Neurologic Disease and Common Sleep Comorbidities

- Stephen Nelson, MD, PhD, FAACPDM, FAAN, FAAP, FANA
- Professor of Pediatrics, Neurology, Neurosurgery and Psychiatry
- Epileptologist
- Section Head, Tulane University School of Medicine
- CHNOLA Pediatric Neurology

Disclosure slide

All opinions are mine, and are based on my knowledge, training and expertise. I do not represent Tulane University, CHNOLA, the AAP, or any other organization with these opinions.

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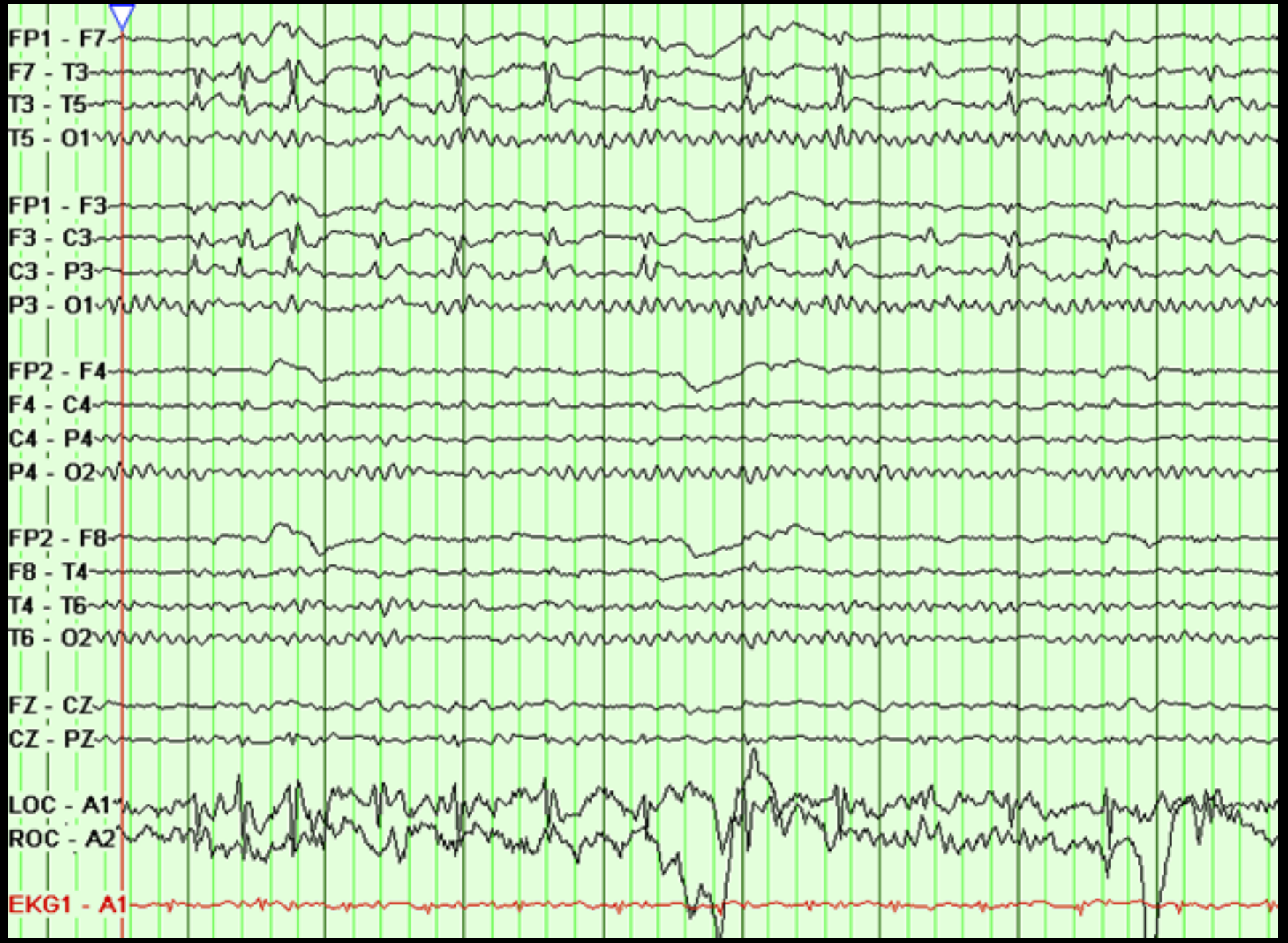
Epilepsy and sleep

