SEIZURES AND SLEEP

ARCS 2016
Epidemiology of Epilepsy

- 1 in 26 people will develop epilepsy during their lifetime
- 2.5 million people in the U.S. have epilepsy
- Epilepsy is the 3rd most common neurological disorder after stroke and Alzheimer’s disease in the U.S.
- More common than autism, cerebral palsy, MS and Parkinson’s disease combined
Neuron Structure
Seizure

- Hyper-excitability of the neuron
- Provoked or unprovoked
- Inherited gene mutations
- Secondary etiology
  (head injury, stroke, degenerative disease)
- For >50% with epilepsy, exact cause is unknown
Seizure Work Up

- Brain imaging – MRI
- EEG
- Labwork
- Medication Review
EEG

- Routine EEG
- Video EEG
- Epileptiform changes
- Ictal / Interictal
Epileptiform Changes
Spike and Wave on PSG
Does the EEG always show epileptiform changes in epilepsy?

- Sensitivity of EEG is 30-60%
- Sensitivity improves to 80-90% with repeated EEGs
- 51% of EEGs are abnl if <24 hours post seizure
- 34% of EEGs are abnl if > 24 hours post seizure
- Sleep deprivation – increases yield in 30-70%
EEG False Positives

- Medications
  - Cefepime
  - Bupropion
  - Lithium
  - Tramadol
  - Clozapine

- Uremia

- Thyrotoxicosis

- Autoimmune Encephalopathies
Seizure Classification

Partial
Seizure activity starts in one area of the brain

Simple
Retains awareness

Complex
Altered awareness and behaviour

Generalized
Seizure involves whole brain & consciousness is affected

Tonic Clonic
“grand-mal” or convulsion

Absence
“petit mal” or staring fit

Atonic / Tonic
“drop attack”

Myoclonic
Sudden muscle jerks
Brain Function
Simple Partial Seizures

- **Somatosensory:** Tingling of contralateral limb, face, or side of body
- **Focal motor:** Tonic-clonic movements of upper (or lower) limb
- **Visual:** Sees flashes of light, scotomas, unilateral or bilateral blurring
- **Auditory:** Hears ringing or hissing noises

**EEG:** Focal motor seizure, left arm and hand

- Fp1-F3
- F3-C3
- C3-P3
- P3-O1
- Fp2-F4
- F4-C4
- C4-P4
- Pa-O2

Repetitive sharp waves over right central region

**Autonomic:** Sweating, flushing or pallor, and/or epigastric sensations

**Grimacing:**

**Contraversive:** Head and eyes turned to opposite side
Complex Partial Seizures

- Impairment of consciousness: cognitive, affective symptoms
  - Dreamy state; blank, vacant expression; déjà vu; jamais vu; or fear

- Brain diagram with regions:
  - Frontal lobe
  - Parietal lobe
  - Posterior temporal gyrus
  - Occipital lobe

- EEG: left temporal lobe seizure
  - Fp1-F7
  - F7-T3
  - T3-T5
  - T5-O1
  - Fp2-F8
  - F8-T4
  - T4-T6
  - T6-O2
  - Repetitive sharp waves over left temporal region

- Complex Partial Seizures symptoms:
  - Formed auditory hallucinations: Hears music etc.
  - Formed visual hallucinations: Sees house, trees that are not there
  - Bad or unusual smell
  - Olfactory hallucinations
  - Psychomotor phenomena: Chewing movements, wetting lips, automatisms (picking at clothing)
  - Dysphasia
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Generalized Seizures

- Generalized seizures rapidly engaging, bilaterally distributed networks.
- Consciousness may be impaired and this impairment may be the initial manifestation.
- Motor manifestations are bilateral.
Seizures and Sleep

- **Study of 850 institutionalized:**
  - 21% of patients had seizures exclusively at night
  - 42% only during the day
  - 37% either during the night or day.

