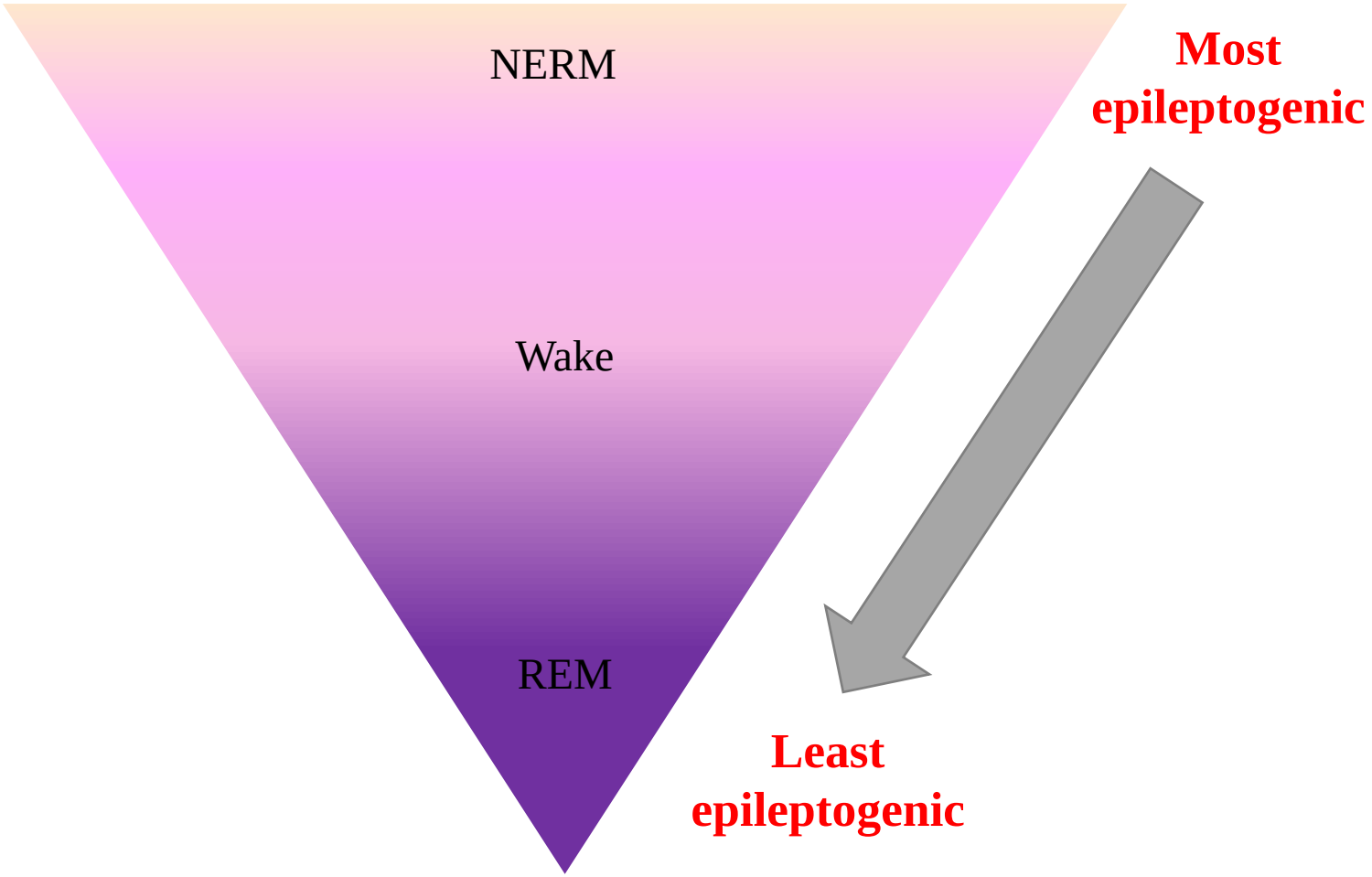
- ✓ Excessive diffuse cortical synchronization
- ✓ Enhancement in interhemispheric impulse traffic

DESYNCHRONIZED SLEEP

- ✓ Inhabitation of thalamocortical synchronization
- ✓ Tonic reduction in interhemispheric impulse traffic

Sleep State as a Facilitator of Epilepsy

Seizures vs. State Epileptogenicity



Regional Anatomy in Epilepsy Facilitation

- **Patients with frontal lobe epilepsy experience most of their seizures during sleep, whereas those with temporal lobe epilepsy experience most of their seizures while awake**

- **The frontal lobe receives significant ascending input from the thalamus and has rich interconnections, demonstrating its propensity as a region to facilitate seizures during sleep.**

The elements for consideration of Diagnosis of sleep-related seizures

- ✓ **The patient has a history of epilepsy, even if the epilepsy is well controlled.**
- ✓ **The patient experiences stereotyped events that are repetitive and disruptive to the sleep of the patient and the patient's bed partner.**

The elements for consideration of Diagnosis of sleep-related seizures

- ✓ **Episodes occur at any time of night (more commonly during NREM sleep than during REM sleep).**
- ✓ **Similar events may occur during the day.**
- ✓ **A trial of antiepileptic drugs produces a favorable response**

Nocturnal Epilepsy

- **It has long been known that seizures, both convulsive and non convulsive, often occur during sleep, especially in children.**
- **Seizures may occur soon after the onset of sleep or at any time during the night, but mainly in stages 1 and 2 of NREM sleep or, rarely, in REM sleep.**
- **They are also common during the first hour after awakening.**

- **If the nocturnal seizure is unobserved, the only indication of it may be disheveled bedclothes, a few drops of blood on the pillow from a bitten tongue, wet bed linen from urinary incontinence, or sore muscle.**

- **Rarely, a patient may die in an epileptic seizure during sleep, sometimes from smothering in the bed clothes or aspirating vomitus or for some obscure reason (possibly respiratory or cardiac dysrhythmia).**

- **Epilepsy occasionally occurs in conjunction with night terrors and somnambulism; the question then arises whether the latter disorders represent postepileptic automatisms.**

- **Usually no such relationship is established.**

- **EEG studies during a nocturnal period of sleep are most helpful in such cases.**

- **Measurement of serum creatine kinase concentration in the hours following an event may distinguish seizure from night terrors, and the other described sleep-related motor behaviors.**

Nocturnal Frontal Lobe Epilepsy

- **Nocturnal frontal lobe epilepsy (NFLE) represents a type of partial epilepsy in which seizures appear mainly or almost exclusively during NREM sleep.**

- **Seizures are usually described as episodes of paroxysmal motor behaviors characterized by bizarre hyperkinetic patterns or distonic postures with a high frequency of nightly episodes, internight repetition, and stereotypy.**

Nocturnal Frontal Lobe Epilepsy

Classification of the episodes into different semiologic patterns.

