Chap. 7. Sleep

Arousal

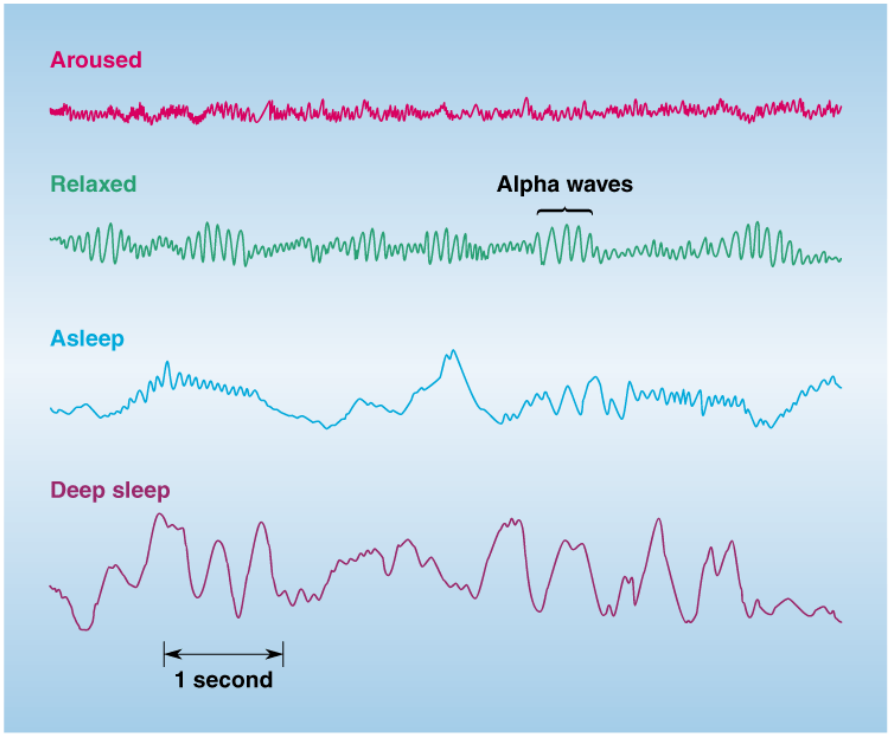
Constant dialogue with the outside world
Different levels of arousal
    sleep, arousal, and higher arousal
Measuring arousal states
    1875 Richard Caton: electrical activity in the animal brains
    1929 Hans Berger: electrical current in the human brain

Electroencephalography

<u>electrical potentials amplified from scalp</u>
-high temporal resolution
-low spatial resolution
-cortical tissue only

