Control of sleep in mammals

Ronald McGregor and Jerome Siegel

Sleep in most mammals, including humans, consists of rapid eye movement (REM) and nonREM phases. Deprivation of sleep per se or of REM sleep results in a 'rebound' of the deprived states, but the amount lost is not completely recovered. Studies, mostly conducted in rodents and cats, show that neurons that are active during non REM sleep are scattered in groups from the basal forebrain to the medulla. By contrast, the pons contains neurons that are active during REM sleep and indeed this area is sufficient for REM sleep generation.

Sleep Basics

Normal human sleep is comprised of two distinct states: REM and nonREM sleep. When going to sleep, individuals usually enter the NonREM state; direct transitions from waking to REM sleep are generally seen only under pathological conditions such as narcolepsy. REM sleep usually follows nonREM sleep and the two states alternate throughout the period of sleep. Individuals can experience awakenings from either state. NonREM in humans is characterized by high-voltage cortical waves (as seen on electroencephalograms, EEG) slow, regular respiration and heart rate and a reduction in muscle tone from waking levels (as seen on electromyograms, EMG). Human REM sleep is characterized by low-voltage cortical waves, resembling those observed during wakefulness in humans, cats and dogs. In rodents, prominent cortical theta (4-10 Hz) waves are seen in REM sleep. REM sleep in all mammals is characterized by irregular respiration and heart rate, REMs, and paradoxically, by muscular tone. The basics below show EEG and EMG data from a rat.

Sleep cycle and neural correlates of the different sleep-wake states

NonREM sleep

REM sleep

Sleep cycle

AWAKE brain

REM sleep brain

The majority of cells in the midbrain, pontine and medullary reticular formation are active in both waking and REM sleep, and inactive in nonREM sleep.

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Sleep-active GABAergic neurons have been identified in the basal forebrain, anterior hypothalamus and substantia nigra, and in the paraventricular nucleus of the thalamus.

Glutamate cell groups throughout the brain are major participants in REM and nonREM sleep but are more difficult to study because they cannot easily be distinguished from surrounding neurons.

Glutamate neurons in the lateral pons fire before and during PGO waves.

Loss of muscle tone in REM sleep is linked to an activation of the GABAergic motor inhibitory system in the medulla (REM and the inactivation of the noradrenergic motor facilitatory system from the locus coeruleus SC) triggering on motor neurons. Noradrenergic agonists can reduce cataplexy in human narcoleptics. In normal individuals, a major caudal projection from the hypocretin cells to the LC maintains the activity of these cells in awake.

Hippocampus neurons in the lateral pons fire before and during PGO spikes.

Basal cells that are maximally active in REM sleep and inactive in waking are also found in the substantia nigra and medial medullary regions.

Circadian control of sleep

The suprachiasmatic nucleus (SCN), which is the major generator of 24h rhythms in mammals, has a potent effect on sleep states. In humans, the SCN regulates a circadian signal that counters sleepiness as the day progresses. When this alerting influence subsides, the nonREM-REM cycle resumes. The circadian rhythm also affects the relationship between REM and nonREM sleep, with the duration and intensity of REM sleep peaks increasing at the end of the night. Light acts through the retina-hypothalamic melatonin system to entrain the circadian rhythm to the solar cycle.

Sleep pathologies and current treatments

Disorder

Clinical features

Underlying deficit

Common treatments

Insomnia

Inability to fall asleep, feeling of inadequate sleep, not refreshed

Unknown in most cases; rarely, brain lesion.

Behavior modification

Sleep apnea

Interrupted, obstructed breathing, excessive sleepiness

Small airways and reduced tone in airway muscles during sleep

Continuous Positive Airway Pressure (COP) which is delivered through a mask

REM behavior disorder

Acting out of dream on injury during sleep

Brainstem damage

Clonazepam

Periodic leg movements

Regular twitch, causing sleep

Unknown; potentially a brainstem abnormality

Benzoazepines; dopamine agonists

Narcolepsy

Sleepiness, cataplexy

Loss of hypocretin neurons, increased number of histamine neurons

Stimulants for sleepiness; antidepressants or noradrenergic agonists for cataplexy

Why we sleep

There is little agreement on the purpose of sleep states. Daily sleep duration varies tremendously across mammalian species, ranging from 2 to 20 hours. This variation in duration is not strongly correlated with brain size or basal body weight, but is linked to diet, with HARD sleepers sleeping the least and carnivores sleeping the most. This pattern is consistent with the idea of sleep as a privative and consoling energy.

Abbreviations: AH, anterior hypothalamus; CRI, dorsal raphe; EEG, electroencephalogram; EMG, electromyogram; GABA, gamma-aminobutyric acid; GABAergic, GABAergic neurons; GC, granule cells; GCL, granule cell layer; HC, hypothalamus; HVC, hyperpallium ventrale; IPL, intermediate pituitary lobe; LP, lateral geniculate nucleus; MCH, melanin-concentrating hormone; MA, medulla inhibitory area; NAC, nucleus accumbens; SDL, sleep deprivation; TRH, thyroid-releasing hormone; VTA, ventral tegmental area; 22H, in the retina.