- ✓ ***Minor events*, or *paroxysmal arousals*, are characterized by a sudden arousal and no major movements.**
- ✓ ***Major episodes* include hyperkinetic seizures with complex movements, vocalization, screaming, and repetitive movements of the trunk and limbs; *asymmetric bilateral tonic seizure*.**

Nocturnal Frontal Lobe Epilepsy

- **Seizures have been thought to originate from mesial frontal zones and orbitofrontal regions.**

- **Approximately 30% of the seizures arose from the extra frontal region and subsequently involved cingulate and frontal regions.**

- **Nowadays, a family history of possible NFLE is seen in about 25% of cases.**

Nocturnal Frontal Lobe Epilepsy

- **Not uncommonly, interictal and even ictal EEG findings are normal or nonspecific in patients with NFLE**

- **Reliable characterization of the episodes by the observers is lacking because they may be asleep or they may miss the beginning of an episode, leading to an ambiguous or partial description. Furthermore, nocturnal epileptic episodes may have auras and postictal periods that tend to be masked by sleep.**

Nocturnal Frontal Lobe Epilepsy

- **Home video recording could be useful, but video PSG is required for the diagnosis.**

- **A natural history of the episodes that appear to increase in frequency after childhood, occurrence of more than one episode per night, and semiology of the attacks (stereotypy, diskinetic and distonic components, clear onset and offset) are indicative of epileptic seizures.**

Nocturnal Frontal Lobe Epilepsy

- **Epileptic and parasomniac attacks often co-occur in the same family and even in the same patients.**

- **NFLE could be differentiated from REM sleep behavior disorder, which is characterized by later age of onset, relationship of the episodes with dream-enacting behavior, less stereotypy, and presence of REM without atonia during PSG recording.**

Nocturnal Frontal Lobe Epilepsy

- **The attacks may begin at any age, affect both sexes, and are usually nonfamilial.**
- **All respond to treatment with carbamazepine.**
- **Ictal and interictal EEGs during wakefulness and sleep are normal.**

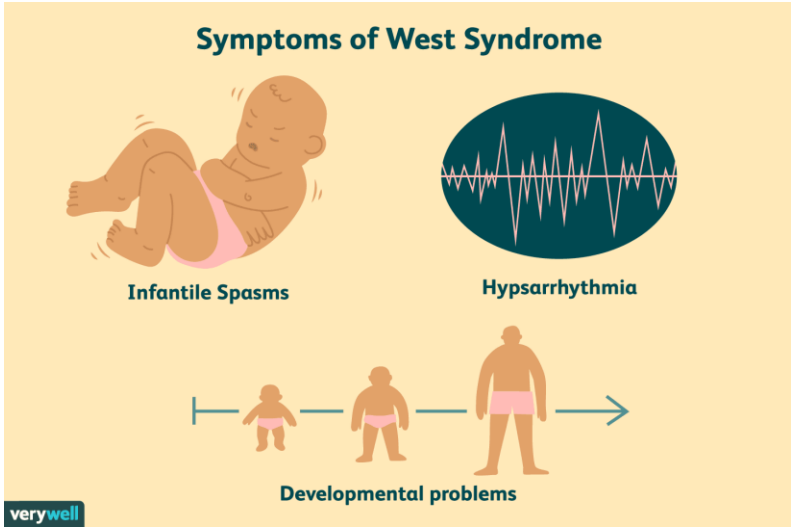
Sleep-Related Epilepsies

- **Patients with generalized tonic-clonic seizures on awakening have generalized seizures that occur in the morning.**
- **Juvenile myoclonic epilepsy is characterized by myoclonic, absence, and generalized tonic-clonic seizures.**
- **Myoclonus occurs soon after awakening, which may progress to a generalized seizure.**

Sleep-Related Epilepsies

West Syndrome

- is a catastrophic epilepsy syndrome characterized by a triad of epileptic flexor-extensor spasms of the body, variable intellectual disability, and chaotic hypsarrhythmic EEG, with onset between ages 3-18 months.
- The spasms or tonic seizures tend to cluster on awakening in the morning.
- At the onset of the disorder, hypsarrhythmia first occurs in NREM sleep



Sleep-Related Epilepsies

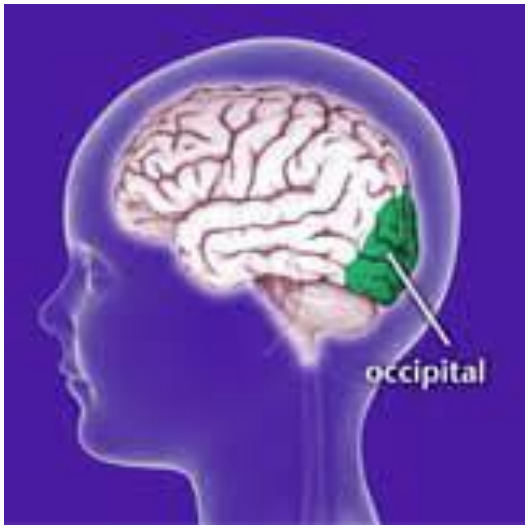
Benign Occipital Lobe Epilepsy

- **A benign epilepsy syndrome seen in children ages 2-6 years.**
- **characterized by prolonged periods of eye deviation and autonomic instability (temperature, heart rate, respiration, and blood pressure) and hemiconvulsive and generalized tonic-clonic seizures in sleep, with vomiting on awakening.**

Sleep-Related Epilepsies

Benign Occipital Lobe Epilepsy

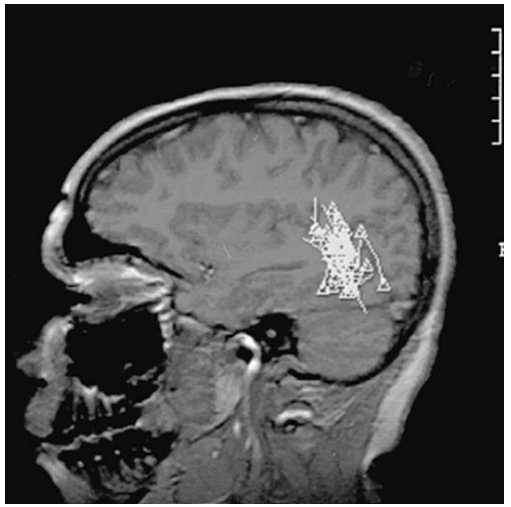
- **Interictal EEGs show occipital spikes, whereas Interictal EEGs show electrographic seizures emanating from the occipital region during sleep.**
- **Remission occurs within 2 years of onset.**



