Sleep Dysfunction in Psychiatric Illness

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Objectives

1. Briefly review Normal Sleep Architecture
2. Learn the effects of Sleep Deprivation on Body and Brain
3. Review interaction between Psychiatric Illness and Sleep
4. Look at Sleep Hygiene & CBT for Insomnia
5. Review medication effects on Sleep Architecture
Effects of Sleep Deprivation

**Body**
- ↑ Adrenaline (Epinephrine)
  - ↑ BP & HR → Cardiovascular disease
- ↑ Cortisol
  - ↑ Glucose → DM type 2
  - ↑ Weight gain → obesity
  - ↓ Immune function
- Fatigue, Weakness

**Brain**
- ↓ Serotonin = ↑ irritability, ↓ attention
- ↓ Dopamine = ↓ pleasure/reward
- ↑ Norepinephrine = ↑ anxiety/anger
  - ↓ Memory
  - ↓ Concentration
  - ↓ Judgement
- ↓ Memory
- ↑ Adrenaline (Epinephrine)
- ↑ Cortisol
- ↑ Glucose → DM type 2
- ↑ Weight gain → obesity
- ↓ Immune function
- Fatigue, Weakness

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

*Other:
- Growth suppression
- Risk of obesity
- Decreased temperature
Normal Sleep Architecture

- **Stage 1 (N1)**
  - “half” asleep
  - Easily aroused

- **Stage 2 (N2)**
  - Light sleep
  - Reduced movements

- **Stage 3 (N3)**
  - Slow-wave (deep) sleep
  - Delta (δ) waves – 0.5-4 Hz
  - “Refreshing sleep”
    - Replenish pre-synaptic vesicles

- **REM sleep**
  - Dreaming
  - Memory Consolidation
  - 5HT & DA receptor re-sensitization
Neurochemicals & Sleep Architecture
Circadian Rhythm

**Melatonin**
- made by Pineal Gland
- ↑ after sunset
- Daylight inhibits
- Light delays by 2-3 hrs

**Adenosine**
- made by all cells
- breakdown of ATP
- ↑ throughout the day
- blocked by caffeine

Sleep Deprivation

- Pre-synaptic cannot keep up with demand
- Pre-synaptic neuron gets depleted

- Harder to trigger post-synaptic neuron
- Post-synaptic receptors become desensitized
- Only fully restored during deep sleep
Sleep Deprivation

• Well rested:
  ↓ Norepi  ↑ Serotonin  ↑ Dopamine

• Sleep Deprived:
  ↑ Norepi  ↓ Serotonin  ↓ Dopamine

Norepinephrine (Fight/Flight)  Serotonin (calm)  Dopamine (pleasure)
Trauma & Stress

Posttraumatic Stress

A. Exposure to actual or threatened death, serious injury, or sexual violence

B. Intrusion symptoms:
   1. Involuntary, and intrusive distressing memories
   2. Distressing dreams
   3. Dissociative reactions (e.g., flashbacks)
   4. Intense / prolonged psychological distress to cues (triggers)
   5. Marked physiological reactions to cues (triggers)

C. Avoidance

↑ Norepinephrine

↑ Norepinephrine
Trauma & Stress

Posttraumatic Stress

E. Marked alterations in arousal and reactivity:
   A. Irritable behavior and angry outbursts (with little or no provocation)  
   B. Reckless or self-destructive behavior.  
   C. Hypervigilance.  
   D. Exaggerated startle response.  
   E. Problems with concentration.  
   F. **Sleep disturbance** (e.g., difficulty falling or staying asleep or restless sleep).
PTSD & Insomnia

- Nightmares & Sleep Fragmentation most common symptoms in PTSD
- Sleep disruption reported in 70-87% of PTSD pts
- Sleep disturbance may predict the development of PTSD
  - Sleep complaints (insomnia, nightmares) at 1 month (not at 1 week) after trauma, are significant predictor of PTSD at 12 months
  - Absence of sleep symptoms during 1st month strong predictor of NOT developing PTSD
- Untreated sleep symptoms can persist for years and intensify daytime PTSD symptoms
- Sleep Architecture Changes:
  - ↑ REM density
  - ↑ brief awakenings
  - ↑ shifts from REM to NREM per hour
  - ↓ SWS (N4) sleep

↑ PTSD sx
↑ Triggers

↑ Norepinephrine
↓ Serotonin
↓ Dopamine

↑ Latency
↑ Nightmares
↑ Fragmentation
↑ WASO
↓ SWS (N4)
↓ Efficiency

↓ SWS (N4)
PTSD & Sleep-disordered Breathing

Central Events

- ↑ PTSD sx
- ↑ Triggers
- ↑ Sleep Fragmentation
- ↓ RR
- ↓ P_{O2}
- ↑ AHI/RDI
- ↑ Nightmares

