SLEEP & INSOMNIA

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OVERVIEW

I. What is sleep?
II. Sleep deprivation and consequences.
III. Clinical diagnoses of sleep disorders.
IV. Treatments for insomnia.
SLEEP

SLEEP: is the integration of 2 oscillating processes: 1. Sleep homeostasis which regulates the accumulation and dissipation of sleep debt and 2. Circadian clock which accounts for the daily rhythm in sleep and arousal cycles in a 24hr day (note however that a human’s natural day clock has 25hrs/d)
SLEEP

PURPOSE: Although essential the specific purpose and function of sleep has yet to be definitively determined but many theories exist including:

- Restorative Theory of Sleep
- Adaptive Theory of Sleep
- Energy Conservation Theory
SLEEP STAGES
(2007 DEFINITION VS 1968 DEFINITION)

1. Non-REM: aka slow wave sleep or S sleep
   - **Stage 1** ($\theta$): lightest sleep usually a few seconds to minutes, transition into sleep from wakefulness, people usually awakened from this state do not perceive themselves as having been asleep, accounts for 2-5% of sleep
   - **Stage 2** (sleep spindles & K-complex): intermediate sleep, accounts for 40-50% of sleep, benzos increase this stage of sleep at the expense of stage 3 sleep
   - **Stage 3** ($\delta$): aka Deep sleep or Delta wave sleep, accounts for 20% of sleep. Was previously subdivided into stage 3 and stage 4 sleep (difference being that stage 3 has < 50% delta waves vs stage 4 has > 50%)
II. REM (Rapid Eye Movement): aka D sleep for dreaming sleep or paradoxical sleep 2/2 activated EEG, accounts for 25% of sleep
NORMAL SLEEP ARCHITECTURE

- Sleep cycles are typically 90-120min
- 4-5 cycles/night
- First half of sleep: More deep sleep occurs with more alt between N2 and N3.
- Last half of sleep: More REM sleep occurs with more alt between N2 and REM.
- As one ages Stage 3 sleep decreases and Stage 2 increases
- Neonates (<1 month) spend more 50% in REM and go straight into REM from wakefulness.
SLEEP DEPRIVATION

- More than one third of participants reported sleeping less than 7 hours during the work week according to the 2005 to 2008 National Health and Nutrition Examination Survey.

- As few as five arousals per hour of sleep can result in daytime sleepiness and/or performance deficits, even after a single night of disruption.

- Sleep deprivation affects alertness, performance, health and quality of life and can present with mental status changes that look like depression and anxiety including decreased alertness, poor concentration and memory, irritability, poor mood, decreased libido and pleasure in activities.
SLEEP DEPRIVATION

It’s the second leading cause of car crashes and a major cause of truck crashes in the United States. Three Mile Island (on March 28, 1979 near Harrisburg, Pennsylvania) and Chernobyl nuclear power plant disasters (On April 26, 1986 in Chernobyl, Ukraine), the Exxon Valdez oil spill, and the Space Shuttle Challenger disaster have been attributed to the poor judgment of sleep-deprived workers.
FEELING THE EFFECTS OF SLEEP DEPRIVATION

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

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

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

- Risk of diabetes Type 2
MORTALITY

• 2x increase in mortality rate if sleep onset latency is >30min or <80% efficient sleep
• Increased mortality if one sleeps < 4hrs or >10hrs also those who using sleeping pills had 1.5 times the mortality
• 4x increase in mortality if sleep was <6hrs for men
• Night work may increase cancer risk
DSM IV Primary Sleep Disorders

**Dyssomnias**: disturbances in amount, quality or timing of sleep ≥ 1 mo
- 1° insomnia
- 1° hypersomnia
- Narcolepsy
  - Sleep related breathing d/o: OSA or central sleep apnea
  - Circadian rhythm sleep d/o: delayed sleep phase, jet leg, shift work
    - NOS: RLS, Nocturnal Myoclonus

**Parasomnias**: abnormal physiological events in connection with stages of sleep
- Nightmare d/o-REM
- Sleep terrors-N3
  - Somnambulism aka sleep walking-N3
- NOS: REM behavior d/o, sleep paralysis, enuresis, bruxism, sleep related hemolysis
PSYCHIATRIC NUANCES OF SLEEP

Insomnia is often a coexisting disorder as many diagnostic criteria are related to sleep disturbances. Insomnia may also be predictive of developing a psychiatric illnesses therefore separate treatment may be warranted in treating both conditions.

