Sleep and Psychiatry

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Conflict of Interest Disclosures

- NONE ☹
Outline

- Sleep Disruption and Psychiatric Disorders
- Hypersomnia
- Sleep Apnea
- Restless Legs Syndrome
- PTSD Nightmare Disorder
- Insomnia
EEG Changes Seen On PSG

- Depression
  - Prolonged Sleep Onset Latency
  - Increased WASO/Decreased Total Sleep Time
  - Increased Early Morning Wake Time
  - Decreased Slow Wave Sleep
  - Increased total REM and REM Density
  - Decreased REM latency and Prolonged REM duration for first episode of REM
Hypersomnia

- Narcolepsy with or without cataplexy
- Idiopathic Hypersomnia
Narcolepsy With and Without Cataplexy

- Narcolepsy Type 1
  - Daily periods of irrepressible need to sleep or lapses into sleep
  AND
  - Cataplexy and mean sleep latency less than 8 minutes and 2 or more Sleep Onset REM Periods (SOREMPs) on PSG/MSLT
  OR
  - Decreased CSF Hypocretin-1 concentration

- Narcolepsy Type 2
  - No Cataplexy and normal or untested CSF Hypocretin-1 concentration
Idiopathic Hypersomnia

- Daily periods of irrepressible need to sleep or lapses into sleep
- Cataplexy is absent
- Less than 2 SOREMP on PSG/MSLT

AND

- Mean sleep latency less than 8 minutes

OR

- Total 24 hour sleep time is greater than 660 minutes
- Insufficient sleep syndrome is ruled out
Hypersomnia Disorders

- Significant impact on quality of life.
- Patients with narcolepsy are at increased risk for depression and anxiety
- Also found in:
  - Major Depression
  - Bipolar Disorder
  - Schizophrenia
  - Seasonal Affective Disorder
    - ICSD-3 suggests prolonged time in bed; however, Plante et al, 2017 found that patients with MDD and hypersomnia complaints did have objective increased sleep time
- Treatment Consideration: Bupropion
Physiology of Sleep Apnea

- Decrease or cessation of air flow associated with oxygen desaturation and/or brief arousal
- Leads to hyperactivation of the sympathetic nervous system and hypothalamic pituitary axis
- Obstructive: complete or partial upper airway obstruction
- Central: no observable inspiratory effort
Obstructive Sleep Apnea

- More likely to suffer from MDD (Gupta and Simpson, 2015)
- More likely to suffer from insomnia if untreated
- Can exacerbate PTSD, Anxiety, Schizophrenia
- Can mimic nocturnal panic attacks
- More likely to occur in patients on psychiatric medications due to associated weight gain/metabolic syndrome
Restless Legs Syndrome

- Irrepressible urge to move the legs due to sensation of discomfort which is exacerbated by periods of rest or inactivity and relieved by movement
- More likely to suffer from depression/anxiety (Mackie and Winkleman, 2015)
- Decreased quality of life (Stevens, 2015)
- Conflicting data about exacerbation by SSRIs, SNRIs, TCAs, antipsychotics
  - Medications that act on serotonin
Post-Traumatic Stress Disorder - Nightmares

- Treatment: Prazosin and Image Rehearsal Therapy
  - Prazosin: Start at 1mg QHS and titrate up by 1mg per week until symptoms resolve/significantly improve
  - Most common side effects: Orthostatic Hypotension, Headaches, Insomnia
Insomnia

- Patients with insomnia:
  - 2 fold risk of developing depression (Baglioni et al, 2011)
  - Increased risk for suicidal ideation, attempts, and success (Pigeon et al, 2012)
  - Increased risk for chronic pain (Smith et al, 2007)
  - Predictor of recurrence in absence of mood symptoms (Benca RM, Peterson MJ, 2008)
Prevalence

- 10% of the adult population meet full criteria
- 30-35% report transient symptoms
- 10-30% of children experience behavioral insomnia of childhood
Previously Used Insomnia Categories