Hyperventilation
- ↓ P_{CO2}

Obstructive Events

- ↑ PTSD symptoms
- ↑ Apneas/Hypopneas
- ↓ P_{crit}
- ↑ Airway Collapse
- ↑ Insomnia
- ↑ Nightmares
- ↑ Sleep Fragmentation
Anxiety

Generalized Anxiety Disorder

A. Excessive anxiety/worry, >6 month ↑ Norepinephrine

B. Difficult to control the worry ↑ Norepinephrine

C. 3+/6 of the following symptoms:

• Restlessness, feeling “keyed up” or “on edge” ↑ Norepinephrine

• Being easily fatigued. ↓ Sleep Quality

• Difficulty concentrating or mind going blank. ↑ Norepinephrine ↓ Serotonin

• Irritability. ↑ Norepinephrine ↓ Serotonin

• Muscle tension. ↑ Norepinephrine & Adrenaline

• Sleep disturbance (difficulty falling/staying asleep, or restless, unsatisfying sleep). ↑ Norepinephrine
Anxiety & Insomnia

- Anxiety disorder in 33.1% of those who report insomnia
- Insomnia occurs in up to 2/3 of patients with social anxiety
- 7x Higher lifetime prevalence of sleep disturbance in GAD.
- Anxiety often occurs before (43.5%) or at time of (38.6%) onset of insomnia
- PSG results vary but trend...
  - ↑↑ Sleep Latency
  - ↓ Total Sleep Time
  - ↑ Wake After Sleep Onset
Depression

Major Depressive Disorder

A. 5+ of following symptoms:

- Depressed mood or Anhedonia (lack of interest/pleasure) \(\downarrow\) Dopamine
- Weight loss/gain or decrease/increase in appetite \(\uparrow\) Norepinephrine & Adrenaline \(\uparrow\) Cortisol & Ghrelin
- **Insomnia** or **hypersomnia** nearly every day. \(\uparrow\) Norepinephrine
- Psychomotor agitation/retardation \(\uparrow\) Norepinephrine
- Fatigue or loss of energy \(\downarrow\) Sleep Quality
- Feelings of worthlessness or excessive/inappropriate guilt \(\downarrow\) Serotonin \(\downarrow\) Dopamine
- Poor concentrate or indecisiveness \(\uparrow\) Norepinephrine \(\downarrow\) Serotonin
- Recurrent thoughts of death or suicidal ideation \(\downarrow\) Serotonin
Depression & Insomnia

- Depression can present as insomnia
  - Insomnia is seen in >90% of patients with clinical depression.
- Depression is a risk factor for developing insomnia
  - Odds ratio of 6.2
- Insomnia is a risk factor for developing depression
  - Odds ratio of 6.2
- Insomnia is an indicator for relapse
- Higher levels of insomnia and depression corresponded to significantly greater intensity of suicidal thinking
- Need N3 to replenish presynaptic vesicles
- Need REM to desensitize 5HT & DA receptors

Bipolar Disorder

Bipolar I disorder

A. Persistently elevated, expansive, or irritable mood and increased activity/energy. >1 week

B. 3+ of the following symptoms:

1. Inflated self-esteem or grandiosity  
   - Dopamine

2. Decreased need for sleep (e.g., feels rested after only 3 hours of sleep)  
   - Norepinephrine

3. More talkative or pressured speech  
   - Norepinephrine

4. Flight of ideas or racing thoughts.  
   - Norepinephrine

5. Distractibility  
   - Norepinephrine

6. Increase in goal-directed activity or psychomotor agitation  
   - Norepinephrine & Adrenaline

7. Increased risk-taking behavior  
   - Dopamine  
   - Norepinephrine
Bipolar & Insomnia

- Decreased need for sleep (while maintaining energy) is hallmark of Mania
  - Present is very few other disorders
  - Many pts have died from total sleep deprivation

- Sleep deprivation is one cause of mania, triggered by...
  - Drugs of abuse / prescribed medications
  - Travel (jet lag)
  - Postpartum
  - Bereavement

- ↓↓ Total Sleep Time (TST)
  - TST is a predictor of manic episodes
  - TST may be a marker of response
## Substance Abuse – Drug Effects on Sleep