- **Circadian pattern of seizures**
  - Nocturnal seizures 5 to 6 AM and 1 to 2 hours after sleep onset
  - Diurnal seizures clustered in the early morning and late afternoon.

Gowers WR. Epilepsy and Other Chronic Convulsive Diseases: Their Causes, Symptoms and Treatment. Churchill London: 1985

Langdon-Down M, Brain WR. Time of day in relation to convulsions in epilepsy. Lancet 1929; 1: 2029-2032
Seizure rate per sleep stage

<table>
<thead>
<tr>
<th></th>
<th>NREM Stage 1</th>
<th>NREM Stage 2</th>
<th>NREM Stage 3-4</th>
<th>REM</th>
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<tr>
<td>Sleep Laboratory Patients</td>
<td>0.30</td>
<td>0.42*</td>
<td>0.36</td>
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<tr>
<td>Epilepsy Laboratory Patients</td>
<td>0.36*</td>
<td>0.42*</td>
<td>0.24</td>
<td>0.06</td>
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<tr>
<td>Combined Groups</td>
<td>0.36*</td>
<td>0.42*</td>
<td>0.30*</td>
<td>0.06</td>
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</tbody>
</table>

All nights of sleep were included in this Table.
*Higher seizure rate compared to REM sleep (p < 0.05) in that particular group of laboratory patients. See text for detailed p-values.
Seizures in Sleep Stages

Seizure occurrence

- Stage N2
- Wakefulness
- Stage N1
- Stage N3
- Stage REM
Seizures in NREM sleep

- NREM sleep is a state of synchronization between the brainstem reticular activating system, thalamus, and cortex (pyramidal neurons). Deepening NREM sleep is associated with removal of acetylcholine and progressive hyperpolarization of thalamocortical neurons.

The generation of REM sleep is associated with the disinhibition of mesopontine cholinergic cells, resulting in an increased brainstem cholinergic input to thalamocortical neurons, producing a relative state of cortical activation.

Seizures in REM vs wakefulness

- We hypothesize that the impact of REM sleep on epilepsy is due to a maximally desynchronized EEG pattern which reduces the likelihood of spatial and temporal summation of aberrant depolarizations.

- Although at first glance similar to wakefulness, recent connectivity studies demonstrate a further strategic loss of connectivity in REM sleep which we hypothesize accounts for its unique antiepileptic influence on seizures.
Sleep Complaints in Epilepsy

- Sleep Deprivation
- Insomnia
- Excessive daytime sleepiness
Sleep Deprivation

Effects of Sleep deprivation

- Irritability
- Cognitive impairment
- Memory lapses or loss
- Impaired moral judgement
- Severe yawning
- Hallucinations
- Symptoms similar to ADHD
- Impaired immune system
- Risk of diabetes Type 2

- Increased heart rate variability
- Risk of heart disease
- Increased reaction time
- Decreased accuracy
- Tremors
- Aches

Other:
- Growth suppression
- Risk of obesity
- Decreased temperature
Sleep Deprivation

- Greater interictal epileptiform discharges yield following total sleep deprivation compared with routine wake and drug induced sleep EEGs; interictal epileptiform discharges were recorded in 28% of their subjects only following total sleep deprivation, and total sleep deprivation activated a new epileptic focus in 7% of cases.

- Prospective study of 721 subjects who had a second EEG (routine, drug induced sleep, or total sleep deprivation) after an inconclusive initial EEG found a significantly greater percentage containing interictal epileptiform discharges after total sleep deprivation as compared with a second routine record (22.6% vs. 9.5%).