- Improvements in sleep can improve epilepsy
- Both sleep deprivation and oversleeping can provoke seizures
- Epilepsy patients at increased risk for co-morbid sleep disorders
- Seizures - more likely during non-REM sleep (especially N1/N2)
- Interictal epileptiform discharges (IEDs) more frequent in non-REM sleep (especially N3) so better estimate of seizure risk
- REM sleep protective, and thus better for localization of IED

Benign epilepsy of childhood with centrotemporal spikes (BECTS or Rolandic epilepsy)

- One of the most common forms of epilepsy in children (8-20%)
- 75% start between 7 - 10 years (range 1 – 14)
  - Seizures are somatosensory and motor focal
  - Hemifacial and oropharynx, with speech arrest and hypersalivation
  - In some cases involving the upper limb
  - Brief lasting for 1 - 3 minutes
- Occur in the first 1/3 of the night in non-REM sleep
- Usually the interictal discharge appears only during sleep
- Infrequent seizures that usually resolve within 2 years

BECTS


FP1 - F7
F7 - T3
T3 - T5
T5 - O1
FP1 - F3
F3 - C3
C3 - P3
P3 - O1
FP2 - F4
F4 - C4
C4 - P4
P4 - O2
FP2 - F8
F8 - T4
T4 - T6
T6 - O2
FZ - CZ
CZ - PZ
LOC - A1
ROC - A2
EKG1 - A1

Benign childhood epilepsy with occipital spikes - Panayiotopoulos syndrome

- Mean age of onset < 5 years old
- Vomiting is the most characteristic and frequent ictal sign (70 – 85%)
- Autonomic signs and symptoms - syncope-like seizures, with sudden loss of muscle tone and unresponsiveness; pallor, miosis, incontinence, coughing, and hypersalivation
- Progressive impairment of consciousness along with staring or head and eye deviation
- Usually nocturnal and last > 5 minutes and can result in nonconvulsive status epilepticus
- Seizures are infrequent (~1/2 single seizure), spontaneous remission ~2 – 3 years from onset

Benign occipital epilepsy of childhood - Gastaut syndrome

- Mean age of onset 8 - 9 years old
- Seizures often include visual symptoms, either blindness or visual hallucinations
- **Most seizures occur in the daytime**
- Hemiclonic activity, automatisms, migraine-like headache, and versive movements can occur, and seizures may secondarily generalize
- Seizures typically < 5 minutes long but can be frequent and persistent

Nocturnal (sleep-related) focal epilepsies

- Most common is sleep-related hypermotor epilepsy (SHE)
  - Autosomal dominant nocturnal frontal lobe epilepsy (ADNFLE) – nicotinic receptor mutations
  - Focal cortical dysplasia (FCD) is the most common structural cause
- Brief (<2 minutes) seizures with stereotyped motor pattern and abrupt onset and offset
- Hypermotor semiology: vigorous hyperkinetic and/or asymmetric tonic or dystonic features, with or without impaired awareness
- Occurs predominantly in sleep, either in nighttime or daytime hours
- Mean age of onset = 14 years

SHE seizures

- Short (2 - 4 seconds) stereotyped movements involving the limbs, axial musculature, and/or head that may or may not correspond with ictal discharges
- Sudden and brief (5 - 10 seconds) arousals from sleep ("paroxysmal arousals"), sometimes accompanied by stereotyped movements, vocalization, frightened expression, or fear - mimic confusional arousals
- Longer seizures lasting up to 2 minutes characterized by highly stereotyped hyperkinetic ("hypermotor") and/or asymmetric dystonic movements, often with prominent vocalization - complex movements, such as pedaling, choreoathetoid movements, and ballistic movements of the limbs also can occur – appear nonepileptic

SHE seizures

- Longer events include ambulatory behavior, known as episodic nocturnal wandering, can occur - difficult to distinguish clinically from sleepwalking or postictal confusion
- Seizures occur multiple times per night, almost exclusively during NREM sleep
- Although seizure duration and the amount of motor activity may vary across the night, all events tend to begin similarly and remain highly stereotyped and stable within a given individual

Sleep-Accentuated Epilepsies - Lennox-Gastaut syndrome

- Epileptic encephalopathy with onset during childhood
- Multiple seizure types, including atypical absence, myoclonic, generalized tonic-clonic, prominent and frequent nocturnal tonic seizures with nocturnal tonic status epilepticus, and prominent astatic (atonic) seizures with loss of postural tone and falling (helmets)
- EEG shows characteristic slow spike-wave discharges
- Usually have cognitive impairment and severe psychomotor disability
- Antiseizure drug therapy is incompletely effective in most cases, and seizures are often medically refractory

