Rhythms of the Brain

Recording brain waves
EEG rhythms
Mechanical and meaning of brain rhythms
Sleep
Neural mechanisms of sleep

Introduction

- Rhythmic Controls of Brain
  - Sleeping and waking, hibernation, breathing, walking, electrical rhythms of cerebral cortex
  - Cerebral cortex: Range of rapid electrical rhythms
  - EEG: Classical method of recording brain rhythms
  - Circadian rhythms: Change in physiological functions according to daily clocks in brain

The Electroencephalogram

- The Electroencephalogram (EEG)
  - Measurement providing glimpse of generalized activity of cerebral cortex
  - Function
    - Diagnose neurological conditions such as epilepsy, research purpose
  - Richard Caton in 1875, electrical recordings from surface of dog and rabbit brains using primitive device sensitive to voltage
  - Hans Berger in 1929, human EEG

The Electroencephalogram

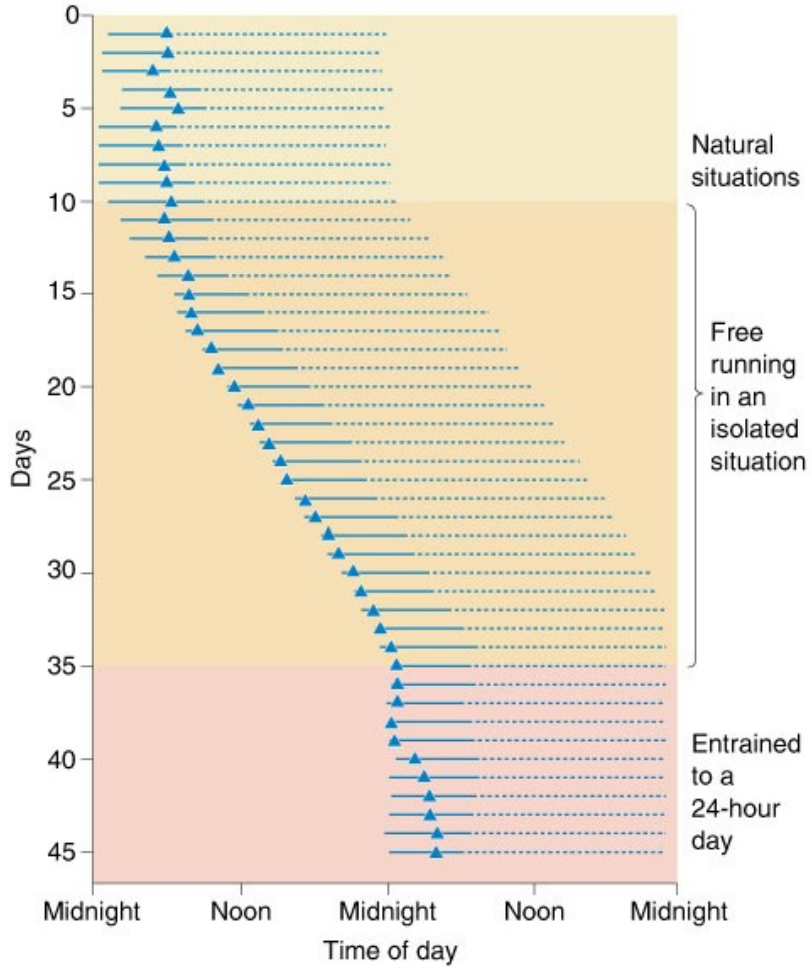
- Recording Brain Waves
  - Electrodes to scalp, low-resistance connection
  - Connected to banks of amplifiers and recording devices
  - Voltage fluctuations measured (tens of microvolts)
  - Electrode pairs: Measure different brain regions
  - Set of simultaneous squiggles, voltage changes between electrode pairs

Sleep

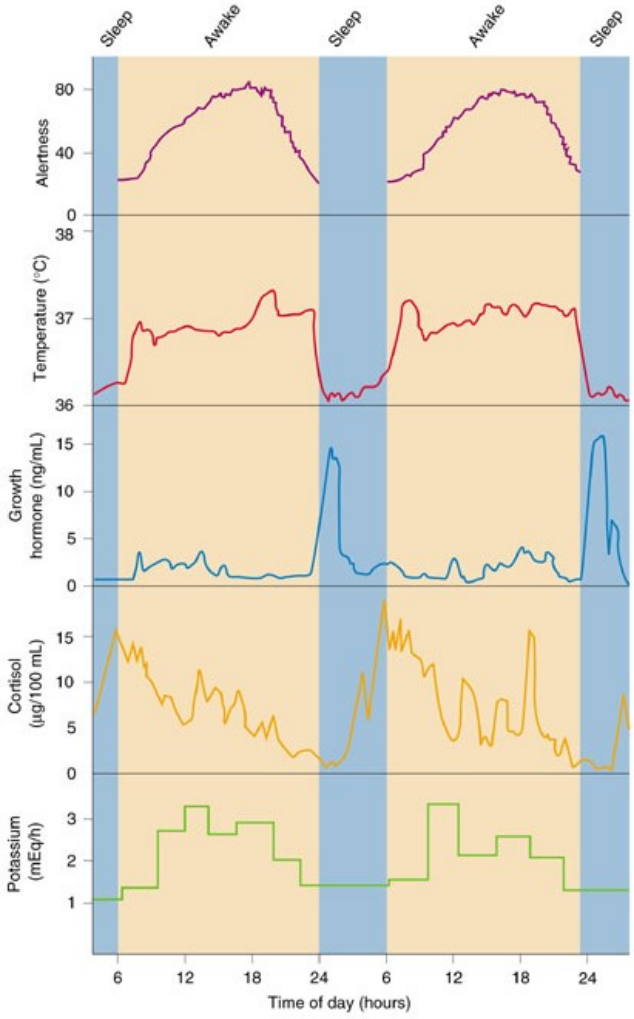
- Reflected in the rest/activity cycles of all organisms by the circadian rhythm
- Sleep itself is defined by rather strict electrophysiological criteria
- Function of sleep is unknown
  - Circadian
  - Homeostatic

Circadian functions

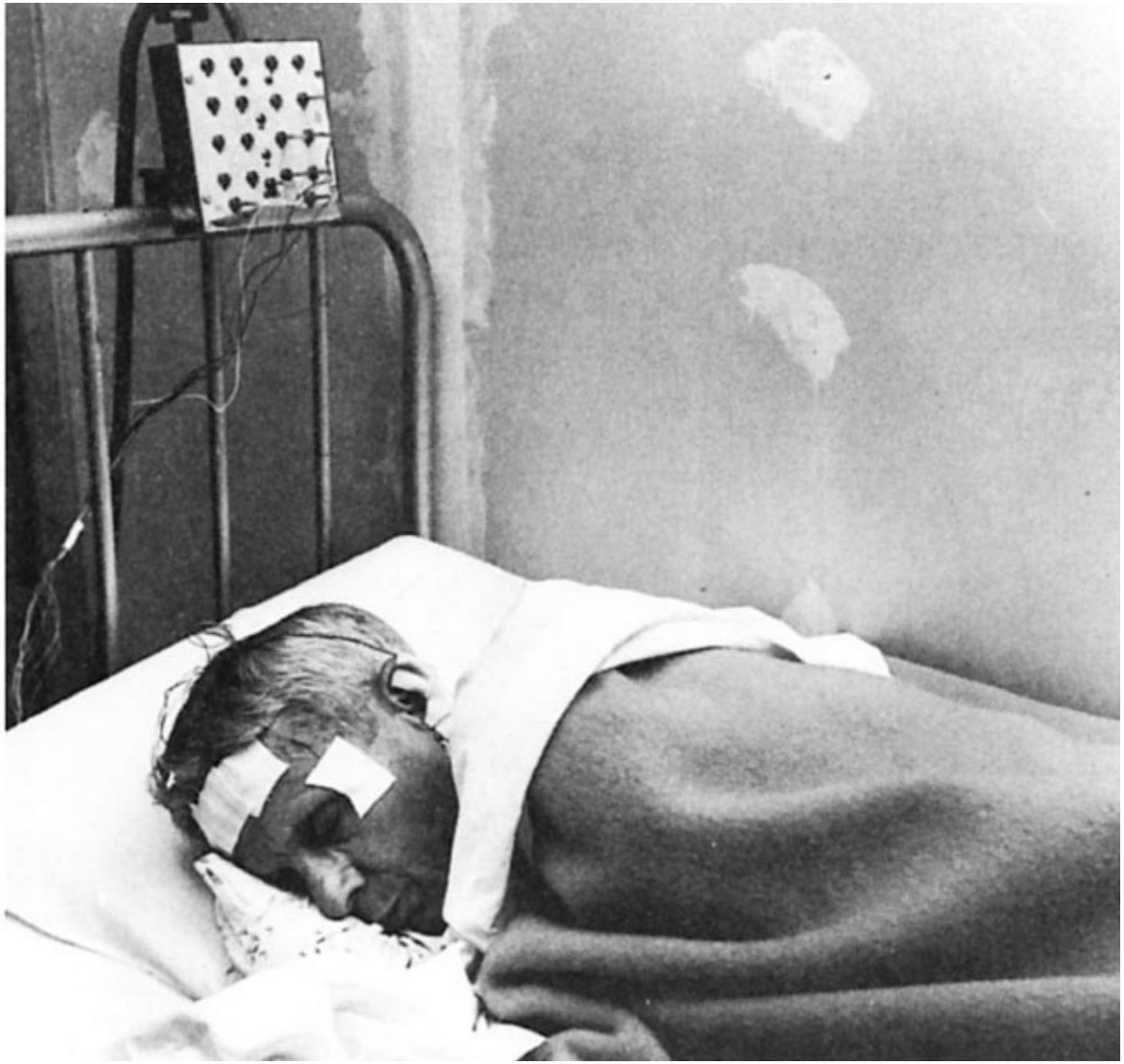
Circadian rhythms of sleep and wakefulness. Shown here is a daily plot of one person's sleep-wake cycles. Each horizontal line is a day; solid lines indicate sleep, and broken lines indicate waking. A triangle indicates the point of the day's lowest body temperature. The subject was first exposed to 9 days of natural 24-hour cycles of light and dark, noise and quiet, and air temperature. During the middle 25 days, all time cues were removed, but the subject was free to set his own schedule. Notice that the sleep-wake cycles remained stable, but each lengthened to about 25 hours. The subject was now free-running. Notice also that the low point of body temperature shifts from the end of the sleep period to the beginning. During the last 11 days, a 24-hour cycle of light and meals was reintroduced, the subject again entrained to a day-long rhythm, and body temperature gradually shifted back to its normal point in the sleep cycle.
(Source: Adapted from Dement, 1976, Fig. 2.)



Circadian rhythms of physiological functions. Fluctuations over two consecutive days are shown here. Alertness and core body temperature vary similarly. Growth hormone and cortisol levels in the blood, however, are highest during sleep, although at different times. The bottom graph shows the excretion of potassium by the kidneys, which is highest during the day. (Source: Adapted from Coleman, 1986, Fig. 2.1.)



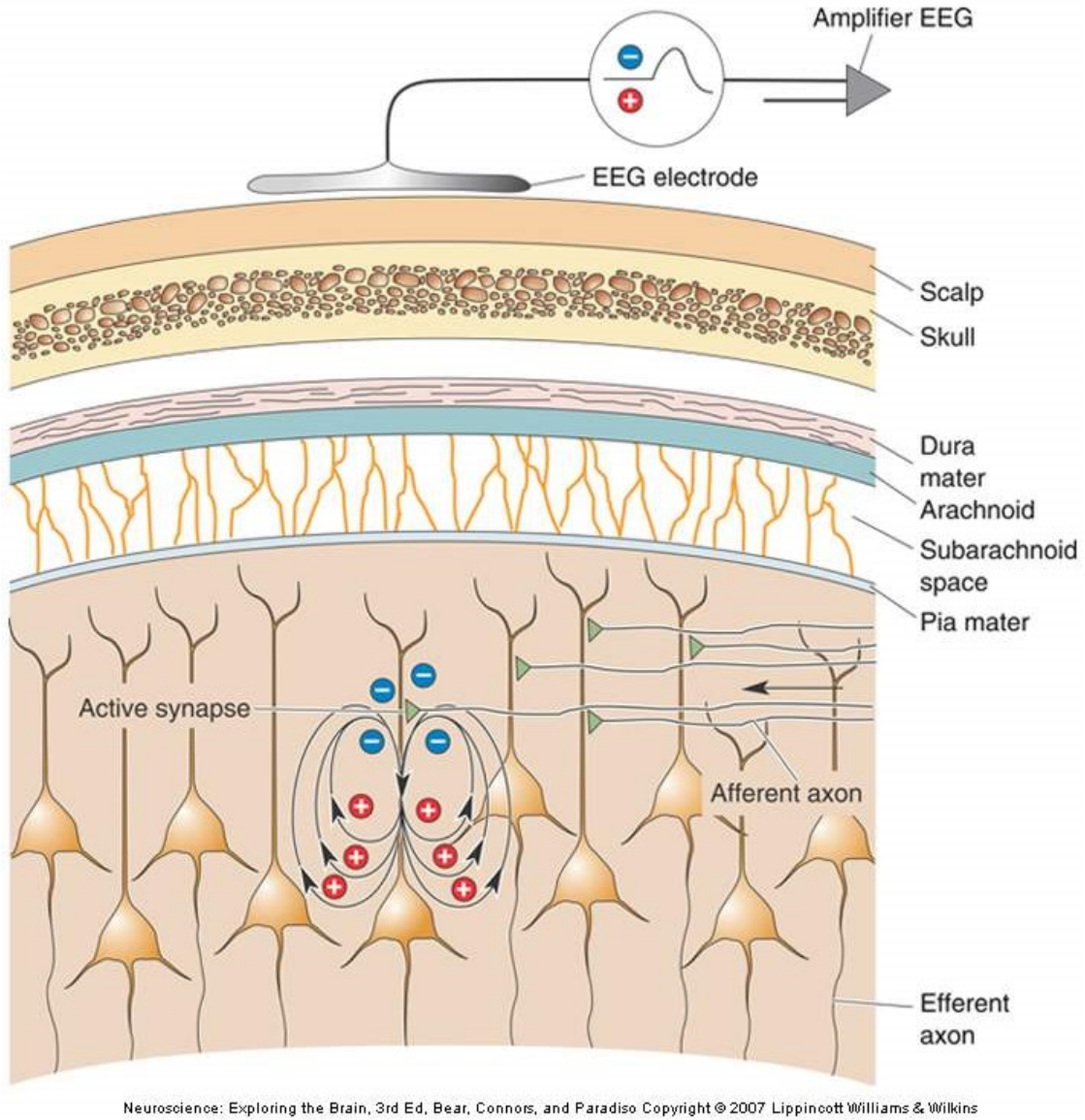
A subject in a sleep research study. This is American sleep researcher Nathaniel Kleitman, codiscoverer of REM sleep. The white patches on his head are pieces of tape holding EEG electrodes, and those next to his eyes hold electrodes that monitor his eye movements. (Source: Carskadon, 1993.)



