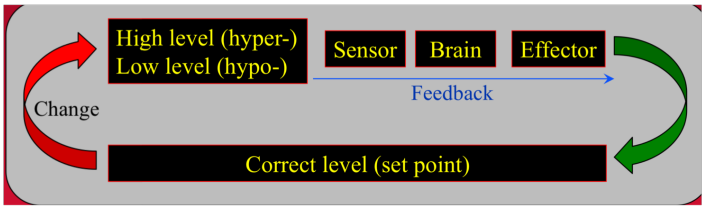
# Circadian rhythm and Sleep

- ## Homeostasis

Maintenance of equilibrium by active regulation of internal states:

- Cardiovascular function (blood pressure, heart rate)
- Body temperature
- Food and energy regulation
- Fluid regulation




- ## Summary of homeostatic control

Multiple mechanisms control homeostasis

- Emphasises the importance to survival
- Set points are not fixed:

- Many homeostatic functions show daily rhythms
- Maintain levels appropriate for the level of activity
- Therefore efficient in energy use.

**Example**
**• During sleep body temperature decreases • Heart rate decreases**
**• Respiration rate decreases**

➢ **Energy conservation**

## Biorhythms

Many functions show natural biological rhythms

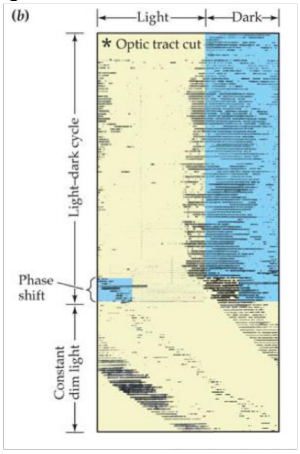
- Circadian rhythms (daily cycle)
- Body temperature, heart rate, respiration, sleep
- Circannual rhythms (yearly cycle)
- Hibernation, mating behaviour, migration

Linked to:

- Light/dark cycle
- Season (day length probably critical)

## Circadian rhythms

- