Kathryn

Class 13-Sleep continued

Neural Control of Arousal

-Neural control of arousal: neuromodulators

-ACh from the pons and basal forebrain. Behavioral activity levels correlate with the ACh levels. Desynchronized the EEG. Controls neural excitability. ACh high in REM sleep.

-Norepinephrine from the locus coeruleus: Vigilance, attention. Amphetamines (NE agonists) produce arousal

**Figure 8.10

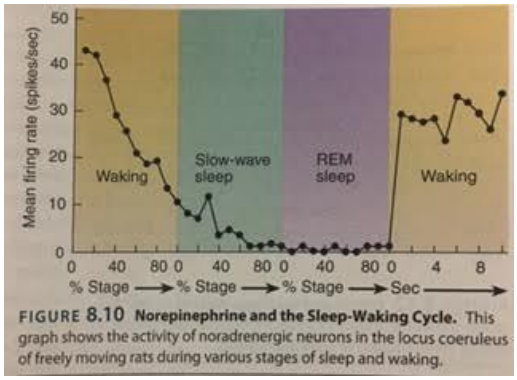


FIGURE 8.10 **Norepinephrine and the Sleep-Waking Cycle.** This graph shows the activity of noradrenergic neurons in the locus coeruleus of freely moving rats during various stages of sleep and waking.

-5HT (Serotonin) from the raphe nuclei (in the Pons). Correlates with sleep stages. Active during the transitions out of REM sleep.

-Histamines (Tuberomammilary nucleus, hypothalamus):

→activate the cortex directly, and indirectly (through basal forebrain ACh). Anti-histamines promote drowsiness

-Orexin (aka Hypocretin, lateral hypothalamus):

→Excitatory projections to cortex and many neuromodulatory centers. Wakefulness promoting. Indirect arousal effects. Narcolepsy when damaged.

**Figure 8.12

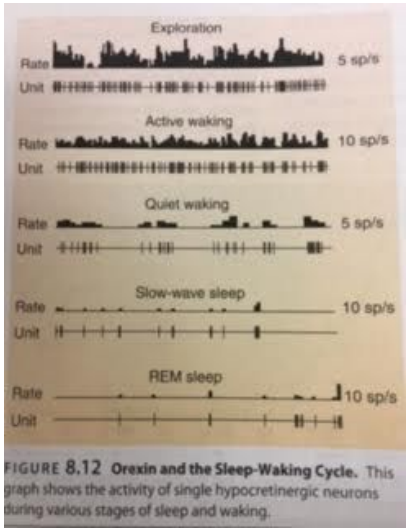


FIGURE 8.12 **Orexin and the Sleep-Waking Cycle.** This graph shows the activity of single hypocretinergic neurons during various stages of sleep and waking.

Neural Control of Sleep

-What makes us go/transition to sleep?

-**Adenosine Hypothesis:** adenosine accumulation during the awake period. Adenosine as a 'sleep promoting substance'

-Awake state: adenosine secreted by astrocytes. Astrocytes providing glycogen (fuel) to neurons if needed. Astrocytes providing neurons with energy

**Glycogen depletion→increase in adenosine→progressive increase in general inhibition→increase in sleep tendency

-Sleep state: Glycogen→Astrocytes

Neural Bases of Sleep: SWS

-Ventrolateral PreOptic Area (vLPOA)

-Destruction→no sleep→death

-Stimulation→drowsiness and delayed sleep

-Mutual inhibition:

→vLPOA sends inhibitory projections to Histamine, NE, 5HT, ACh systems. These systems in turn inhibit the vLPOA

-Flip-Flop circuitry: **Figure 8.13

-If flip-flop is on, meaning the sleep-promoting region in vLPOA is inhibited, you're in alert waking state, if flip-flop is off, you're in slow-wave sleep because the sleep-promoting region in vLPOA is activated