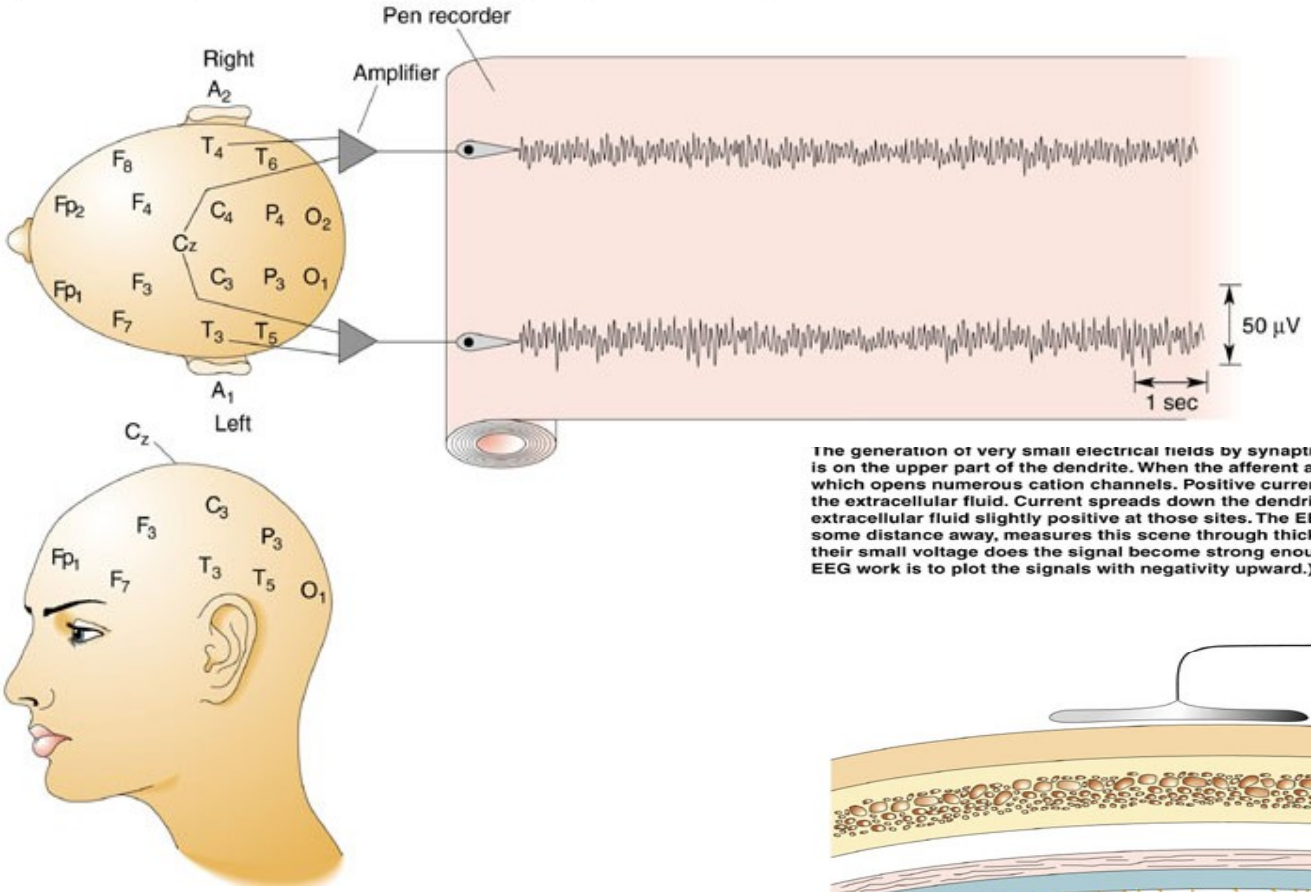
EEG

The Electroencephalogram

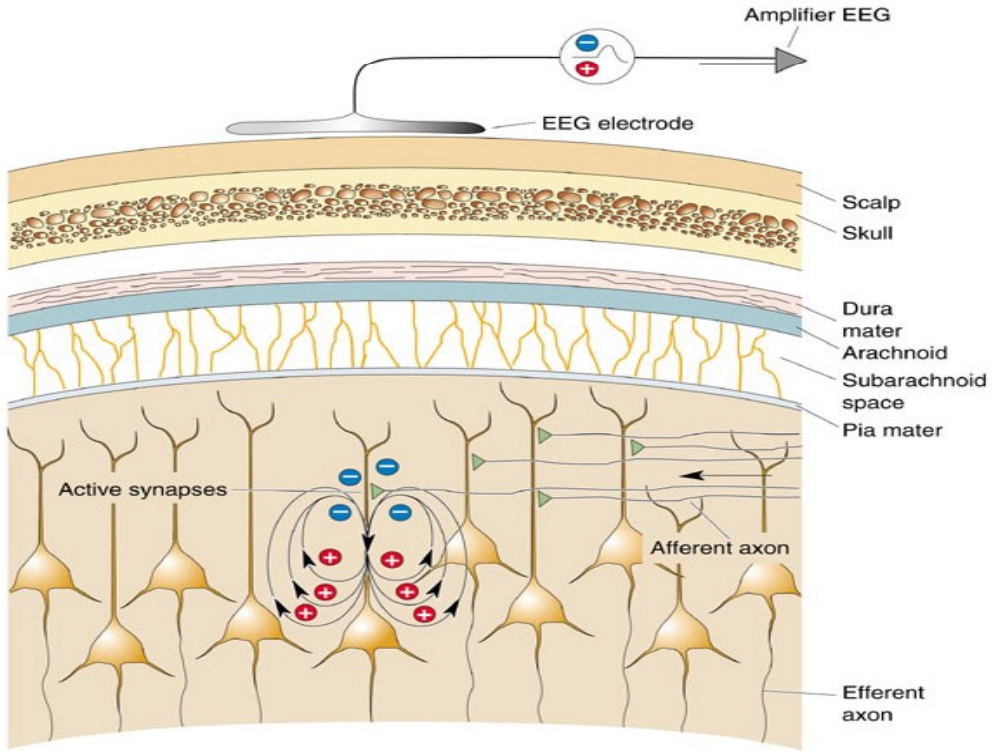
- EEG Fluctuations and Oscillations



Standard positions for the placement of EEG electrodes. A, auricle (or ear); C, central; Cz, vertex; F, frontal; Fp, frontal pole; O, occipital; P, parietal; T, temporal. Wires from pairs of electrodes are fed to amplifiers, and these drive pen recorders.



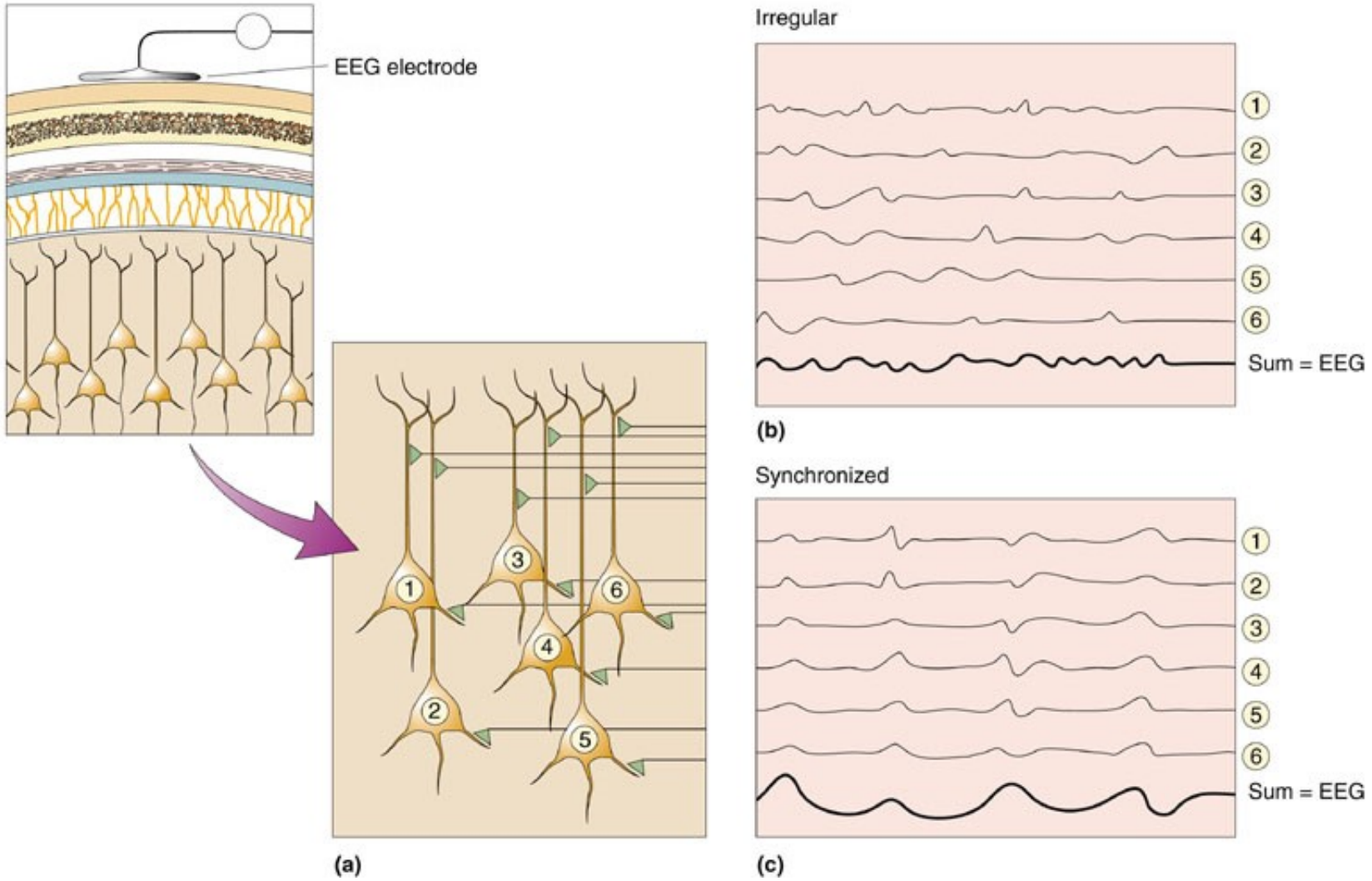
The generation of very small electrical fields by synaptic currents in pyramidal cells. In this case, the synapse is on the upper part of the dendrite. When the afferent axon fires, the presynaptic terminal releases glutamate, which opens numerous cation channels. Positive current flows into the dendrite, leaving a slight negativity in the extracellular fluid. Current spreads down the dendrite and escapes out of its deeper parts, leaving the extracellular fluid slightly positive at those sites. The EEG electrode, which is referred to a second electrode some distance away, measures this scene through thick layers of tissue. Only if thousands of cells contribute their small voltage does the signal become strong enough to see at the surface of the scalp. (The convention in EEG work is to plot the signals with negativity upward.)



Recording of EEG

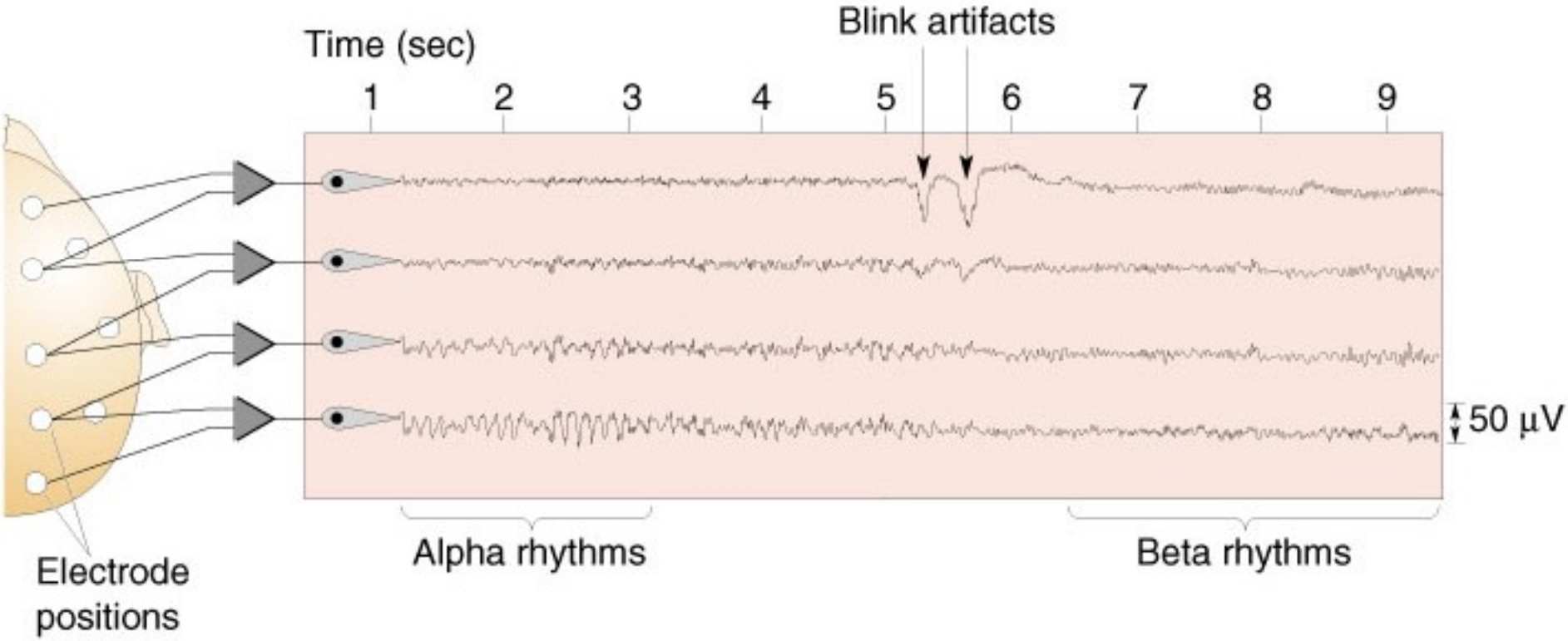
Generation of large EEGs

The generation of large EEG signals by synchronous activity. (a) In a population of pyramidal cells under an EEG electrode, each neuron receives many synaptic inputs. (b) If the inputs fire at irregular intervals, the pyramidal cell responses are not synchronized, and the summed activity detected by the electrode has small amplitude. (c) If the same number of inputs fire within a narrow time window so that the pyramidal cell responses are synchronized, the resulting EEG sum is much larger.



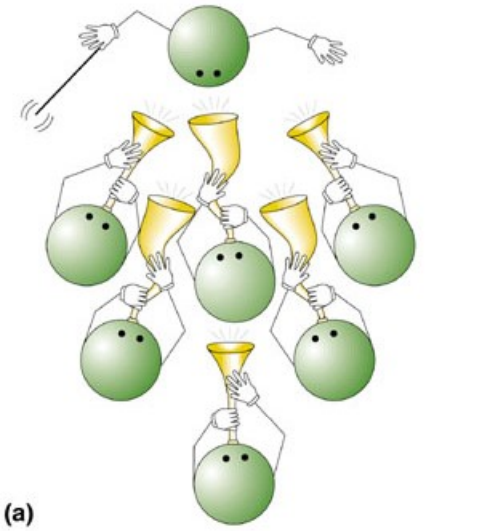
A normal EEG

A normal EEG. The subject is awake and quiet, and recording sites are indicated at the left. The first few seconds show normal alpha activity, which has frequencies of 8–13 Hz and is largest in the occipital regions. About halfway through the recording, the subject opened his eyes, signaled by the large blink artifacts on the top traces (arrows), and alpha rhythms were suppressed.

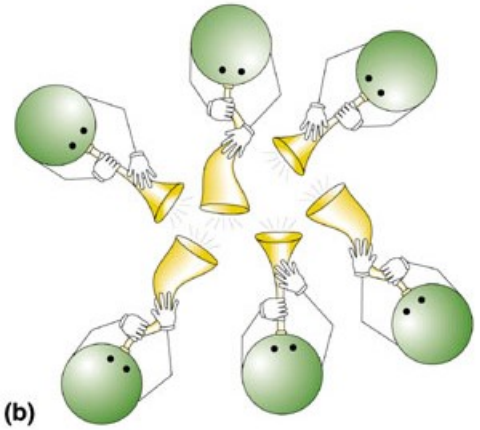


Generation of synchronous rhythms I

Two mechanisms of synchronous rhythms. Synchronous rhythms may (a) be led by a pacemaker or (b) arise from the collective behavior of all participants.



