Biological Rhythms, Sleep, Dreaming (Ch.14) II

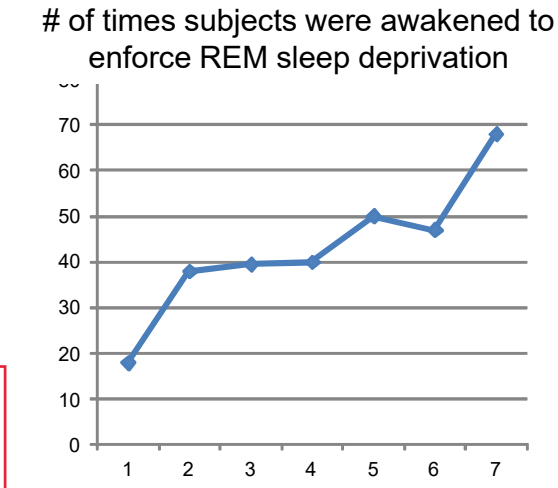
- How much sleep do we need?
- Neural Circuits Underlying Sleep
  - Arousal, Slow wave and REM sleep centers
- Neurochemistry, Pharmacology of Sleep
  - 5-HT, Acetylcholine, Norepinephrine, GABA
- When good sleeping goes bad
  - Narcolepsy

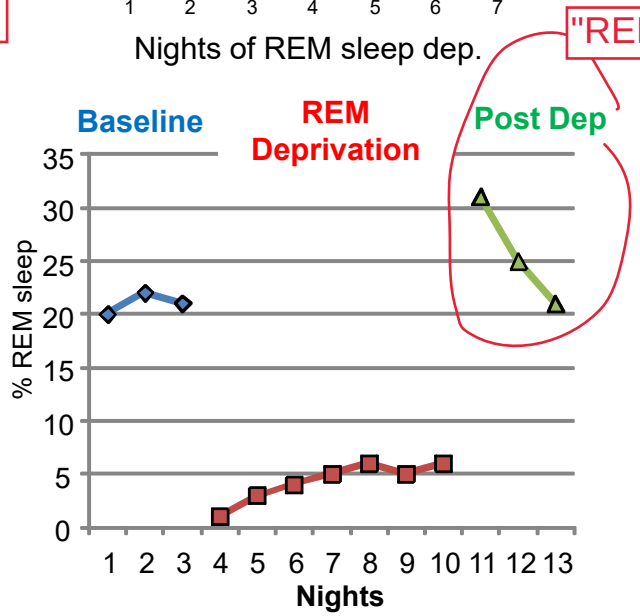
REM-Sleep Deprivation

- Cognitive effects of sleep deprivation seem due to reduced REM sleep
  - Effects can be observed after a few nights of less than normal sleep
  - Waking subjects up from ***only*** REM sleep has similar consequences
  - After repeated REM sleep deprivation, subjects have rebound increases in bouts of REM

Depriving someone of REM sleep has the primary negative effect

- Following sleep deprivation, subjects try to make up sleep loss with more REM sleep
  - After deprivation, sleep time increases for a few days
  - More Stage 3, at the expense of Stage 2
  - REM episodes become more frequent, are longer, and/or more intense, individuals become more "efficient" sleepers

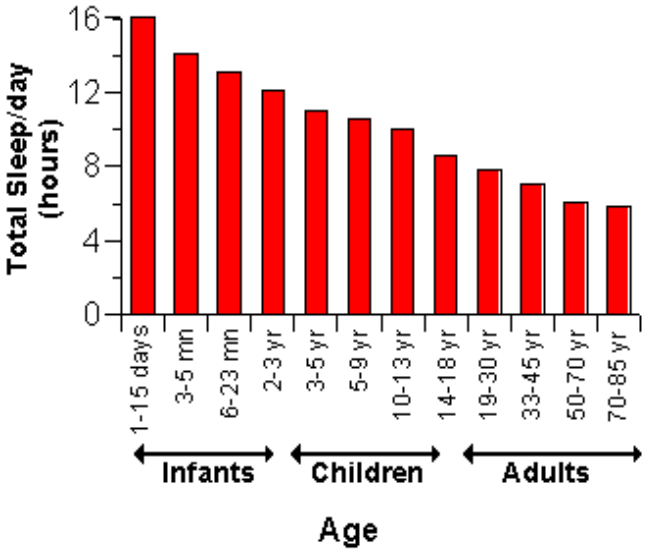




Brain waves enter REM stage more per night after REM deprivation & less stage 2

How much sleep do we really need?