Sleep-Related Epilepsies

Landau-Kleffner Syndrome

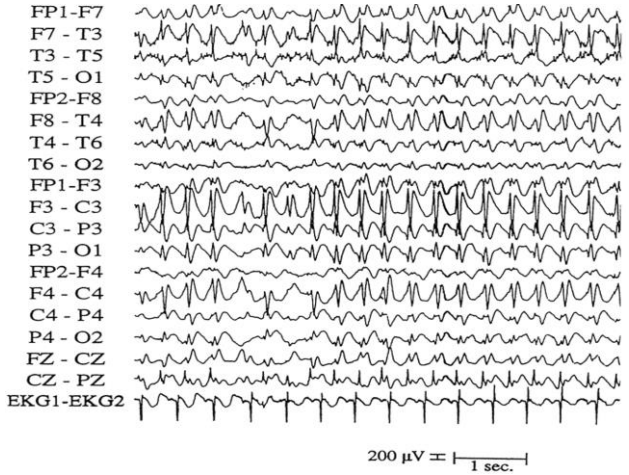
- **Landau-Kleffner syndrome, also called acquired epileptic aphasia, is a rare childhood neurologic disorder in which children present with language regression or verbal auditory agnosia.**
- **Onset is usually between 3 and 8 years of age.**
- **Epileptiform Activity during sleep, behavioral disturbances, and sometimes overt seizures are seen.**
- **In Landau-Kleiner syndrome spike wave activity is mainly in the temporal lobe channels.**



Sleep-Related Epilepsies

Benign Epilepsy with Centrotemporal Spikes

- **Benign epilepsy with centrotemporal spikes, or benign rolandic epilepsy, is the most common partial epilepsy syndrome in children, with an onset between 3 and 13 years of age and remission in adolescence.**
- **The typical presentation is a partial seizure with paraesthesias and tonic or clonic activity of the lower face, associated with drooling and dysarthria.**
- **The seizures are mostly nocturnal, with 55%-59% of patients having seizures exclusively during sleep.**



Sleep-Related Epilepsies

Benign Epilepsy with Centrotemporal Spikes

- **On EEG, central and temporal lobe spikes are seen.**
- **despite the increased frequency of seizures and spikes IEDs during sleep, the sleep architecture is unaffected.**
- **The response to medications is excellent, and the prognosis is universally good from an epilepsy perspective.**
- **The syndrome is no longer considered benign as cognitive deficits have been described in children with it.**

Sleep-related Epilepsy Syndromes

- **Temporal lobe epilepsy is the most common type of partial epilepsy in adults.**

- **Patients may lack an aura or may not recall the event. Spells consist of experiential, autonomic, or special sensory components associated with brief periods of impaired consciousness with motionless starting or automatisms.**

NOCTURNAL PAROXYSMAL DYSTONIA

- **Nocturnal paroxysmal dystonia is a form of frontal lobe epilepsy that consists of a sudden arousal associated with a complex sequence of movements, repeated dystopia, or a dyskinetic (ballistic or choreoathetotic) pattern .**

NOCTURNAL PAROXYSMAL DYSTONIA

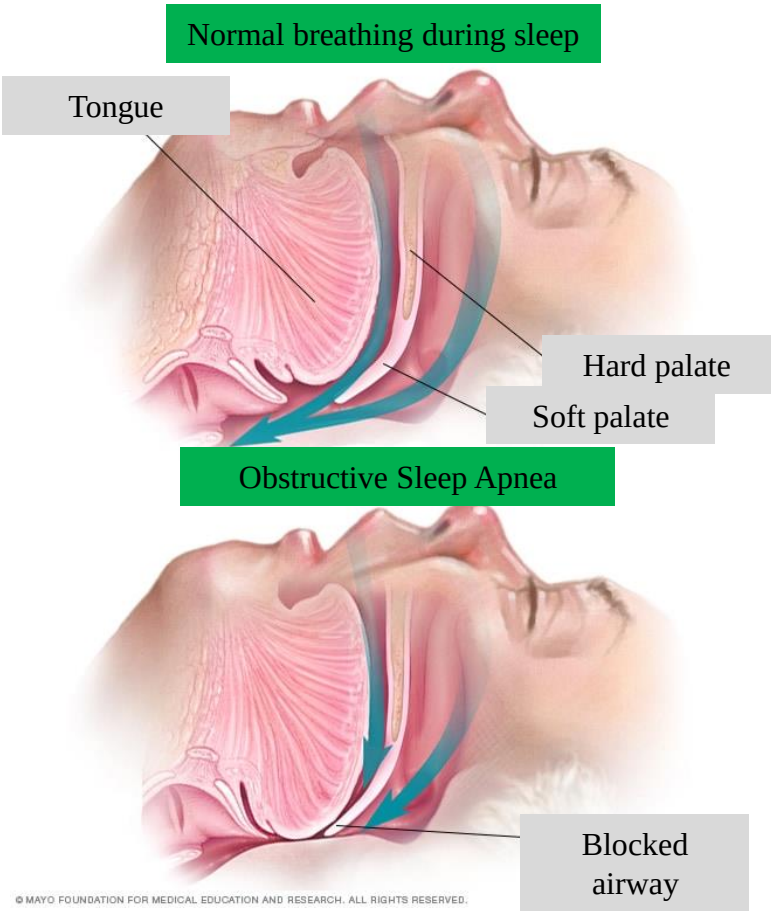
- **Patients may also move their legs and arms with cycling or kicking movements.**
- **Consciousness is often preserved.**
- **Carbamazepine is the agent of choice and provides an excellent response.**

Sleep Disorders in Epilepsy

Obstructive Sleep Apnea

- **A study by Malow et al. in adults with refractory epilepsy showed that 33% had OSA.**

- **The predictors for OSA were increasing age, male sex, and seizures during sleep.**