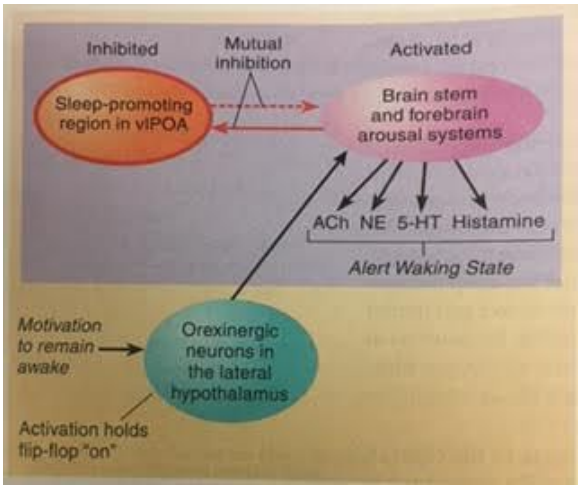
-Can be unstable : narcolepsy, sleep attacks (low arousal state)

-Turning the flip-flop 'ON': Orexin neurons

-Orexin neurons active during awake state and project to the arousal systems

-ON: 'Motivation to remain awake,' 'stimulus driven,' medicated by external signals, Biological clocks, hunger signals…

**Figure 8.14



-Turning the flip-flop 'OFF': The adenosine hypothesis
- -Active state: glucose consumption from blood
- -When blood glucose not sufficient, use glycogen
- -Glycogen→(locally) glucose + adenosine (nucleoside transmitter)
- -Adenosine accumulate in those parts of the brain that were the most active
- -Adenosine is inhibitory→decrease brain stem activity→increase vLPOA→SWS
- -OFF: also related to food consumption:
  - →Satiety signals inhibit orexin neurons

Therapeutic Manipulations of SWS

-Prolonged total sleep deprivation leads to:
- -loss of body weight
- -temperature deregulation
- -(eventually) death

-However: 1 night sleep deprivation (total, or 2nd half of night) has *antidepressant* effect

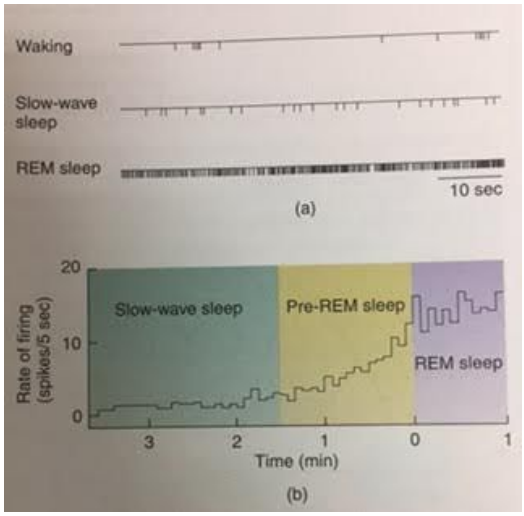
Neural Control of Sleep: REM

-Dreams=windows to the 'Psyche'.
- →65% sad, angry
- →20% happy excitement
- → 1% sexual

-Executive Mechanism ('switch,' 'flip-flop')

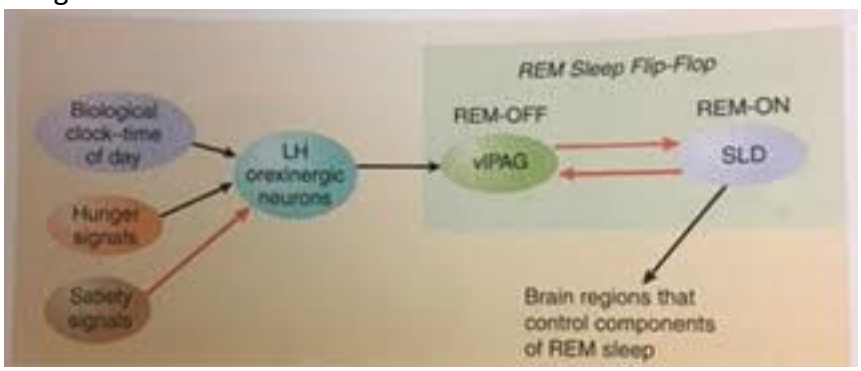
-ACh levels are high during REM (and awake). From Pons

**Figure 8.16



-REM position: likely in the 'fetal' position while asleep
-REM flip-flop
-Mutual inhibition: sublaterodorsal nucleus (SLD) and ventrolateral PAG (vlPAG)
-Orexin neurons also influence the R EM flip-flop. Cataplexy.

