Sleep

**Neural Control of Arousal: 8.10, 8.11, 8.12**

Neural Control of Arousal: Neuromodulators
- ACh from the pons & basal forebrain, behavioral activity levels correlate with ACh levels, desynchronize the EEG, controls the neural excitability, ACh high in REM sleep
- NE from the locus coruleus: vigilance, attention, amphetamines, (NE agonist) produce arousal
- 5HT from the raphe nuclei (in the pons), correlates with sleep stages, active during the transitions out of REM sleep
- Histamines (tuberomammillary nucleus, hypothalamus): activates the cortex directly and indirectly (through basal forebrain ACh), anti-histamines promote drowsiness
- Orexin (hypocretin, from lateral hypothalamus): excitatory projections to cortex and many neuromodulatory centers, wakefulness promoting, indirect arousal effects, narcolepsy when damaged

**Neural Control of Sleep**

Central question: What makes us go/transition to sleep?
- Adenosine hypothesis: adenosine accumulation during the awake period, adenosine as a sleep promoting substance

Glycogen depletion > increase in adenosine > progressive increase in general inhibition > increase in sleep tendency

Sleep state: restorative process
Glycogen > astrocytes

**Neural Bases of Sleep: SWS: 8.13, 8.14, 8.15**

Ventrolateral Pre-Optic 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
Can be unstable: narcolepsy, sleep attacks (low arousal state)
Turning the Flip-Flop ON: orexin neurons:
  Orexin neurons are active during awake state and project to the arousal system
  ON: motivation to remain awake, stimulus driven, mediated by external signals:
  biological clocks, hunger signals

Turning the Flip-Flop OFF: the adenosine hypothesis
  - Active state: glucose consumption from blood
  - When blood glucose not sufficient, use glycogen (ch. 11)
  - 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 (ch. 11)

**Therapeutic Manipulations of SWS?**
Prolonged total sleep deprivation leads to loss of body weight, temperature deregulation and (eventually) death
  However: 1-night sleep deprivation (total, or 2nd half of the night) has antidepressant effect

**Neural control of sleep: REM: 8.16, 8.17**
Dreams: window to the psyche, 65%: sad/angry, 20%: happy
Executive mechanism (‘switch’, ‘flip-flop’)
- ACh levels are high during REM (and awake) from pons

REM Flip-Flop
Mutual inhibition: sublaterodorsal nucleus (SLD) and venrolateral PAG (vPAG)
- Orexin neurons also influence the REM flip-flop, cataplexy

**Neural control of REM Sleep: 8.20**
SDL projections explain the normal features of REM sleep
- Cortical activation: thalamus (dream content), medial pontine reticular formation (dream intensity)
- REM: tectum (superior colliculi)
- Genital activity: lateral Pre Optic are (sexual preparedness)
- Lesion of paralysis neurons (in medulla) yield REM without atonia

**Neural control of sleep: 8.18, 8.19**
Putting it all together
- When orexin neurons are damaged: emotional stimuli take over (cataplexy), amygdala and hypothalamus

**Biological rhythms: 8.21, 8.24, 8.26**
Internal clocks
- InfraDiem (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 (8600 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

SCN sends inputs to the SWS flip-flop, inhibits vLPOA (decreases drowsiness), excite orexin neurons (promote wakefulness)

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, wake up 3-4 am, genetic mutation
- Delayed sleep phases syndrome: sleep onset 2-3 am, wake up 10-11 am, genetic mutation

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

**Circadian Rhythms**

Pineal gland: CircaDian/Cirannual

- 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 with jet-lag (take before adjusted bed-time), side effects: depression, low sex drive, weight loss
- Melatonin helps blind people to sleep better

https://language101.com/learn-any-language/jet-lag/