Epilepsy Syndromes
&
Sleep
# Differential Diagnosis of Nocturnal Events

<table>
<thead>
<tr>
<th></th>
<th>NREM Parasomnia</th>
<th>REM Behavior Disorder</th>
<th>Nocturnal Seizures</th>
<th>Psychogenic Events</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Time of Occurrence</strong></td>
<td>First 1/3 of night</td>
<td>During REM; latter 2/3 of night</td>
<td>Any time (most common during first 2 hours and last 2 hours of sleep)</td>
<td>Anytime</td>
</tr>
<tr>
<td><strong>Memory of Event</strong></td>
<td>Usually none</td>
<td>Dream recall</td>
<td>Usually none but frontal lobe may have some recall</td>
<td>None</td>
</tr>
<tr>
<td><strong>Stereotypical Movements</strong></td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td><strong>PSG Findings</strong></td>
<td>Arousal from delta sleep</td>
<td>XS EMG tone during REM sleep</td>
<td>Potentially epileptic activity</td>
<td>Occur from awake state</td>
</tr>
</tbody>
</table>
# Frontal Lobe Seizures vs NREM Parasomnias

## Differential Diagnosis

<table>
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<tr>
<th></th>
<th>Frontal Lobe Seizures</th>
<th>NREM Parasomnias</th>
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<tbody>
<tr>
<td><strong>Age of onset</strong></td>
<td>11.8 +/- 6.3</td>
<td>Usually &lt; 10 yo</td>
</tr>
<tr>
<td><strong>Attacks per month</strong></td>
<td>20 to 40 (multiple events per night)</td>
<td>1-4</td>
</tr>
<tr>
<td><strong>Clinical course</strong></td>
<td>Increasing frequency or stable</td>
<td>Decreasing/disappearing</td>
</tr>
<tr>
<td><strong>Movement semiology</strong></td>
<td>Stereotypic</td>
<td>Polymorphic</td>
</tr>
<tr>
<td><strong>Attack onset</strong></td>
<td>Any time during night</td>
<td>First third of night</td>
</tr>
<tr>
<td><strong>Attack distribution</strong></td>
<td>2- NREM (65%)</td>
<td>3-4 NREM</td>
</tr>
<tr>
<td><strong>Motor Pattern</strong></td>
<td>2-3 repetitive types of attacks</td>
<td>Absence of motor pattern</td>
</tr>
<tr>
<td><strong>Duration of attacks</strong></td>
<td>&lt; 1 minute (usually 15 to 30 sec)</td>
<td>Several minutes</td>
</tr>
</tbody>
</table>

## Diagnostic Evaluation

1) **Daylab video EEG (awake only): essentially all normal**
2) **Daylab video EEG (after sleep deprivation): 52.2% abnormal**
3) **24 hour video EEG (daytime and nocturnal): 87% abnormal**
Importance of Sleep in Epilepsy Patients

- Sleep disorders are frequently overlooked
- Diagnosis and treatment can improve daily functioning
- Diagnosis and treatment can (in some cases) improve seizure control
Influence of Sleep on Epilepsy

• Nocturnal seizures occur in 60% of children with epilepsy, many of whom have seizures limited to sleep
• Most nocturnal seizures arise during nonREM sleep (primarily stage 2)
• Localization of seizure focus—frontal onset associated with sleep
• REM-onset seizures rare
Effects of Sleep Deprivation on Epilepsy

• Sleep deprivation occurs in the real world from inadequate sleep and associated primary sleep disorders, even in children with epilepsy

• Direct effects of epilepsy and medication on sleep duration and sleep architecture

• Correction of sleep-deprivation from any source can improve seizure control
Epilepsy and Sleep Apnea

• Importance of sleep apnea
  – Apnea associated with higher seizure rate
  – Almost 1/3 of patients with intractable epilepsy have evidence of sleep apnea
  – Treatment of apnea decreases seizure frequency

• Weight gain from AEDs (i.e. VPA, GBP, Lyrica) may induce or worsen apnea

• Sedating AEDs (i.e. PB, BZDs) produce upper airway relaxation and reduce arousability
Impact of Epilepsy on Sleep

• Seizures can disrupt the regulation of the sleep-wake cycle
  – Frequent seizures (and even frequent interictal discharges):
    • produce sleep fragmentation
    • suppression of REM
    • increased spontaneous arousals

• Untreated epilepsy associated with feelings of non-restorative sleep
Using Sleep Knowledge to Improve Understanding of Epilepsy