- **Individual differences**: varies among people and with age
  - Older people spend less time in Stage 3
  - Leonardo da Vinci slept for 15 mins every 4 hours and for 1.5 hours a day
- 8 hrs/night may not be right for everyone- one study showed that those averaging 7 hrs/night had the lowest mortality rates (vs longer/shorter periods)
- Reducing sleep time in short-term can have consequences, but if reduction occurs over prolonged period, fewer problems



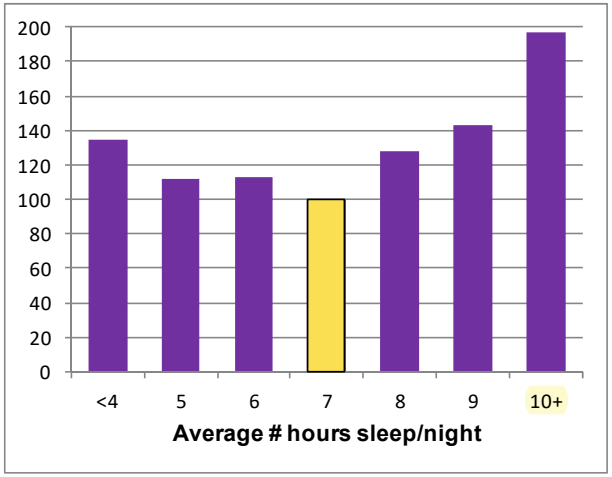
- **Long-term reduction study**: subjects reduced sleep time by 30 min every 2-4 weeks until they were at ~4.5 hrs sleep/night
- No adverse effects: ↑ efficiency of sleep (↓ time to fall asleep and awakenings, ↑ Stage 4 sleep)
- 1 year follow-up showed all were sleeping 2-3 hrs less per night

- Mullaney et al (1977) Sleep during and after gradual sleep reduction. *Psychophysiology* 14, 237-244.
- Stampi (1992) Why we nap: Evolution, chronobiology and functions of polyphasic and ultrashort sleep

How much sleep?

- **Is 8 hours/night sleep the "right" amount?**
- **Study**: track mortality rates of adults (with no other sleep disorders) over 10 years
- Organize data by how much sleep individuals normally got per night
- **Results:** Those who slept either less, or more than **7 hours** tended to have higher mortality rates (bigger effects with 9+ hrs)

Mortality rate (per +100k subjects) as a % of those who slept 7 hrs/night

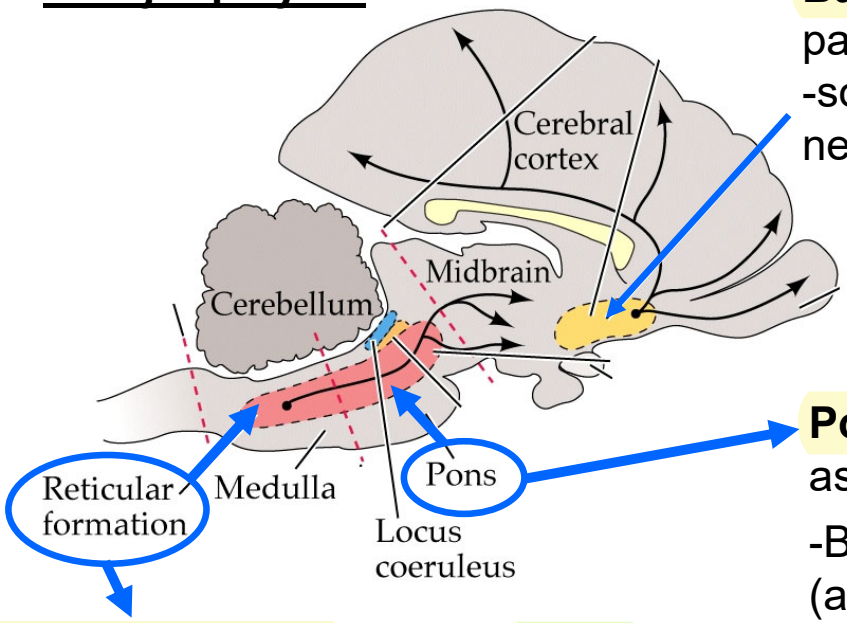


- **Note: Correlational evidence**
- There may be numerous other facts as to why those who sleep more than 9+ hours may die sooner than those sleep less
- However, this shows that getting less than 8 hours/night does not appear to be the risk of life and health as it is often made out to be

Cat studies: Big sleepers!!!