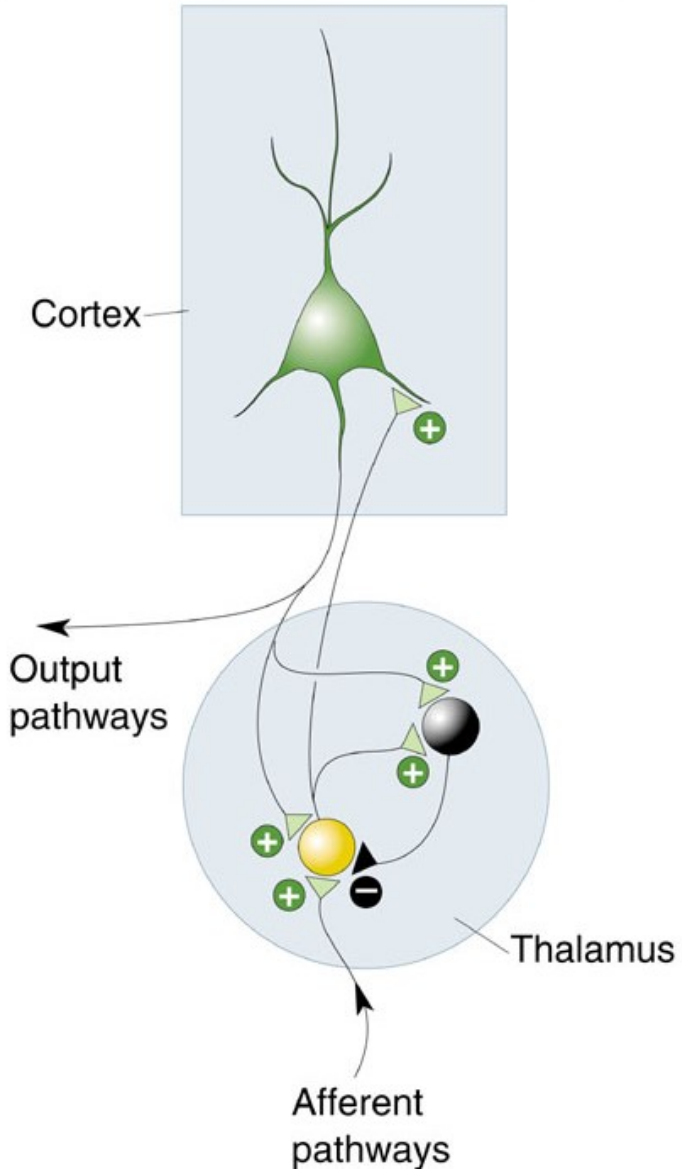
(a)



(b)

Generation of synchronous rhythms II

Rhythms in the thalamus drive rhythms in the cerebral cortex. The thalamus can generate rhythmic activity because of the intrinsic properties of its neurons and because of its synaptic interconnections. Yellow indicates a population of excitatory neurons, and black indicates a population of inhibitory neurons.



The Electroencephalogram

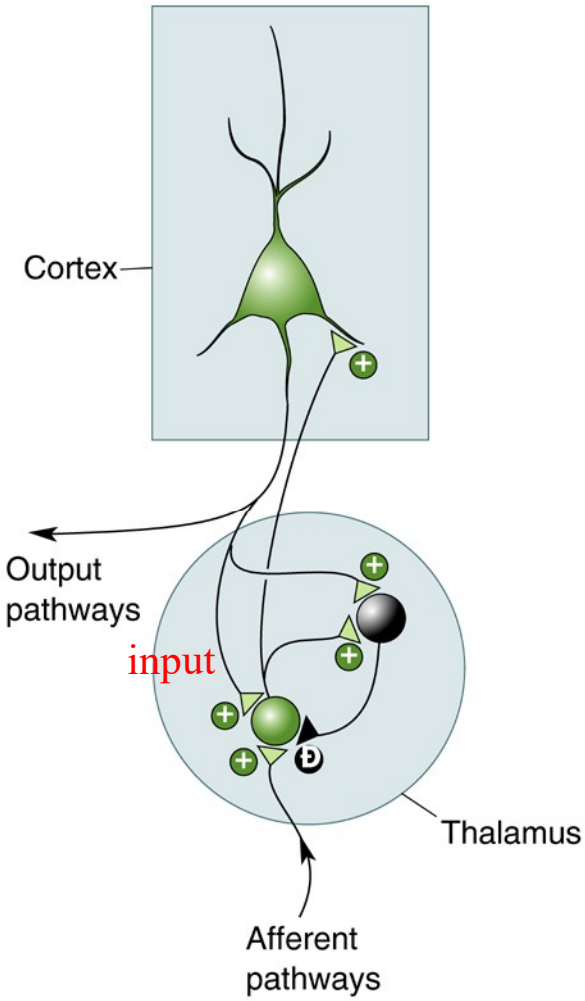
- Magnetoencephalography (MEG)
  - Recording miniscule magnetic signals generated by neural activity
- Comparison with EEG, fMRI, PET
    - MEG localizes sources of neural activity better than EEG
    - MEG cannot provide detailed images of fMRI
    - EEG, MEG - measure neuron activity
    - fMRI, PET - changes in blood flow, metabolism

The Electroencephalogram

- EEG Rhythms
  - Categorization of rhythms based on frequency
    - Beta: Greater than 14 Hz, activated cortex
    - Alpha: 8-13 Hz, quiet, waking state
    - Theta: 4-7 Hz, some sleep states
    - Delta: Less than 4 Hz, deep sleep
  - Deep Sleep
    - High synchrony, high EEG amplitude

The Electroencephalogram

- Mechanisms and Meanings of Brain Rhythms
  - Synchronized oscillation mechanisms
    - Central clock/Pacemaker
    - Collective methods ("jam session")
  - Thalamus - massive cortical input - influence cortex (**Powerful pacemaker**)
    - Neuronal oscillations
    - Voltage-gated ion channels (allow each cell to generate rhythmic self sustaining discharge patterns)



The Electroencephalogram

- Functions of Brain Rhythms
  - Scarcity of data: No satisfactory answers
  - Hypotheses for sleep-related rhythms
    - Brain's way of disconnecting cortex from sensory input
    - No direct function, by-products of strongly interconnected circuits
- Walter Freeman: a neurobiologist
  - Neural rhythms coordinate activity, synchronize oscillations, bind together

The Electroencephalogram

- The Seizures of Epilepsy
  - Epilepsy: Repeated seizures
  - Causes: Tumor, trauma, infection, vascular disease, many cases unknown
  - Generalized: Entire cerebral cortex, complete behavior disruption, consciousness loss
  - Partial: Circumscribed cortex area, abnormal sensation or aura
  - Absence: Less than 30 sec of generalized, 3 Hz EEG waves

Sleep

- Sleep
  - Universal among higher vertebrates
  - Sleep deprivation, devastating
  - One-third of lives in sleep state
  - Defined: “Sleep is a readily reversible state of reduced responsiveness to, and interaction with, the environment.”

Sleep

- The Functional States of the Brain

Table 19.1 **Characteristics of the Three Functional States of the Brain**

BEHAVIOR	AWAKE	NON-REM SLEEP	REM SLEEP
EEG	Low voltage, fast	High voltage, slow	Low voltage, fast
Sensation	Vivid, externally generated	Dull or absent	Vivid, internally generated
Thought	Logical, progressive	Logical, repetitive	Vivid, illogical, bizarre
Movement	Continuous, voluntary	Occasional, involuntary	Muscle paralysis; movement commanded by the brain but not carried out
Rapid eye movement	Often	Rare	Often

Do you know??????????????

In fact, 17 hours of continuous sleeplessness leads to a decrease in performance that is equivalent to a blood alcohol level of two glasses of wine (0.05%).

REM Sleep

- It is an active, hallucinating brain in a paralyzed body.
- Occurs several times during night (only in mammals and birds), sometimes characterized by dreams, indicated by bursts of rapid eye movements.
- Called “paradoxical sleep”. EEG looks more awake than asleep. Brain consumes more O_2 even compared to when it is awake, and involved in problem solving. Brain seems doing everything except resting.
- Physiological control systems are dominated by activity of the sympathetic division of the ANS
- Decreases as we age

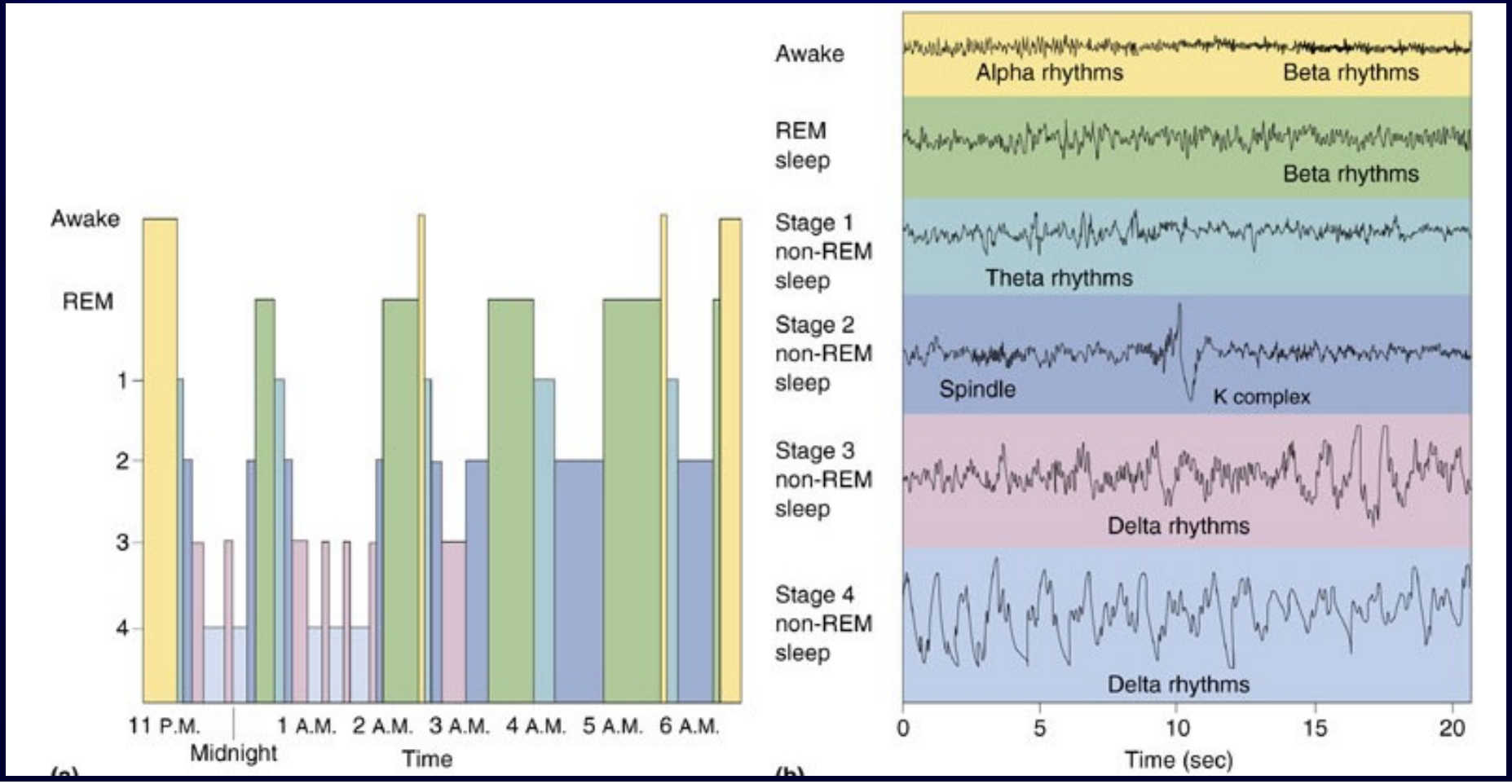
Non-REM

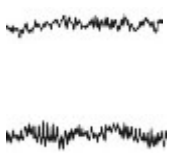
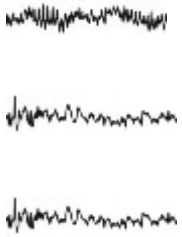
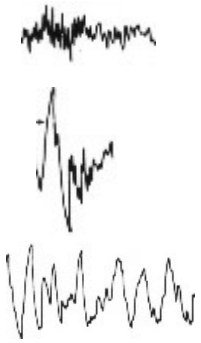
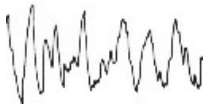
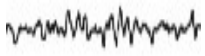
- It is an idling brain in a movable body.
- Brain does not usually generate complex dreams.
- The temperature and energy consumption are lowered
- Synchronized activity of neurons
- Increased glycogen synthesis
- Physiological control systems are dominated by activity of the parasympathetic division of the ANS

The Sleep cycle (non REM:REM- 75:25%)

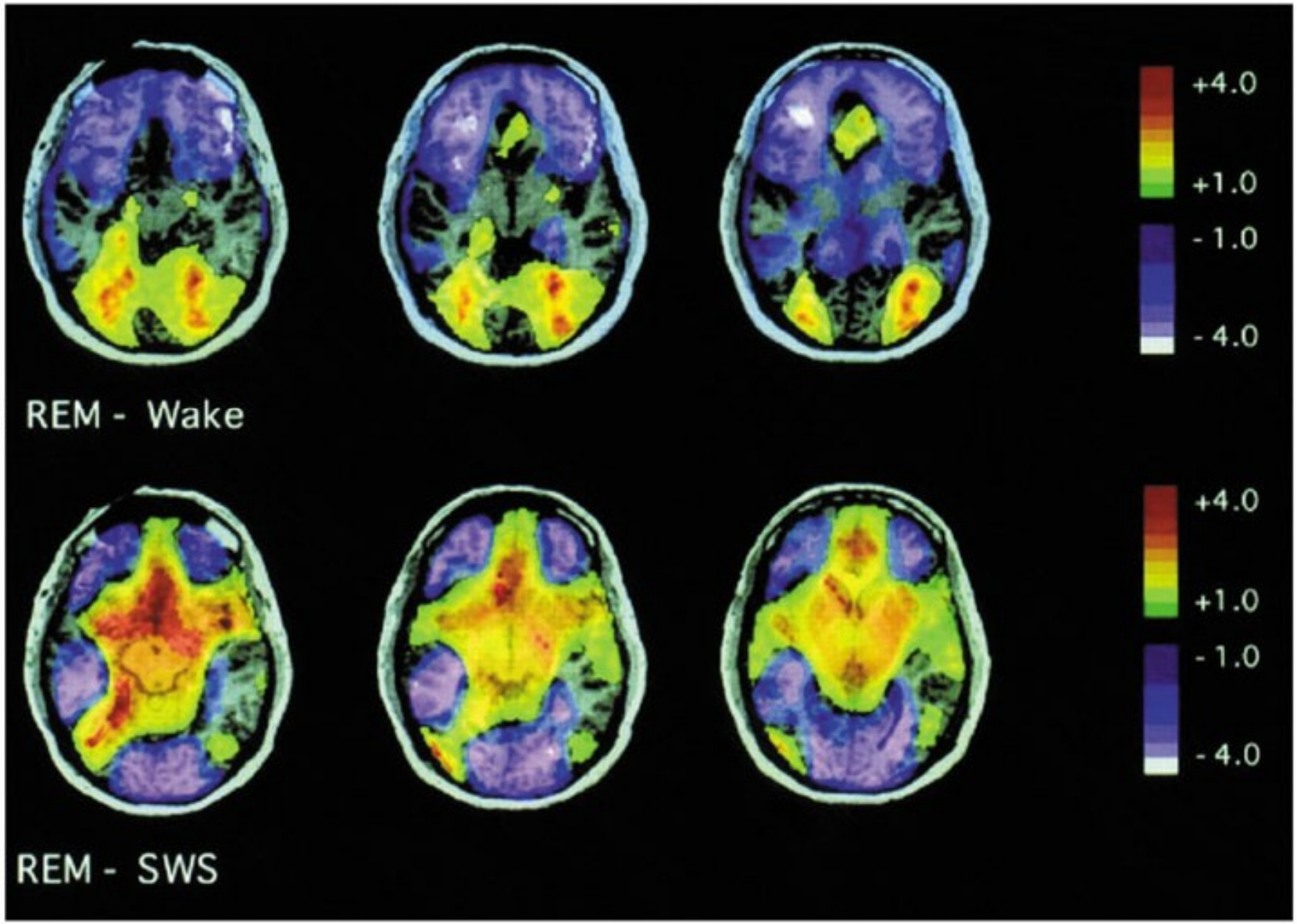
Sleep occurs in a recurring cycle of 90 to 110 minutes

- The night's sleep progresses through the deeper stages of non-REM sleep.
- The cycle is repeated several times.
- Each cycle tends, however, to have shorter and shallower non-REM periods and longer REM periods.

