Sleep, Epilepsy and Development Disabilities: A Fitting Topic for Child Neurologists

Lawrence W. Brown, MD
Director, Pediatric Neuropsychiatry Program
The Children’s Hospital of Philadelphia
“Sleep is an essential, a health-giving restorative... Yet, darkness is also a cloak for hobgoblins and evildoers.... Phenomena such as extreme restlessness, excessive swallowing movements, nightmares and sleepwalking may possibly be seizures, masked and disguised by the altered physical and mental state of sleep.”

*Lennox and Lennox, 1960*
Goals of Presentation

■ To distinguish seizures from other nocturnal events including normal phenomena and primary sleep disorders in children
■ To describe the impact of sleep on epilepsy
■ To describe the impact of seizures and AEDs on sleep and daytime alertness
■ To outline how knowledge of sleep can improve epilepsy care
What are we seeing every day on the Epilepsy Service?

- Admissions for sleep resistance and nocturnal arousals
  - Many developmentally delayed and/or on the autistic spectrum
  - Some with documented epilepsy, but medication adjustment did not help

- Admissions for children with autism and history of language regression
Nocturnal events are not all due to seizures even in those with Epilepsy

- Normal sleep phenomena
  - Sleep myoclonus – infants
  - “Sleep starts” – all ages

- NREM arousal disorders (parasomnias)
  - Somniloquy, somnambulism, confusional arousals, night terrors

- Non-epileptic movement disorders
  - Head banging, RLS, PLMD

- Psychiatric disorders
  - Nocturnal panic disorder, PTSD, non-epileptic seizure

- Seizures
When is the arousal a seizure?

- Clinical features
  - Stereotyped presentation, timing of events, additional daytime abnormalities
  - Supported by neurological and psychiatric history as well as family history
  - Response to medication

- Video EEG
  - Ictal/interictal features
  - LTM good for establishing epilepsy but may miss abnormal sleep architecture and primary sleep disorders
  - PSG with simultaneous EEG may be necessary to confirm diagnosis
Sleep-Epilepsy Interactions: Impact of Sleep on Epilepsy
Sleep and Risk of Seizure Recurrence

- Prospective study of first unprovoked seizure in childhood (n=347)

- State of first seizure predicts second event
  - If awake - 2nd seizure 78% awake, 22% asleep
  - If asleep - 2nd seizure 66% asleep, 34% awake

- Sleep or wake most important in idiopathic seizure
  - If normal history, exam, EEG – recurrence rate 18% awake, 42% asleep
  - Recurrence rate unaffected if remote symptomatic

*Shinnar et al. Pediatrics 107:115, 2001*
Influence of Sleep on Epilepsy

- Nocturnal seizures in 60% of children with epilepsy, many of whom have seizures limited to sleep
- Most nocturnal seizures arise during NREM sleep
- Frontal localization associated with sleep
- REM-onset seizures rare, but highly localizing

*Kothare et al. Sleep Medicine 11:674, 2010*
Sleep and Epilepsy Syndromes

- **Infantile spasms**
  - Great majority of clusters on awakening or falling asleep
  - EEG deterioration with sleep including hypsarrhythmia and burst suppression

- **Lennox-Gastaut Syndrome**
  - Sleep increases spike wave activity
  - Nocturnal tonic seizures almost pathognomonic

- **Juvenile Myoclonic Epilepsy**
  - Myoclonic and GTCS on awakening
  - Sensitivity to sleep deprivation
Sleep and Epilepsy Syndromes

- **Benign rolandic epilepsy**
  - Sleep-activated central-temporal spikes
    - 30% occur only in sleep*
  - 65% sleep-related seizures only; 35% sleep and wake

- **Complex partial seizures of frontal lobe onset**
  - Bizarre clinical manifestations may suggest night terror or nightmare
  - Events typically brief with rapid recovery
  - Ictal EEG often obscured by artifact

* Dalla Bernardina, Behghini, Epilepsia 17: 161, 1976
Sleep Deprivation and Epilepsy