Neural Control of Sleep (I)

4 major players



Basal Forebrain: group of nuclei (including parts of hypothalamus) which regulates SWS
-some neurons in this region use GABA as neurotransmitter

Pons: group of nuclei which regulate different aspects of REM

-Brain activity patterns, shut down of muscles (atonia)

Reticular formation: group of nuclei which regulate waking/ arousal

Raphe nucleus sends serotonin inputs that inhibit reticular formation neurons

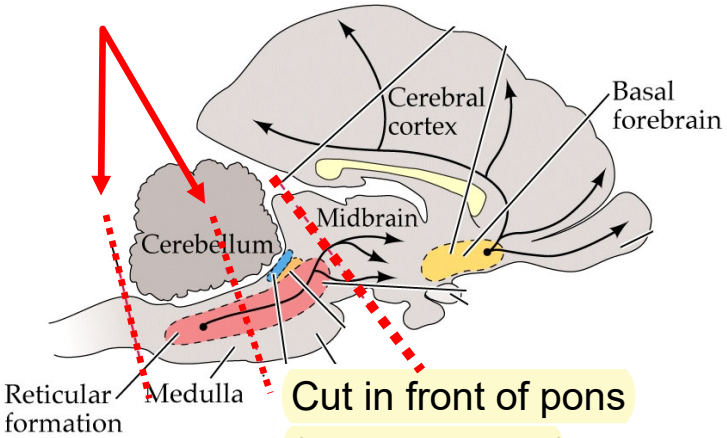
Multiple brain regions interact to control different stages of sleep

Neural Control of Sleep (II)

can't get into REM phase

- Cut spinal cord (***encephale isole***), or right behind pons = **normal SWS and REM sleep**
  - Sleep controlled by brain in front of pons

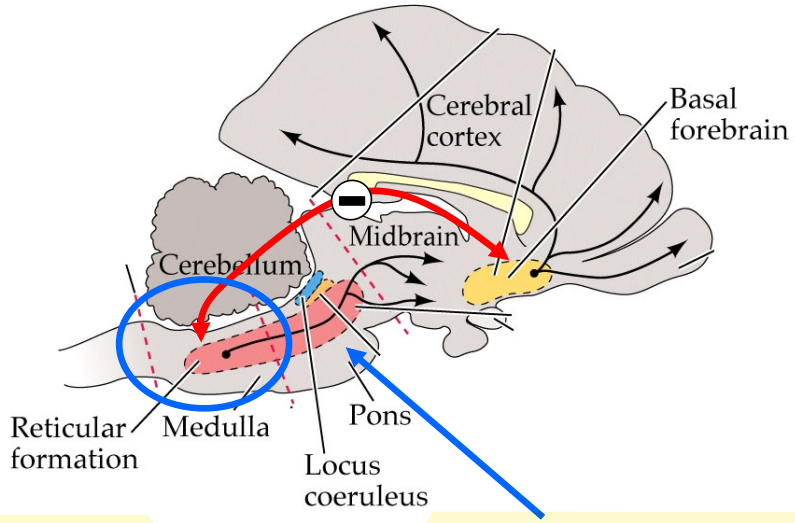
-Lesion basal forebrain= abolish SWS
-Stimulate basal forebrain=induce SWS



-Neurons in the basal forebrain release GABA in the adjacent **tuberomamilliary** nucleus to promote SWS

Cut in front of pons (***cerveau isole***) =
- **CONSTANT SWS**
-NO REM sleep

Neural Control of Sleep (III)



-Lesion reticular formation = **persistent sleep**

-Stimulate reticular formation = **rapid awakening from sleep**

-Sends input to thalamus and is reciprocally connected with basal forebrain

-**Lesion** or *stimulate* region of pons = **Abolish** or *activate* REM sleep

-Some neurons in this region are active ONLY during REM

-Lesion the subcoeruler nucleus (a subregion of the pons) = **Loss of uncoupling of motor systems during sleep**

Sleep walking behavior

PBS video:
- disable the "paralysis" of muscles in REM
- cats: dreaming of running, chasing prey
- humans: dreaming of smoking cigarette

one group of 5-HT neurons helps you go to sleep by *inhibiting wakefulness* part of brain

5-HT and Acetylcholine Systems and Sleep

•Serotonin (5-HT) released by axons originating in raphe nuclei.