Roupakiotis SC, Gatzonis SD, Triantafyllou N. The usefulness of sleep and sleep deprivation as activating methods in electroencephalographic recording: contribution to a longstanding discussion. Seizure 2000; 9(8): 580-584

Foldvary-Schaefer N, Grigg-Damberger M. Sleep and epilepsy: what we know, don’t know, and need to know. J Clin Neurophysiol 2006; 23(1): 420
Insomnia and Seizures

- Insomnia triggers in Epilepsy
  - Stress related insomnia
  - Medications adverse event: Lamotrigine (Lamictal), Felbamate (Felbatol) …
  - Coexisting medical disorders: fibromyalgia, arthritis, CHF, GERD…
  - Coexisting psychiatric disorders: Depression, anxiety, nocturnal panic attacks …
Insomnia and Seizures

- Sleep aids can cause seizures as side effect
  - Diphenhydramine (Benadryl), Amitriptyline (Elavil)
  - Zolpidem (Ambien), Zaleplon (Sonata), Eszopiclone (Lunesta)
  - Remelteon (Rozerem)

- Antidepressants can cause seizures:
  - Bupropion (Wellbutrin), Venlafaxine (Effexor), Escitalopram (Lexapro), Citalopram (Celexa), Fluoxetine (Prozac) …
  - Others: Olanazpine (Zyprexa), Quetiapine (Seroquel)
Hypersomnia and Seizures

- Seizure activity during sleep
- Anti-Epileptic Drugs (AED)
- Other sleep disorders
Hypersomnia and Seizures

- Sleep architectural abnormalities in patients with epilepsy:
  - Reduced percentage of sleep time spent in REM sleep
  - Increased wake after sleep onset
  - Prolonged onset of sleep or REM sleep
  - Increased number of arousals, awakenings

- These findings hold true even with the absence of seizures and are observed in patients with idiopathic generalized epilepsy.
## Anti-Epileptic Drugs and Sleep

<table>
<thead>
<tr>
<th></th>
<th>Sleep Efficiency</th>
<th>Sleep Latency</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
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<td>0</td>
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</tr>
</tbody>
</table>

0=no change. -=not reported. ↑ =included data acquired after achieving steady state. REM, rapid eye movement.
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<thead>
<tr>
<th>Sleep Epilepsies</th>
<th>Awakening Epilepsies</th>
</tr>
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<tbody>
<tr>
<td>Benign focal epilepsy with centro-temporal spikes</td>
<td>Juvenile Myoclonic epilepsy</td>
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<tr>
<td>Frontal Lobe Epilepsy</td>
<td>Absence epilepsy</td>
</tr>
<tr>
<td>Lennox Gastaut Syndrome (Tonic seizures)</td>
<td>Epilepsy with grand mal seizures on awakening</td>
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<tr>
<td>Epilepsy with Continuous spike and wave in sleep</td>
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</tr>
</tbody>
</table>
Awakening Epilepsies

Juvenile Myoclonic Epilepsy
Juvenile Myoclonic Epilepsy

- Ages 6 to 22 years (13-16 years +++).
- Myoclonic seizures are present in all patients.
- Family history of epilepsy was present in 66% of 41 studied families.
- 36% had > 2 family members affected by JME.
- No intellectual or neurologic deficits
Juvenile Myoclonic Epilepsy

- Generalized tonic-clonic seizures: 80-97%, and with absence seizures in 12-54% of patients.

- Myoclonic: sudden jerk, lasting <1 second, no clear associated loss of awareness, can happen multiple times per day, especially in the morning or with strobe lights. Occur in all JME patients, but may not be recognized initially as seizures. A history of sudden jerks, clumsiness, or jitteriness, especially in the morning should be questioned.

- Generalized tonic clonic: often begin a repetitive myoclonic seizures that culminate in a generalized bilateral convulsion. Typically self-limited and infrequent, although nearly all JME patients will have at least one. Often the first seizure recognized.