- Inadequate sleep reported by patients with epilepsy as significantly provoking factor
- Sleep deprivation primarily from inadequate sleep and/or associated primary sleep disorders
  - Inadequate sleep leads to increased sleep pressure and more severe apnea with reduced arousability
- Sleep deprivation increases epileptic discharges on EEG
Sleep Deprivation and Epilepsy

- 1 hour of additional sleep on the preceding night decreases odds ratio for seizure by 0.91 (95% CI 0.82)*
- Impact of sleep deprivation most apparent for generalized epilepsies (e.g. JME)
- Correction of sleep-deprivation from any etiology can improve seizure control**
- Routine sleep deprivation for pediatric EEG not recommended***

***Gilbert et al, Pediatrics 114: 658-662, 2004
Sleep-Epilepsy Interactions: Impact of Epilepsy on Sleep
Impact of Epilepsy on Sleep

- Seizures can disrupt normal regulation of sleep-wake cycle
  - Frequent seizures (and even frequent interictal discharges) produce sleep fragmentation, suppress REM and increase spontaneous arousals
- Children with epilepsy have more sleep problems than sibs or controls*
- Children with active epilepsy have more sleep problems than those who are seizure-free

Disturbed Sleep and Circadian Rhythms in Children with Epilepsy

- Ineffectively treated epilepsy associated with feelings of non-restorative sleep, learning/behavior disorders and daytime sleepiness
- Altered melatonin release in epilepsy *
  - Treatment can lead to improved sleep quality, fewer seizures

AEDs Can Alter Sleep Architecture as well as Neuronal Excitability

- Reduced sleep latency and/or improved sleep efficiency
  - Gabapentin, tiagabine, pregabalin, clobazam and carbamazepine
- Increased daytime sleepiness
  - Phenobarbital, valproate and high dose levetiracetam
- Reduced daytime sleepiness
  - Felbamate, VNS
- No effect on daytime sleepiness
  - Topiramate, zonisamide

Jain, Glauser Epilepsia 55: 26, 2014
Other Epilepsy Treatments and Effects on Sleep

- Epilepsy surgery may improve nocturnal sleep, but only in subgroup of patients with reduced seizure frequency
- VNS reduces daytime sleepiness
- Ketogenic diet increases stage N3
Choosing AED with Known Sleep Disorders

- Obstructive sleep apnea
  - TPM, ZNS
  - avoid VPA, BZD
- Narcolepsy
  - avoid BZD
- NREM Parasomnias
  - BZD
- RLS/PLMD
  - BZD, GBP
- Bruxism
  - BZD
- Myoclonus
  - BZD
- Insomnia
  - avoid FBM
Using Sleep Knowledge to Improve Epilepsy Care: What the Neurologist Already Knows!

- Synchronization of EEG during drowsiness and NREM sleep facilitates epileptic discharges syndrome
- Sleep deprivation can increase interictal abnormalities and seizure frequency
- Severely disturbed sleep architecture associated with cognitive-behavioral deterioration (i.e. Landau-Kleffner)
Using Sleep Knowledge to Improve Epilepsy: What Sleep Medicine can Add

- Good sleep hygiene with adequate sleep leads to optimal daytime functioning
- Sedation from any cause can exacerbate epilepsy
- Treating associated primary sleep disorder will often improve seizure control and daytime alertness
  - Epileptogenic effects of sleep loss, sleep fragmentation and oxygen desaturation
Using Sleep Knowledge to Improve Epilepsy: A Few More Pointers

- Avoid sedating drugs and ETOH which can worsen sleep architecture and exacerbate epilepsy
- Use sleep promoting agents sparingly
  - Melatonin, clonidine and hypnotics are generally safe options for insomnia, but first exclude treatable causes and practice effective sleep hygiene
- Consider “after-loading” AED to avoid daytime somnolence
  - All or majority of dose at bedtime to maximize medication levels at night while minimizing daytime sedation
Pleasant dreams!!