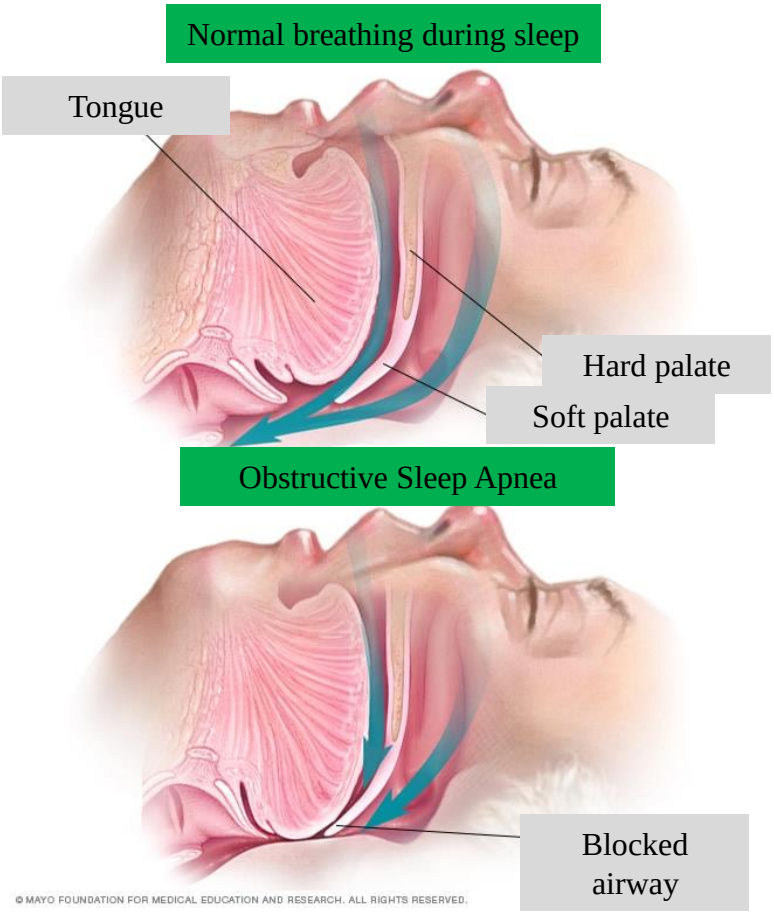


Sleep Disorders in Epilepsy

Obstructive Sleep Apnea

- **No correlation was identified with seizure frequency or type, AED number or type, seizure localization, and sleepiness.**

- **In a retrospective review in children with epilepsy, uncontrolled epilepsy was a risk factor for OSA as compared with primary snoring.**

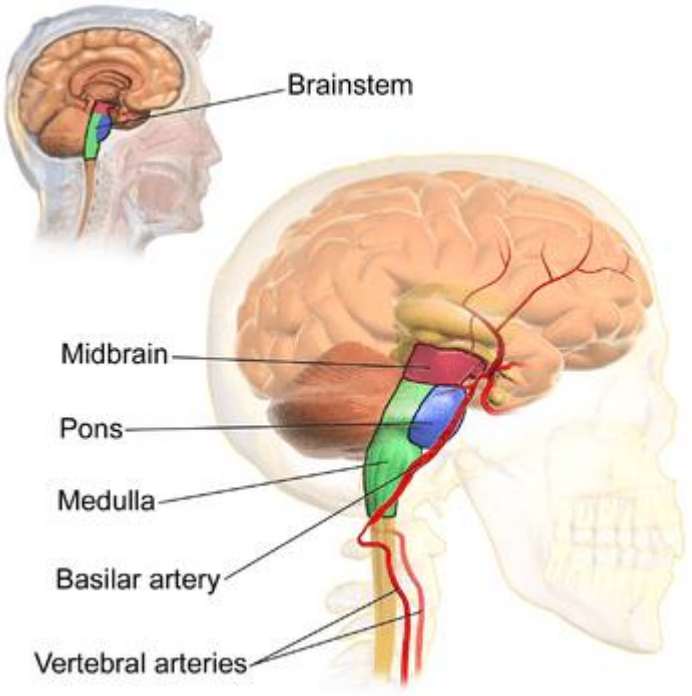


Sleep Disorders in Epilepsy

Central Sleep Apnea

- ✓ **In a study by Vendrame et al., 3.7% of patients with epilepsy had central sleep apnea (CSA) and 7.9% had complex sleep apnea.**

- ✓ **CSA was more common among men. Focal seizures were more prevalent in patients with CSA.**



Sleep Disorders in Epilepsy

Restless Leg Syndrome or Periodic Limb Movement Disorder

- **n children with epilepsy, referred to sleep laboratory, periodic limb movements or periodic limb movement disorder was found in 5%-10%.**
- **In studies in adults with epilepsy, 15% had periodic limb movement disorder and 17% had periodic limb movements in sleep.**

Sleep Disorders in Epilepsy

Insomnia

- **In children with epilepsy referred for sleep evaluation, insomnia was identified in 11%.**
- **In adults with epilepsy, 40%-55% of patients had insomnia.**
- **Insomnia correlated with number of AEDs, and higher scores on depression scales.**
- **In 100 consecutive adult patients with epilepsy, sleep-onset insomnia was reported in 34% and maintenance insomnia in 52%.**

Sleep Disorders in Epilepsy

Sleepiness or Hypersomnia

- **Overall, 28%-48% of patients with epilepsy report daytime sleepiness. In a questionnaire-based study, 70% of the neurologists attributed sleepiness to AEDs.**

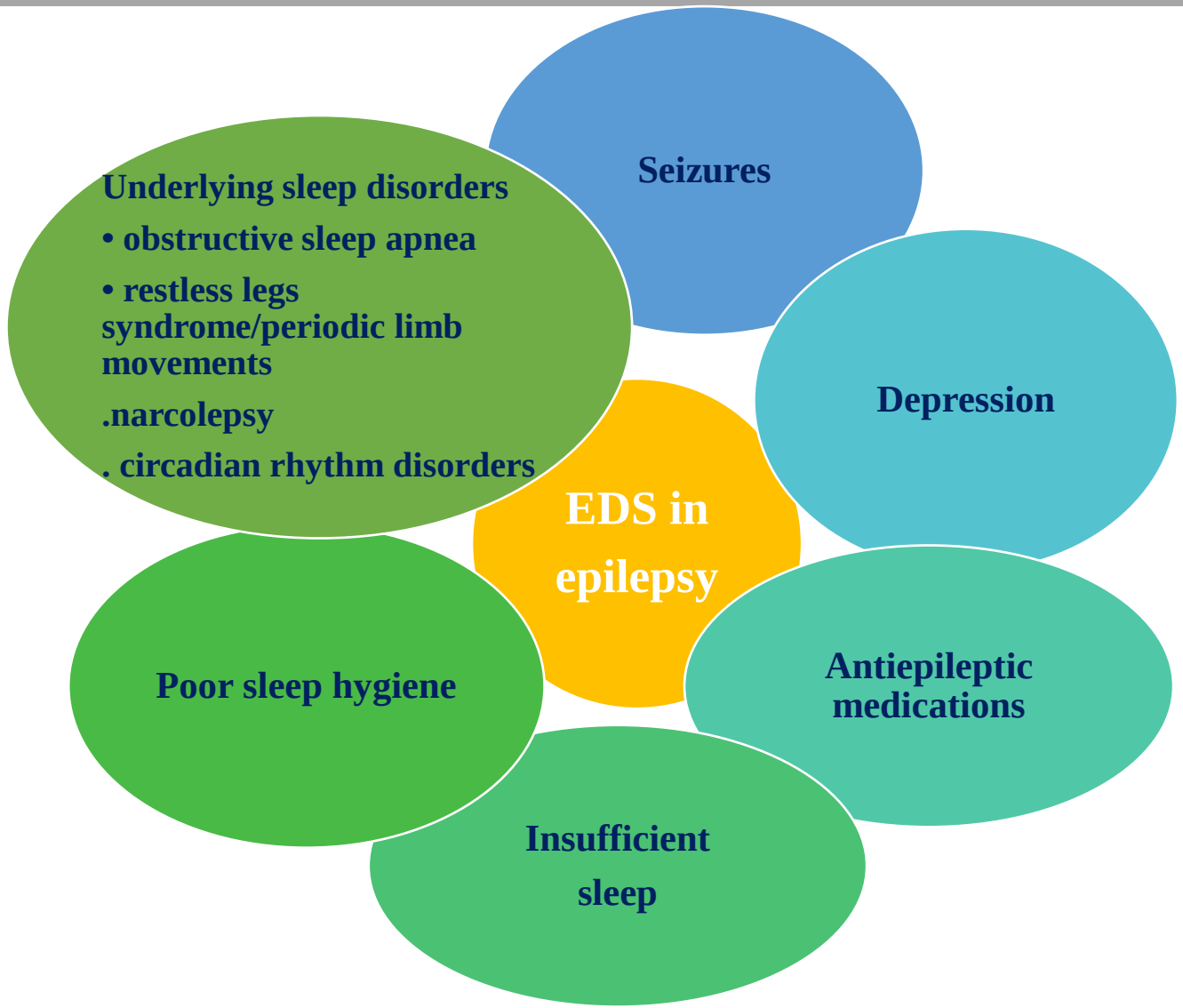
- **However, prospective studies in adults with epilepsy evaluating sleepiness with subjective and objective tools identified that sleepiness correlated with sleep apnea and restless leg syndrome symptoms, habitual snoring, observed apneas, recurrence of seizures, neck circumference, and anxiety.**