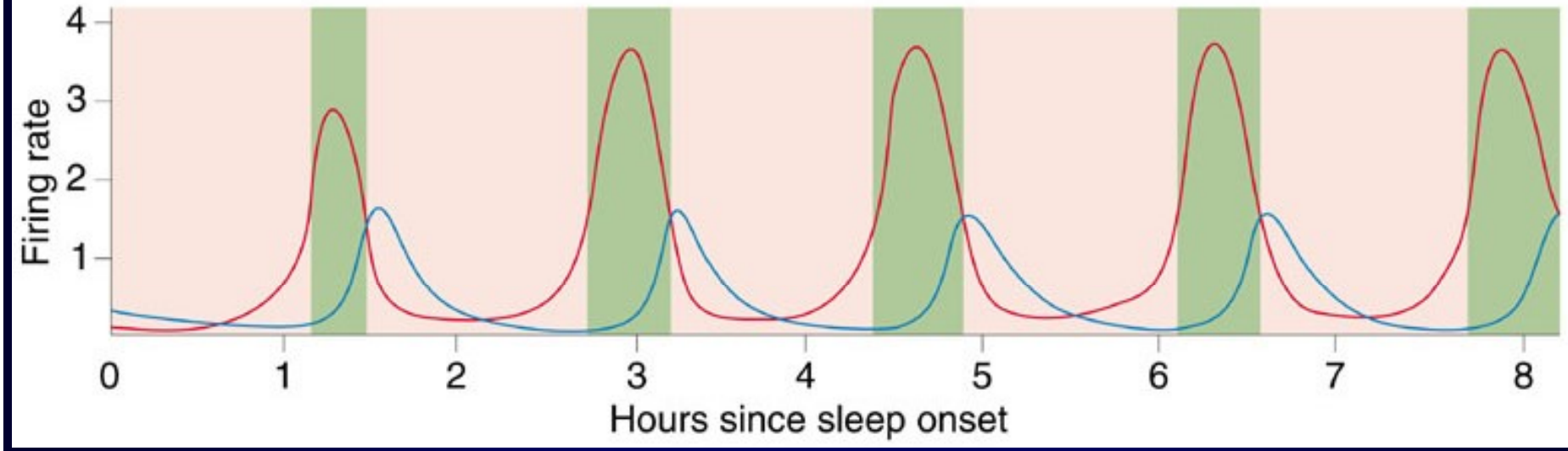


Stage	Waveform	Characteristic wave	% total sleep time	Associated with
Waking		Beta waves Alpha waves	-	Awake, vigilant, eyes open Relaxed, eyes closed
Stage 1		Alpha waves Vertex Spike Theta waves	5-10%	Drowsiness, decrease in heart rate, decreased muscle tension
Stage 2		Theta waves Sleep spindles K-complex	45-50%	Preconscious state upon waking and just before falling asleep Dreaming characterised by 'thinking'
Stage 3		Delta waves	(8%)	Profound relaxation & deep sleep
Stage 4		Delta waves	(12%)	Profound relaxation & deep sleep
REM			5->60 min (20%)	Dreaming characterised by imagery

PET images of the waking and sleeping human brain. (a) These images show brain activity in three horizontal sections in which color represents changes in activity between REM sleep and waking (yellow and red areas are more active during REM sleep). The dark notch at the bottom (posterior) edge of the sections indicates that striate cortex is equally active in the two states. (b) In these three horizontal sections, REM sleep is compared with non-REM sleep (SWS). In REM, striate cortex is less active. (Source: Braun et al., 1998, Fig. 1.)

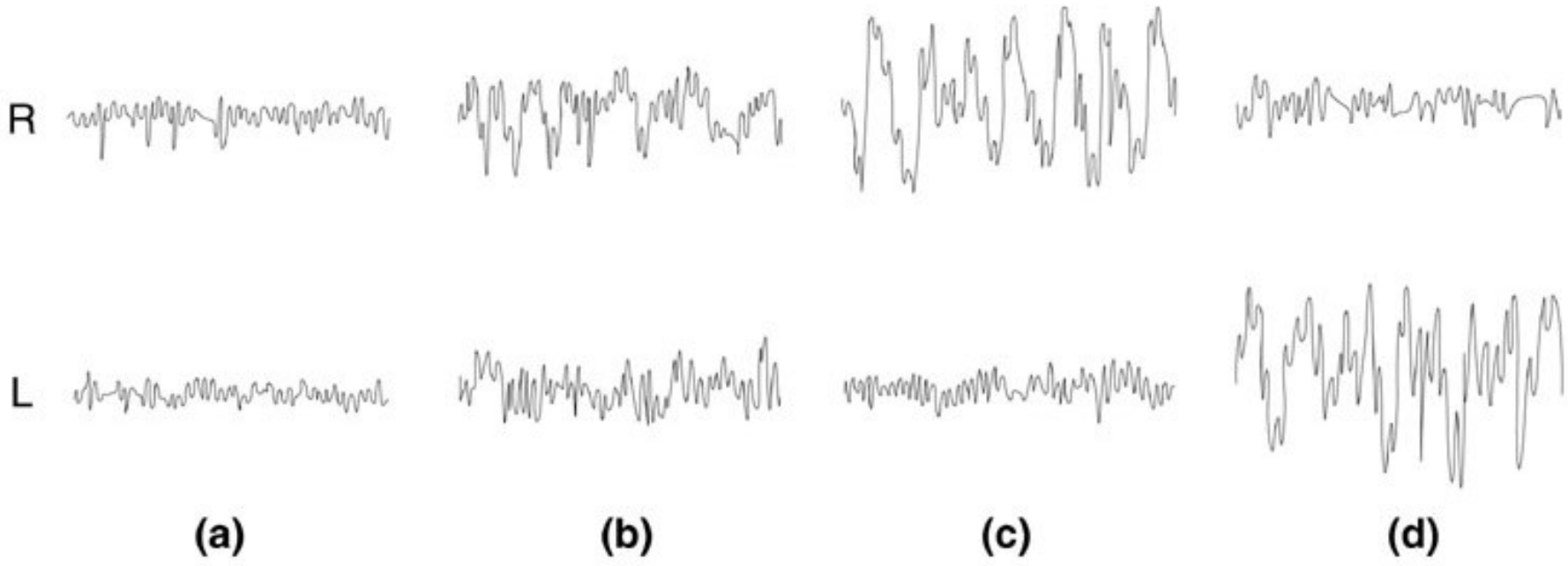


Control of the onset and offset of REM periods by brain stem neurons. This graph shows the relative firing rates of REM-associated neurons during a single night. Periods of REM sleep are green. REM-on cells are cholinergic neurons of the pons, and they increase their firing rates just before the onset of REM sleep (red line). REM-off cells are noradrenergic and serotonergic neurons of the locus coeruleus and raphe nuclei, respectively, and their firing rates increase just before the end of REM sleep (blue line). (Source: McCarley and Massaquoi, 1986, Fig. 4B.)



- Green: Periods of REM sleep.
- Red line: REM-on cells are cholinergic neurons of the Pons, they increase their firing rates just before the onset of REM sleep.
- Blue line: REM-off cells are nonadrenergic and seratonergic neurons of the Locus coeruleus and raphe nuclei, respectively, and their firing rates increase just before the end of REM sleep.

Sleep in the bottlenose dolphin. These EEG patterns were recorded from the right (R) and left (L) hemispheres. (a) High-frequency activity on both sides during alert wakefulness. (b) Low-amplitude delta rhythms of an intermediate sleep stage on the right side and, to some extent, on the left. (c) Large delta rhythms of deep sleep only on the right side, with fast activation on the left. (d) The patterns shift to opposite hemispheres some time later. (Source: Mukhametov, 1984, Fig. 1.)



Functions of Sleep

- Restoration theory - body wears out during the day and sleep is necessary to put it back in shape
- Preservation and protection theory - sleep emerged in evolution to preserve energy and protect during the time of day when there is little value and considerable danger

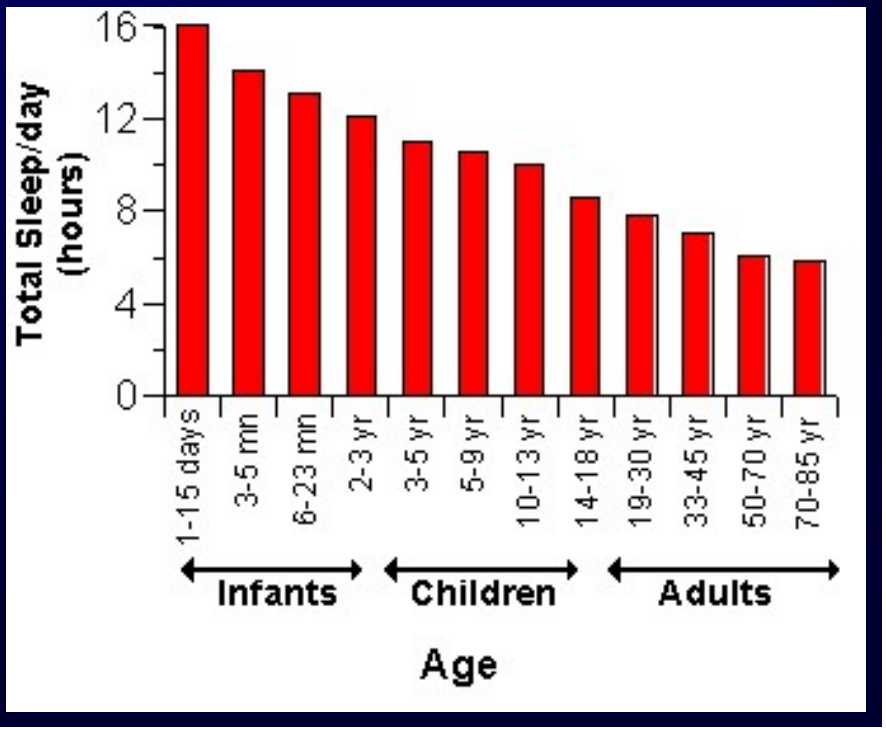
Sleep Disorders

- Somnambulism - sleepwalking
- Nightmares - frightening dreams that wake a sleeper from REM
- Night terrors - sudden arousal from sleep and intense fear accompanied by physiological reactions (e.g., rapid heart rate, perspiration) that occur during slow-wave sleep
- Narcolepsy - overpowering urge to fall asleep that may occur while talking or standing up
- Sleep apnea - failure to breathe when asleep

How much sleep is required?

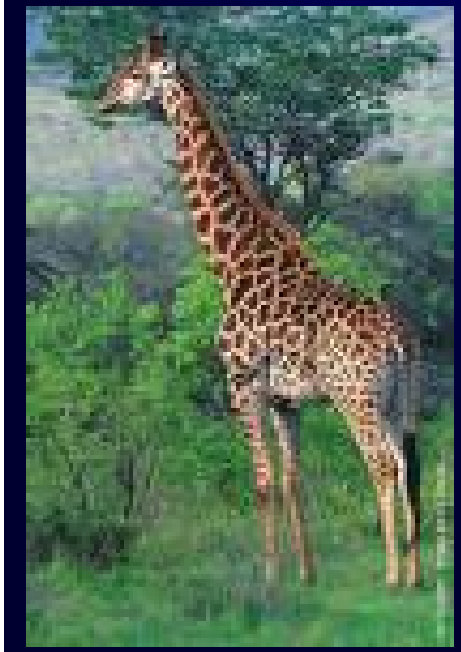
- There is no set amount of time that everyone needs to sleep, since it varies from person to person. Results from the sleep profiler indicate that people like to sleep anywhere between 5 and 11 hours, with the average being 7.75 hours

- How long people sleep a day on average:



Animal Sleep

- Animals, like humans also have a required certain amount of sleep:



SPECIES	Average total sleep time per day
Python	18 hours
Tiger	15.8 hours
Cat	12.1 hours
Chimpanzee	9.7 hours
Sheep	3.8 hours
African Elephant	3.3 hours
Giraffe	1.9 hours

Brain Structures in Arousal & Sleep

Brain Structure	Brain Area	Neurotransmitter	Behavioural Effect
Basal forebrain	Cerebral cortex	2 transmitters: ACh	Excites the thalamus and cortex, switches sleep from NREM to REM
		GABA	Inhibits thalamus and cortex
Pontomesence-phalon	Reticular system, brain stem	ACh, glutamate	Increases cortical arousal
Dorsal raphe and pons	Brain stem	5-HT	Interrupts REM sleep
Locus coeruleus	Brain stem	NE	Suppresses REM sleep; increases information storage during wakefulness
Hypothalamus	Midbrain	Histamine	Increases arousal