•One group of 5-HT neurons project to ***reticular formation*** that can **inhibit activity** (and ↓ wakefulness)

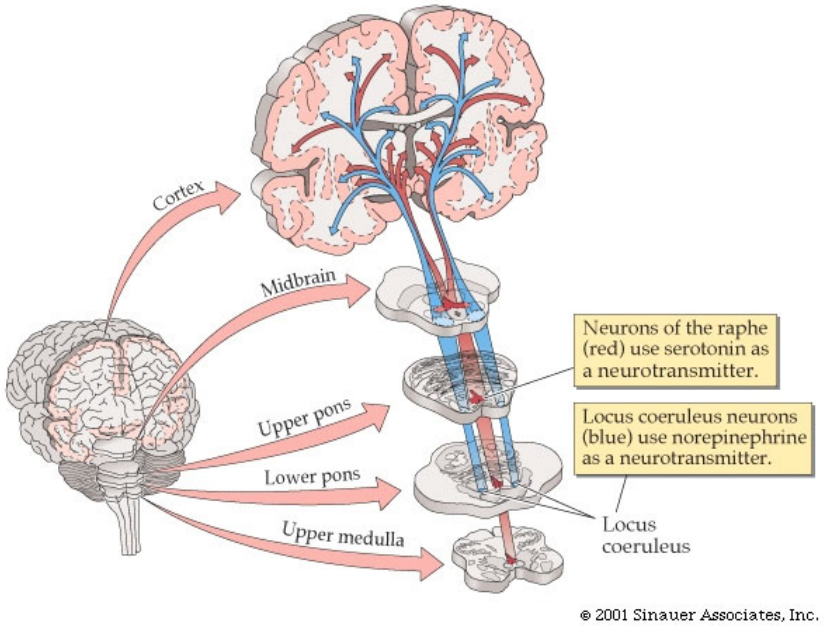
- ➢ Lesions of raphe = insomnia

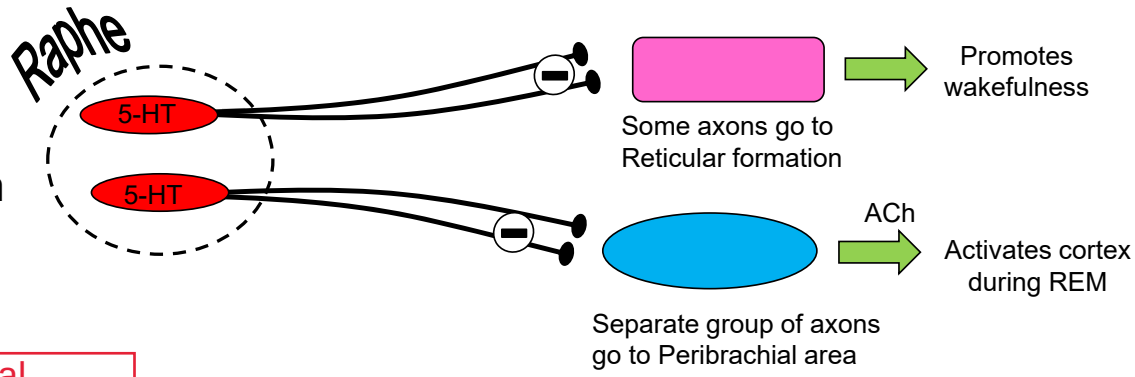
•However, raphe projects to other regions, including centers mediating REM sleep, such as…

back of brain

•**Peribrachial Area**: group of nuclei in pons which mediate REM sleep. Use **acetylcholine** (Ach) as a neurotransmitter

• ***Another group of 5-HT neurons*** from raphe inhibits peribrachial neurons. ↑ 5-HT = **decrease REM sleep**





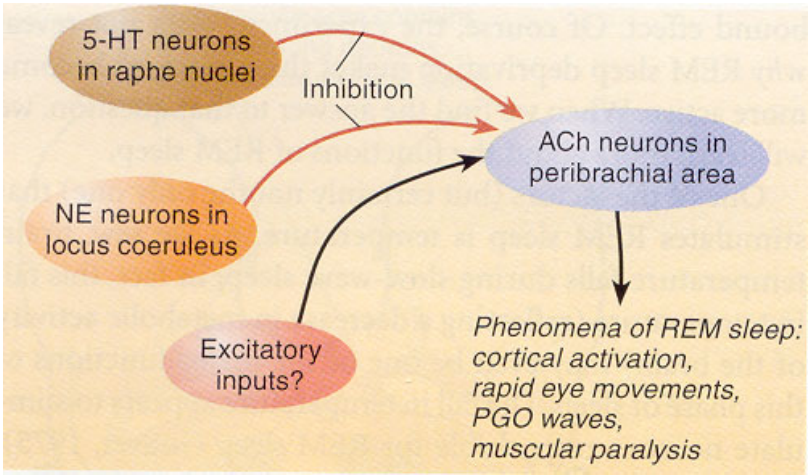
another group of 5-HT inhibits peribrachial neurons to *decrease REM sleep*
completely silent during REM