Sleep Disorders in Epilepsy

Sleepiness or Hypersomnia

- **No correlation was found for type of AED, number of AEDs, type of seizures, and seizure frequency.**
- **In 46.2% of children with epilepsy had sleepiness that was associated with symptoms of sleep disordered breathing and parasomnia.**

Obstructive Sleep Apnea and Epilepsy



Sleep Disorders in Epilepsy

Parasomnia

- **Parasomnias are also common in children with epilepsy.**
- **Nocturnal seizures may be difficult to differentiate from parasomnias.**

Nocturnal Frontal Lobe Epilepsy

Characteristics of Nocturnal Frontal Lobe Epilepsy (NFLE) vs. Parasomnias

Clinical Feature	NFLE	PARASOMNIAS
Age at onset (years)	11.8±6.3	usually< 10
Attacks/months (n)	36±12	1-4
Clinical course	Increasing or stable	Decreasing/disappearing
Movement semiology	Stereotypic	Polymorphic
Attack onset	Any time during the night	First third of the night
Attack distribution	2-NREM (65%)	3-4 NERM
Motor pattern	2-3 repetitive types of attacks	Absence of motor pattern
Duration of the attacks	Less than 1 min (excl. prolonged episodes)	Some minutes


Nocturnal Seizures
Polymorphic
Complex
Fighting
Sensation of fear
Tachycardia
Running
Bicycling
Kicking
Thrashing movements
Shouting
Screamin g
Laughing

Effect of Treatment of Sleep Disorders on Epilepsy

- **Treatment of sleep disorders improves the seizure control.**
- **A retrospective review in adult patients with OSA and epilepsy, treated with continuous positive airway pressure (CPAP) at least for 6 months, showed decreased seizure frequency.**
- **Of 28 CPAP-compliant subjects, 16 became seizure free. In the noncompliant group, no significant differences were seen.**
- **CPAP also improved IEDs in wakefulness and sleep except for REM sleep.**

Effect of Treatment of Sleep Disorders on Epilepsy

- **In a randomized study, 50% or more seizure reduction was seen in 28% of subjects on CPAP as compared with 15% of controls.**
- **Additionally, treatment of underlying OSA with adenotonsillectomy resulted in improvement in seizure frequency.**
- **in a randomized study, in patients with insomnia and epilepsy, melatonin improved seizure frequency; however, no significant improvement in sleep was noted.**
- **In a recent randomized placebo-controlled study, melatonin improved sleep with nonsignificant improvement in IEDs and seizure frequency.**

Obstructive Sleep Apnea and Epilepsy

Effects of Antiepileptic Drugs on Sleep

Drug	EDS	INSOMNIA	SL	REM	SLOW WAVE	AWAKENINGS	OTHER
Gabapentin	++			↑		↓	↑Weight
Lamotrigine		+		↑	↑	↑	
Levetiracetam	+						
Oxcarbazepine	+						
Tiagabine	+++				↑		
Topiramate	++						↓Weight
Zonisamide	+	+					
Carbamazepine	+			↓			↑PLMs
Phenytoin	+	+	↓				
Valproate	+		↑			↑	↑Weight
Phenobarbital	+++					↓	↑OSA
Ethosuximide		+			↓		
Felbamate		++					↑Weight

+: mild effect; ++: moderate effect; +++: severe effect; EDS: excessive daytime sleepiness; SL: Sleep latency

Sudden Unexpected Death in Epilepsy, Sleep, and Cardiorespiratory Abnormalities

- **Sudden unexpected death in epilepsy is defined as a "sudden, unexpected, witnessed or unwitnessed, nontraumatic and non-drowning death in patients with epilepsy with or without evidence for a seizure and excluding documented status epilepticus in which postmortem examination does not reveal a toxicologic or anatomic cause for death.**

- **The incidence is as high as 6.0-9.3 per 1000 patient-years among patients evaluated for or treated with epilepsy surgery or vagus nerve stimulation for epilepsy.**