- BAD I, II (7 days vs 4 days of decreased need for sleep)
- Depression (melancholic with early morning awakening vs atypical with hypersomnia) On hypnogram will see decrease REM latency with more REM sleep shifted towards first half of night
- GAD (sleep disturbance: difficulty falling asleep, staying asleep, restless unsatisfying sleep)
- PTSD (nightmares, hyper-arousal)
- Substance Abuse esp EToH causing rebound awakening
SECONDARY SLEEP DISTURBANCES

Inadequate/Poor Sleep Hygiene

Medical Conditions
  - Pulmonary Disease: ≥50%
  - Pain: 30-50% with CA
  - Heart Failure: 30%

Medications
INADEQUATE/POOR SLEEP HYGIENE

5-10% of patients who are evaluated in sleep centers have poor sleep hygiene

- Irregular sleep schedule
- Sleep disturbing substances
- Mentally/physically stimulating activities
- Activities that are not related to sleep
- Failure to maintain a comfortable sleep environment
- Other learned sleep-preventing behaviors

"No wonder you have insomnia... lying there awake all night."
MEDICATIONS

- Central nervous system stimulants (caffeine)
- Respiratory stimulants (theophylline)
- Appetite suppressants
- Calcium channel blockers
- Antidepressants (TCAs, MAOIs, SSRIs, SNRIs, Wellbutrin)
- Beta antagonists (propranolol, metoprolol, pindolol)
- Glucocorticoids (prednisone, cortisol)
OTHER SLEEP CONDITIONS

• **Idiopathic Insomnia**: ≤1% of young adults and adolescents
• **Behavioral insomnia of childhood**: 10-30% of children beginning at six months of age
• **Paradoxical insomnia**: aka sleep state misperception, subjective insomnia, pseudoinsomnia, or sleep hypochondriasis. Consistently overestimate how long it takes to fall asleep and to underestimate their total sleep time.
TREATMENT FOR INSOMNIA

Insomnia may present independently but is often a comorbid condition in our population and is worth treating and addressing separately as successful treatment of insomnia may also improve their comorbid conditions. Furthermore any medical condition, psychiatric illness, substance abuse, or sleep disorder that may be precipitating or exacerbating the insomnia should be adequately treated.
TYPES OF TREATMENT

- **Behavioral Therapies**: sleep hygiene education, stimulus control, relaxation, sleep restriction therapy, cognitive therapy, and cognitive behavioral therapy

- **Medication**: benzodiazepines, nonbenzodiazepine sedatives, and melatonin agonists

- **Combination Therapy**
SLEEP HYGIENE

Sleep only as much as you need to feel rested and then get out of bed
Keep a regular sleep schedule
Avoid forcing sleep
Exercise regularly 4 to 5 hours before bedtime
Avoid caffeinated beverages after lunch
Avoid alcohol near bedtime
Avoid smoking, especially in the evening
Avoid naps esp those longer than 20-30min and late in day
Adjust bedroom environment
Deal with your worries before bedtime
STIMULUS CONTROL

Attempting to break any anticipatory anxiety or other stimulating associations with sleep that perpetuates the difficulty in falling asleep and maintaining quality sleep.

Go to bed only when tired
If not asleep in 20 minutes remove yourself from bedroom
Bedroom is only for sleep and sex
RELAXATION TECHNIQUES

Progressive Muscle Relaxation
SLEEP RESTRICTION

Minimizes extended periods of time in bed to produce more efficient sleeping patterns i.e. time in bed is spent sleeping. This relies on the body’s sleep homeostatic process. As sleep debt is accumulated the drive to sleep increases therefore awakening at the same time each morning regardless of when one fell asleep the night before will eventually aid the person to fall asleep earlier and more efficiently on subsequent nights.
COGNITIVE THERAPY focus on erroneous automatic thoughts that stimulate wakefulness

COGNITIVE BEHAVIORAL THERAPY usually incorporates all of the previous therapies with use of sleep logs/diaries and attention to teaching skills that can be applied to future relapses
MEDICATIONS

- Benzodiazepines
- Nonbenzodiazepine sedatives
- Melatonin agonists
BENZODIAZEPINES

