Introduction

- The primary function of sleep remains a matter of debate
- Cognitive and restorative benefits well-known
- Learning & memory
- *There is a very strong interplay of epilepsy and sleep*
Objectives

- Introduction to normal sleep
- Common sleep disorders
- Common tools used to evaluate sleep

- Physiologic relationship of sleep to epilepsy
  - Effect of sleep disturbances on seizure frequency and epileptiform activity

- Effect of epilepsy on sleep
  - Effect of seizures & EEG abnormalities on sleep
  - Effect of antiseizure treatment on sleep

- Management strategies
Normal Sleep
<table>
<thead>
<tr>
<th>Non-REM Sleep</th>
<th>REM Sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Very synchronous automatic functions (breathing, heart rate)</td>
<td>• Dreams</td>
</tr>
<tr>
<td>• Stages N1, N2, N3</td>
<td>• Muscle tone absent</td>
</tr>
<tr>
<td>• Declarative memory consolidation</td>
<td>• Irregular breathing, rapid eye movements</td>
</tr>
<tr>
<td></td>
<td>• Nondeclarative &amp; emotional memory</td>
</tr>
</tbody>
</table>
Sleep Is Divided Into Rapid Eye Movement (REM) and Non-REM sleep

<table>
<thead>
<tr>
<th>Non-REM Sleep</th>
<th>REM Sleep</th>
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</table>
| - Electrical and clinical seizure activity more prevalent  
  - Especially stages N1 and N2 | - Seizures rare  
  - Low tone increases risk of obstructive sleep apnea |
Sleep Progresses Predictably

- *Cycling* between non-REM and REM may be important to learning.

- Any disruption to sleep (e.g. arousals, sleep-disordered breathing, seizures, medications, etc.) can affect sleep architecture.
Normal Sleep Amounts

- **Newborns:**
  - Total *10-19* hours/24h
  - No circadian pattern for several weeks

- **Infants:**
  - Total *12-13* hours (9-10 at night)
  - Gradual decrease in # of naps

- **Toddlers (up to 3 years):**
  - Total *11-13* hrs (9.5-10.5 at night)

- **Preschool (3-5 years):**
  - Total *9-10* hours
  - 1 or 0 naps (15% of 5 yr olds nap)

- **School-aged:**
  - Total *9-10* hours

- **Adolescents:**
  - Actual: *7-7.5* hours;
  - Recommended: 9-9.5 hours
  - Physiologic phase delay (2 hours)
Common Sleep Disorders
Common Sleep Disorders
Obstructive Sleep Apnea (OSA)

• Repeated episodes of upper airway obstruction – despite respiratory effort

• Leads to cessation of airflow
  ○ Complete (apnea)
  ○ Partial (hypopnea)

• Repeated arousals & poorer quality of sleep

• 4-11% (parent-defined); 1-4% (sleep studies)
• Highest prevalence in children: 2-8 years
**Obstructive Sleep Apnea (OSA)**

<table>
<thead>
<tr>
<th>Nighttime Symptoms</th>
<th>Daytime Symptoms</th>
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<tbody>
<tr>
<td>Snoring</td>
<td>Daytime sleepiness</td>
</tr>
<tr>
<td>Pauses in breathing</td>
<td>Irritability, depression, anxiety</td>
</tr>
<tr>
<td>Restlessness</td>
<td>Inattention/hyperactivity</td>
</tr>
<tr>
<td>Enuresis (bedwetting)</td>
<td>Learning/academic difficulties</td>
</tr>
<tr>
<td>Mouth breathing</td>
<td>Behavioural problems</td>
</tr>
</tbody>
</table>

- Daytime Symptom
  - Daytime sleepiness
  - Irritability, depression, anxiety
  - Inattention/hyperactivity
  - Learning/academic difficulties
  - Behavioural problems
<table>
<thead>
<tr>
<th>Obstructive</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Adenoidal/tonsillar hypertrophy</td>
<td></td>
</tr>
<tr>
<td>- Craniofacial abnormalities</td>
<td></td>
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<tr>
<td>- Allergies</td>
<td></td>
</tr>
<tr>
<td>- Septal deviation</td>
<td></td>
</tr>
<tr>
<td>- Obesity</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Reduced/altered muscle tone (e.g. cerebral palsy)</td>
</tr>
<tr>
<td>- Reduced central drive</td>
</tr>
<tr>
<td>- Brain malformations (esp brainstem)</td>
</tr>
<tr>
<td>- Medications</td>
</tr>
<tr>
<td>- Genetic</td>
</tr>
</tbody>
</table>
• Inability to stay awake during day
• Unintended lapses into drowsiness or sleep
• May be confused with fatigue