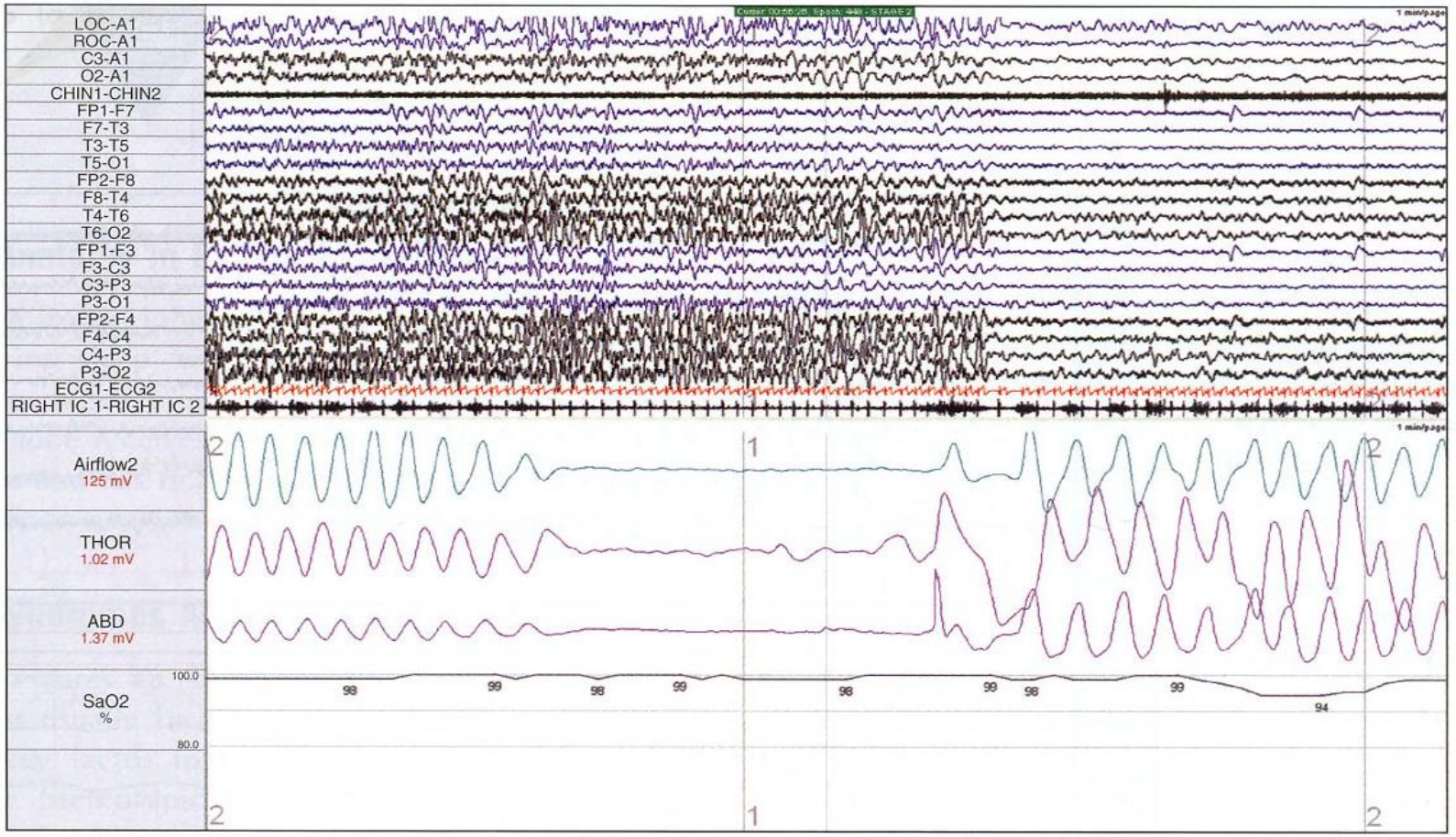
Sudden Unexpected Death in Epilepsy, Sleep, and Cardiorespiratory Abnormalities

- **The risk factors in children are major neurologic impairment, refractory seizures, and generalized tonic-clonic seizures. The death typically occurs in bed.**
- **One of the mechanisms thought to be responsible for sudden unexpected death in epilepsy is respiratory and cardiac changes during seizures.**
- **The respiratory abnormalities include central and obstructive apneas, hypoventilation, hypercapnia, and desaturation with acidosis, bradypnea, and tachypnea.**

Sudden Unexpected Death in Epilepsy, Sleep, and Cardiorespiratory Abnormalities

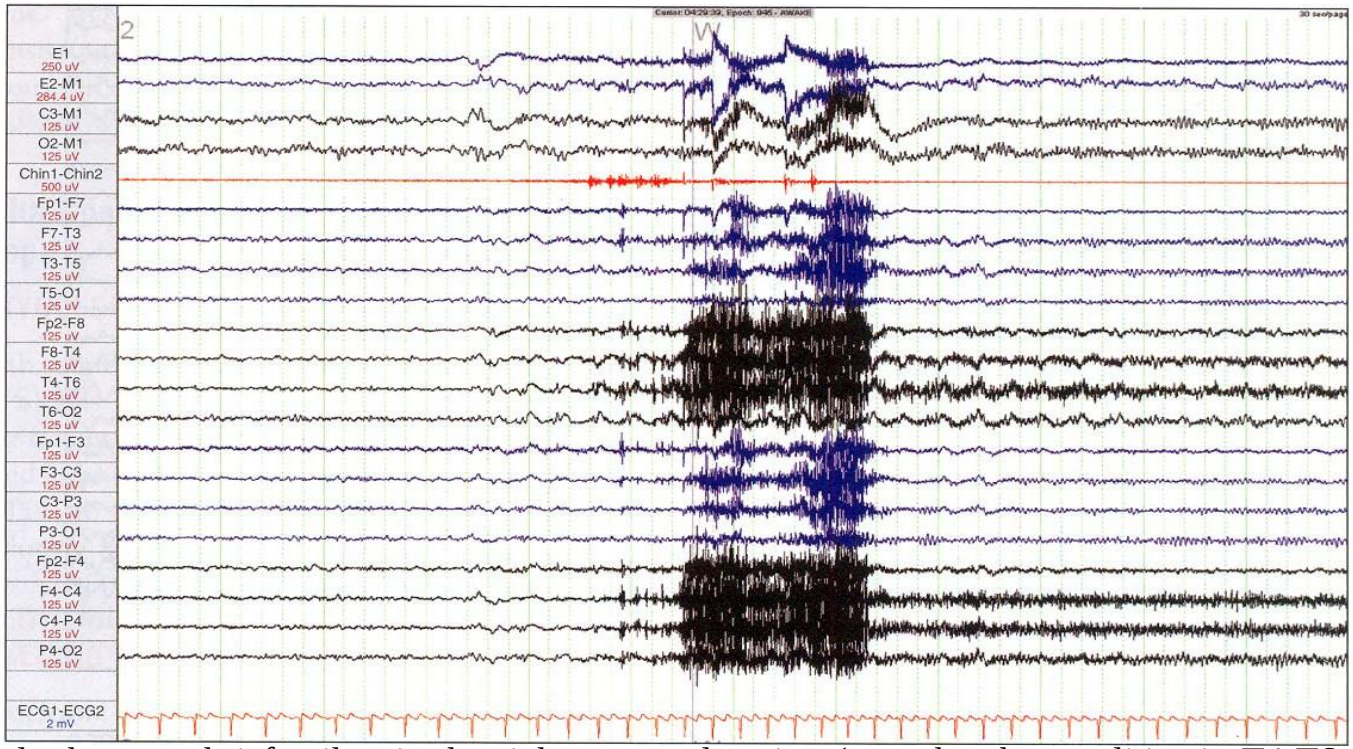
- **The cardiac abnormalities include postictal changes in heart rate variability caused by sympathetic activation, ictal bradycardia, asystole, repolarization anomalies (prolonged or shortened QTc interval), and atrial fibrillation.**
- **Moreover, cerebral shutdown seen as postictal EEG suppression may be another mechanism.**