**Figure 8.17

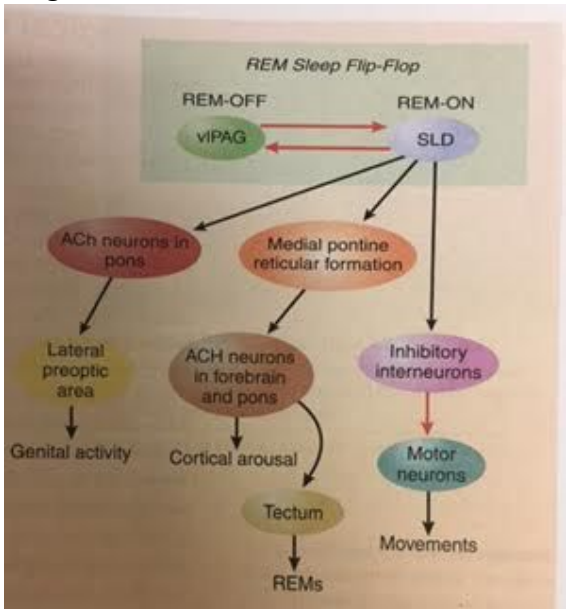


Neural Control of REM Sleep

-SLD projections explain the normal features of REM sleep:
-Cortical Activation: Thalamus (dream content), **M**edial **P**ontine **R**eticular Formation (dream intensity)
-REM: Tectum (superior colliculi)
-Genital activity: Lateral preoptic area (sexual preparedness?)
-Atonia: medulla, prevents the 'acting out' of dreams

-Lesion of ‘paralysis neurons’ (in medulla) yield REM without atonia

**Figure 8.20

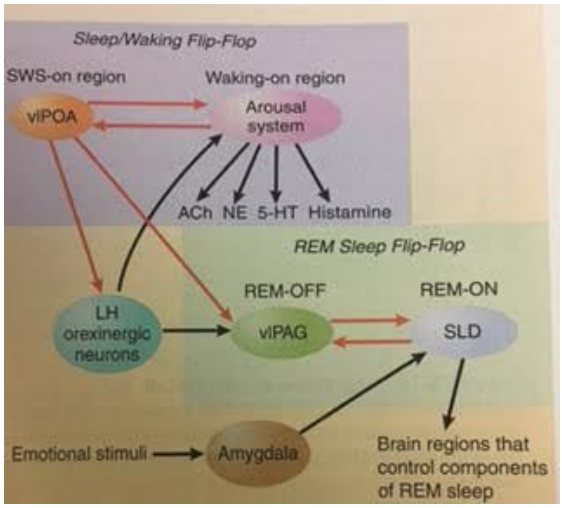


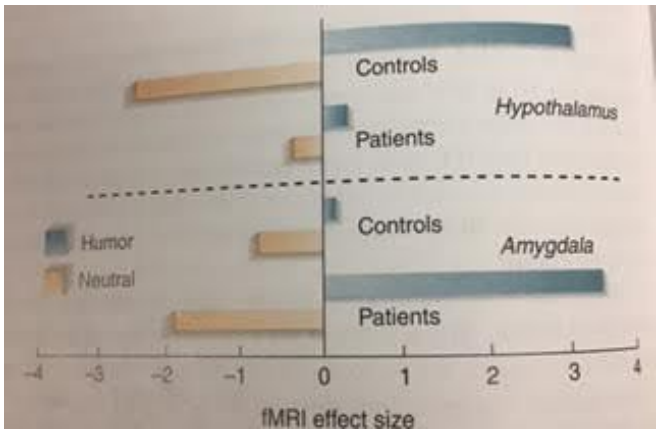
Neural Control of Sleep

-When Orexin neurons are damaged: Emotional stimuli take over (cataplexy). Amygdala and hypothalamus