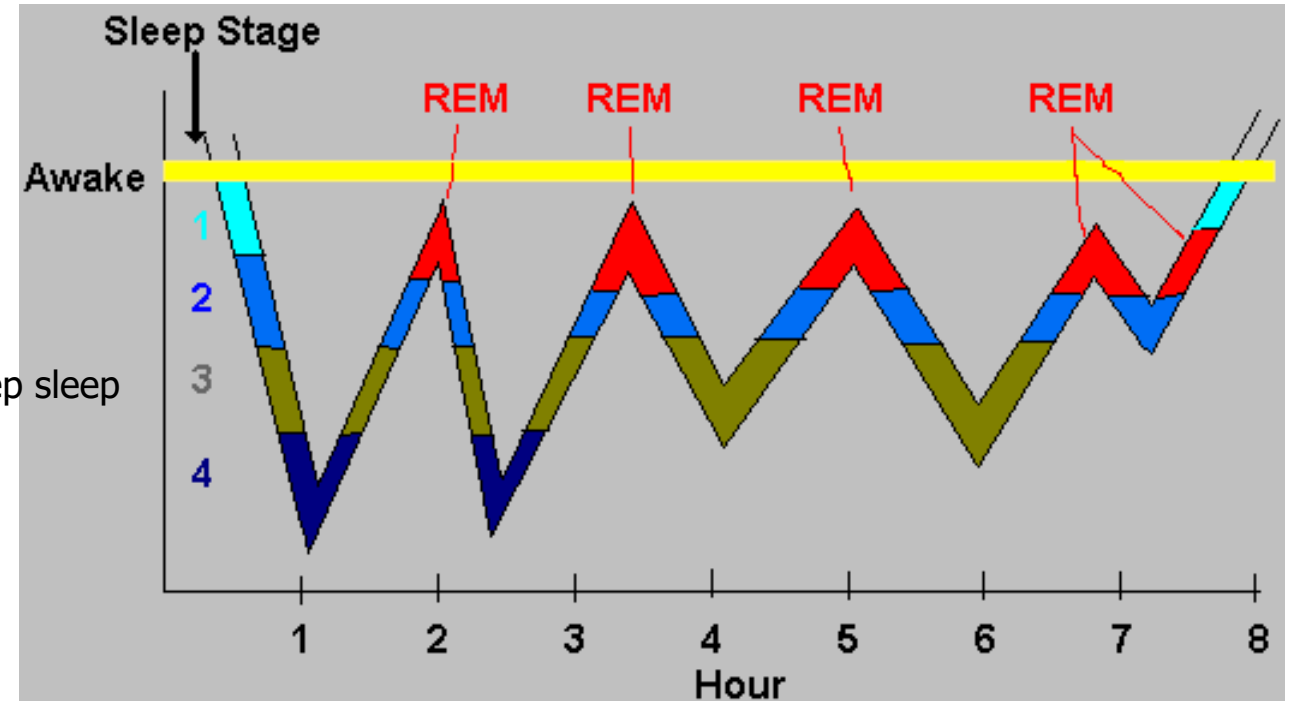
Electroencephalograghy (EEG) recording

► Typical EEGs



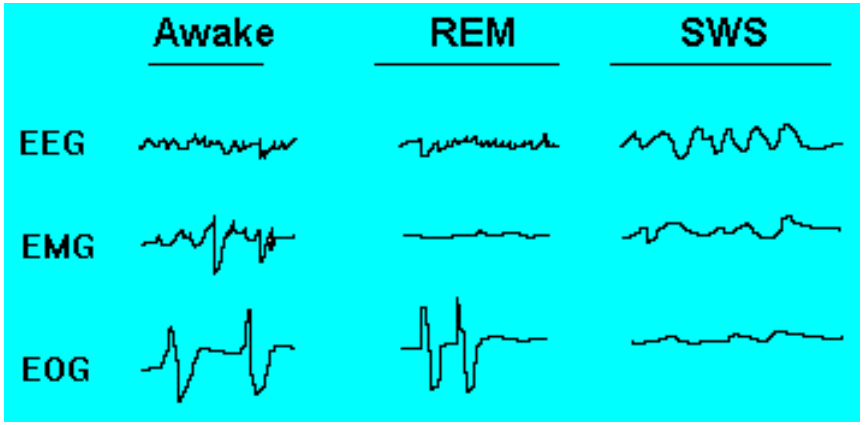
Sleep

Rapid eye movement (REM)
Slow wave sleep (SWS) Deep sleep



http://www.univ.trieste.it/~brain/NeuroBiol/Neuroscienze%20per%20tutti/sleep.html

Electroencephalograpy
Electromyography
Electrooculography

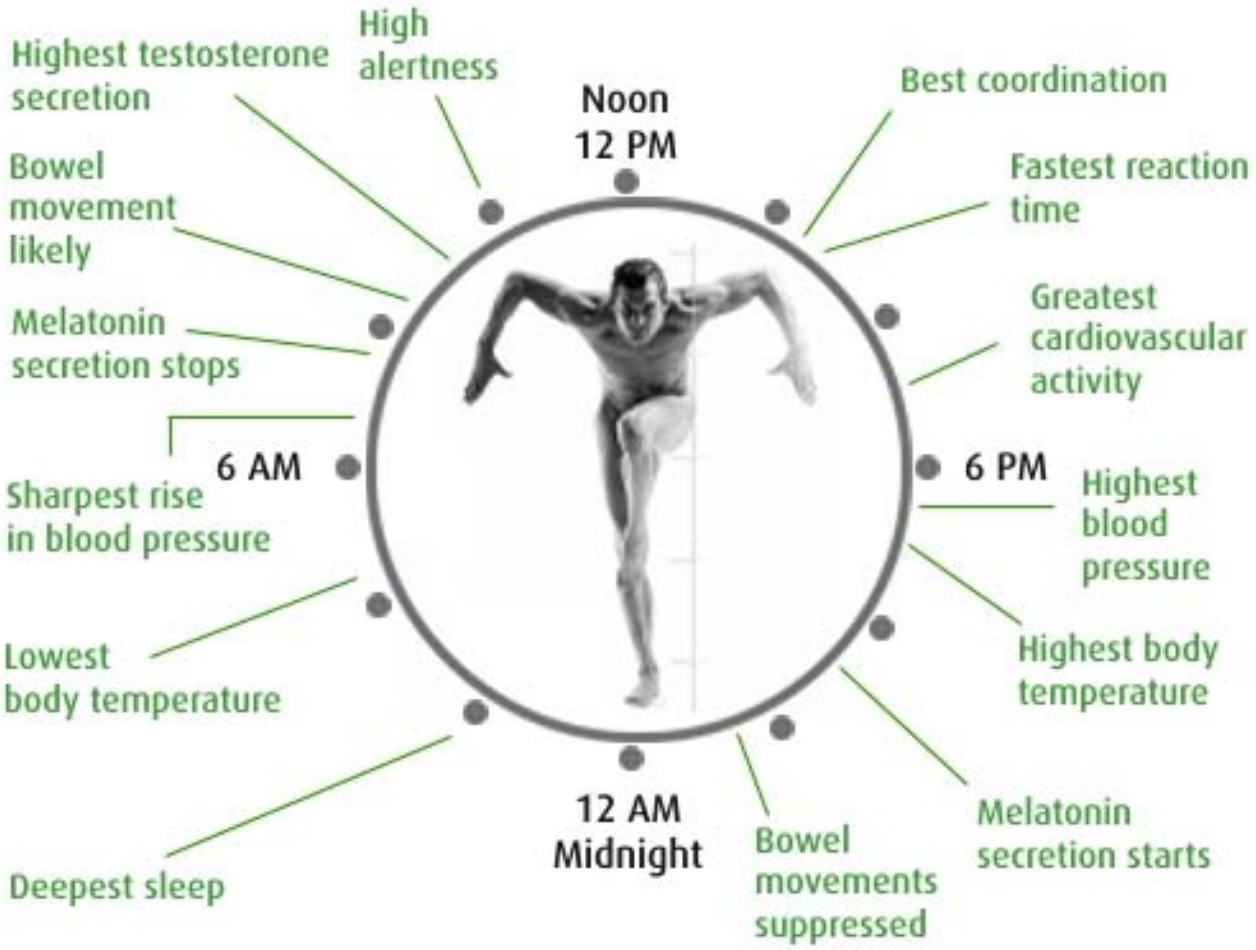


Stage 1: theta activity is 3.5-7.5 Hz. A stage between sleep and wakefulness. The muscles are active, and the eyes roll slowly, opening and closing moderately.