PSG example of right-sided seizure resulting in central apnea



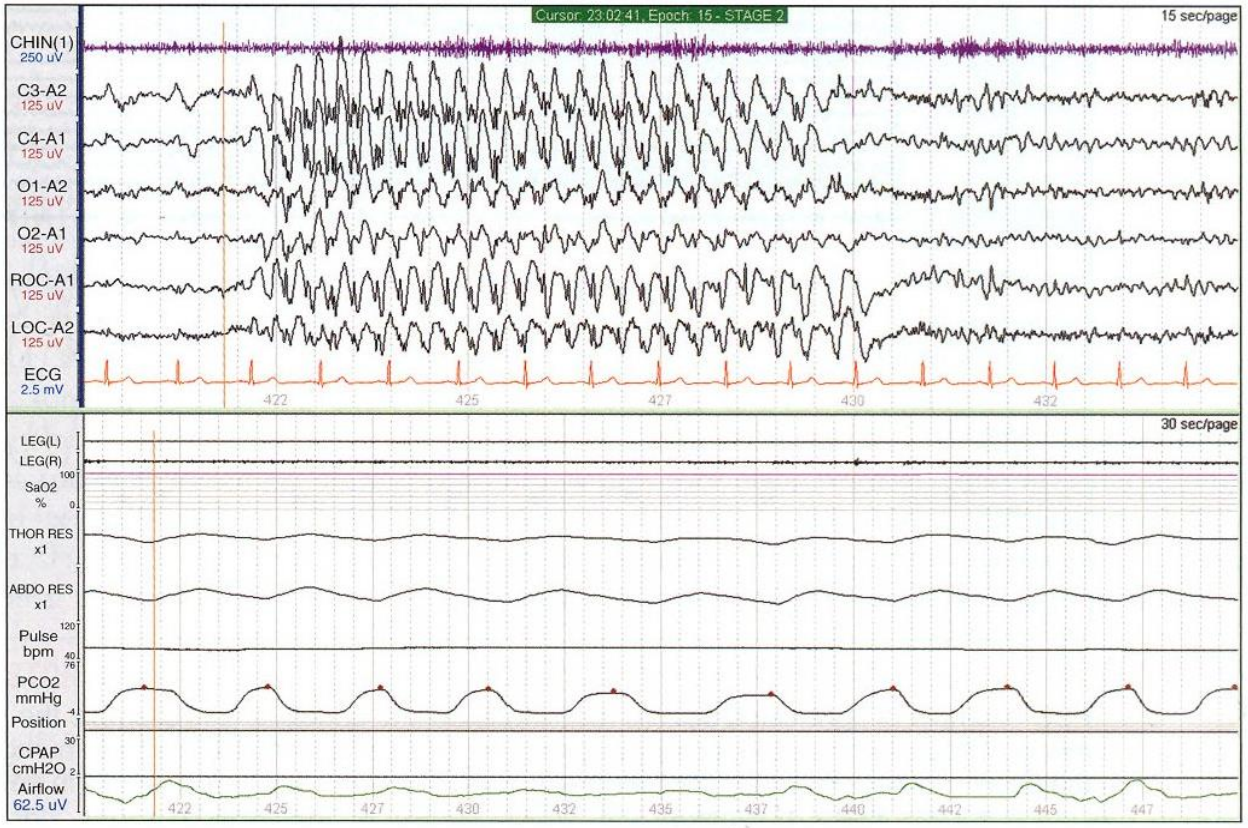
In this example the seizure was originally missed because the seizure activity was only on the right side (notice the even-numbered electrodes) and the scoring montage did not include them. Such a seizure montage is useful in cases of unexplained central apneas (black, right; blue, left). (PSG courtesy M. Mahowald.)

PSG example of temporal seizure.



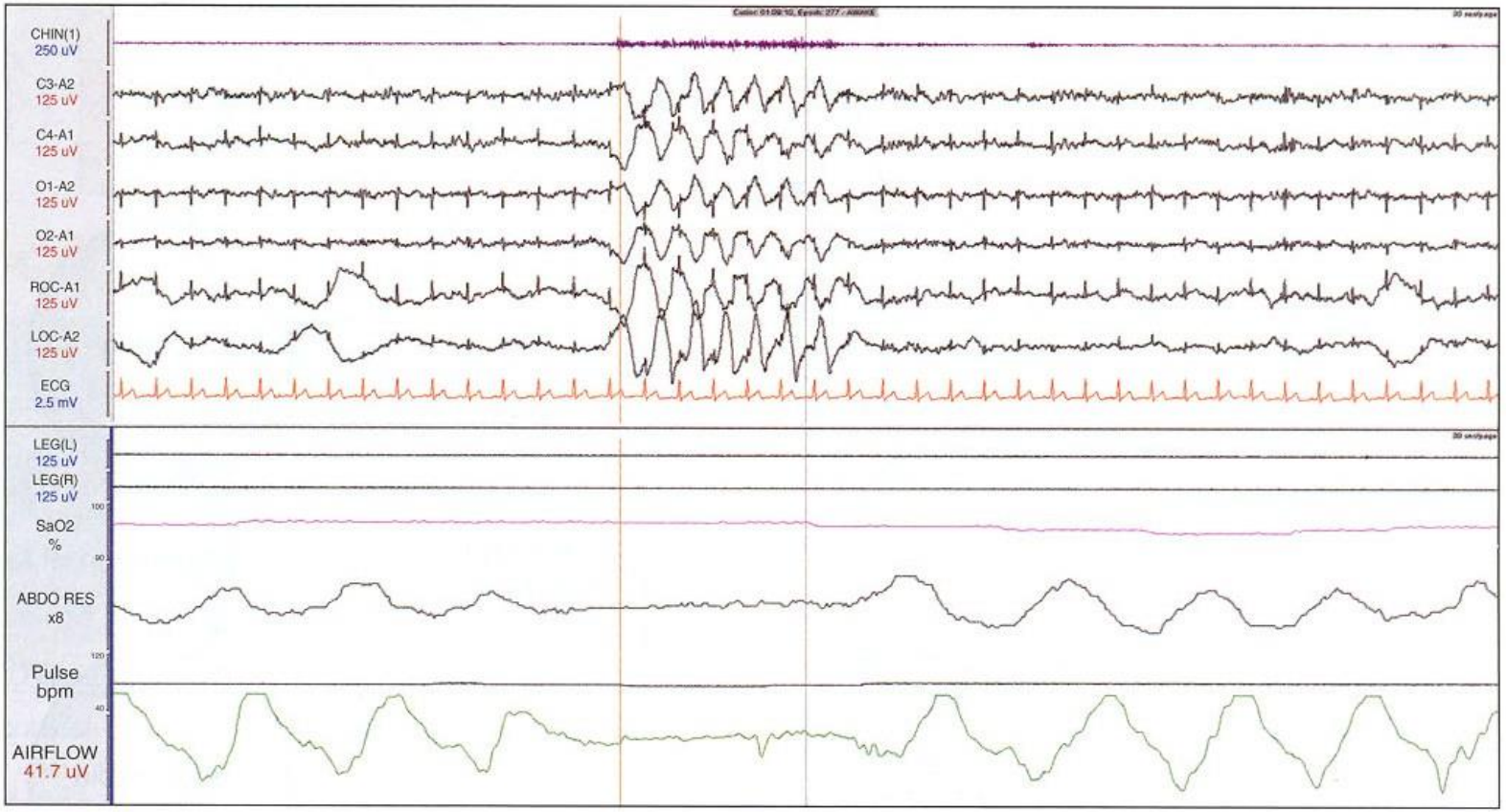
In this example there are brief spikes in the right temporal region (note the abnormalities in T4-T6 and T6-02) that begin just before the increased activity in the chin electrodes. This is followed by arousal. On the conventional sleep scoring montage, this would appear to be a simple, nonspecific arousal. The EEG montage reveals periodic spikes from the right mid-temporal region culminating in an arousal followed by residual postictal slowing over the same region. This "arousal" was actually the sole clinical manifestation of a focal temporal lobe epileptic discharge. (These may occur hundreds of times a night, resulting in frequent arousals (sleep fragmentation) presenting as excessive daytime sleepiness.) For this reason, it is prudent to employ a full seizure montage in all patients with a history of seizures and the complaint of excessive daytime sleepiness. If these arousals are associated with extremity movements, an erroneous diagnosis of periodic leg movements could be made (black, right; blue, left). (PSG courtesy M. Mahowald.)