- Direct effects of sleep loss, fragmentation and oxygen desaturation predispose to seizures
- Daytime sleepiness from disturbed sleep may exacerbate epilepsy
- Treating associated primary sleep disorder improves seizure control and daytime alertness
Effects of Sleep Deprivation on EEG

- Activation of interictal discharges, especially in presence of sleep-related seizures
- Age-dependent sleep deprivation may yield epileptic abnormalities in 35% of patients with initially normal waking EEG
- Sleep-deprived EEG not recommended as standard for initial study
Certain types of epilepsy are closely associated with sleep

- **Idiopathic generalized epilepsy**
  - awakening grand mal
  - juvenile myoclonic epilepsy

- **Idiopathic partial epilepsies**
  - benign rolandic
  - childhood epilepsy with occipital paroxysms
  - autosomal dominant frontal lobe epilepsy
  - Landau-Kleffner syndrome
Sleep and Epilepsy: Seizure Type

• Frontal lobe seizures more commonly begin during sleep, while temporal lobe seizures begin more commonly awake
• Temporal and occipital lobe seizures in particular generalize more during sleep whereas frontal lobe seizures less commonly generalize
• All types of partial seizures are rare in REM sleep

In what stage of sleep do seizures happen?

Effects of Seizures on Sleep

• Seizures during sleep result in brief awakening
• Many patients, however, report decreased functioning after even a brief nocturnal seizure
• Investigation of seizure effects in patients with temporal lobe epilepsy, using all-night polysomnography in patients hospitalized for video-EEG monitoring
Seizure Effects on Sleep Efficiency

Effects of Nocturnal Seizure

Patients with Partial Seizures AND Sleep Disturbance Have Worse Quality of Life

Mean SF-36 subscale score

**SF-36 Mental health**

**Mean SF-36 subscale score**

**SF-36 Physical health**

- *P<0.05, **P<0.01, ***P<0.001 vs. controls
- † P<0.001 vs. undisturbed sleep within group

Sleep and Epilepsy

I. Mechanisms

- influence of sleep supported by specific seizure disorders have seizures only during sleep
  - Temporal lobe seizures are most common nocturnal seizures
  - Frontal lobe seizures have higher prevalence during sleep
    - possible thalamocortical activation
  - Frontal > temporal > parietal > occipital
- interictal epileptiform discharges more prevalent in NREM
  - Light sleep (Stage 1 & 2) > Deep Sleep (Stage 3 & 4)
  - NREM sleep is a state of neuronal synchronization with thalamocortical networks allowing recruitment of a critical mass of neurons to initiate and sustain a seizure

Seizure Promoter
Synchronized sleep
- xs diffuse cortical synchronization
- enhanced interhemispheric impulses

Seizure Protector
Desynchronized sleep
- inhibition of thalamocortical synchronization
- tonic reduction of interhemispheric impulses
Do different seizures have a tendency to start during sleep?

![Bar chart showing the percentage of seizures beginning in sleep for different brain regions.

- Frontal: Approximately 60% begin in sleep.
- Temporal: Approximately 70% begin in sleep.
- Posterior: Approximately 80% begin in sleep.

Statistical significance: P<0.0001

Do some seizures generalize more often during sleep?

Effects of Treatment on Sleep
Effects of AEDs on Sleep

• Complex interaction between direct effects of drugs on sleep architecture and stabilization of neuronal excitability
  – Sedating side effects with most older AEDs
  – Insomnia associated with some drugs (ACTH, felbamate)
  – Insomnia with AED withdrawal (PB, BZD)

• Incomplete data on newer AEDs
AEDs Effect on Sleep Organization

• Barbiturates and benzodiazepines
  – Shorten sleep latency
  – Decrease arousals from sleep

• Phenobarbital
  – Decreases sleep latency, arousals
  – Increases Stage 2, decreases REM
  – Restlessness in latter part of night
  – REM rebound with drug withdrawal

• Benzodiazepines
  – Reduces sleep latency and awakenings
  – Increases Stage 2, decreases SWS
  – REM rebound with drug withdrawal
Effects of AEDs on Sleep

- **Carbamazepine**
  - Decreases sleep latency, arousals; improves sleep efficiency
  - REM unchanged
  - Increase PLMS

- **Valproate**
  - Increases SWS
  - Decreases REM

- **Phenytoin**
  - Shorten sleep latency

- **Lamotrigine**
  - Decreased stage shifts and arousals
  - Increased REM sleep

- **Topiramate**
  - No sleep studies

- **Zonisamide**
  - Occasional reports of insomnia

- **Levetiracetam**
  - Increases stage 2, decreases SWS