• Major causes:
  ○ Disrupted/poor quality sleep*
    ▷ E.g. sleep apnea, restless legs, frequent seizures, pain, etc.
  ○ Insufficient quantity of sleep
    ▷ E.g. poor sleep hygiene
  ○ Due to increased need for sleep
    ▷ E.g. narcolepsy, idiopathic hypersomnia, secondary hypersomnia etc.
Common Sleep Disorders

Insomnia

- Difficulty falling asleep or maintaining sleep
  - Results in decreased “sleep efficiency” (time asleep/time in bed)

- Primary insomnia (psychophysiological)
  - No other disturbance
  - Predisposition (heightened arousal) + learned associations (e.g. excessive worry about sleep)

- Behavioural insomnia
  - Related to difficulties setting limits and managing behaviour

- Secondary insomnia
  - Due to another medical condition (e.g. seizures, sleep-disordered breathing, pain)
**Common Sleep Disorders**

**Restless Legs Syndrome/Periodic Limb Movement Disorder**

- **Restless legs syndrome:**
  - Uncomfortable sensation in lower extremities, usually in evening and worse when lying still
  - Urge to move – symptoms improve only while moving

- **Periodic limb movement disorder:**
  - Repetitive, brief (<10 seconds) limb jerks that occur periodically (20-40 sec)
  - Diagnosis requires PSG

- **Related to altered iron metabolism**
  - Association with low serum ferritin
Common Sleep Disorders
Circadian Rhythm Disorders

- **Abnormal timing** of sleep-wake cycles

- **Advanced & delayed sleep phase disorders**

- **Free-running (non-24h) circadian rhythm**
  - (Completely) sightless individuals may have free-running rhythm disorder – unable to “reset” circadian clock to external cues

- **Irregular circadian rhythm**
  - Severe neurological abnormalities (e.g. brain injury, malformation) are risk factor
# Common Sleep Disorders

## Parasomnias

<table>
<thead>
<tr>
<th>Non-REM Parasomnias</th>
<th>REM Parasomnias</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sleepwalking</td>
<td>• Nightmares</td>
</tr>
<tr>
<td>• Confusional arousals</td>
<td>• Other REM parasomnias uncommon in children (e.g. REM behaviour disorder)</td>
</tr>
<tr>
<td>• Sleep terrors</td>
<td></td>
</tr>
<tr>
<td>○ Prolonged, dramatic</td>
<td></td>
</tr>
<tr>
<td>○ Differential diagnosis:</td>
<td></td>
</tr>
<tr>
<td>nocturnal seizures</td>
<td></td>
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</tbody>
</table>
Diagnostic Difficulties

- Nocturnal events may be difficult to distinguish:
  - Nocturnal seizures
  - Partial arousal (non-REM) parasomnias
    - E.g. sleep terrors
  - REM parasomnias
    - Nightmares
Sleep And Neurodevelopmental Disorders

- Higher prevalence of sleep disorders
- Common:
  - Short sleep duration
  - Irregular sleep pattern
  - Insomnia
- Specific:
  - Sleep-disordered breathing in children with genetic disorders, craniofacial abnormalities
  - Brain malformations: abnormal sleep-wake regulation (central)
  - Decreased sensitivity to social/environmental cues in autism: irregular sleep-wake patterns (extrinsic)
Evaluation Tools
# Modified Epworth Sleepiness Scale

For each of the following situations, indicate how likely your child is to fall asleep or doze.

<table>
<thead>
<tr>
<th>Situation</th>
<th>Chance of Dozing or Sleeping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td>None</td>
</tr>
<tr>
<td>Watching TV</td>
<td>None</td>
</tr>
<tr>
<td>Sitting inactive in a public place</td>
<td>None</td>
</tr>
<tr>
<td>Being a passenger in a motor vehicle for an hour or more</td>
<td>None</td>
</tr>
<tr>
<td>Lying down in the afternoon when circumstances permit</td>
<td>None</td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td>None</td>
</tr>
<tr>
<td>Sitting quietly after lunch</td>
<td>None</td>
</tr>
<tr>
<td>While in a car stopped in traffic for a few minutes</td>
<td>None</td>
</tr>
</tbody>
</table>

**TOTAL SCORE:** __________ (maximum 24)
INSTRUCTIONS:
1. Write the date, day of the week, and type of day: Work, School, Day Off, or Vacation.
2. Put the letter “C” in the box when you have coffee, cola or tea. Put “M” when you take any medicine. Put “A” when you drink alcohol. Put “E” when you exercise.
3. Put a line (I) to show when you go to bed. Shade in the box that shows when you think you fell asleep.
4. Shade in all the boxes that show when you are asleep at night or when you take a nap during the day.
5. Leave boxes unshaded to show when you wake up at night and when you are awake during the day.