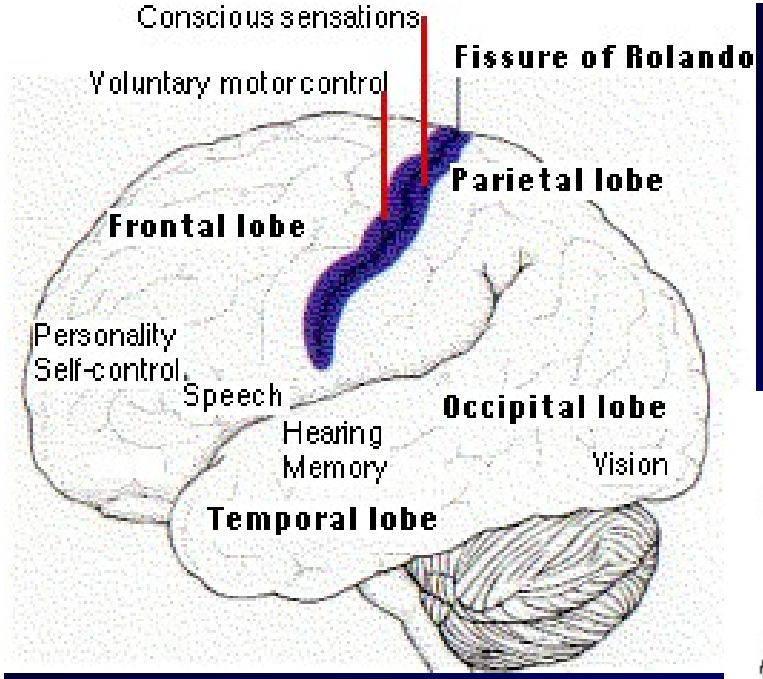
Kalat (2004). *Biopsychology*

Sleep-Antagonists

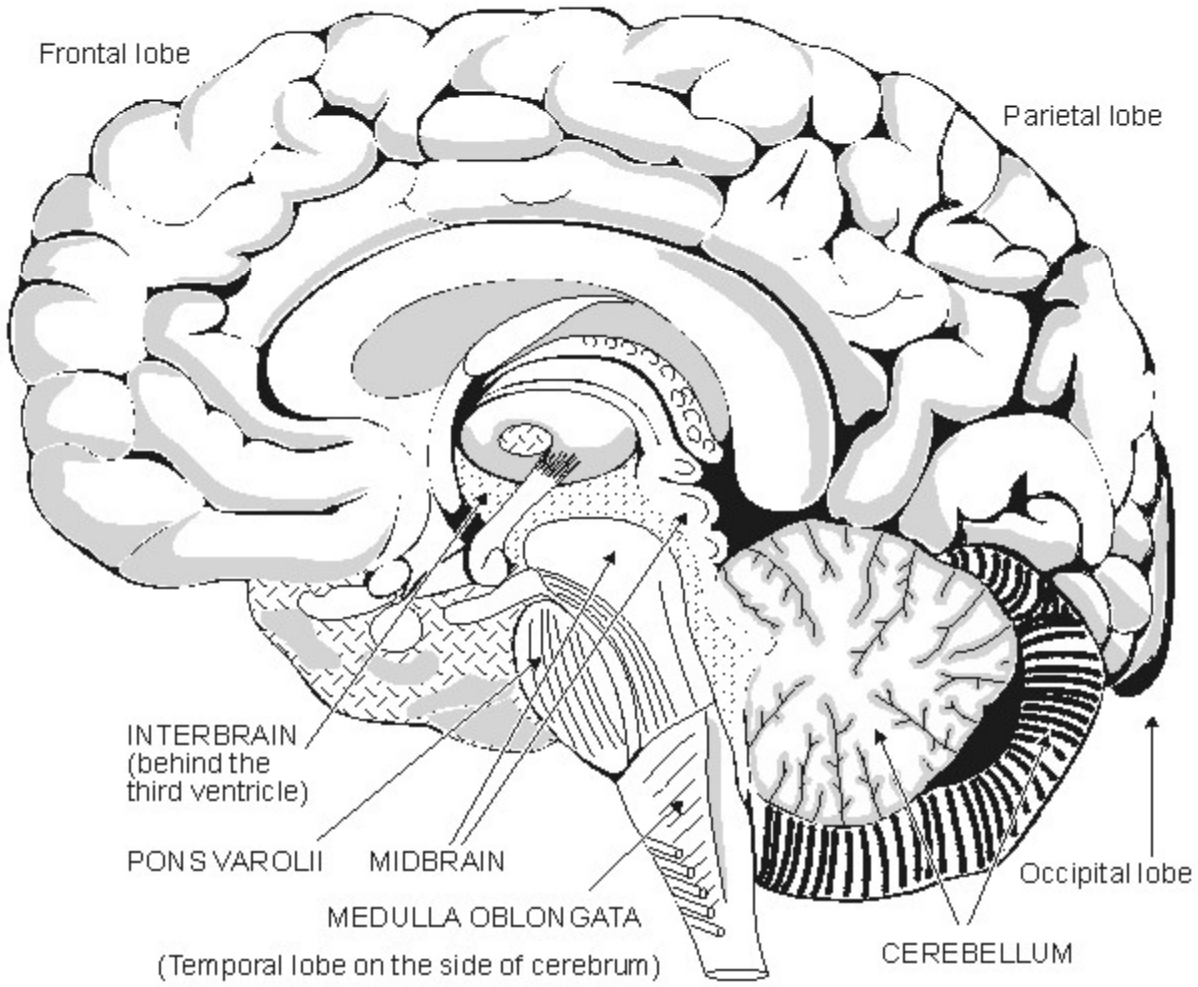
- Raphe nucleus
- Locus coeruleus
- Tuberomamillary nucleus
- Perifornical lateral hypothalamus

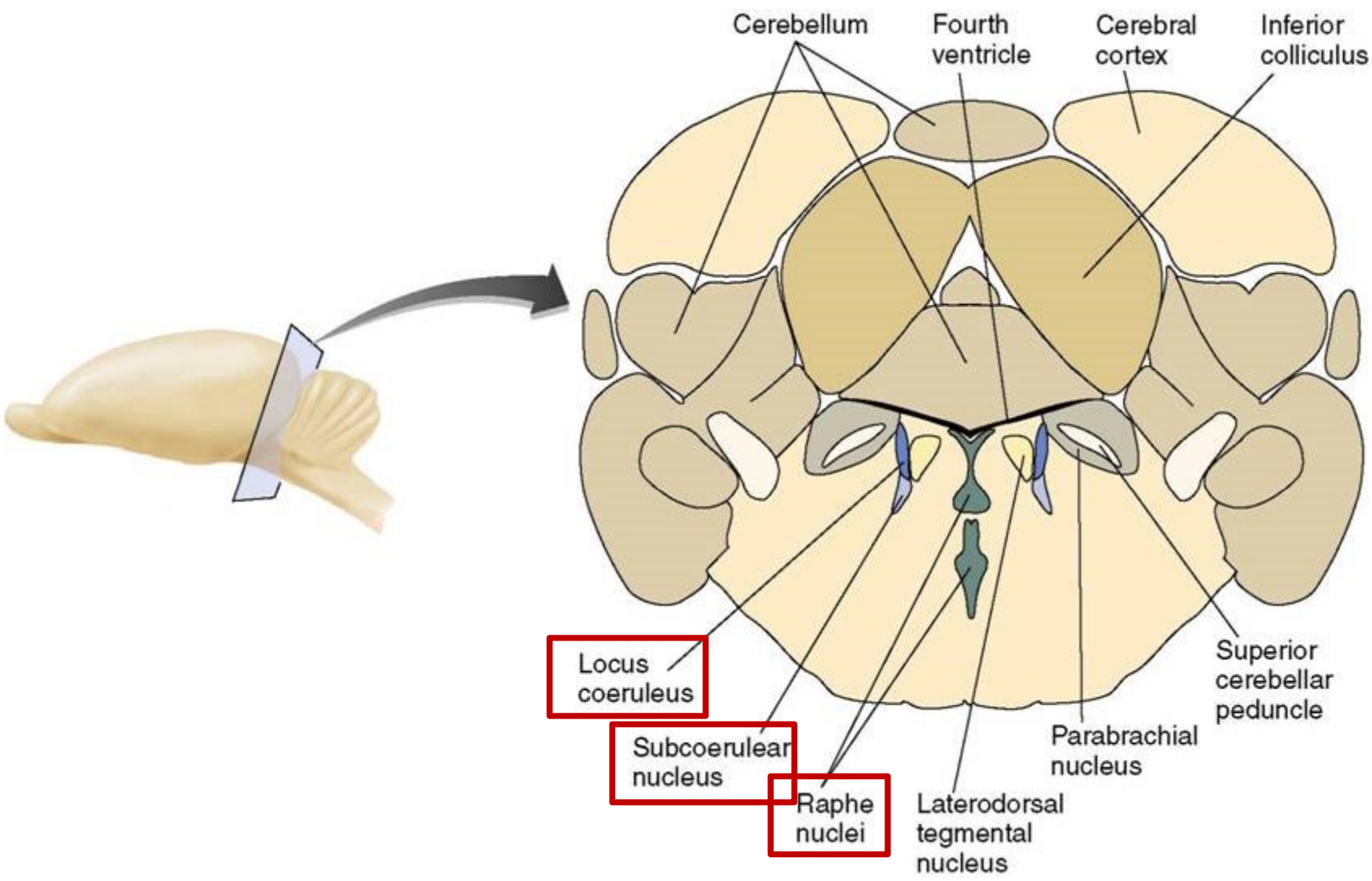
Sleep-Agonists

- Pineal gland – Melatonin
- Pre-optic Area (POA)
- Pre-optic Area (POA): Median Pre-optic nucleus
- Pre-optic Area (POA): Ventrolateral Pre-optic nucleus
- Thalamus


Conscious sensations
Fissure of Rolando
Voluntary motor control
Parietal lobe
Frontal lobe
Personality
Self-control
Speech
Occipital lobe
Hearing
Memory
Vision
Temporal lobe

CEREBRUM


Frontal lobe
Parietal lobe
INTERBRAIN
(behind the
third ventricle)
PONS VAROLII
MIDBRAIN
Occipital lobe
MEDULLA OBLONGATA
(Temporal lobe on the side of cerebrum)
CEREBELLUM



- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Arousal
  - Acetylcholine:
    - One of the most important neurotransmitters involved in arousal.
    - Two groups of acetylcholinergic neurons located in the pons and basal forebrain, produce activation and cortical desynchrony when they are stimulated

A

- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Arousal

  - Norepinephrine:

    Locus ceoruleus:

    - A dark-colored group of noradrenergic cell bodies located in the pons near the rostral end of the floor of the fourth ventricle; involved in arousal and vigilance.

- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Arousal

  - Serotonin (5-HT):
    - Appears to play a role in activating behavior; almost all of the brain's serotonergic neurons are found in the raphe nucleus, located in the medullary and pontine regions of the brain.

  - Raphe nucleus:
    - A group of nuclei located in the reticular formation of the medulla, pons, and midbrain, situated along the midline; contain serotonergic neurons.

- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Arousal

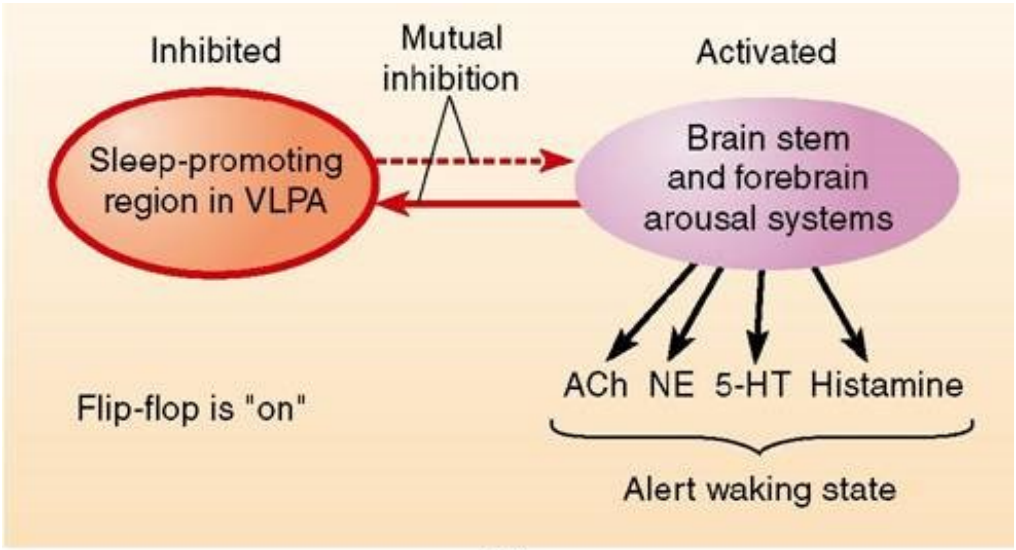
  - Histamine: S
    - A neurotransmitter implicated in control of wakefulness and arousal; a compound synthesized from histidine, an amino acid. Antihistamines block H1 receptors and promote drowsiness.
  - Tuberomammillary nucleus: A
    - A nucleus in the ventral posterior hypothalamus, just rostral to the mammillary bodies; contains histaminergic neurons involved in cortical activation and behavioral arousal.

- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Arousal

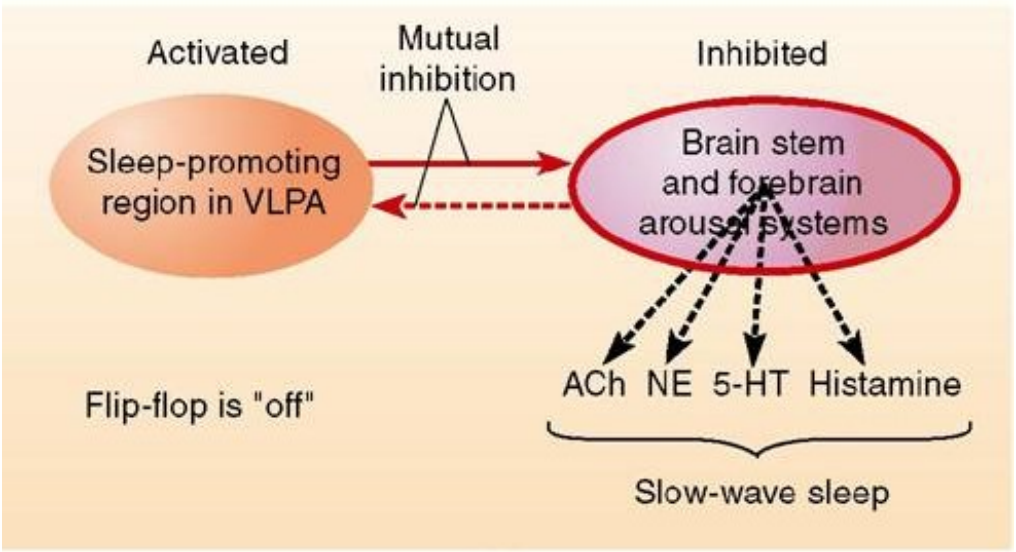
  - Hypocretin:
    - A peptide also known as orexin, produced by neurons whose cell bodies are located in the lateral hypothalamus; their destruction causes narcolepsy and difficulty in sleeping for extended time.

    - Involved in regulating the sleep on/off cells in the ventro lateral preoptic area (VLPA).

- Physiological Mechanisms of Sleep and Waking
  - Neural Control of Slow-Wave Sleep
  - Ventrolateral preoptic area (VLPA): S
    - A group of GABAergic neurons in the preoptic area whose activity suppresses alertness and behavioral arousal and promotes sleep.
    - Destruction of this area has been reported to result in total insomnia, coma, and eventual death in rats.



