

Open Line
with
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- Introduction - Insomnia
- Bible Verses
 - Psalms 4:8 – I will both lay me down in peace, and sleep: for thou, Lord, only makest me dwell in safety.
 - Psalms 127:2 – It is vain for you to rise up early, to sit up late, to eat the bread of sorrows: for so he giveth his beloved sleep.
 - Proverbs 3:24 – When thou liest down, thou shalt not be afraid: yea, thou shalt lie down, and thy sleep shall be sweet.
- Sleep
 - Sleep is the recurring rest for the body during which there is little conscious thought. Sleep consists of REM (rapid eye movement or dream) sleep and NREM (non-rapid eye movement) sleep. In depression one often has more early morning awakening (EMA); whereas in anxiety there is more difficulty falling asleep (DFA). However, since depression and anxiety often coexist, both EMA and DFA may be present in depressed individuals. Also, depressed individuals often have a shortened REM latency and begin to dream more quickly.
- Sleep hygiene
 - Sleep hygiene includes:
 - regular sleep schedule
 - exercise in late afternoon but not at night
 - removal from bedroom of lights, noise, cold, pets
 - avoid alcohol, caffeine, smoking, daytime naps, staying in bed awake, large meals
- Insomnia, mental disorders, neurochemistry, and neurocircuitry
 - depression
 - ↑ REM with ↓ REM latency
 - ↓ stage 3 and 4 (delta)
 - ↓ 5HT
 - PTSD
 - ↑ REM with ↓ REM latency, ↑ nightmares
 - ↓ stage 3 and 4 (delta)
 - ↑ locus coeruleus → ↑ NE
 - panic disorder
 - ↑ hyperarousal
 - schizophrenia
 - ↓ melatonin → phase advance sleep syndrome such that one is sleepy in early evening and awakes in early morning
 - ↓ REM
 - ↓ total sleep time

- ↓ stages 2, 3, and 4 (less stage 4 with ↑ negative symptoms)
 - ↑ restless sleep
 - ↑ stage 2 latency
 - ↑ insomnia precedes relapse
 - ↑ D
- dementia
 - ↑ restless sleep
 - ↑ HPA axis hyperactivity
 - ↑ cortisol at night
- Parkinson's disease
 - narcolepsy-like symptoms with nocturia, pain, nightmares, hallucinations, sleep talking, hypersexuality, REM disturbance
 - ↓ total sleep time
 - ↑ restless sleep
- obstructive sleep apnea and metabolic syndrome
 - activation of HPA axis
 - ↑ leptin → ↑ appetite
- Insomnia is the inability to sleep. Many drugs have been tried for insomnia:
 - chloral hydrate in the 1860's
 - bromides in the 1870's
 - paraldehyde in the 1880's
 - barbiturates in the 1930's
 - benzodiazepines in the 1960's and beyond (Dalmane, Restoril, Halcion, ProSom, Doral)
 - zolpidem (Ambien), zaleplon (Sonata), and eszopicolone (Lunesta) in the 1990's
 - ramelteon (Rozerum) in 2005
 - zolpidem extended release (Ambien CR) in 2006 with 7.5 mg released immediately and 5 mg released in two hours
 - ropinirole (Requip) in 2006 and pramipexole (Mirapex) a little later for RLS
 - Circadin, a synthetic melatonin analog approved in Europe 2007
 - Vanda, a beta analog of melatonin is being tested
 - tigabine (Gabitril) is being tested
 - antihistamines, such as diphenhydramine (Benedryl) and doxylamine (Unisom), are sometimes not great sleeping pills since they often lose their effect in seven to ten days; they are used off-label
 - Tylenol PM with diphenhydramine plus acetaminophen is popular as a sleep aide
 - Desyrel (trazadone), Elavil (amitriptyline), Sinequan (doxepin), and Remeron (mirtazepine) have been used off-label for insomnia
 - alcohol, perhaps the number one sleeping agent tried, is a terrible sleeping agent since it disturbs sleep
- DSMIV R has organized the etiologies of insomnia into five categories:
 - primary insomnia
 - sleep apnea

- RLS (restless leg syndrome)
 - PLMD (periodic limb movement disorder)
 - insomnia related to another mental disorder
 - MDD (major depressive disorder)
 - bipolar disorder
 - anxiety disorders
 - schizophrenia
 - insomnia related to a general medical condition
 - Alzheimer's disease
 - back pain
 - cancer
 - cardiac disease
 - diabetes mellitus
 - renal disease
 - GI disease
 - GERD
 - HIV
 - menopause
 - nocturia
 - pain
 - Parkinson's disease
 - pulmonary disease
 - thyroid disease
 - insomnia—substance induced
 - albuterol
 - alcohol
 - antidepressants
 - beta blockers
 - caffeine
 - diuretics
 - levodopa
 - oral contraceptives
 - steroids
 - theophylline
 - thyroxine
 - other categories of insomnia
 - circadian rhythm disturbance
 - transient/adjustment insomnia—identifiable stressor
- Insomnia and diphenhydramine
 - Diphenhydramine (Benadryl, Tylenol PM) is often used OTC for insomnia. At 50 mg it improves sleep in 70%; at greater than 50 mg anticholinergic delirium increases (especially in the elderly). Incidentally, Unisom OTC is doxylamine not diphenhydramine.
- Insomnia: pharmacologic treatments
 - Pharmacologic treatments of insomnia include:

- GABA alpha-1 subunit drugs with hypnotic effect
 - eszopiclone (Lunesta)
 - zolpidem (Ambien)
 - zaleplon (Sonata)
 - Incidentally, alpha-2 subunits as benzodiazepine have anxiolytic effects
 - alpha 2 + alpha 3 + alpha 5 = muscle relaxation and alcohol potentiation
- benzodiazepine with alpha and gamma subunits (Dalmane, Restoril, ProSom, Doral)
 - all have GABA_A effects
 - a GABA_B effect
 - a gamma-2 effect
 - any of four alpha subunits (alpha 1, 2, 3, or 5) effects
- melatonin receptor agonist
 - ramelteon (Rozerum)—MT1 and MT2 receptors
 - melatonin
 - Vanda is a beta analog of melatonin. It is in testing.
- antihistamine drugs
 - trazadone (Desyrel)—antidepressant approved
 - Seroquel (quetiapine)—antipsychotic approved
 - Tylenol PM (acetaminophen-diphenhydramine)
 - doxylamine (Unisom)
 - Levoprome (methotrimeprazine)—antipsychotic with antipain effects
 - hydroxazine (Vistaril)—antipain effects
- barbiturate-like drugs
 - chloral hydrate (Somnote)
- other possible GABA acting drugs with antipain effects
 - gabapentin (Neurontin)
 - pregabalin (Lyrica)
- Conclusion
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