Norepinephrine (NE) Systems and Sleep

•Neurons from **locus coeruleus** also project to peribrachial area; use NE as transmitter

•NE inhibits neurons that mediate REM sleep

•NE projects widely through brain/cortex; also mediates arousal



•REM sleep episodes occur when neurons in the raphe and locus coeruleus decrease firing, so that peribrachial neurons can increase firing

Raphe and L.C. ↓

Peribrachial neurons ↑

REM occurs

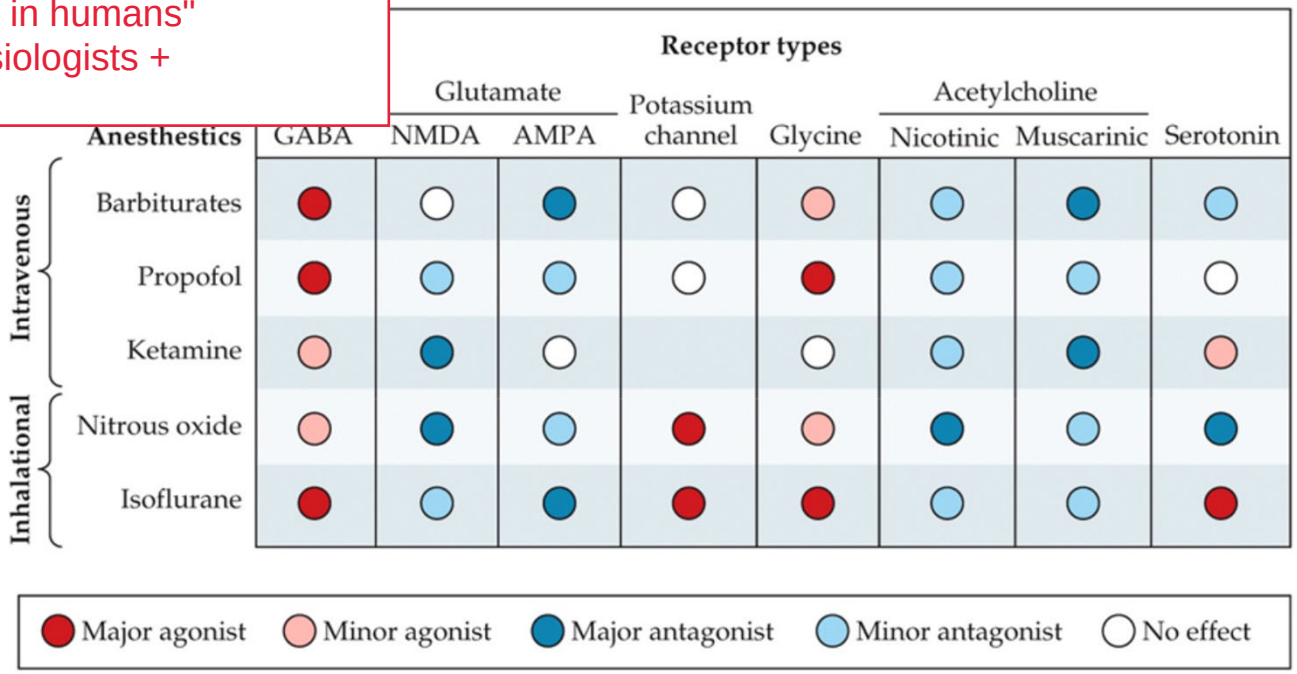
REVIEW GIF!!!!!

Animation of sleep circuits uploaded to CANVAS as a gif file

Pharmacology of Sleep (I)

- **General anesthetics**, that cause unconsciousness, produce slow waves in EEG that resemble SWS.
- Almost all general anesthetics are agonists of GABA-A receptors
  - Supports idea that some brain system uses GABA to promote SWS.

"single most dangerous (group of) drug approved for use in humans"
thank u anesthesiologists + anesthetists!