Stage 2: eyes dart back and forth.

Stage 3: formerly divided into stages 3 and 4, is called slow wave sleep - which is caused by the preoptic area which consists of delta activity, high amplitude waves at less than 3.5 Hz. The sleeper is less responsive to the environment; environmental stimuli that may have distracted them in stage one, no longer produce any reactions.
http://en.wikipedia.org/wiki/Sleep

The human biological clock



Why sleep?

Repair and Restoration Theory

sleep enables the body and brain to repair itself after working hard all day

going without sleep causes people to be irritable, dizzy, and to have hallucinations and impaired concentration

sleep-deprived rats' bodies work harder

BUT, how much we sleep does not depend on how much we worked that day

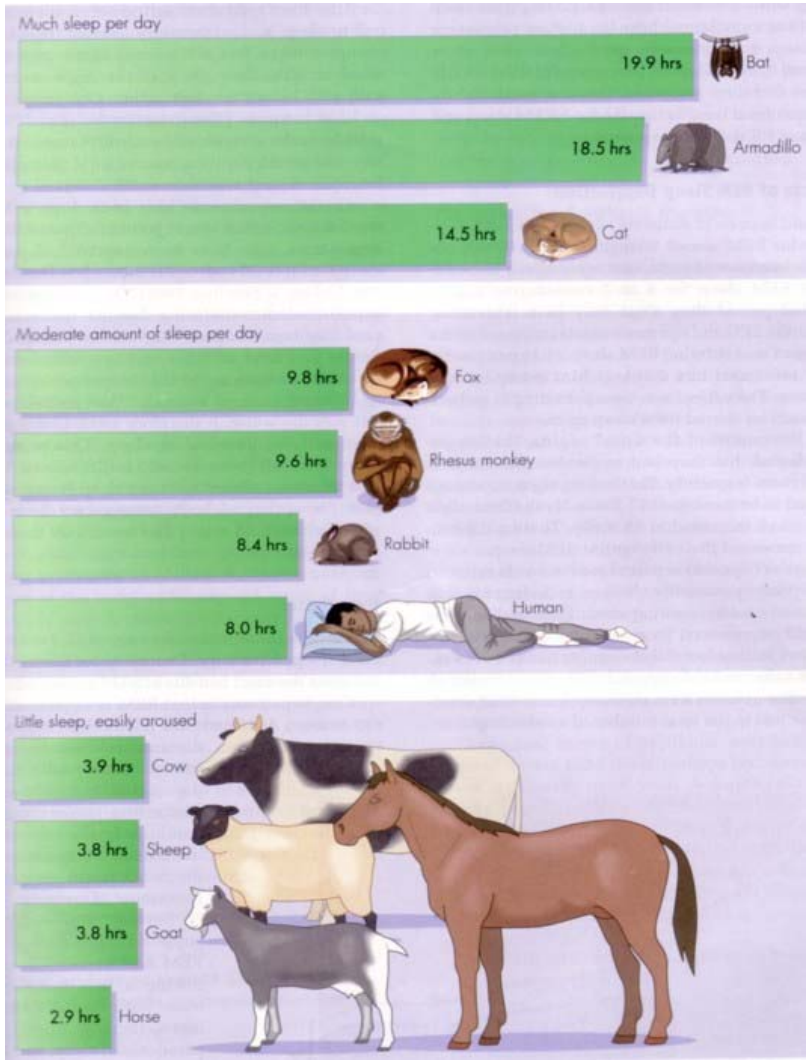
Evolutionary Theory

- we evolved to sleep so that we would conserve energy when we were least efficient

- during sleep body temperature decreases

- predicts that species will sleep different amounts depending on how much they must look for food and watch for predators