<table>
<thead>
<tr>
<th>Medication</th>
<th>Sleep latency</th>
<th>N1</th>
<th>N2</th>
<th>N3 (deep)</th>
<th>REM latency</th>
<th>REM</th>
<th>WASO</th>
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</thead>
<tbody>
<tr>
<td>Alcohol</td>
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<td>Barbiturates</td>
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<td>Benzodiazepines</td>
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<td>Stimulants</td>
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<td>Caffeine</td>
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<td>Phase delay in circadian rhythm</td>
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<td>Steroids (Prednisone)</td>
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<td>THC (Acute use)</td>
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<td>THC (Chronic use)</td>
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Treatments - Sleep Hygiene

• Keep a **consistent sleep schedule**. Get up at the same time every day, even on weekends.
• Set a bedtime that is early enough for you to get **at least 7 hours** of sleep.
• Establish a relaxing **bedtime routine**.
• If you don’t fall asleep after **20 minutes**, get out of bed.
• Use your bedroom only for **sleep and sex**.
• Make your bedroom **quiet, dark and relaxing**. Keep the room at a comfortable, cool temperature.
• Limit exposure to **bright light** in the evenings. (Blue light filters)
• Turn off **electronic devices** at least 30 minutes before bedtime.
• Don’t eat a large meal before bedtime. If you are hungry at night, eat a light, healthy snack.
• Exercise regularly and maintain a healthy diet.
• Avoid consuming **caffeine** in the afternoon or evening.
• Avoid consuming **alcohol** before bedtime.
• Reduce your **fluid intake** before bedtime.

modified from [http://www.sleepeducation.org/essentials-in-sleep/healthy-sleep-habits](http://www.sleepeducation.org/essentials-in-sleep/healthy-sleep-habits)
Visible Spectrum – Light
What color temperature is right for me?

Understanding Kelvin temperature (K) makes it easier to choose lighting that gives you the look and feel you want.

<table>
<thead>
<tr>
<th>Color Temperature (Kelvin)</th>
<th>2000K - 3000K</th>
<th>3100K - 4500K</th>
<th>4600K - 6500K</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Appearance</td>
<td>Warm White</td>
<td>Cool White</td>
<td>Daylight</td>
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<tr>
<td>Ambience</td>
<td>Cozy, calm, inviting, intimate</td>
<td>Bright, vibrant</td>
<td>Crisp, invigorating</td>
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</tbody>
</table>
Treatments – CBT for Insomnia (CBT-i)

• 6 sessions, once per week.
• Keep a sleep journal
• Focus on:
  • sleep hygiene
  • stimulus control
  • sleep restriction
  • cognitive restructuring
• Interdepartmental Referral
• **CBT-i Coach** – VA mobile app [https://mobile.va.gov/app/cbt-i-coach](https://mobile.va.gov/app/cbt-i-coach)

[https://www ptsd va gov/professional/co occurring/sleep problems veterans ptsd asp](https://www.ptsd.va.gov/professional/co-occurring/sleep_problems_veterans_ptsd.asp)
## Medication Effects

<table>
<thead>
<tr>
<th>Medication</th>
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<th>N1</th>
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<th>N3</th>
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<tr>
<td>Barbituates</td>
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<td>Benzodiazepines</td>
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<td>GABA&lt;sub&gt;A&lt;/sub&gt; agonists</td>
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<td>Pregabalin</td>
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<td>Phenobarbital</td>
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<td>Phenytoin</td>
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<td>Carbamazepine</td>
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- **Phase delay in circadian rhythm**
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<tr>
<td>Diphenhydramine</td>
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<td>Melatonin</td>
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<td>Phase advance in circadian rhythm</td>
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<td>Ramelteon (melatonin-RS)</td>
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<td>Suvorexant (orexin-RA)</td>
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<td>SSRIs</td>
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<td>Tertiary TCAs (doxepin, amitriptyline)</td>
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<td>Mirtazapine</td>
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<td>Atypical Antipsychotics</td>
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<tbody>
<tr>
<td><strong>β-blockers (lipophilic)</strong></td>
<td>reduce melatonin production</td>
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<td>Prazosin (α₁-antagonists)</td>
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<td>Clonidine (α₂-agonists)</td>
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</table>

**General rules:**
- Any medication that gets in to the brain will effect sleep.
- Anticholinergic effects (cumulative effect) will reduce Sleep latency, REM, and next day cognitive performance.
- Benzodiazepines, like alcohol, block Stage 3 (deep sleep)
Reference

• Taheri S, Lin L, Austin D, Young T, Mignot E (December 2004). "Short sleep duration is associated with reduced leptin, elevated ghrelin, and increased body mass index". PLOS Medicine. 1 (3): e62. doi:10.1371/journal.pmed.0010062. PMC 535701. PMID 15602591.


• PTSD: National Center for PTSD, Sleep Problems in Veterans with PTSD; https://www.ptsd.va.gov/professional/co-occurring/sleep_problems_veterans_ptsd.asp