-i.e. guy who was playing the ‘slap the hand’ game and falls asleep from high arousal

**Figure 8.18 and 8.19

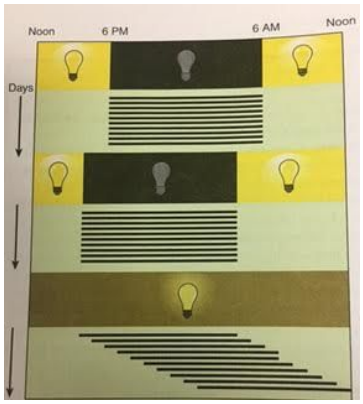




Biological Rhythms

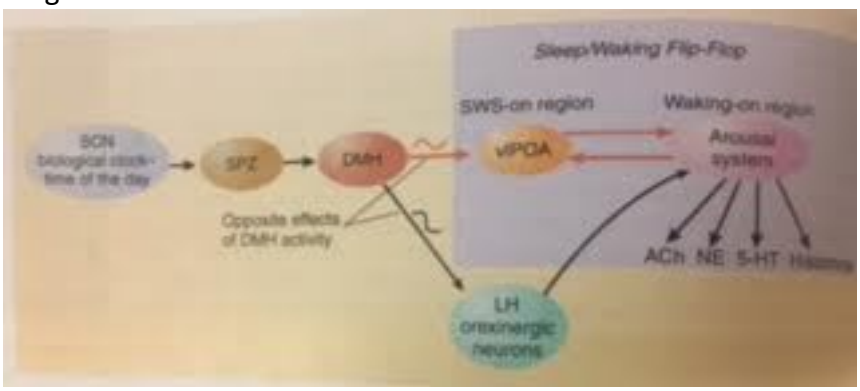
- -Internal clocks
  - -InfraDian (less than 1 day)
  - -Circadian (one day): Sleep/wake cycle. ~25 hours free running
  - -SupraDian (more than one day): menstrual cycle
  - -Circannual (one year): hibernation
- -SupraChiasmatic Nucleus: Circadian/Supradian
  - -Time scale: day→month
  - -Small (8,600 cells), within the Hypothalamus
  - -Reset by light (retino-hypothalamic tract). Melanopsin in 'special' retinal ganglion cells projecting to SCN. Light is a 'zeitgeber' ('giver of time')
  - -Intrinsic and network rhythmic phenomena: SCN neurons by themselves, or as a group in a dish, have a circadian rhythm
  - -Transplantation studies indicate the SCN uses chemical non-synaptic connection to affect its targets

**Figure 8.21



-SCN sends inputs to the SWS flip-flop. Inhibits vlPOA (decrease drowsiness), excite Orexin neurons (promote wakefulness)

**Figure 8.24



-SCN ticking=slow production of a self-inhibiting protein

-'Normal' sleep onset: 10-11 pm. Average length 8 hours

-Advanced sleep phase syndrome sleep onset 6-7 pm, wakeup 3-4 am. Genetic mutation

-Delayed sleep phase syndrome: Sleep onset 2-3 am, wakeup 10-11 am. Genetic mutation

→Normal genetic variations may explain 'normal' variations in sleep onset time and sleep duration

**Figure 8.26

Circadian Rhythms

-Pineal Gland: Circadian/Circannual

-In midbrain (near cerebellum).

→Secretes Melatonin (during night)

-Melatonin has slow (cumulative) actions in the periphery (sympathetic system): Seasonal time keeper in most animals (humans?)
-Melatonin: highest levels just before bedtime
-Melatonin helps jet-lag (take before adjusted bed-time).
    -Side effects: Depression, low sex drive, weight loss
-Melatonin helps blind people to sleep better