Don't need to memorize

Pharmacology of Sleep (II)

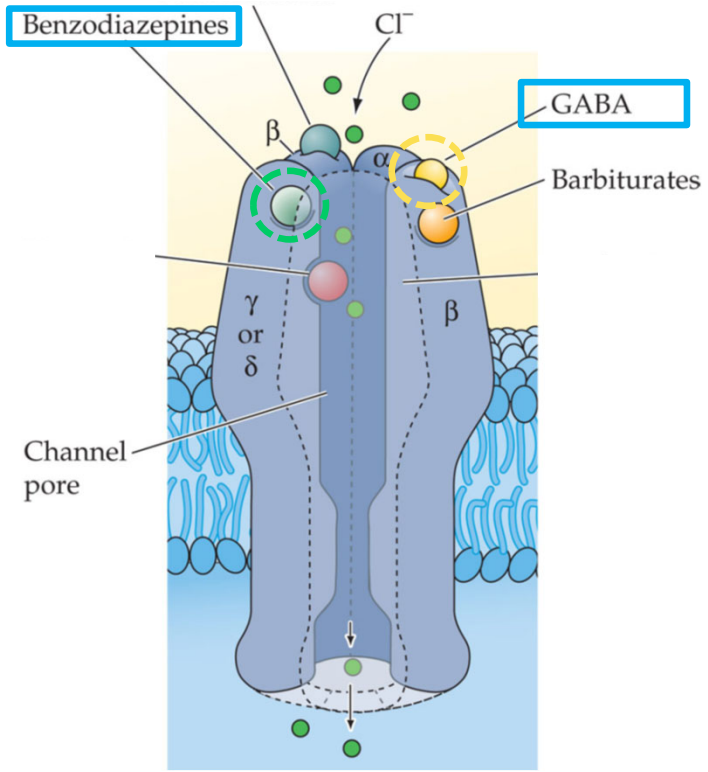
➢ **Hypnotics (sedatives)**

- Benzodiazepines (eg: Valium, Ativan, Ambien) act on GABA transmission
  - Are not direct agonist, but facilitate binding of GABA to the GABA-A receptor
- Causes decrease in cortical activity

- When drug binds to the this site, it increases potency of GABA to open receptor channel, but **does not** open channel if GABA is not also bound
  - I.E: act as positive allosteric modulators

NOT agonist

(from Google) benzodiazepines do *not* stimulate the GABA receptor directly, they simply make GABA receptors more efficient. Benzodiazepines still produce a calming effect but don't have as depressive an effect on the central nervous system as barbiturates



Pharmacology of Sleep (III)

➢ **Problems with benzodiazepine use:**

Suppress REM sleep

- Tolerance and addiction develops
  - » Can lead to insomnia when drugs are discontinued
  - » Distort normal pattern of sleep
  - » ↑Stage 2 sleep, but ↓ REM and Stage 3 sleep;
  - » Hangover effect; REM rebound

spend more time in REM than before (like REM deprivation studies)

- Alcohol works on a similar mechanism: also ↓ REM sleep
  - Alcohol and benzodiazepines can work synergistically to cause death!
- Serotonergic drugs are not effective in treating insomnia
  - However, increasing the brains 5-HT (eg: increased tryptophan) can aid sleeping

Pharmacology of Sleep (IV)

➢ **Antihypnotics (stimulants)**

- Promote release of catecholamines (dopamine, NE)
- ↑ Wakefulness, alertness but almost totally suppress REM, even at doses that do not effect sleep patterns
- Some can be addictive

➢ **Caffeine**

- acts as an antagonist to **adenosine**
- Adenosine is inhibitory transmitter distributed throughout brain (cortex, reticular formation)
- Adenosine accumulates with activity in the brain, decreases during sleep.
- Caffeine (or theophylline from tea) can block adenosine, increase arousal

Narcolepsy

- Sudden intense attacks of sleep
  - Patients go directly from waking state to REM sleep
  - Attacks come on during periods of intense emotion
  - Loss of muscle tone (cataplexy) during attack
  - Regular sleep stages when they choose to go to sleep

- **Causes:** Disruption in neural circuits that mediate REM sleep
  - Gene that encodes for peptide neurotransmitter **hypocretin** (aka: ***orexin***) is involved: humans with narcolepsy lose ~90% of hypocretin neurons
  - Hypocretin projections from hypothalamus coordinate activity in sleep-centers (basal forebrain, reticular formation, locus coeruleus)
- **Treatments:** NE and 5-HT agonists to reduce attacks. Development of orexin-like drugs continues