Things To Keep In Mind

- Many drugs effect sleep either causing insomnia or sedation
- Disruption of sleep and wakefulness may not be as important as therapeutic gain from medicine
- Drug that theoretically disrupts sleep may in fact improve sleep quality in a sick patient
Prototypical Drugs Affecting Sleep

- Psychiatric medications!!
Neurotransmitters

- **Dopamine**
  - ↔ in wakefulness, NREM, REM
  - DA promotes wakefulness

- **Serotonin (5-HT)**
  - ↑ in wakefulness; ↓ in NREM; ↓↓ in REM

- **Norepinephrine**
  - ↑ in wakefulness; ↓ in NREM; ↓↓ in REM

- **Histamine**
  - ↑ in wakefulness; ↓ in NREM; ↓↓ in REM

- **Acetylcholine**
  - ↑↑ in REM; ↑ in wakefulness; ↓ in NREM
Monoamine Oxidase Inhibitors

- Inhibit MAO which metabolize 5-HT, NE, DA

- Subjective sxs:
  - insomnia; sedation

- PSG
  - Decreased TST
  - Marked REM suppress
Selective Serotonin Reuptake Inhibitors

- **Symptoms**
  - Insomnia: fluoxetine
  - Sedation: paroxetine, fluvoxamine

- **PSG**
  - Suppress REM
  - Increase WASO
  - Decrease TST
  - Increase PLMS
  - Excessive eye movements
  - REM without atonia
Venlafaxine

- Selective Serotonin and NE reuptake inhibitor
  - Inhibits reuptake of both 5-HT and NE

- Symptoms
  - Insomnia: 4-18%
  - Somnolence: 12-31%

- PSG
  - Increased waking
  - Increases Stage 1
  - Decrease REM
  - PLMS
  - REM without atonia
Trazadone & Nefazadone

- 5-HT Antagonist and reuptake inhibitor

- Trazadone
  - ↓ Sleep latency
  - ↑ Sleep efficiency
  - ↑ SWS
  - ↔ REM

- Nefazadone
  - ↔ Sleep latency
  - ↑ Sleep efficiency
  - ↔ SWS
  - ↔ REM

- Both sedating: traz>>nefa
Buproprion

- NE and DA reuptake inhibitor
- Symptoms
  - Insomnia
- PSG
  - ↔ Sleep latency
  - ↓ REM latency
  - Little effect on PLMS
  - ↔ TST
  - ↑ REM
Mirtazapine

- NE and specific 5-HT antagonist
- Also acts on histamine
- Very sedating
Tricyclic Antidepressants

- **Tertiary amines**
  - 5-HT and NE reuptake; blk M1, H1, alpha1
  - amitriptyline, imipramine, trimipramine, doxepin, clomipramine
    - More sedation than secondary
    - ↓ SL, ↑ SWS, ↓ REM; REM w/o atonia

- **Secondary amines**
  - NE>5-HT reuptake
  - nortriptyline, desipramine, protriptyline, and amoxapine
Lithium

- Mechanism unknown
- In bipolar patients, associated with improved sleep but daytime sleepiness
Antipsychotics

- Not dirty dancing
- Dirty drugs
Traditional

- **Chlorpromazine**
  - Blks D2, 5-HT2, alpha1, H1, cholinergic

- **Thioridazine**
  - Blks D2, 5-HT2, alpha1, H1, cholinergic, D1

- **Haloperidol**
  - Blks D2, 5-HT2 and alpha1

- **All sedating:**
  - chlorpromazine > thioridazine > haloperidol
Atypicals

- **Clozapine**
  - D2, D1, 5-HT2, alpha1, H1, M1

- **Quetiapine**
  - D2, 5-HT2, alpha1, H1

- **Ziprasidone**
  - D2, D1, 5-HT2, alpha1

- **Olanzapine**
  - D2, D1, 5-HT2, alpha1, H1, M1

- **Risperidone**
  - D2, 5-HT2, alpha1

- **All sedating:** clozapine and olanzapine >> quetiapine > risperidone and ziprasidone
Benzodiazepines

- GABA_\textsubscript{A} agonists
  - Short acting: half life less than 12 hrs
    - Triazolam, temazepam, midazolam, alprazolam
    - Few residual effects if taken before bedtime
    - Rebound insomnia common; withdrawal
  - Intermediate acting: 12-24 hrs
    - Lorazepam, estazolam
    - Morning sedation
  - Long acting: > 24 hrs
    - Clonazepam, diazepam, chlordiazepoxide
    - Daytime sedation b/c accumulation with repeated dosing
Other classes of drugs

- Cardiovascular medicines
Beta-Blockers

- Effects on sleep
  - Insomnia, sleepiness, nightmares
  - Related to degree cross BBB (lipophilicity)
    - Propranolol > pindolol > metoprolol > carvedilol > atenolol
  - Degree of blockade of 5-HT receptors
    - Propranolol, pindolol, carvedilol

- PSG
  - Decrease sleep efficiency; ↓ REM
Clonidine

- Alpha2 agonist on presynaptic receptors
  - Autoinhibition of catecholamine release

- Symptoms
  - Sedation

- PSG
  - Increase sleep efficiency
  - Incr SWS
  - Decr REM
Prazoson, terazosin

- Alpha1 antagonists
  - Remember used to treat prostatic hypertrophy

- Symptoms
  - Can cause transient sedation

- Treatment
  - Used to treat nightmares in PTSD
Little sleep effects

- ACE inhibitors
- Calcium channel blockers
Statins

- Disrupt sleep quality subjectively; insomnia
- Related to lipophilicity
  - Lovastatin
  - Simvastatin
Parkinson’s drugs

- Levodopa
  - Disrupt sleep at higher and evening doses
  - Nightmares

- Selegiline
  - MAOI

- Ropinorole, pramipexole
  - Insomnia; daytime sedation
  - Sleep attacks
  - Nightmares