www.psy.fsu.edu/undergrad.prog/hull/Sleep.ppt



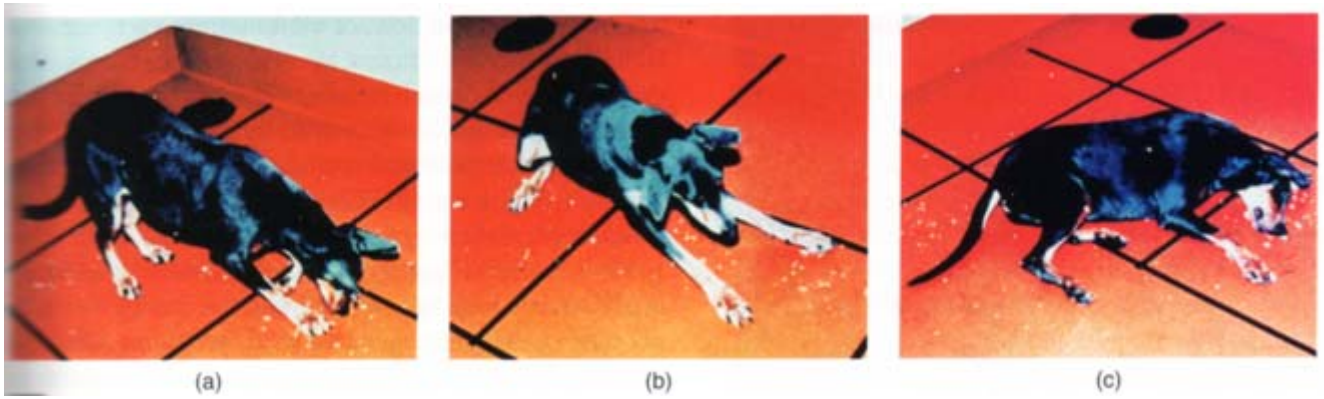
Sleep Disorders

Insomnia (불면증)

- habitual sleeplessness
- possible causes: excessive noise, stress, drugs, medications, pain, uncomfortable temperature, sleep apnea, periodic limb movement disorder
- followed by functional impairment while awake

Narcolepsy (기면발작) (cataplexy 탈력발작)

- Frequent, unexpected periods of sleepiness during the day
- affects about 1 in 1000 people
- symptoms: extreme daytime sleepiness, cataplexy, sleep paralysis, hypnagogic hallucinations (입면환각)
- involvement of orexin



Night Terrors (야경증)

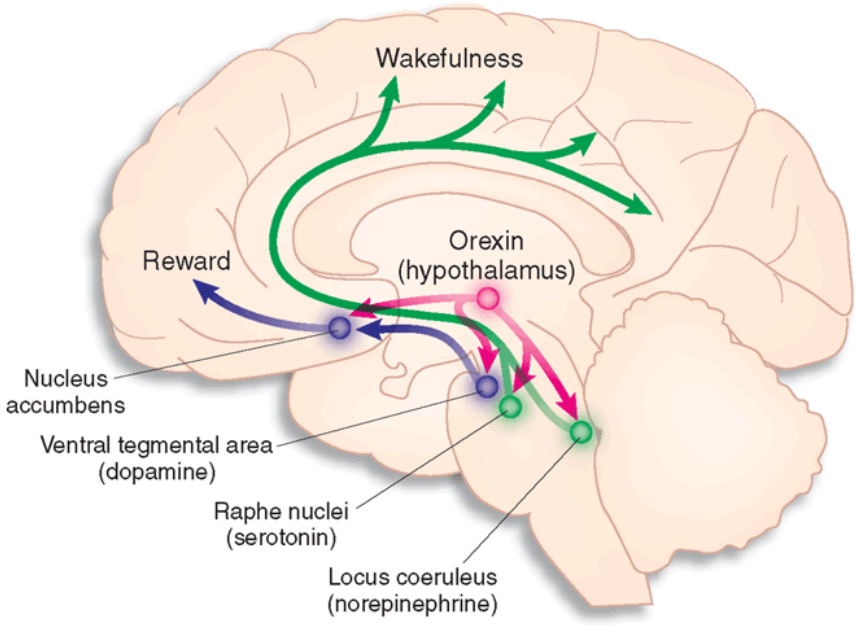
- experience of intense anxiety from which a person awakens screaming in terror
- occur during nonREM sleep
- more common in children

Sleep Walking

- occurs mostly in children
- runs in families
- expressed early in the night during stage 3 and 4 sleep

Orexin (hypocretin) neuron in hypothalamus promotes wakefulness

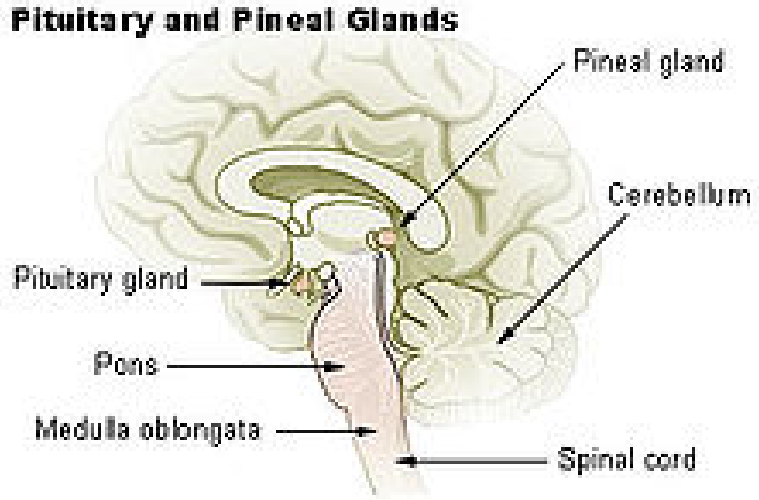
- Suppresses REM sleep
- Excitatory signal to the arousal system
- KO mice was narcoleptic
- Abnormal receptor in narcoleptic dogs