PSG example of nocturnal frontal lobe epilepsy.



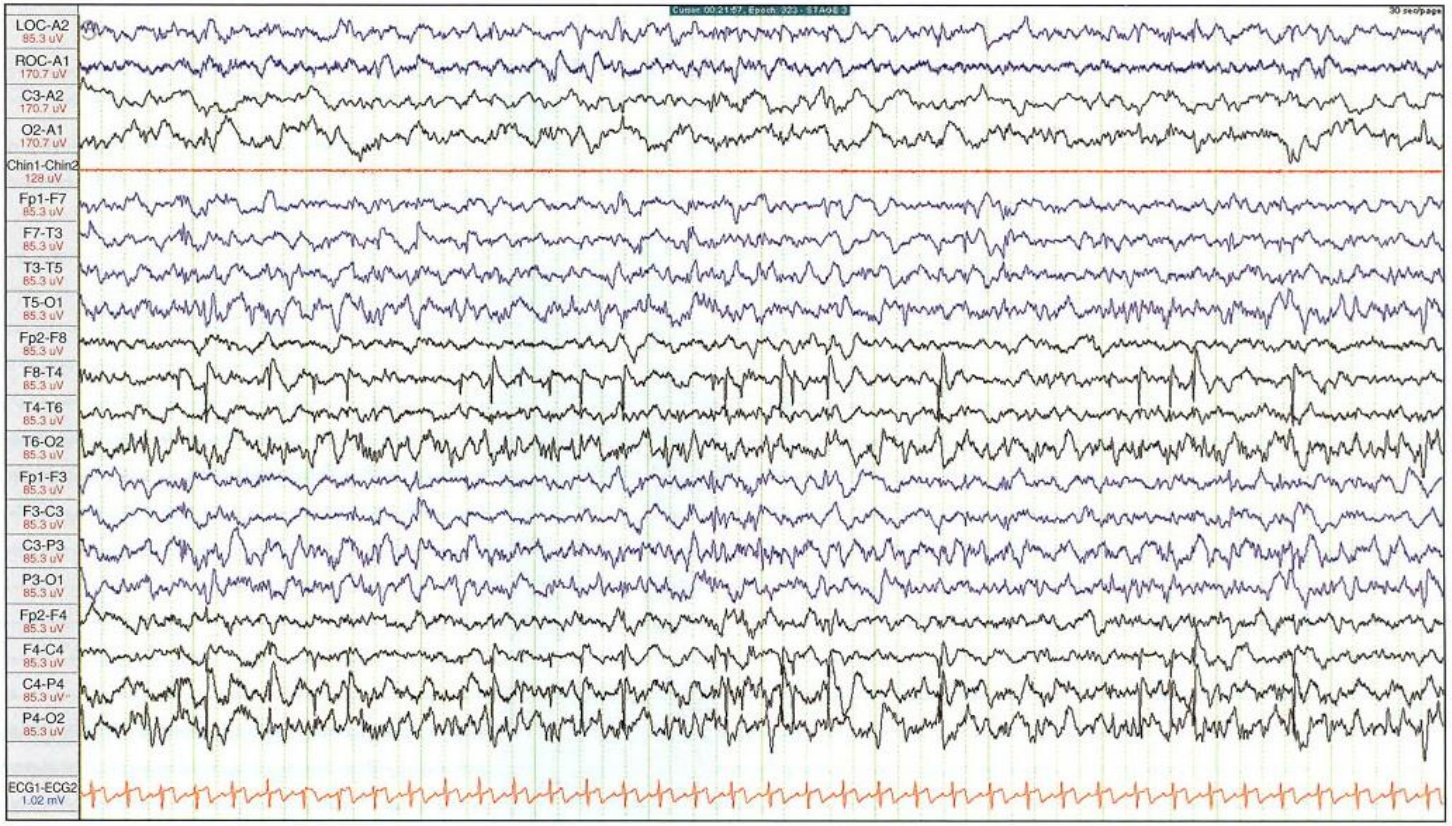
This is a representative PSG sample from a 35-year-old woman with a history of bizarre nocturnal spells in the middle of the night. The episodes are usually brief, less than a minute. This PSG shows spike and slow-wave complexes more prominent centrally during stage N2 sleep. (PSG courtesy M. H. Kryger.)

PSG example of patient referred with infrequent nocturnal seizures



This example is from a 20year-old student who was referred because of a 5-month history of infrequent seizures that occurred only at night. As a result of these, the patient had dislocated his shoulder and bitten his tongue. Notice the seizure activity lasting about 5 seconds in the middle of the epoch, during which time the patient had a central apnea. There were only three similar findings during the night. On synchronized digital video there was absolutely no movement visible. The sleep study may be entirely normal in patients with infrequent seizures. (PSG courtesy M. H. Kryger.)

PSG example of Rolandic spikes



In this example the spikes are right sided (note their presence primarily in even-numbered electrode pairs). These spikes are characteristic of Rolandic spikes (seen in benign Rolandic epilepsy). They are most prominent over the central and midtemporal region and are often present only during NREM sleep, when they may become very active. Clinically, there may be twitching of the mouth on the contralateral side with or without drooling. Occasionally these usually trivial seizures will generalize. The prognosis is generally very good, with the natural history of spontaneous resolution over time, hence the term benign Rolandic epilepsy (black, right; blue, left). (PSG courtesy M. Mahowald.)


Thanks For Your
Attention