SAMPLE ENTRY BELOW: On a Monday when I worked, I jogged on my lunch break at 1 PM, had a glass of wine with dinner at 6 PM, fell asleep watching TV from 7 to 8 PM, went to bed at 10:30 PM, fell asleep around Midnight, woke up and couldn’t get back to sleep at about 4 AM, went back to sleep from 5 to 7 AM, and had coffee and medicine at 7:00 in the morning.

| Today's Date | Day of the week | Type of Day | Noon | 1PM | 2PM | 3PM | 4PM | 5PM | 6PM | 7PM | 8PM | 9PM | 10PM | 11PM | 1AM | 2AM | 3AM | 4AM | 5AM | 6AM | 7AM | 8AM | 9AM |
|--------------|----------------|-------------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|------|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| sample       | Mon.           | Work        | E    |     |     |     |     | A   |     |     |     |     | I    |     |     |     |     |     |     |     |     |     |     |     |

Indications:
Sleep disordered breathing
Hypersomnia (+/- multiple sleep latency test)
Periodic limb movements
Some parasomnias/nocturnal events

Not indication for PSG:
Insomnia
Circadian disorders
Restless legs

Full Night Polysomnography (PSG)
Polysomnography

- Note that standard PSG typically uses a *limited* EEG montage

- Home monitoring options are available
  - Home oximetry
  - Home PSG

  - *Pros*: avoid “first night” effect of being in lab
  - *Cons*: no video, no technologist observing, oximetry does not stage sleep
Actigraphy watch
Physiologic Relationship Between Sleep & Epilepsy

SLEEP AND THE EEG
EFFECT OF SLEEP AND SLEEP DEPRIVATION ON SEIZURES
SLEEP-RELATED EPILEPSY SYNDROMES
Physiology Of Sleep As It Relates To Epilepsy

- Sleep is characterized by increases in the following:
  - Oscillatory brain activity
  - Increased synchrony of brain activity

- Both these factors result in “activation” of epileptiform discharges during sleep
Increase In Spikes With Sleep
Seizures In Sleep

- 20-40% of seizures in children occur in sleep
- 30% of childhood epilepsy syndromes are sleep-related

- Certain seizure types occur almost exclusively in sleep:
  - Focal frontal lobe seizures
  - Rolandic seizures

- Propensity for sleep-wake transition
  - Infantile spasms
Seizures In Sleep

- Certain epilepsy syndromes characterized by continuous abnormal activity during sleep
- May have consequences even in absence of clinical seizures

- Landau-Kleffner syndrome
- Electrical status epilepticus in sleep (ESES)/continuous spike-and-wave in slow sleep (CSWS)
<table>
<thead>
<tr>
<th>Sleep</th>
<th>Sleep-wake transition</th>
<th>Wake</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal lobe seizures</td>
<td></td>
<td>Infantile spasms</td>
</tr>
<tr>
<td>Rolandic seizures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Continuous spike-and-wave in sleep (CSWS)*</td>
<td></td>
<td>Juvenile myoclonic epilepsy</td>
</tr>
<tr>
<td>Landau Kleffner syndrome*</td>
<td></td>
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</tbody>
</table>
Effect Of Sleep On Seizures

- **Activation effect of sleep deprivation (SD)**
  - Makes seizures more likely (even in people without epilepsy)
  - Seizures may be more prolonged or focal
  - Activates abnormal EEG activity (interictal epileptiform discharges)
    - Rationale for SD before EEG

- Disrupted sleep (e.g. in OSA) can trigger seizures
Treatment of OSA in children with epilepsy has been shown to reduce seizure frequency (Koh et al. Pediatric Neurology 2000)

- Greatest reduction (one study) in patients with seizures exclusively in sleep or upon awakening
Sleep Disorders In People With Epilepsy
Effect Of Seizures On Sleep

- Sleep disruption
  - Frank arousals
  - More subtle microarousals without apparent behavioural change

- Decreased total sleep time (TST)
- Frequent awakenings
- Reduction in REM sleep

- Increased sleep onset latency
- Decreased “deep” non-REM sleep (and increased light sleep)
Effect Of Seizures On Sleep

- In certain syndromes with frequent EEG discharges, sleep stages may be hard to score on PSG
- E.g. Lennox-Gastaut

- Sleep maximally disrupted on nights when seizure occurs
  - However, architecture still abnormal even without seizures (e.g. in temporal lobe epilepsy)
Individuals With Epilepsy Have A Higher Prevalence Of Sleep Disorders And Complaints

- *Twice* as prevalent compared to individuals without seizures
- 45% of children with new onset seizures report sleep problems
Sleep Disorders In People With Epilepsy

- Sleepiness: 52%
- Insomnia: 70%

- Among adults with refractory epilepsy: 1/3 OSA

- Also prevalent:
  - Periodic limb movement disorder (PLMD)
  - Restless legs syndrome (RLS)
  - Central sleep apnea (CSA)
Sleep Disorders In People With Epilepsy