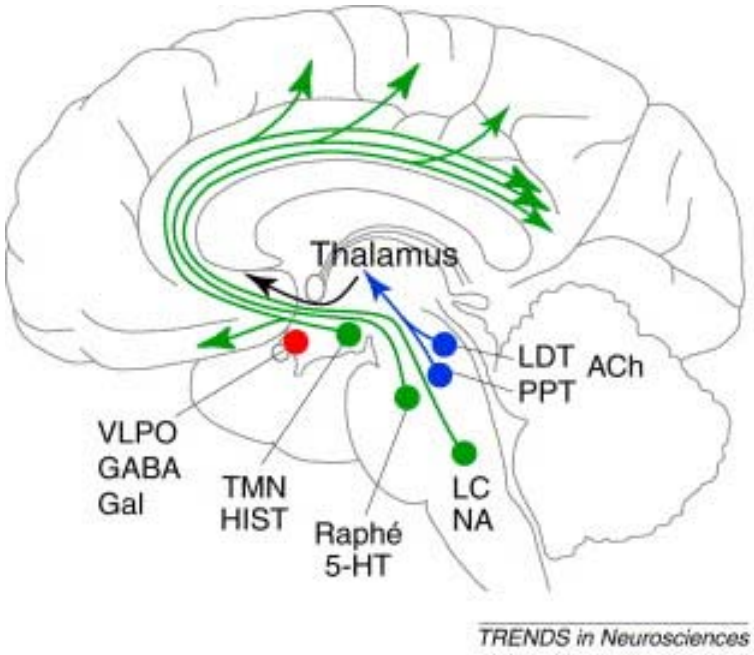
Regulation of sleep

in nonhuman animals: pineal gland is important for sleeping, melatonin secretion

in human controlled by a variety of factors



Some key components of the ascending arousal system excited by orexin

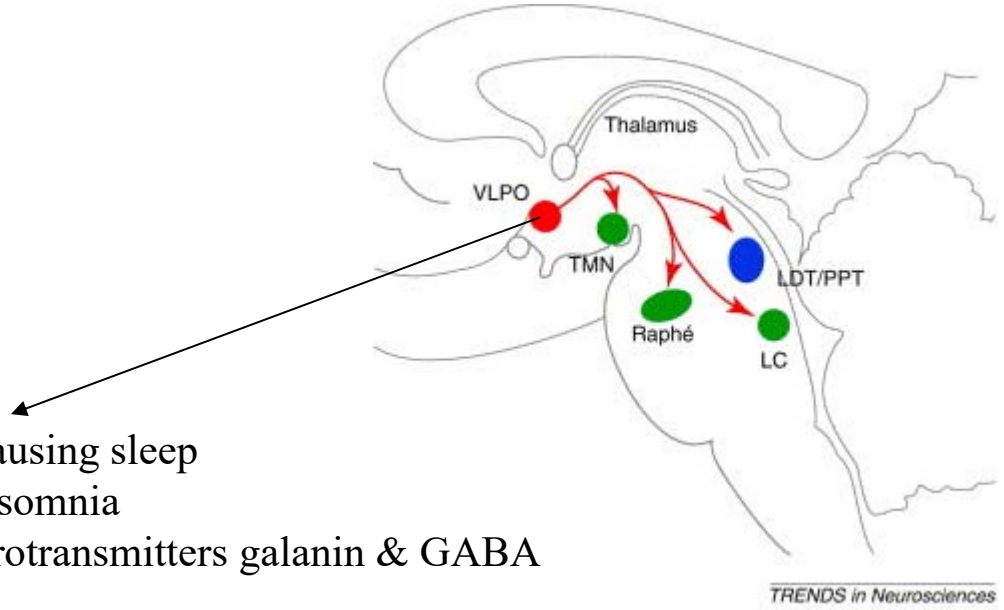


Fire during wake
Slow down during slow wave sleep
Stop during REM sleep

The ascending arousal system sends projections from the brainstem and posterior hypothalamus throughout the forebrain. Neurons of the laterodorsal tegmental nuclei and pedunculopontine tegmental nuclei (LDT and PPT) (blue circles) send cholinergic fibers (Ach) to many forebrain targets, including the thalamus, which then regulate cortical activity. Aminergic nuclei (green circles) diffusely project throughout much of the forebrain, regulating the activity of cortical and hypothalamic targets directly. Neurons of the tuberomammillary nucleus (TMN) contain histamine (HIST), neurons of the raphé nuclei contain 5-HT and neurons of the locus coeruleus (LC) contain noradrenaline (NA). Sleep-promoting neurons of the ventrolateral preoptic nucleus (VLPO, red circle) contain GABA and galanin (Gal). Trends in Neurosciences (2001) 24:726-731

Nature **437**, 1257-1263 (27 October 2005)

The key projections of the ventrolateral preoptic nucleus (VLPO) to the main components of the ascending arousal system



Turn off arousal system, causing sleep
If damaged, irreversible insomnia
Release the inhibitory neurotransmitters galanin & GABA

The projections from the ventrolateral preoptic nucleus (VLPO) to the main components of the ascending arousal system. Axons from the VLPO directly innervate the cell bodies and proximal dendrites of neurons in the major monoamine arousal groups. Within the major cholinergic groups, axons from the VLPO mainly innervate interneurons, rather than the principal cholinergic cells. Abbreviations: LC, locus coeruleus; LDT, laterodorsal tegmental nuclei; PPT, pedunculopontine tegmental nuclei; TMN, tuberomammillary nucleus; VLPO, ventrolateral preoptic nucleus. The blue circle indicates neurons of the LDT and PPT; green circles indicate aminergic nuclei; and the red circle indicates the VLPO.