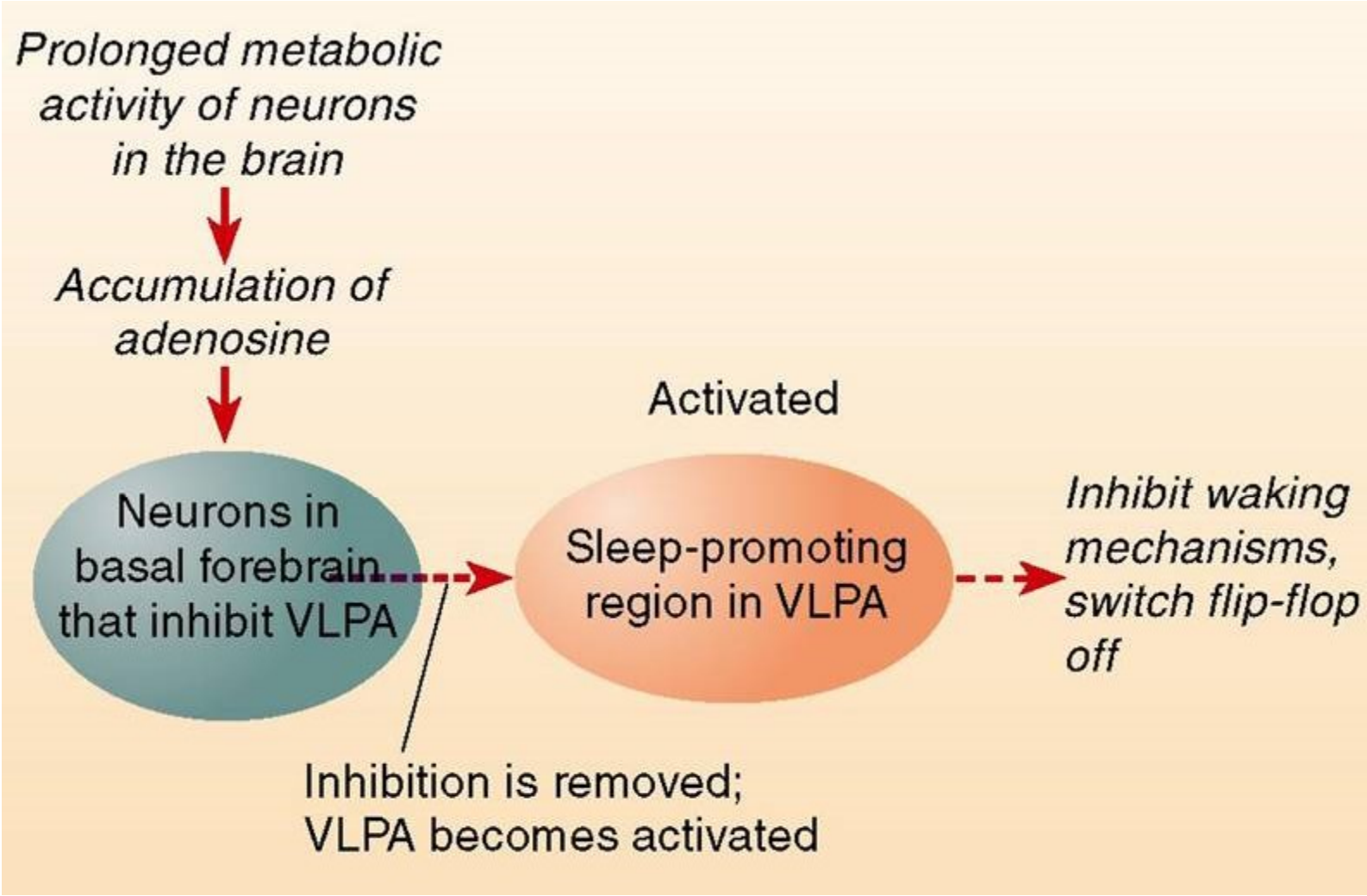
(a)



(b)

Physiological Mechanisms of Sleep and Waking

- Adenosine
  - Inhibitory neuromodulator
  - Increases during prolonged periods of wakefulness, decreases after sleep
  - Inhibited by caffeine
  - Inhibits ACh neurons in forebrain
  - Release inhibition (disinhibition) of histimine neurons in tuberomammilary nucleus, thus promote sleep.



- Physiological Mechanisms of Sleep and Waking
  - Neural Control of REM sleep
  - PGO wave (Pontine, Geniculate, Occipital):
    - Bursts of phasic electrical activity originating in the pons (parabracial area), followed by activity in the lateral geniculate nucleus (LGN) and visual cortex, a characteristic of REM sleep.

- Physiological Mechanisms of Sleep and Waking
  - The Executive Mechanism
  - Peribrachial area:
    - The region located in the dorsolateral pons; contains acetylcholinergic neurons involved in the initiation of REM sleep.
  - Carbachol:
    - A drug that stimulates acetylcholine receptors (ACh agonist).
    - Injections into pons induce REM sleep.

- Physiological Mechanisms of Sleep and Waking
  - The Executive Mechanism
  - Medial pontine reticular formation (MPRF):
    - A region that contains neurons involved in the initiation of REM sleep; activated by acetylcholinergic neurons of the peribrachial area.
  - Magnocellular nucleus:
    - A nucleus in the medulla; involved in the atonia (muscular paralysis) that accompanies REM sleep.

- Biological Clocks
  - Circadian Rhythms and Zeitgebers
  - Circadian rhythm:
    - A daily rhythmical change in behavior or physiological process.
  - Zeitgeber:
    - A stimulus (usually the light of dawn) that resets the biological clock responsible for circadian rhythms.
    - Artificial light will also work

Biological Clocks

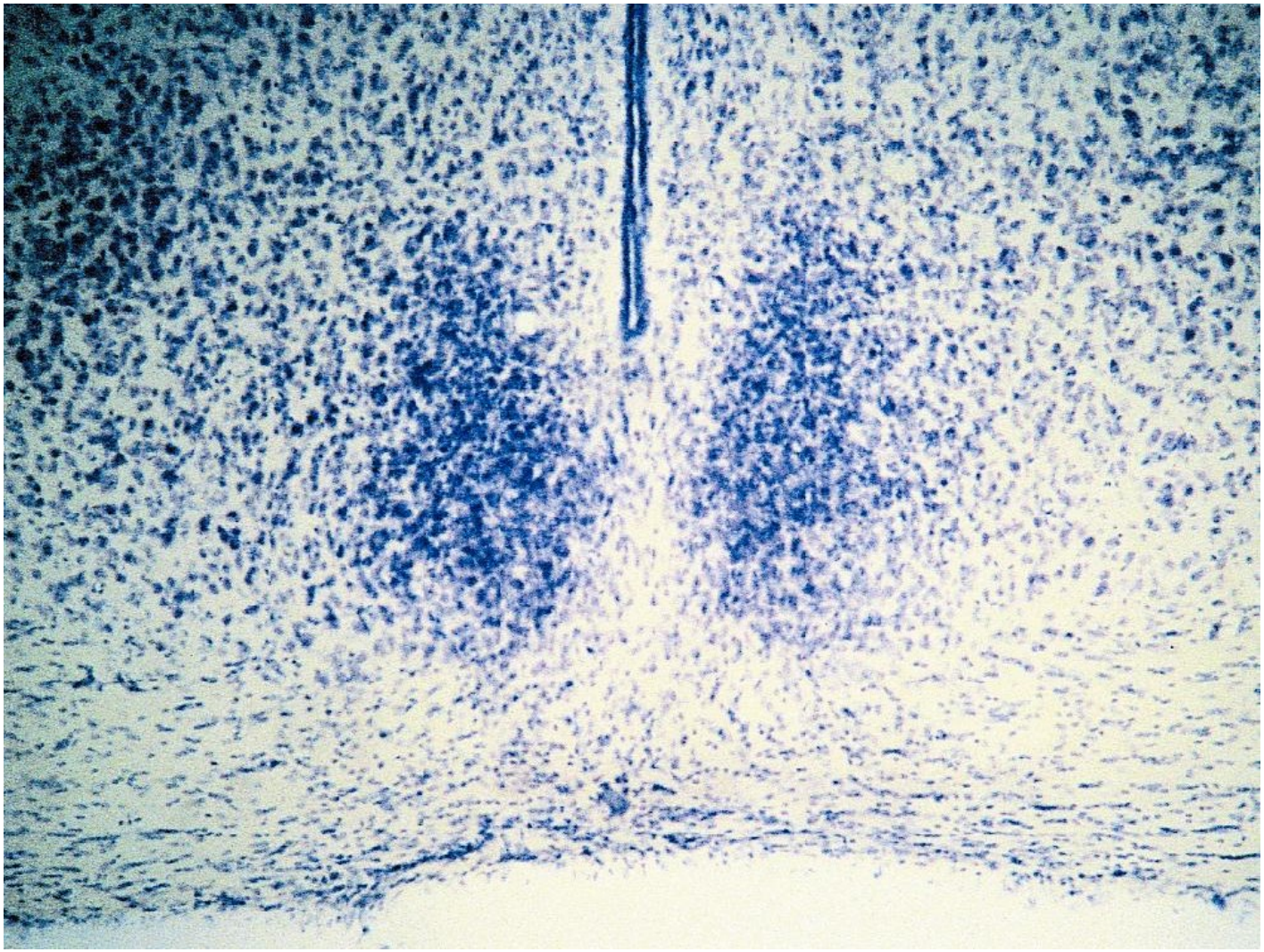
- 12 light/dark cycle
  - With 12 hour l/d cycles circadian rhythms synchronize with light.
    - -activity
    - -hormonal secretion
    - -feeding/drinking
- Constant light
  - Free running
  - 25 hour day

- Biological Clocks
  - The Suprachiasmatic Nucleus

  - Suprachiasmatic nucleus:
    - A nucleus situated atop the optic chiasm. It contains a biological clock responsible for organizing many of the body's circadian rhythms.
    - Lesions disrupt rhythms, transplants restore them!
    - Communication is chemical, not synaptic
  - Melanopsin:
    - A photopigment present in ganglion cells in the retina whose axons transmit information to the SCN, the thalamus, and the olivary pretectal nucleus.
    - Rods and cones are independent of this process

- Biological Clocks
  - The Suprachiasmatic Nucleus
    - Individual SCN neurons behave like clocks

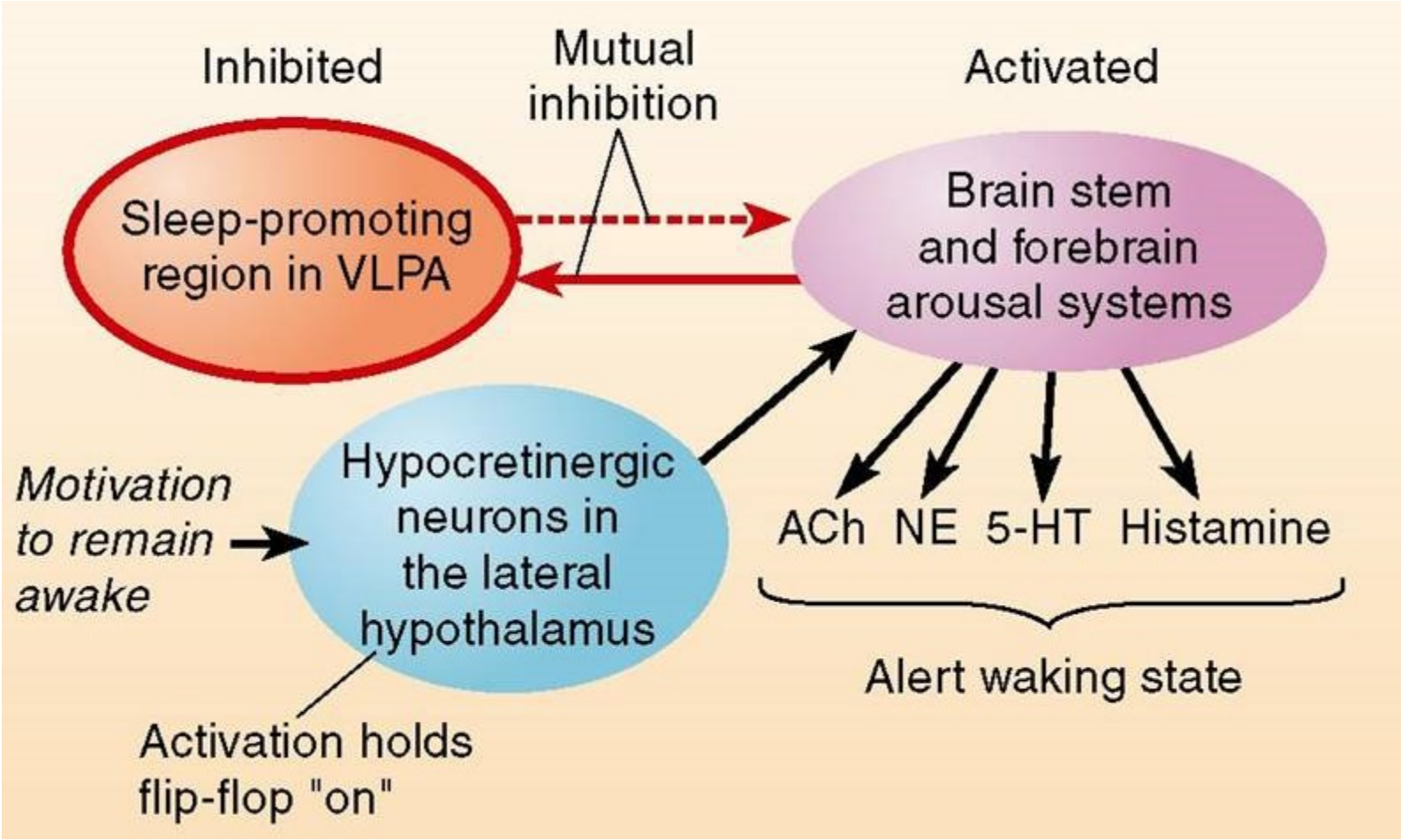
      Cells in culture keep different times if on different cycles
    - Protein synthesis is the clock mechanism
  - Intergeniculate leaflet (IGL):
    - A part of the lateral geniculate nucleus that receives information from the retina and projects to the SCN; terminals release neuropeptide Y at the SCN.
    - IGL stimulation of the SCN also resets circadian rhythms
    - IGL mediates the effects of non-light zeitgebers (noise, temperature)

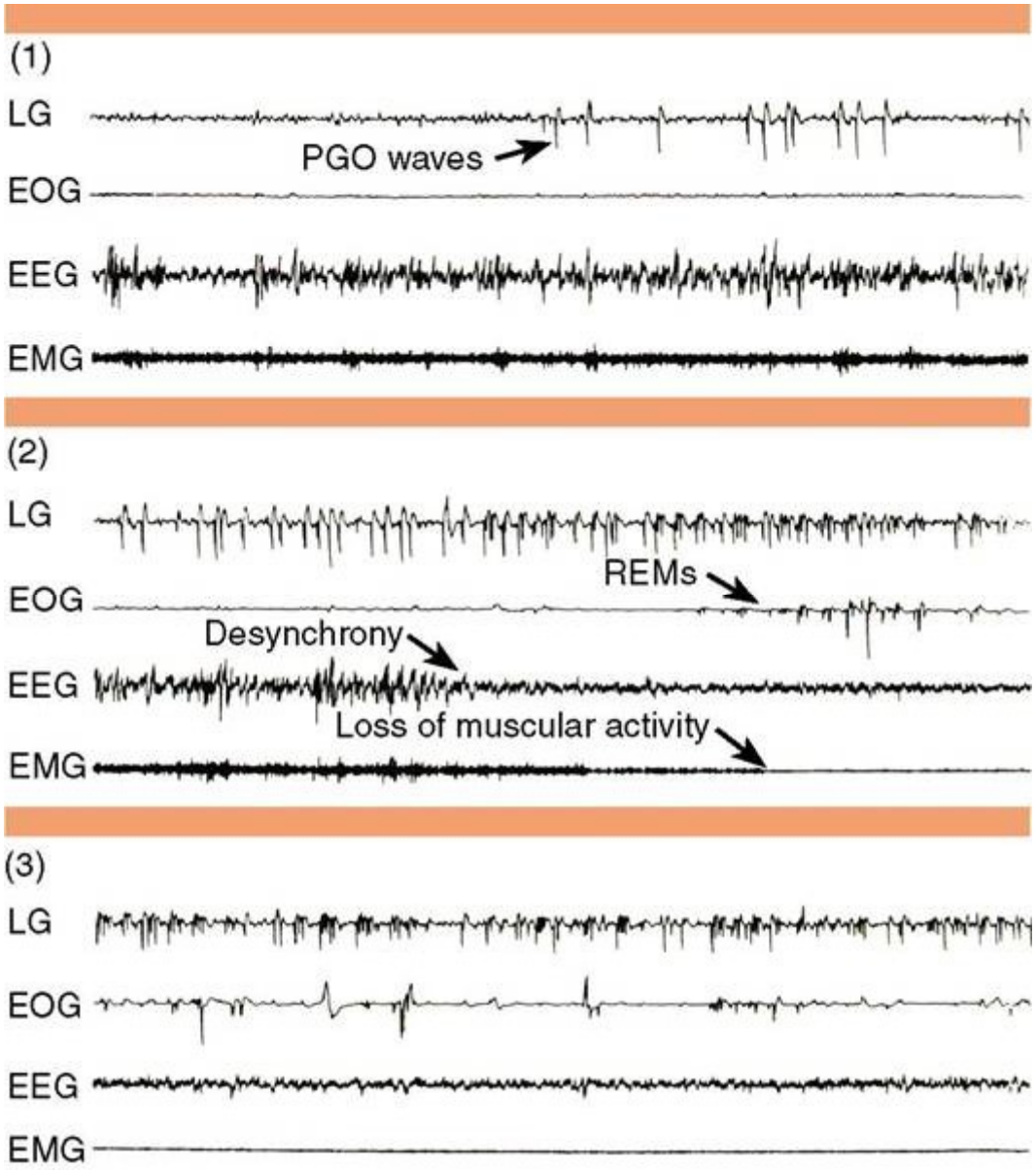


- Biological Clocks
  - Control of Seasonal Rhythms
  - Familial advanced sleep phase syndrome:
    - A 4-hour advance in rhythms of sleep and temperature cycles, caused by mutation of a gene involved in the rhythmicity of neurons of the SCN.
    - Evidence of genetic control over clock
    - Other evidence from “clock” genes in drosophila
  - Pineal gland:
    - A gland attached to the dorsal tectum; produces melatonin and plays a role in circadian and seasonal rhythms.
    - Innervated by the SCN via the paraventricular nucleus and the spinal cord.
    - Pineal lesions disrupt seasonal rhythms