- Absence: staring, behavioral arrest, unresponsiveness. May not be previously recognized and a history of staring spells should be questioned. Occur in approximately 20% of patients with JME.
Grand Mal Seizures
Grand Mal Seizures
Juvenile Myoclonic Epilepsy
Juvenile Myoclonic Epilepsy
Juvenile Myoclonic Epilepsy
Juvenile absence epilepsy
Juvenile absence epilepsy

EEG: Typical absence seizure, 3 Hz spike and wave
Benign Rolandic Epilepsy of Childhood

a.k.a. Benign Rolandic Epilepsy with Centro-Temporal Spikes (BECTS)
Benign Rolandic Epilepsy

- The most common epileptic syndrome in childhood
- Age of onset: 4-10 years (spontaneous remission by age 15)
- Duration: self-limited, status epilepticus is uncommon
- Frequency: typically low
- Sleep Related: 75% of all seizures occur in NREM sleep.
Benign Rolandic Epilepsy

- EEG: High amplitude centrotemporal spikes and sharp waves with dramatic activation during sleep.

- N1 and N2 abundant spikes-wave (localized to temporal area), during N3 more generalized.
Rolandic Epilepsy

- A typical seizure in people with benign rolandic epilepsy (BREC or BECTS) involves:
  - Twitching, numbness, or tingling of the child's face or tongue.
  - Interfere with speech, cause drooling.

- Partial seizure that lasts no more than 2 minutes and the child remains fully conscious.

- Sometimes the child also may have tonic-clonic seizures, typically during sleep. The seizures are usually infrequent, but they may occur in clusters of a few at a time.
Benign Rolandic Epilepsy
Benign Rolandic Epilepsy
Sleep Related Seizures

Lennox Gastaut Syndrome
Lennox Gastaut Syndrome

- Age of onset – 1-7 years of age
- Seizure types – tonic (mostly nocturnal), atonic, myoclonic, atypical absence, generalized tonic clonic, focal.
- Common etiologies – variety of etiologies, proceeded by infantile spasms in 9-40% of cases. Variable degrees of learning disorders. Half have perinatal hemorrhage, tuberous sclerosis, ... 
- Prognosis – moderate to severe intellectual impairment, usually correlates with etiology and seizure control
LennoxF  Gastaut Syndrome

- EEG multifocal, generalized Spike and Wave pattern.
- During sleep Polyspike activity, with basal continuous epileptiform activity.
Lennox Gastaut Syndrome
Lennox Gastaut Syndrome

- Associated EEG patterns – generalized 1-2hz slow spike and wave, generalized slowing, paroxysmal fast activity (recruiting rhythm) during sleep.
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Sleep Related Seizures

Frontal Lobe Epilepsy
Frontal Lobe Epilepsy

- Almost exclusively during sleep, N2++

- Frontal Lobe:
  - Motor events, short duration
  - Post-ictal confusion

- Autosomal Dominant Nocturnal Frontal Lobe Epilepsy (ADNFLE): Chromosomes 20q13 and 15q24 with mutations in the transmembrane region of the neuronal nicotinic acetylcholine receptor
Frontal Lobe Epilepsy

**FIGURE 6-1** Dorsolateral (left) and medial (right) schematics of the brain highlighting the symptomatogenic areas in nocturnal frontal lobe epilepsies. Activation of the precentral (primary motor) region produces contralateral clonic movements; premotor region activation produces tonic posturing, usually proximal, bilateral, asymmetric, and version; dorsolateral prefrontal region activation produces hypermotor behavior, complex automatisms, and version; frontal operculum region activation produces facial grimacing and salivation; activation of the ventromedial prefrontal region produces hypermotor behavior, autonomic activation, and affective changes (eg, agitation, fear). Activation of the premotor and prefrontal regions is characteristic of nocturnal frontal lobe epilepsy.
Frontal Lobe Epilepsy
Sleep Related Seizures

Epilepsy with Continuous Spike-Wave during sleep
Continuous Spike-Wave during sleep

- Occurs mainly in Children
- Some degree of learning disability common

- EEG: multifocal, mainly frontal spike-wave
- ESES: Continuous, >85% of the recording (Electrical Status Epilepticus in Sleep). Seen in CSWS and Landau Kleffner Syndrome
Continuous Spike-Wave during sleep
Massod, S., Ralls, F. - Sleep Review – Electrical Status Epilepticus during Sleep – June 14, 2013
Thank You For Your Attention