A schematic diagram of the flip-flop switch model

The regulation of a circuit containing mutually inhibitory elements (orexin & VLPO neurons)

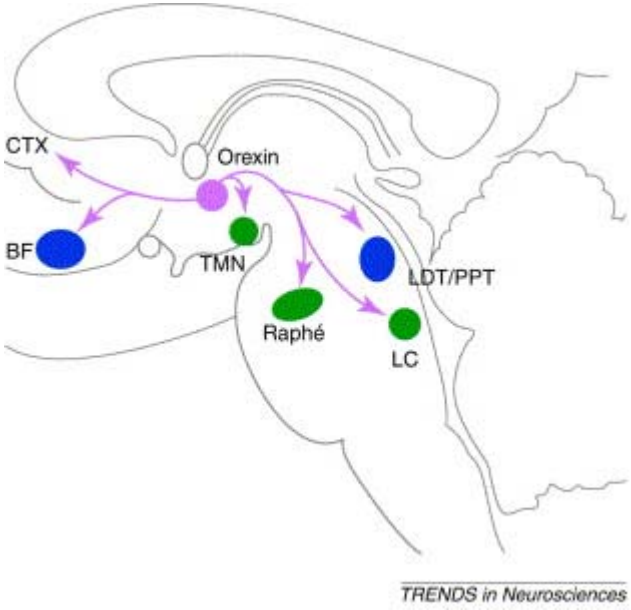
orexin: stimulate wakefulness

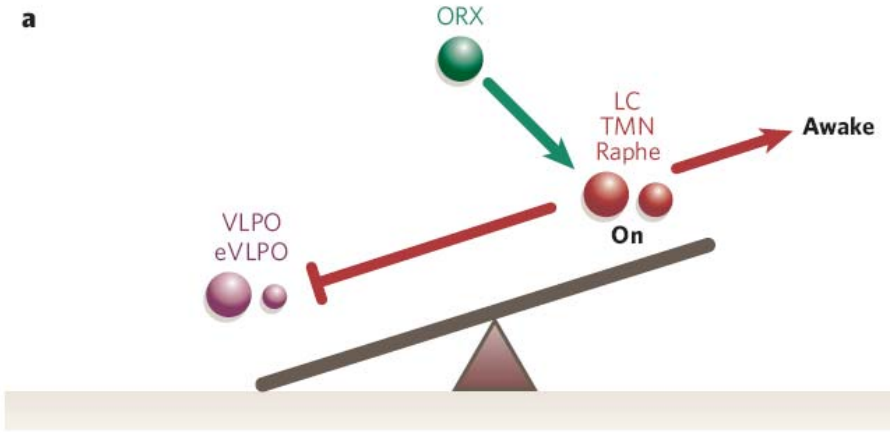
VLPO: inhibit wakefulness (via galanin & GABA)

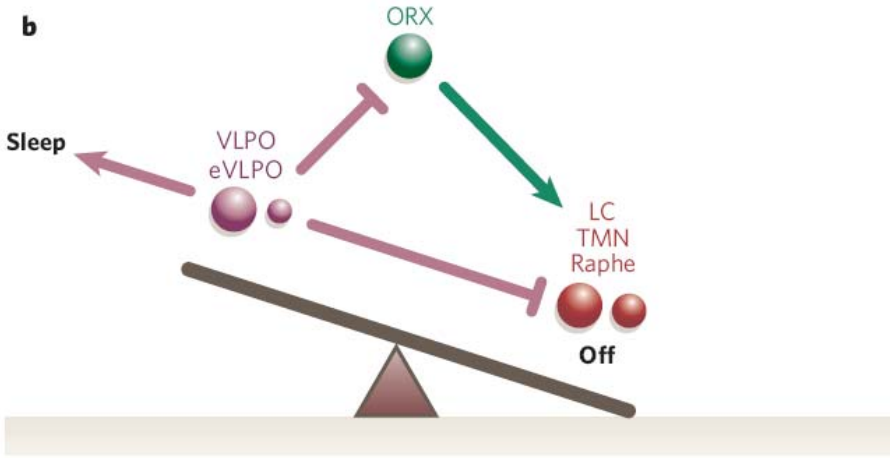
Wake-sleep transitions are relatively abrupt

Unwanted transitions with little warning

Stabilized by orexin



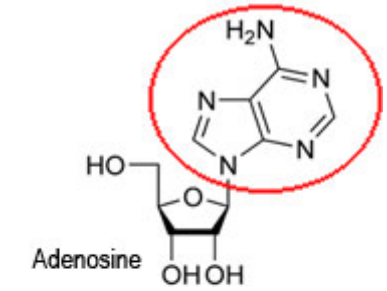




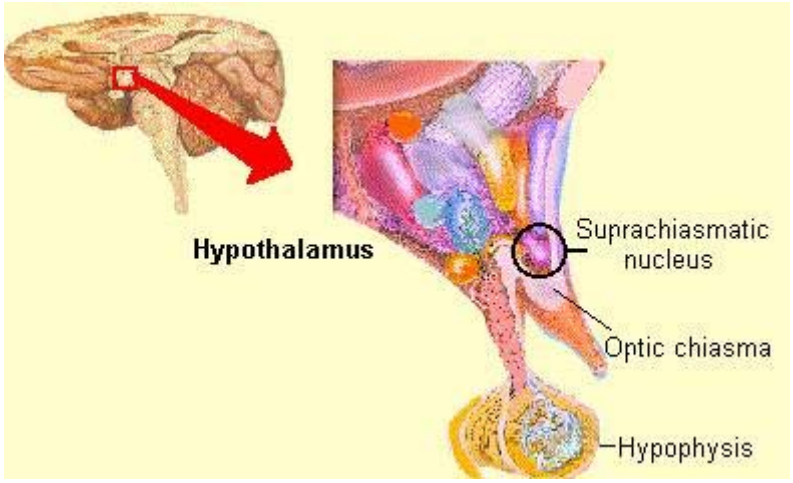
Two main signals control our need for sleep and its circuitry