- Factors contributing to sleep disruption:
  - Seizure frequency
  - Interictal EEG abnormalities
  - Antiepileptic drugs (AEDs)
  - Comorbidities (e.g. abnormal tone, irregular circadian rhythm, etc.)
Excessive Daytime Sleepiness

- Among the most common complaint in children with epilepsy

- One study identified presence of sleep-disordered breathing and parasomnias as predictors of EDS
  - Seizure syndrome, AED, and seizure frequency were not predictors

- Seizures (nocturnal), medications, presence of primary sleep disorders important factors
Disrupted Sleep In Children With Epilepsy & Their Families

Impact of pediatric epilepsy on sleep patterns and behaviors in children and parents


Pediatric Epilepsy Program, Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts, U.S.A.
Disrupted Sleep In Children & Families

- Higher rates in children with epilepsy (vs. controls):
  - Parental co-sleeping
  - Parasomnias
  - Bedtime resistance
  - Sleep onset delay
  - Decreased sleep time
  - Daytime sleepiness
  - Nighttime wakings

- Parents:
  - Greater fatigue & sleep dysfunction
  - 69% worried about nighttime seizures
  - 44% feel rested rarely or never
A Word About SUDEP

Postulated link between OSA and sudden unexplained death in epilepsy (SUDEP)
- Disruption of autonomic function in sleep in OSA
- May promote cardiac arrhythmias
- Increased frequency of seizures in OSA

Any disruption of sleep that may exacerbate seizures may increase risk of SUDEP
Antiepileptic Therapy And Sleep

ANTIEPILEPTIC DRUGS (AEDS)
KETOGENIC DIET
VAGAL NERVE STIMULATOR
EPILEPSY SURGERY
Antiepileptic medications typically cause daytime sedation
- Phenobarbital, carbamazepine, valproic acid
- Phenytoin relatively less
- “Newer” AEDs cause relatively less daytime sedation
Antiseizure Treatment And Sleep

- Antiepileptic medications and non-drug treatments affect sleep architecture

  - Relative paucity of data
  - However, evaluation can be difficult due to the effect of improved seizure frequency on sleep

Effects of epilepsy treatments on sleep architecture and daytime sleepiness: An evidence-based review of objective sleep metrics
Sejal V. Jain and Tracy A. Glauser
Epilepsia, 55(1):26–37, 2014
doi: 10.1111/epi.12478
Antiseizure Treatments

- **Most AEDs affect sleep architecture**
  - However, the changes are not consistent from medication to medication

- **Vagal nerve stimulator:**
  - Improves daytime sleepiness and increases slow-wave sleep

- **Epilepsy surgery:**
  - Greater total sleep time & reduced arousals IF seizures effectively treated

- **Ketogenic diet:**
  - Increases REM sleep
Consequences Of Sleep Architecture Disruption

- **Slow-wave sleep (Non-REM stage N3):**
  - Increased: more partial arousal parasomnias (e.g. terrors)
  - Decreased: feeling of less restorative sleep

- **REM sleep:**
  - Increased: potential increase in nightmares, may worsen sleep-disordered breathing
  - Decreased: impairment of memory consolidation
Increased frequency of seizures

Sleep disruption/deprivation

Sleep Disorder (e.g. OSA)

Neuro-developmental abnormality

Antiseizure Treatment
Management Strategies
Management Approach

- Proper evaluation of sleep complaints
- History & physical
  - Special attention to medications, comorbidities, etc.
- Questionnaires (Epworth, Insomnia scales, Sleep Diary)
- Laboratory testing (if indicated)
  - PSG (in-lab or home) or home overnight oximetry
  - EEG (video-EEG, ambulatory EEG)
  - Actigraphy
  - Bloodwork: med levels, iron, thyroid studies, etc.
Management Approach

• Optimization of seizure management
  - Special attention to medications
    - Dosages
    - Levels (if applicable)
    - Side-effects (e.g., GI upset)
    - Timing/distribution

• Treatment of medical and neurological comorbidities
  - Pain (e.g., from spasticity)
  - Reflux

• Correction of underlying sleep disorder
  - Adenotonsillectomy for OSA
  - Iron supplementation for RLS
Management Approach

- **Behavioural management**
  - Establishment of bedtime routines and limits
  - Fading
  - Reward systems & positive reinforcement

- **Sleep hygiene**
  - Avoidance of naps
  - Avoidance of caffeine
  - Exercise
  - Appropriate sleep environment
  - Morning light exposure

- (Medications)
Conclusions

- Sleep & Epilepsy are closely interrelated!
- High prevalence of sleep disorders in individuals with epilepsy
- Identification and treatment of sleep disorders (whether primary or secondary) can greatly improve seizure control and quality of life
- Effective management of seizures can improve sleep
THANK YOU!
Questions?