- FDA indications: anxiety, panic d/o, insomnia (short term tx), status epilepticus, preoperative sedation, chemo-related nausea/vomiting
- Class D associated with development of cleft lip and palate and is excreted into the breast milk
- Tolerance develops to sedative effects but not antianxiety effects
- Decreases REM sleep and therefore will have REM rebound

List: triazolam/Halcion, estazolam, lorazepam/Ativan, temazepam/Restoril, flurazepam/Dalmane
NONBENZODIAZEPINES

- Binds more specifically at GABA A α1 subunit therefore have less anxiolytic and anticonvulsant properties.
- FDA indications: insomnia
- Class C: animal studies show adverse fetal effects but no controlled human studies

List: zaleplon/Sonata, zolpidem/Ambien/AmbienCR, eszopiclone/Lunesta
SPECIAL CONSIDERATIONS

• Pregnancy – risk of malformations
• Alcohol consumption – risk of excessive sedation
• Renal or hepatic disease – metabolic clearance may be delayed in patients leading to accumulation and excessive sedation
• Pulmonary disease or sleep apnea – worsen obstructive sleep apnea or hypoventilation
• Nighttime decision makers – eg, clinicians on-call or single parents responsible for the care of young children
• Older adults – risk of adverse effects is increased in older adults, especially those who are older than 75 years.
• Substance Use Disorder – possess risk of abuse and dependence
WHICH MEDICATION TO SELECT?

Sleep initiation vs sleep maintenance or both?
Comorbidities? Substance abuse history? Hepatic disease?
<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>Half-life</th>
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</thead>
<tbody>
<tr>
<td>Short Acting</td>
<td>tiazolam/Halcion</td>
<td>(1.5-5.5hrs)</td>
</tr>
<tr>
<td></td>
<td>zolpidem/Ambien/AmbienCR</td>
<td>(2.5-3.1hrs)</td>
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<tr>
<td></td>
<td>zaleplon/Sonata</td>
<td>(1hr)</td>
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<tr>
<td>Intermediate Acting</td>
<td>lorazepam/Ativan</td>
<td>(14hrs)</td>
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<tr>
<td></td>
<td>temazepam/Restoril</td>
<td>(8.8hrs)</td>
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<tr>
<td>Long Acting</td>
<td>flurazepam/Dalmane</td>
<td>(active metabolite 40-100hrs)</td>
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ADVERSE EFFECTS

• residual daytime sedation, drowsiness, dizziness, lightheadedness, cognitive impairment, motor incoordination, and dependence
• complex sleep-related behaviors (eg, driving, making telephone calls, eating, having sex while not fully awake) and hallucinations esp noted with Ambien
• Lunesta-metallic taste and unpleasant dreams
Melatonin is a hormone that is produced by the pineal gland, a small endocrine gland located in the center of the brain. It regulates the sleep-wake cycle by chemically causing drowsiness. Its production by the pineal gland is inhibited by light to the retina and permitted by darkness.

ramelteon/Rozerem: binds to MT1/MT2 receptors, half life 2-5hrs
OTHER MEDICATIONS

- **ANTIDEPRESSANTS**: doxepine FDA approved at 10-50mg, trazadone at 25-50mg
- **ANTIPSYCHOTICS**: not recommended
- **HERBAL**: not regulated by FDA
  - **Valerian**: flowering plant has sedative effects
  - **Melatonin**: may help in delayed phase sleep syndromes
SUMMARY

• Insomnia affects nearly 1/3 of the population and 70% in the primary care setting.

• Patients with insomnia should receive tx for any medical condition, psychiatric illness, substance abuse, or sleep disorder that may be precipitating or exacerbating insomnia.

• Long-term medication alone is not the optimal initial treatment strategy for patients with insomnia.

• Cognitive behavioral therapy (CBT) is tx of choice as the initial therapy. An alternative type of behavioral therapy is reasonable if CBT is not available.

• Patients given behavioral plus pharmacologic therapy should continue for six to eight weeks. In patients who respond to therapy, the medication can be tapered while continuing the behavioral therapy.

• Patients whose symptoms recur may require evaluation in a sleep disorders center, prior to the institution of long-term therapy.
REFERENCES

- Mark R Pressman, PhD. Definition and consequences of sleep deprivation. Retrieved from UpToDate. Literature review current through: Sep 2012. |This topic last updated: Jun 5, 2011.