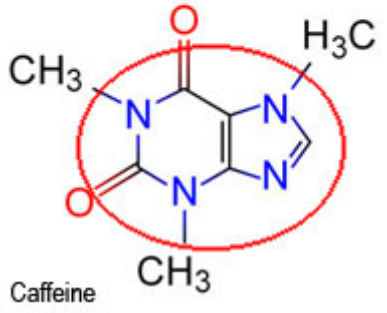
1. Body's circadian clock: the suprachiasmatic nucleus (SCN) in the hypothalamus

2. Homeostasis:
   - ex. Adenosine accumulation during wake: energy depletion
     - caffeine is an adenosine blocker
   - sleep debt



SCN: acts as a master clock





The link between SCN and the sleep system

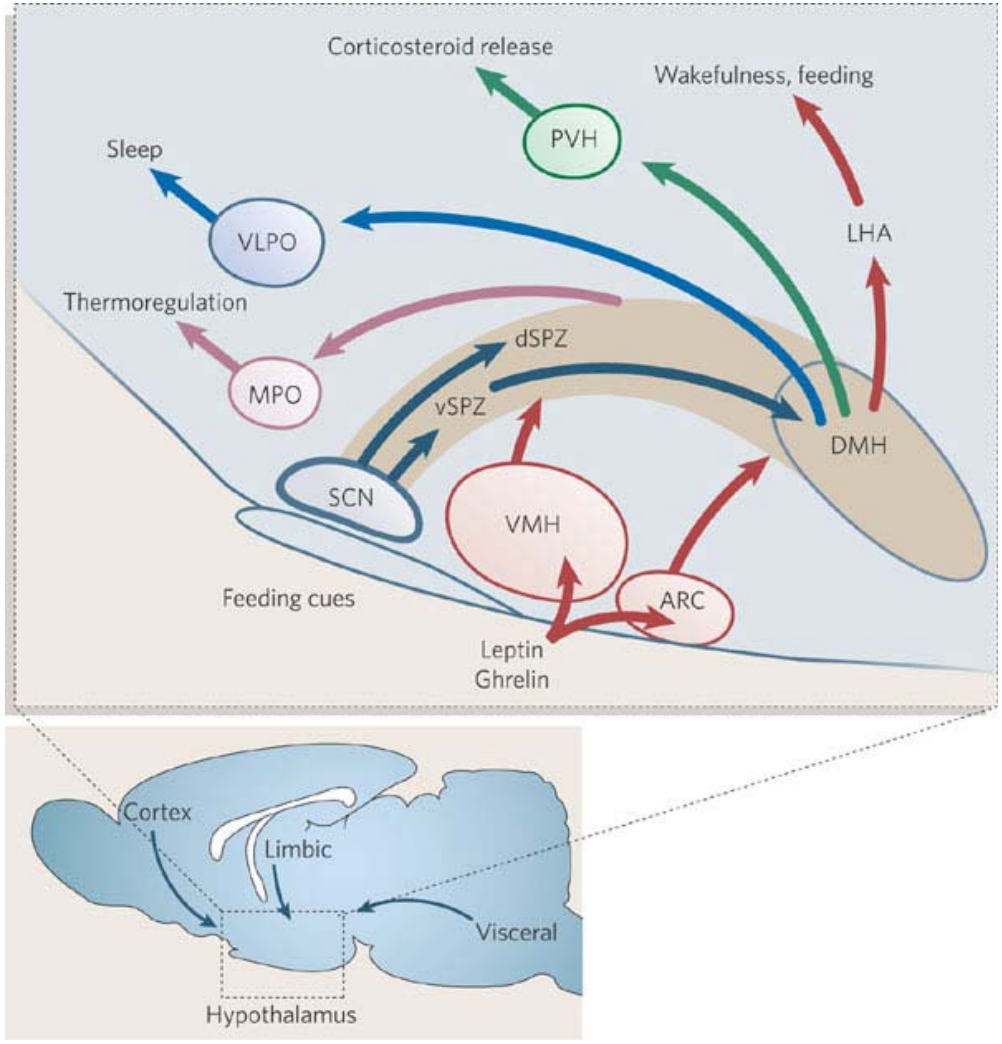
Suprachiasmatic nucleus (SCN) is a tiny region located in the hypothalamus, situated directly above the optic chiasm. It is responsible for controlling circadian rhythms. The neuronal and hormonal activities it generates regulate many different body functions in a 24-hour cycle, using around 20,000 neurons.

