

Sleep and Epilepsy: Pediatric population

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Topics we will cover

- Prevalence of sleep disorders in children with epilepsy
- Physiology of sleep and epileptic networks
- Sleep-related epilepsies in children

Sleep Disorders in Children with Epilepsy

- Prevalence of sleep disorders in children with epilepsy is under-recognized, estimated to be at least 80%
- Sleep quality is related to perceived quality of life, often independent of seizure control
- Good sleep quality is related to improved seizure control
- Poor sleep quality is associated with suboptimal seizure control

Sleep Disorders in Children with Epilepsy

- Higher incidence of sleep-related anxiety among children with epilepsy and their parents
 - Co-sleeping or parental presence at sleep onset reported to be higher among children with epilepsy
- Parents also report disturbed/aberrant daytime behavior, poor quality sleep

Sleep Disorders in Children with Epilepsy

- Factors associated with increased incidence of sleep disorders
 - Nocturnal seizures
 - Polytherapy
 - Refractory/poorly controlled seizures
 - Epileptic encephalopathies

Sleep Disorders in Children with Epilepsy

- Broad spectrum of sleep disturbances in children with epilepsy
- PSG has demonstrated the following:
 - Decreased total sleep time
 - Poor sleep efficiency
 - Decreased REM sleep
 - Disturbed sleep architecture
 - Increased sleep latency
 - Increased spontaneous arousals and sleep fragmentation
 - Sleep disordered breathing

Sleep Disorders in Children with Epilepsy

- Also increased incidence of the following sleep disorders:
 - Frequent daytime drowsiness
 - Increased incidence of parasomnias
 - Higher incidence of OSA
 - Higher incidence of RLS
 - Higher incidence of PLMS

Sleep Disorders in Children with Epilepsy

- Good seizure control improves sleep while good consolidated sleep improves seizure control
 - Sleep disorders associated with increased fragmentation (i.e. OSA) are associated with worsened seizure control
- Good sleep is associated with reported better behavior and health-related quality of life
 - >50% of children with epilepsy have reported behavioral problems

Physiology

- Epileptic networks most commonly involve brain structures involved in sleep plastic functions
 - Thalamocortical system
 - Hippocampal-limbic-frontal system

Physiology

- NREM sleep is potently associated with activation of epileptic activity (interictal and ictal), and represents a state of synchronization between the brainstem reticular activating system and thalamocortical circuits
- In contrast, REM sleep inhibits thalamocortical synchronization and inhibits spread of epileptiform discharges

Physiology

- Sleep transitions are associated with increased incidence of seizures as well as increased interictal epileptiform activity
 - This is felt to be due to changes in synchronicity as well as changes in concentrations of inhibitory neuromodulators such as adenosine
 - Adenosine levels drop during transition from wakefulness to sleep

Physiology

- Frequent epileptiform discharges during NREM sleep are postulated to interfere with memory consolidation
 - High frequency oscillations (HFOs) have been associated with epileptogenesis and are more frequent during slow wave sleep
- Discharges involving the thalamocortical network and the perisylvian network are often associated with cognitive dysfunction
- The degree of cognitive dysfunction seems to parallel the burden of interictal epileptiform discharges present during slow wave sleep

Sleep-influenced Epilepsies in Children

Absence Epilepsy

- Most common idiopathic/generalized epilepsy of childhood
- Absence seizures are characterized by brief periods of behavioral arrest/cognitive impairment lasting seconds

Absence Epilepsy

- Thalamocortical dysfunction
- Reportedly 'vigilance dependent'; spike-wave discharges are more frequent during periods of low/decreased vigilance

Absence Epilepsy

- Cognitive, behavioral, and emotional disorders common
 - Anxiety/depression
 - ADHD
 - Decreased language and verbal memory scores

Juvenile Myoclonic Epilepsy

- Idiopathic/genetic generalized epilepsy type commonly diagnosed in adolescence
- Most common epilepsy type encountered in adolescent patients
- Myoclonic jerks most frequently occurring within 1-2 hours of awakening
 - Less frequent seizure types include absence seizures and GTCs

