

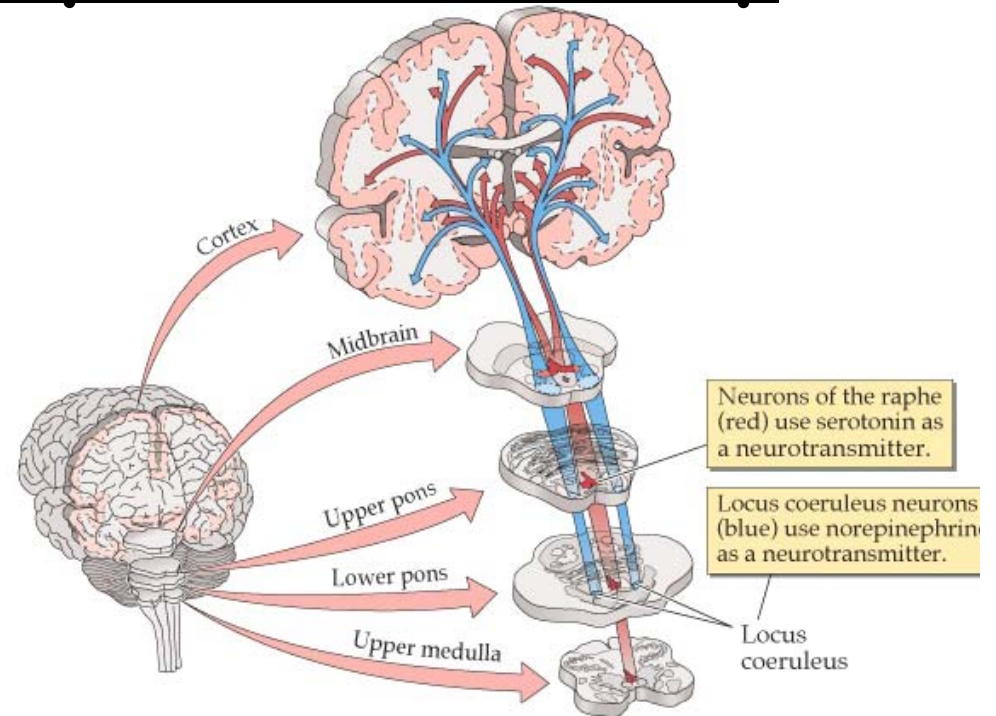
# Biological Rhythms, Sleep, Dreaming (Ch.14) III

- Neural Circuits Underlying Sleep
  - Reticular formation, Pons
  - Serotonin and the Raphe Nucleus
  - Other transmitter systems
- Pharmacology of Sleep
  - Drugs that promote sleep
  - Drugs that interfere with sleep
- When Good Sleeping Goes Bad
  
- MONDAY: there will be a MOVIE!!! ("What are dreams: inside the sleeping brain")
- For next week: Start reading Ch. 15 (from the beginning)



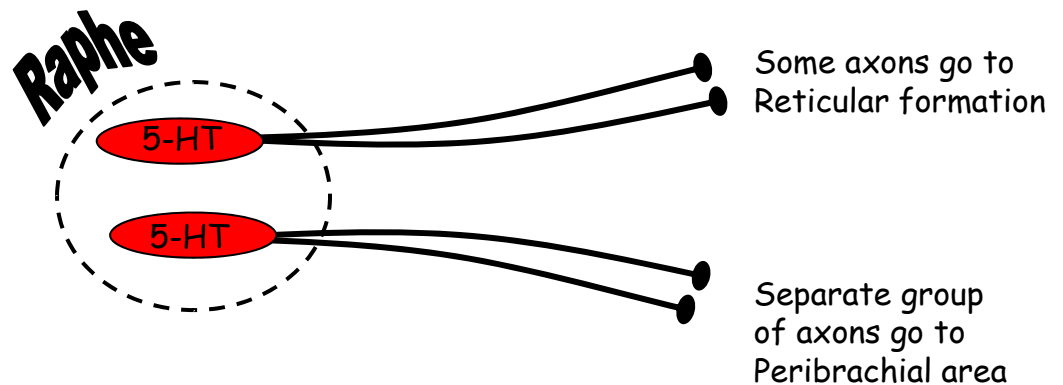
# Serotonin (5-HT) Systems and Sleep

- Serotonin (5-hydroxy-tryptophan) released by cells in raphe nucleus.
- Projections from raphe can inhibit reticular formation (↓ wakefulness)
- Lesions of raphe = insomnia
- However, raphe projects to many other sites throughout brain, including centers which mediate REM sleep