- Adjustment Insomnia (Acute Insomnia)
- Psychophysiological Insomnia
- Paradoxical Insomnia
- Idiopathic Insomnia
- Insomnia due to Mental Disorder
- Inadequate Sleep Hygiene
- Insomnia Due to Drug or Substance
- Insomnia Due to Medical Condition
- Insomnia Not Due to Substance or Know Physiologic Condition, Unspecified (Nonorganic Insomnia, NOS)
- Physiological (Organic) Insomnia
Chronic Insomnia Criteria

- A. One or more of the following:
  - Difficulty initiating sleep
  - Difficulty maintaining sleep
  - Waking up earlier than desired
  - Resistance to going to bed on an appropriate schedule
  - Difficulty sleeping without parent or caregiver intervention

- B. One or more of the following related to the night time sleep difficulty:
  - Fatigue/malaise
  - Attention, concentration, or memory impairment
  - Impaired social, family, occupational, or academic performance
  - Mood disturbance/irritability
  - Daytime sleepiness
  - Behavioral problems (hyperactivity, impulsivity, aggression)
  - Reduced motivation/energy/initiative.
  - Proneness for errors/accidents
  - Concerns about or dissatisfaction with sleep
Chronic Insomnia Criteria Continued

- C. The reported sleep/wake complaints cannot be explained purely by inadequate opportunity or inadequate circumstances for sleep.
- D. The sleep disturbance and associated daytime symptoms occur at least 3 times a week.
- E. The sleep disturbance and associated daytime symptoms have been present for at least 3 months.
- F. The sleep/wake difficulty is not better explained by another sleep disorder.
Behavioral Insomnia of Childhood

- **Limit-Setting Sleep Disorder**
  - Bedtime stalling or refusal as a result of inadequate limit setting by caregiver
  - “One more glass of water…”

- **Sleep-Onset Association Disorder**
  - Must have a specific set of stimuli, object, or setting to initiate or return to sleep
  - IE: rocking, TV watching, bottle, parents’ bedroom
Insomnia with normal sleep duration

- Lack of physiological hyperarousal (i.e., normal activity of both limbs of the stress system)
- Sleep misperception
- Anxious-ruminative profile
- More likely to remit
- No significant risk of cardiometabolic morbidity and mortality

Insomnia with short sleep duration

- Biological vulnerability (e.g., genetic predisposition, higher sensitivity of sleep to activation of the arousal and stress systems)
- Physiological hyperarousal (i.e., hyperactivity of both limbs of the stress system)
- Impaired neurocognitive functioning
- More likely to persist
- Increased risk of cardiometabolic morbidity and mortality

Vgontzas et al.; Insomnia with objective short sleep duration: The most biologically severe phenotype of the disorder. Sleep Med Review 17(2013)241-254
Spielman’s Model

- **Predisposing Factors**
  - Increased sensitivity to changes in sleep schedule, worries, anxiety/depression, family history, etc.

- **Precipitating Events**
  - Stressful life event, sudden change in schedule, etc

- **Perpetuating Mechanisms**
  - Attempts to regain sleep, excessive worrying about sleep, etc.
Developing Insomnia

Treatment Options

- Pediatrics: Behavioral Interventions
- Cognitive Behavioral Therapy
- Pharmacologic Therapy
Pediatric Behavioral Interventions

- Graduated Extinction
  - Checking on the child at specified intervals that gradually grow longer
  - Minimal interaction when checking on child
  - Ignoring attention seeking behaviors

- Bedtime Routine
  - Quiet and calming activities to help cue the child that bedtime is approaching
  - Scheduled awakenings 15 to 30 minutes prior to child’s usual awakenings
    - Gradually fade out awakenings

- Positive Reinforcement
  - Sticker chart
Cognitive Behavioral Therapy vs Pharmacotherapy

- CBT and BZRAs effective in the short term with CBT providing greater benefit long term (Riemann and Perlis, 2008-Clinical Review)

- Combination therapy (Zolpidem and CBT) vs CBT alone vs zolpidem alone vs placebo – demonstrated improved sleep onset latency and sleep efficiency with combination therapy and CBT alone at conclusion of study when zolpidem had been discontinued (Jacobs et al, 2004)
Cognitive Behavioral Therapy

