

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.

Norepinephrine:

Locus coeruleus:

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.

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.

Histamine:

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 nucleus in the ventral posterior hypothalamus, just rostral to the mammillary bodies; contains histaminergic neurons involved in cortical activation and behavioral 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.

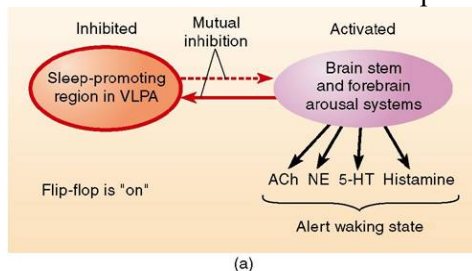
Involved in regulating the sleep on/off cells in the ventro lateral preoptic area (VLPA).

Neural Control of Slow-Wave Sleep

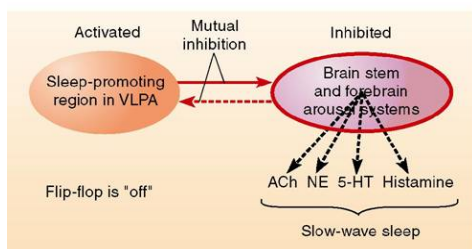
Ventrolateral preoptic area (VLPA):

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)

Adenosine

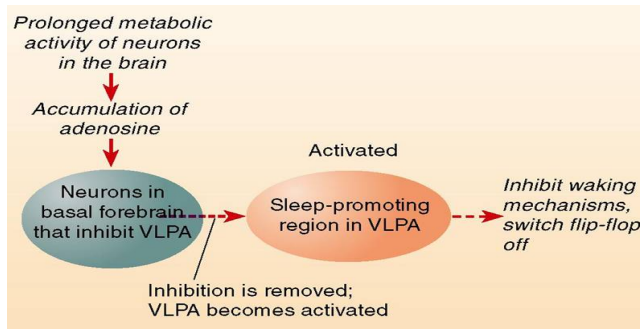
Inhibitory neuromodulator

Increases during prolonged periods of wakefulness, decreases after sleep

Inhibited by caffeine

Inhibits ACh neurons in forebrain

Release inhibition (disinhibition) of histamine neurons in tuberomammillary nucleus, thus promote sleep.



Neural Control of REM sleep

PGO wave (Pontine, Geniculate, Occipital):

Bursts of phasic electrical activity originating in the pons (parabrachial area), followed by activity in the lateral geniculate nucleus (LGN) and visual cortex, a characteristic of REM sleep.

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.

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.

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

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

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

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

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

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)

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

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 (e.g. when traveling east)