- Biological Clocks
  - Control of Seasonal Rhythms

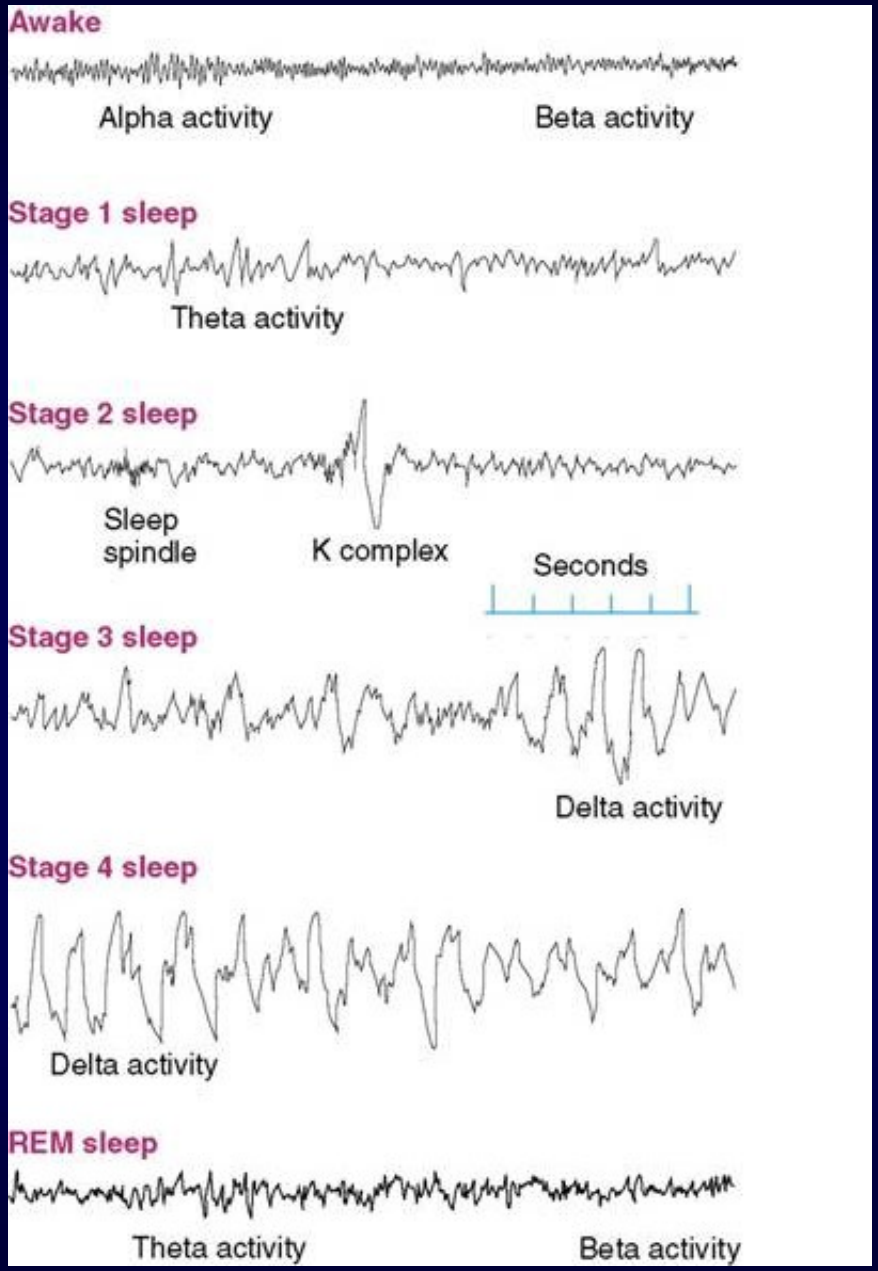
  - Melatonin:
    - A hormone secreted during the night by the pineal body; plays a role in circadian and seasonal rhythms.
    - Highest levels in humans at bedtime
    - Jet-Lag, or disruptions in sleep/wake cycle, can be restored with melatonin.
    - Does not increase sleep time, but does advance circadian phase of sleep (eg., when traveling east)





- A Physiological and Behavioral Description
  - Stages of Sleep
    Measured by EEG
  - Alpha activity:
    - A smooth electrical activity of 8 – 12 Hz recorded from the brain; generally associated with a state of relaxation or meditation.
  - Beta activity:
    - Irregular electrical activity of 13 – 30 Hz recorded from the brain; generally associated with a state of arousal.

- A Physiological and Behavioral Description
  - Stages of Sleep
  - Theta activity:
    - EEG activity of 3.5 – 7.5 Hz that occurs intermittently during early stages of slow wave sleep and REM sleep.
  - Delta activity:
    - Regular, synchronous electrical activity of less than 4 Hz recorded from the brain; occurs during the deepest stages of slow-wave sleep.



Sleep

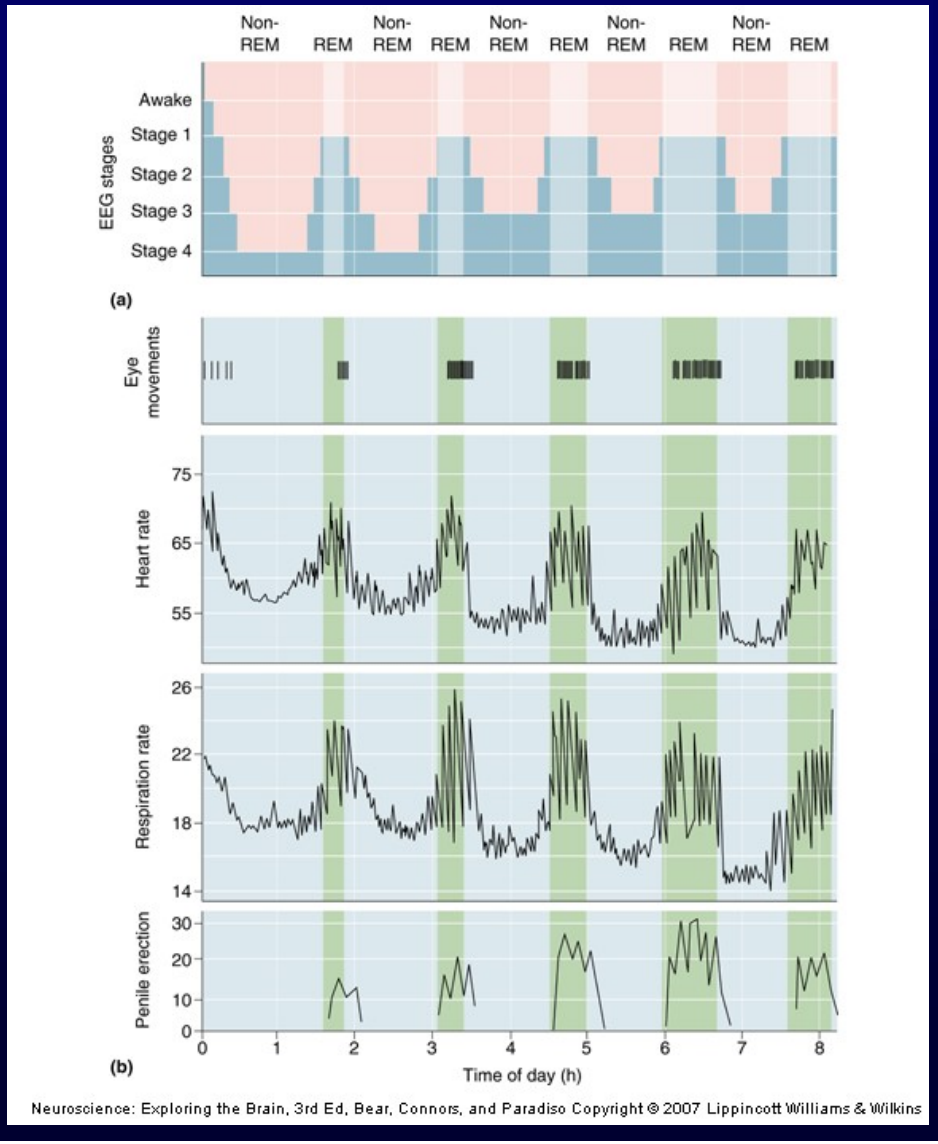
- The Functional States of the Brain

Table 19.1 **Characteristics of the Three Functional States of the Brain**

BEHAVIOR	AWAKE	NON-REM SLEEP	REM SLEEP
EEG	Low voltage, fast	High voltage, slow	Low voltage, fast
Sensation	Vivid, externally generated	Dull or absent	Vivid, internally generated
Thought	Logical, progressive	Logical, repetitive	Vivid, illogical, bizarre
Movement	Continuous, voluntary	Occasional, involuntary	Muscle paralysis; movement commanded by the brain but not carried out
Rapid eye movement	Often	Rare	Often

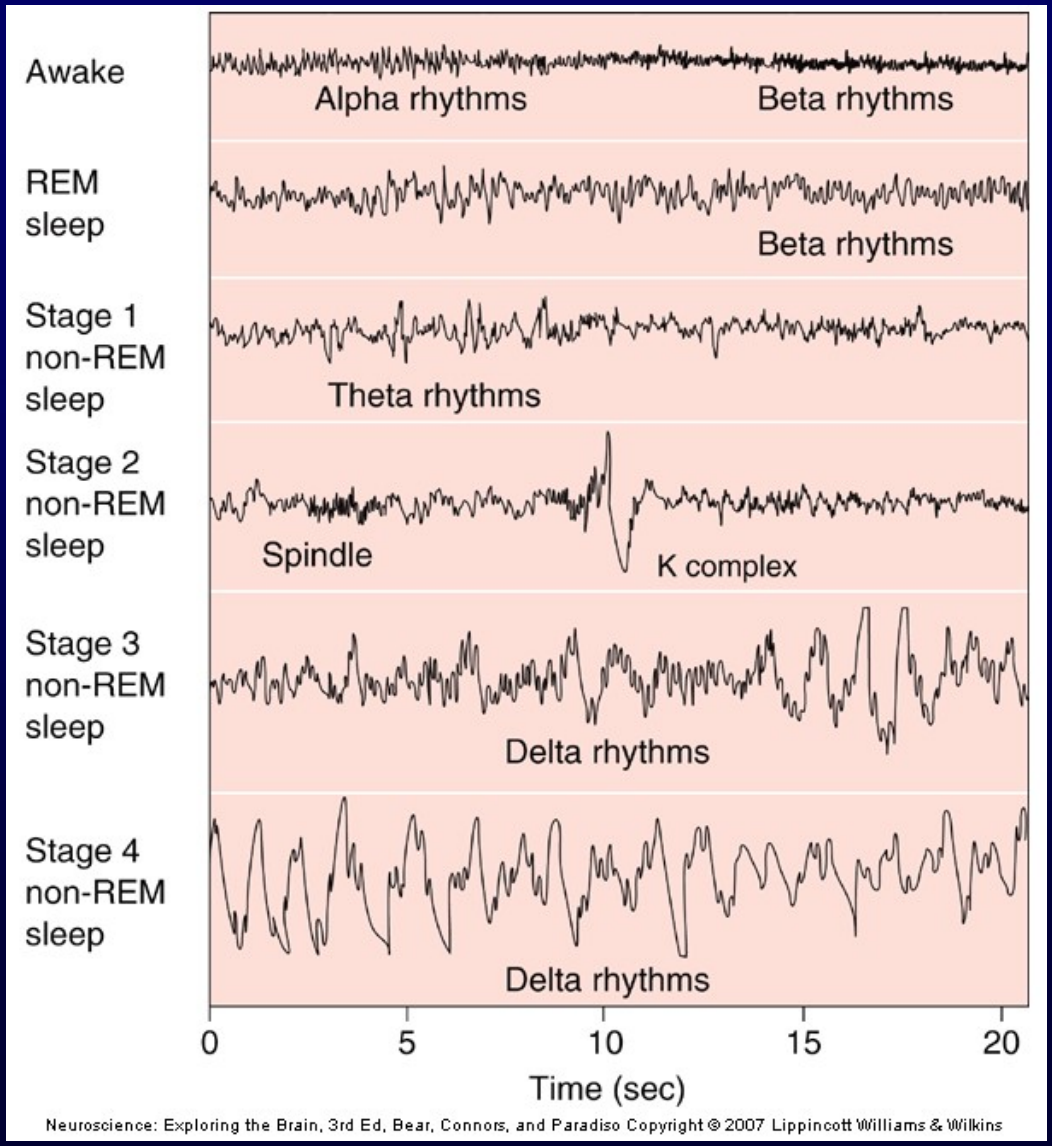
Sleep

- Physiological changes during non-REM and REM sleep



Sleep

- The Sleep Cycle



Sleep

- Why Do We Sleep?
  - Sleep
    - Mammals, birds, reptiles
    - Recovery time for brain
  - Theories of restoration
    - Restoration: Sleep to rest and recover, and prepare to be awake again
  - Theories of adaptation
      - Adaptation: Sleep to keep out of trouble, hide from predators

Sleep

- Functions of Dreaming and REM Sleep
  - Body requires REM sleep
  - Sigmund Freud: Dream functions- Wish-fulfillment, conquer anxieties
  - Allan Hobson and Robert McCarley: Activation-synthesis hypothesis
  - Avi Karni: Certain memories require strengthening period→ REM sleep

Sleep

- Neural Mechanisms of Sleep
  - Basic Principles
    - Critical neurons→ Diffuse modulatory neurotransmitter systems
    - Noradrenergic and serotoninergic neurons: Fire during and enhance waking state
    - Cholinergic neurons: enhance REM events; active during waking
    - Diffuse modulatory system control rhythmic behaviors of thalamus→ controls cortical EEG→ sensory input flow to cortex blocked by slowed thalamic rhythms
    - Activity in descending branches of diffuse modulatory systems (e.g., inhibitory neurons)