Juvenile Myoclonic Epilepsy

- Reduced sleep efficiency
- Increased sleep latency
- Increased total NREM sleep
- Epileptiform discharges may increase with arousal sleep phenomena (K complexes, vertex waves)

Juvenile Myoclonic Epilepsy

- Frontal lobe dysfunction/executive dysfunction
- Mood disorders
- High rates of substance abuse

Idiopathic Focal Epilepsies

- Affect 15-20% of children <15y of age w/epilepsy
 - Centrottemporal (Rolandic) Epilepsy- most common
 - Occipital (Panayitopoulos) Epilepsy

Idiopathic Focal Epilepsies

- Perisylvian epileptic network
 - Communication and cognition → expressive and receptive language, reading, writing, calculations (dominant hemisphere), spatial orientation (non-dominant hemisphere)
- “Human communication network”
- Highly connected to thalamic structures

Epileptic encephalopathies

- During certain developmental windows epileptic activity in sleep ‘hijacks’ normal physiologic systems and hinders function and hence subsequent cognitive development
 - Infantile spasms/West syndrome
 - Lennox-Gastaut syndrome
 - Electrical status epilepticus of sleep
 - Landau-Kleffner
 - Dravet syndrome

Antiepileptic drugs (AEDs) and sleep

- Impact/effect depends on the AED, and reports are often contradictory
 - Negative effects: phenobarbital, phenytoin, benzodiazepines
 - Positive effects: gabapentin (increases SWS and REM sleep)
 - +/-: valproate, carbamazepine, lamotrigine
 - No effect: levetiracetam, topiramate, oxcarbazepine, zonisamide, rufinamide
- Polytherapy is associated with poor sleep
 - Consider obtaining PSG on children taking multiple AEDs
- Ketogenic diet may improve sleep quality

Melatonin and Epilepsy

- Conflicting reports on effects on seizure control
- Reported to enhance hippocampal excitability at high doses, though may have antiepileptogenic effect at low doses
- Data indicate that individuals with refractory epilepsy have lower baseline melatonin levels

Melatonin and Epilepsy

- Mechanism by which it may improve epilepsy could be via its effect on improving sleep
 - Improves sleep efficiency
 - Decreases sleep latency
 - May reduce sleep fragmentation

OSA and children with epilepsy

- Compared to children with OSA without epilepsy, the following has been reported in children with epilepsy and OSA:
 - Longer sleep latency and higher arousal index than children with OSA without epilepsy
 - Lower AHI though more significant desaturations with lower nadir

OSA and children with epilepsy

- Poorly controlled or undiagnosed OSA has been associated with refractory seizure control and increased epileptiform activity
- Adult studies have shown that treatment of OSA may improve seizure control
- VNS may worsen OSA in children with epilepsy

OSA and children with epilepsy

- Special circumstance: Vagal nerve stimulator (VNS)
 - Affects respiration during sleep
 - Associated with worsening pre-existing OSA
 - Increases the AHI
 - Some suggest obtaining PSG prior to VNS implantation in children with epilepsy

- Incidental interictal epileptiform discharges found in 1-2% of children undergoing PSG without reported history of seizures
 - Interictal epileptiform discharges without history of seizure have been reported in 2-4% of children
 - Referral to neurology for formal EEG is indicated
 - Behavioral/cognitive issues may predate development of seizures in some children

Summary

- Sleep disorders in children with epilepsy are very common though are under-reported and under-recognized
- Poor sleep is related to poor quality of life, independent of seizure frequency
- Poor sleep is associated with increased seizure and interictal epileptiform burden
- Improving sleep improves neurobehavioral comorbidities and can improve seizure control
- AEDs can impact sleep and polypharmacy is associated with increased incidence of sleep disturbances
- Patients with incidental epileptiform discharges identified on PSG should be referred to neurology for EEG

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