Pharmacotherapy

- Orexin Receptor Antagonist
- Benzodiazepine Receptor Agonists (BZRAs)
- Benzodiazepines (BZDs)
- Melatonin Receptor Agonists
- Sedating Low Dose Antidepressants
- Anticonvulsants/Antipsychotics
Orexin Receptor Antagonist

- Suvorexant (Belsomra)
  - Half-life: 12 hours, Dose: 5-20mg
  - Faster onset if taken without food
  - Despite long half-life, progressive drop in receptor occupancy throughout the night reduces risk of daytime somnolence
  - At higher than recommended doses, cataplexy can occur
  - Though respiratory depression is listed as a risk, this is primarily due to the drug class it was placed in; however, it is contraindicated in severe COPD.
## BZRAs (Z Drugs)

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Half-Life (hours)</th>
<th>Time to peak concentration (hours)</th>
<th>Dose (mg)</th>
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</thead>
<tbody>
<tr>
<td>Zolpidem</td>
<td>Ambien</td>
<td>1.4-4.5 (~2.5)</td>
<td>1.6-2.2</td>
<td>5-10</td>
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<tr>
<td>Zaleplon</td>
<td>Sonata</td>
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<td>1</td>
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<tr>
<td>Eszopiclone</td>
<td>Lunesta</td>
<td>5-7</td>
<td>1</td>
<td>1-3</td>
</tr>
<tr>
<td>Zolpidem ER</td>
<td>Ambien CR</td>
<td>1.4-4.5 (~2.5)</td>
<td>1.5-4</td>
<td>6.25-12.5</td>
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<tr>
<td>Zolpidem SL</td>
<td>Intermezzo</td>
<td>1.4-6.7 (~3)</td>
<td>0.6-3</td>
<td>1.75-3.5</td>
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BZDs

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand</th>
<th>Half-Life</th>
<th>Dose</th>
<th>Concerns</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flurazepam</td>
<td>Dalmane</td>
<td>48-120</td>
<td>15-30</td>
<td>Half-Life</td>
</tr>
<tr>
<td>Temazepam</td>
<td>Restoril</td>
<td>8-20</td>
<td>15-30</td>
<td>Half-Life</td>
</tr>
<tr>
<td>Triazolam</td>
<td>Halcion</td>
<td>2-6</td>
<td>0.125-0.25</td>
<td>Rebound Anxiety</td>
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<tr>
<td>Estazolam</td>
<td>Prosom</td>
<td>8-24</td>
<td>1-2</td>
<td>Half-Life</td>
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<tr>
<td>Quazepam</td>
<td>Doral</td>
<td>48-120</td>
<td>7.5-15</td>
<td>Half-Life</td>
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<tr>
<td>Clonazepam</td>
<td>Klonopin</td>
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<td>0.25-2</td>
<td>Off Label</td>
</tr>
<tr>
<td>Diazepam</td>
<td>Valium</td>
<td>44-48</td>
<td>2-10</td>
<td>Off Label</td>
</tr>
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</table>
Melatonin Receptor Agonist

- Ramelteon (Rozerem)
  - Half-Life: 1.5-5 hours; Dose: 8mg
  - Better for sleep onset insomnia
Sedating Low Dose Antidepressants

- Potent antihistamine effect
  - Histamine levels rise later in the night
  - May be a better option for those with sleep maintenance issues

- Tricyclic Anti-Depressants
  - Doxepin (Silenor)
    - Half-Life: 15 hours; Dose: 3-6mg
  - Amitriptyline, nortriptyline, trimipramine

- Trazadone
  - Half-Life: 7-10 hours; Dose: 50-200mg

- Mirtazapine (Remeron)
  - Half-Life: 20-40 hours; Dose: 7.5-15mg
Anticonvulsants/Antipsychotics

- Gabapentin, Quetiapine, Etc
  - Only recommended for use when indicated comorbidities are present
  - Gabapentin may be a good choice in alcoholics as one study showed it decreased drinking behaviors (though it did not have much of an effect on sleep)
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