Sleep

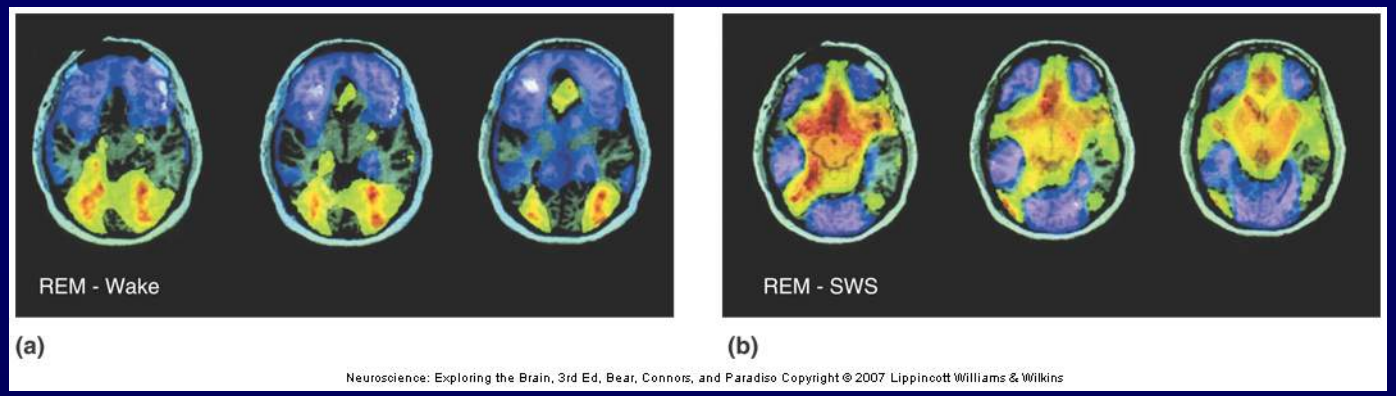
- Wakefulness and the Ascending Reticular Activating System
  - Giuseppe Moruzzi:
    - Lesions in midline structure of brain: State similar to non-REM sleep
    - Lesions in lateral tegmentum: Does not cause non-REM state sleep
    - Electrical stimulation of midline tegmentum of midbrain: Cortex moved from slow, rhythmic EEGs of non-REM sleep to alert and aroused state

Sleep

- Falling Asleep and Non-REM State
  - Sleep: Progression of changes ending in non-REM state
  - Non-REM sleep: Decrease in firing rates of most brain stem modulatory neurons using NE, 5-HT, ACh
  - Stages of non-REM sleep:
    - EEG sleep spindles
    - Spindles disappear
    - Replaced by slow, delta rhythms (less than 4 Hz)

Sleep

- Mechanisms of REM Sleep



- Control of REM sleep
  - Diffuse modulatory systems→ Pons
    - Decreased firing of neurons in locus coeruleus and raphe nuclei→ Concurrent sharp increase in ACh neuron activity
  - REM sleep behavior disorder: Act out dreams

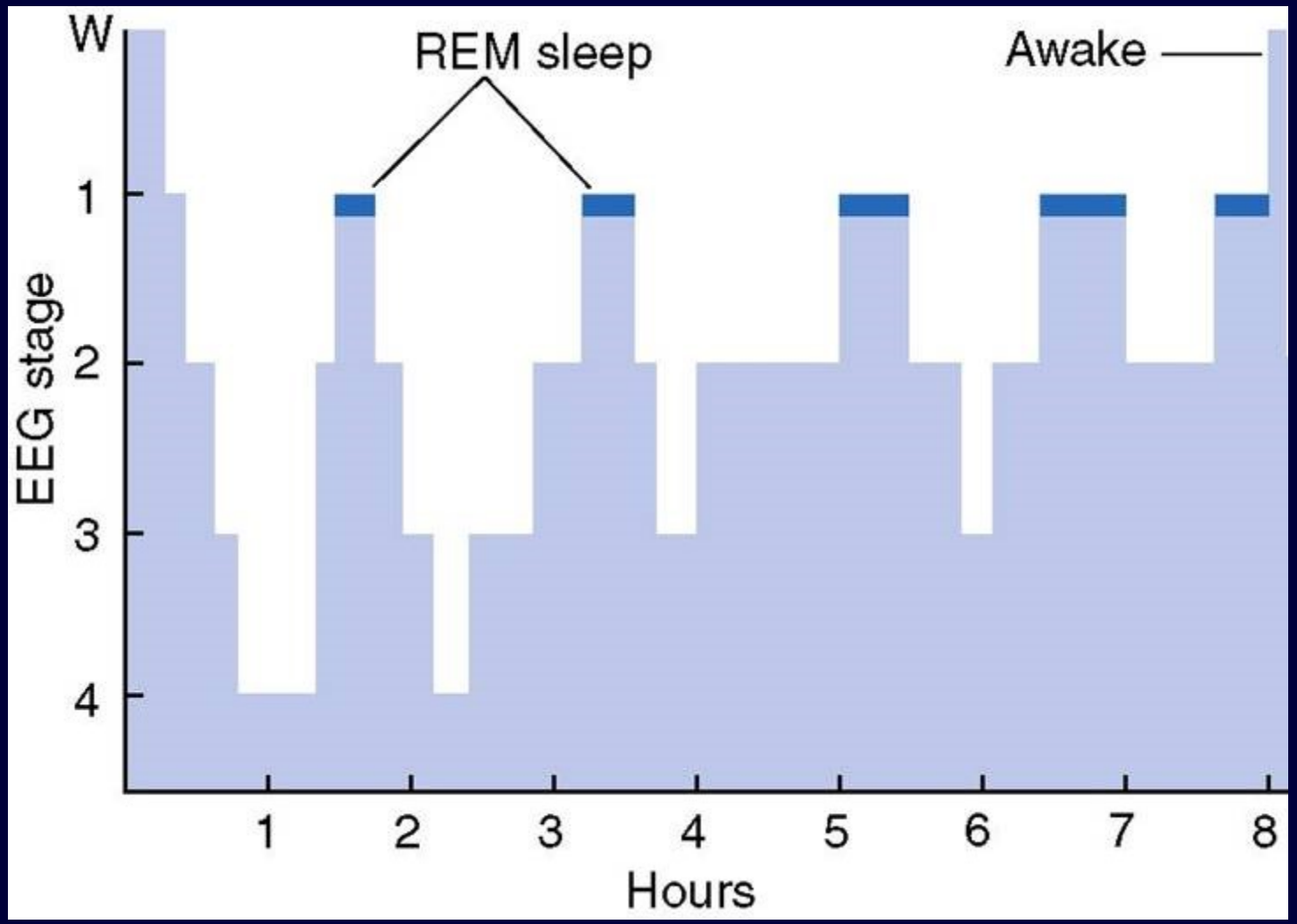
Sleep

- Sleep-Promoting Factors
  - Muramyl dipeptide: isolated from the CSF of sleep-deprived goats, facilitates non-REM sleep
  - Interleukin-1: Synthesized in brain (glia, macrophages), stimulates immune system
  - Adenosine: Sleep promoting factor; released by neurons; may have inhibitory effects of diffuse modulatory systems
  - Melatonin: Produced by pineal gland, released at night-inhibited during the day (circadian regulation); initiates and maintain sleep; treat symptoms of jet lag and insomnia

Sleep

- Gene Expression During Sleeping and Waking
  - Cirelli and Tononi: Comparison of gene expression in brains of awake and sleeping rats
  - 0.5% of genes showed differences of expression levels in two states
  - Increased in awake rats
    - Intermediate early genes
    - Mitochondrial genes
  - Increased in sleeping rats: protein synthesis- and plasticity-related genes
  - Changes specific to brain not other tissues

- A Physiological and Behavioral Description
  - Stages of Sleep
  - REM sleep:
    - A period of desynchronized EEG activity during sleep, at which time dreaming, rapid eye movements, and muscular paralysis occur.
    - Decreased blood flow to inferior frontal lobe associated with distortions of time.
  - Non-REM sleep:
    - All stages of sleep except REM sleep.



- Disorders of Sleep
  - Insomnia
    - Reported to affect approximately 25% of the population occasionally, and 9% regularly.
    - One of the most important causes of insomnia seems to be sleeping medication.
      Ambien acts like a benzodiazapine on GABAa receptors.
    - Insomnia is not a disease, but rather a symptom of another physical ailment or stress.

❑ Disorders of Sleep

- Sleep apnea:
  - Cessation of breathing while sleeping.
  - Increase in CO_2 results in waking
  - SIDS caused by apnea

Disorders of Sleep

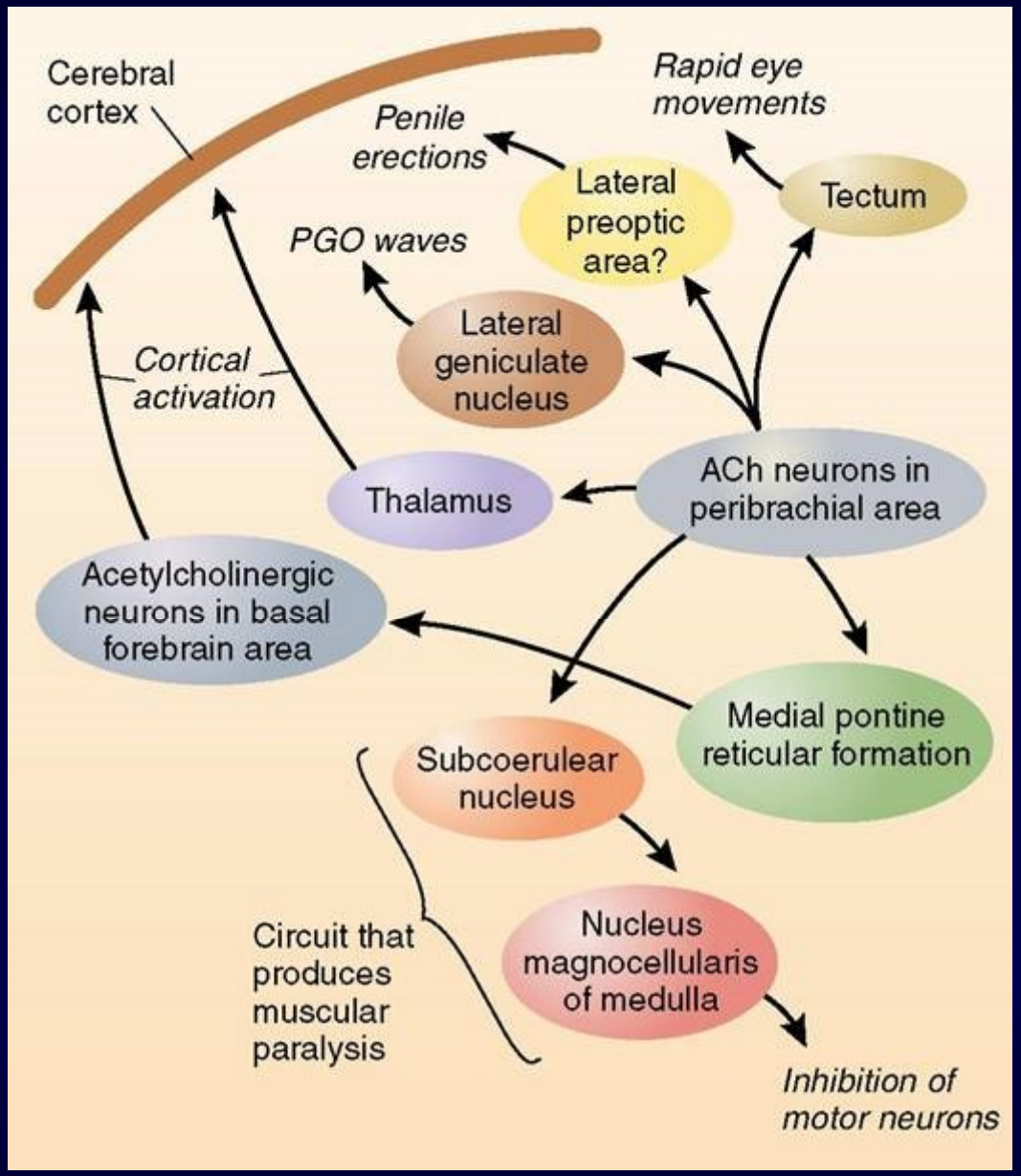
- Narcolepsy:
  - A sleep disorder characterized by periods of irresistible sleep, attacks of cataplexy, sleep paralysis, and hypnagogic hallucinations (dreaming while awake and paralyzed)
- Sleep attack:
  - A symptom of narcolepsy; an irresistible urge to sleep during the day, after which the person awakes feeling refreshed.

- Disorders of Sleep
  - Narcolepsy
  - Cataplexy:
    - A symptom of narcolepsy; complete paralysis that occurs during waking.
  - Sleep paralysis:
    - A symptom of narcolepsy; paralysis occurring just before a person falls asleep.

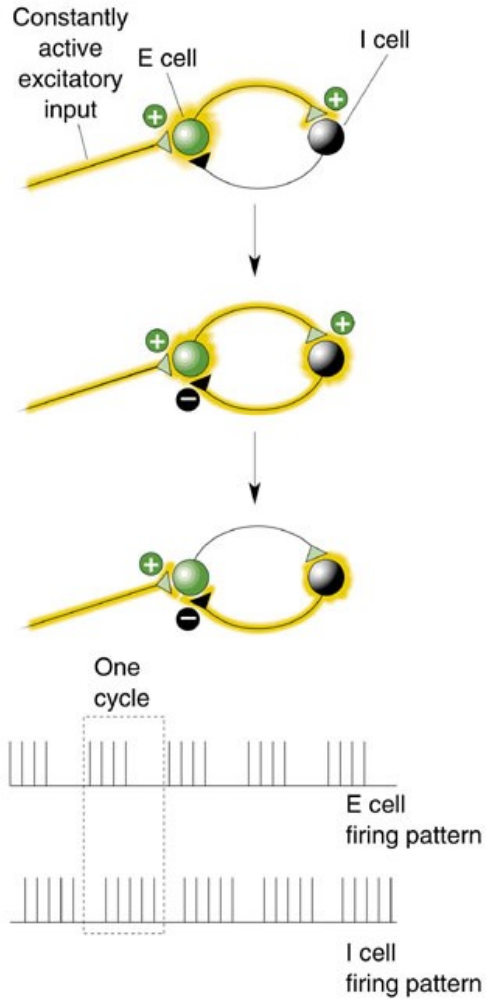
Disorders of Sleep

- Sleep Terrors
  - Emerge from Stage 3-4 sleep
  - Autonomic arousal is interpreted as fear
  - Arousal is abrupt
- Nightmares
  - Occurs in REM sleep
  - Easy to arouse
  - Less intense than sleep terrors
- Sleep Walking (somnambulism)
  - Emerge out of Stage 3 and 4 sleep

- Disorders of Sleep
  - REM Behavior Disorder
    - A rare neurological disorder in which a person does not become paralyzed during REM sleep, and thus acts out dreams.
    - Experiments with cats. Lesions to magnocellular nucleus in the medial medulla near LC. Form inhibitory synapses with motor neurons.



A two-neuron oscillator. One excitatory cell (E cell) and one inhibitory cell (I cell) synapse upon each other. As long as there is a constant excitatory drive, which does not have to be rhythmic, onto the E cell, activity tends to trade back and forth between the two neurons. One activity cycle through the network generates the pattern of firing shown in the box.



Modulating thalamic and cortical rhythmicity. In this case, either ACh or NE shifts cells from (a) an intrinsic burst-firing mode to (b) a single-spiking mode. This may be what happens during transitions from non-REM sleep to the waking state.
(Source: Steriade et al., 1993, Fig. 5D.)