Sleep-Accentuated Epilepsies - Syndromes with electrical status epilepticus during sleep

- Landau-Kleffner syndrome (LKS) and epileptic encephalopathy with continuous spikes and waves during sleep (CSWS) are epileptic encephalopathies of childhood
- Sleep potentiation of epileptiform activity, particularly in the transition from wakefulness to sleep, leading to an EEG pattern of continuous or near-continuous spikes and waves during non-REM sleep, and a regression in different aspects of development
- LKS most often presents subacutely with progressive language regression and verbal and auditory agnosia with onset in early childhood with previously normal developmental milestones.
- CSWS is a more severe syndrome associated with more global developmental regression

AROUSAL EPILEPSIES

- **Juvenile myoclonic epilepsy** - age-related, genetic, generalized epilepsy syndrome characterized by three major seizure types: myoclonic, generalized tonic-clonic, and absence. Seizures typically begin in early adolescence and occur most frequently in the morning hours, often within an hour of awakening. EEG shows generalized interictal epileptiform discharges. Myoclonic jerks in am.
- **Generalized tonic-clonic seizures upon awakening** – generalized tonic-clonic seizures upon awakening but lacking the characteristic myoclonic seizure type seen in JME

Epilepsy and Sleep

- Seizures are noted to cause postictal somnolence, but also evoke more wake after sleep onset, sleep fragmentation, and REM sleep suppression during the sleep period following the seizure
- Interictal discharges also cause sleep fragmentation, potentially by disrupting signals involved in sleep circuitry, thus disrupting the physiologic coordination of sleep
- May have some downstream effect in that nighttime discharges may influence daytime learning and cause daytime sleepiness
- OSA common in epilepsy patients, and treatment can improve epilepsy control
- Different AEDs can impact sleep in different ways (complex)

Sleep and headaches

- Sleep disruption can predispose, provoke, and perpetuate headache issues, whereas sleep may also improve headaches
- Sleep deprivation and excessive sleep increase headaches in both children and adults
- Insomnia and poor sleep quality very common in migraine patients, and improvements in sleep can reduce headache burden
- Patients with OSA may report headaches including upon wakening, and treatment can reduce headache frequency and severity

Headaches and sleep

- 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;
- Hypnic headaches (sometimes called alarm clock headaches) abruptly awaken patients after 1 to 3 hours of sleep
- Chronic paroxysmal hemicrania also may awaken patients suddenly from sleep with abrupt pain
- Improvement in sleep offers a unique pathway to improve headaches
- Patient with sleep related headaches should be referred and get neuroimaging

Sleep and Neuromuscular Disorders

- Duchenne muscular dystrophy causes hypoventilation due to both fixed restrictive and functional restrictive defects, often requiring tracheostomy because of 24 hour/d ventilation
- Myotonic dystrophy can have obstructive and central sleep apnea and hypersomnia; frequent central apneas occur in response to positive airway pressure treatment
- Myasthenia gravis associated with obstructive sleep apnea and restless legs syndrome; nasal continuous positive airway pressure therapy, iron replacement or medications
- Charcot-Marie-Tooth disease associated with restless legs syndrome

Insomnia

- Insomnia Due to a Mental Disorder and Insomnia Due to a Medical Condition Diagnoses of insomnia due to a mental disorder or insomnia due to a medical condition presume the presence of comorbid psychiatric and medical conditions with a clear temporal association with the underlying sleep disturbance and generally are used where the insomnia is severe enough to warrant independent treatment
- Insomnia Due to a Drug or Substance Insomnia due to a drug or substance represents sleep problems clearly and temporally associated with the drug or substance intoxication or withdrawal from a wide range of medications

Insomnia Associations

- Insomnia and poor sleep contribute to worsened pain, anxiety, and depression, which, in turn, worsen the underlying sleep disturbances
- Early morning awakening also may be a sign of a mood disorder
- Insomnia is associated with heavy drinking and physical inactivity, which are also associated with poorer sleep and insomnia symptoms
- Difficulty initiating sleep include anxiety, excessive caffeine use, and symptoms of restless legs syndrome (RLS)
- Sleep apnea and nocturia contribute to sleep maintenance insomnia
- Periodic limb movement disorder may also lead to significant insomnia

Sleep and Neurological Disorders

- Essentially all neurologic disorders are associated $\geq$ 1 sleep disorders
- Identifying and treating sleep dysfunction can reduce sleep-related symptoms and improve quality of life, as well as reduce the underlying neurologic disease symptom severity
- Assessing for sleep disturbances should be part of the routine in all patients with neurologic diseases.

Acknowledgements

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