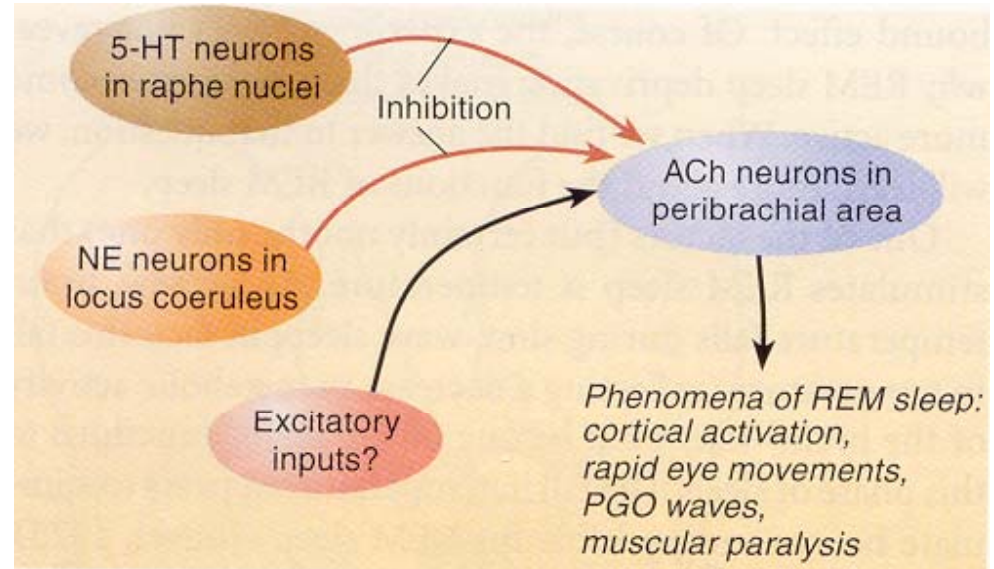
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- **Peribrachial Area:** group of nuclei in pons which mediate REM sleep. Use acetylcholine (ACh) as a neurotransmitter
- 5-HT from raphe inhibits neurons in this region. ↑ 5-HT = **decrease REM sleep**



# 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 the locus coeruleus decrease firing, so that peribrachial neurons can increase firing



	<u>Wakefulness</u>	<u>Activity During</u> <u>SWS</u>	<u>REM</u>
GABA (b. forebrain)	Very Low	High	Low
5-HT (raphe)	High	Low	Very low
NE (l. coeruleus)	High	Low	Very low
Ach (brainstem)	High	Low	High

# Pharmacology of Sleep (I)

- Hypnotics (sedatives)
- Benzodiazepines (eg: Valium, Ativan, Halcion) act on GABA transmission
  - Are not direct agonist, but facilitate binding of GABA to receptor
- Causes decrease in cortical activity
- **Problems:** Tolerance and addiction develops
  - » Can lead to insomnia when taken off drugs
  - » Distort normal pattern of sleep
  - » ↓ REM and Stage 4 sleep; ↑ Stage 2 sleep
  - » Hangover effect; REM rebound
- 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 in sleeping



# Pharmacology of Sleep (II)

- Antihypnotics (stimulants and antidepressants)
- Promote release of catecholamines (dopamine, NE)
- ↑ Wakefulness, alertness but will almost totally suppress REM sleep, even at doses that do not effect sleep patterns
- Highly 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
  - Animal model of narcolepsy (dogs) reveals ↑ Ach in pons
  - Onset of disorder may be related to degeneration in amygdala and basal forebrain
  - Appears have a genetic component as well: gene that encodes for protein neurotransmitter *orexin* may be involved
  - CSF orexin absent in many human narcoleptic patients
- Treatments: NE and 5-HT agonists to reduce attacks. Development of orexin-like drugs continues