vSPZ: ventral subparaventricular zone

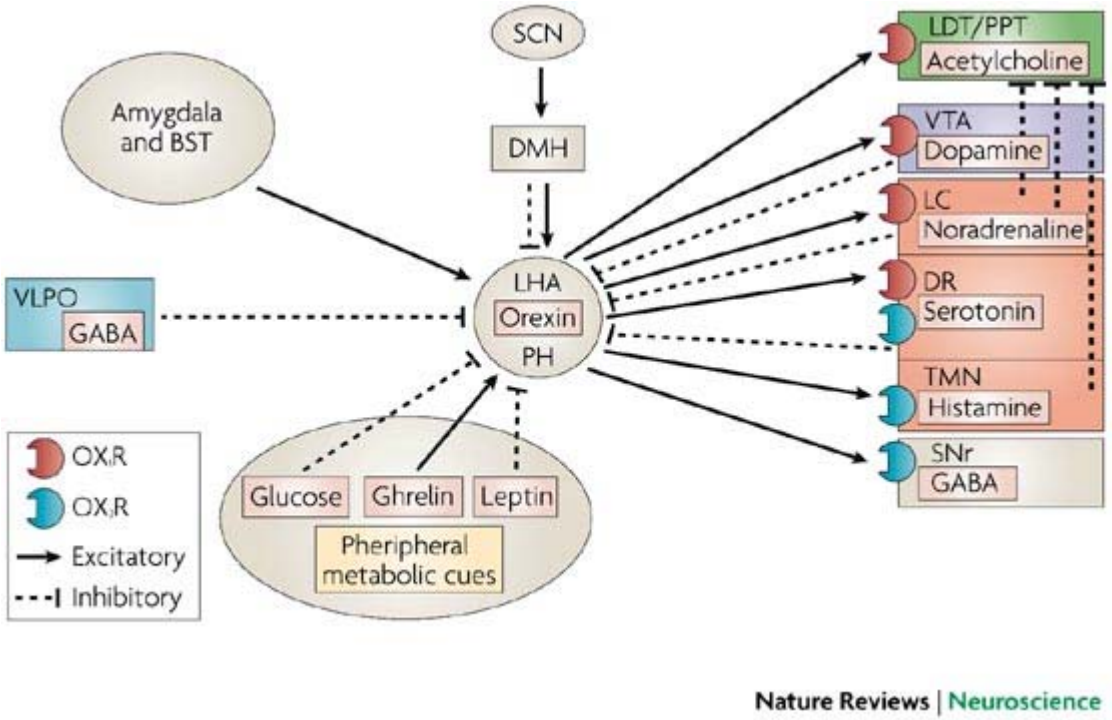
dSPZ: dorsal subparaventricular zone

DMH: the dorsomedial nucleus of the hypothalamus

VLPO: ventrolateral preoptic nucleus



The neural circuit of orexin (hypocretin): maintaining sleep and wakefulness



Orexin neurons in the lateral hypothalamic area (LHA) and posterior hypothalamus (PH) are anatomically well placed to provide a link between the limbic system, systems involved in energy homeostasis and monoaminergic and cholinergic neurons in the brain stem. Solid arrows show excitatory projections, and broken lines inhibitory ones. Wake-active regions, sleep-active regions and REM-active regions are shown by red, blue and green boxes, respectively. Orexin neurons promote wakefulness through the monoaminergic nuclei that are wake-active. Stimulation of dopaminergic centres by orexins can modulate reward systems (purple). Peripheral metabolic signals such as leptin, ghrelin and glucose influence orexin neuronal activity to coordinate arousal and energy homeostasis. The nucleus suprachiasmaticus (SCN), the central body clock, sends signals to orexin neurons via the dorsomedial hypothalamus (DMH). The DMH acts as a food-entrainable ossilator, and influences orexin neuronal activity. Input from the limbic system (amygdala and bed nucleus of the stria terminalis (BST)) might regulate the activity of orexin neurons upon emotional stimuli to evoke emotional arousal or fear-related responses. VLPO, ventrolateral preoptic area; DR, dorsal raphe; GABA, gamma-aminobutyric acid; LC, locus coeruleus; LDT, laterodorsal tegmental nucleus; PPT, pedunculopontine tegmental nucleus; SNr, substantia nigra pars reticulata; TMN, tuberomammillary nucleus. Nature Reviews Neuroscience 8, 171-181 (March 2007)

Homeostatic
Allostatic (McEwen & Steller, 1993)

Rather than maintaining constancy, the physiologic systems within the body fluctuate to meet demands from external forces

How these external forces overcome the homeostatic and circadian systems or reset them?

Dreaming during REM sleep
Why do we dream?

Play around?
Any benefit?

compensation of REM sleep
REM sleep decrease during childhood
consolidation or resolving of experiences: but fetus also dream
A type of consciousness resulting from a less vigorous
dialogue between brain regions

underdeveloped brain
prevailing chemicals in the brain: schizophrenic
failure of processing large amounts of sensory input during asleep

high protein synthesis during sleep

Hayashi Y, Kashiwagi M, Yasuda K, Ando R, Kanuka M, Sakai K, Itohara S. Cells of a common developmental origin regulate REM/non-REM sleep and wakefulness in mice. Science. 2015 Nov 20;350(6263):957-61. doi: 10.1126/science.aad1023. Epub 2015 Oct 22. PubMed PMID: 26494173.
http://www.sciencetimes.co.kr/?news=%ec%9e%a0-%ec%a7%80%eb%b0%b0%ed%95%98%eb%8a%94-%ec%84%b8%ed%8f%ac-%eb%b0%9c%ea%b2%ac%eb%90%98%eb%8b%a4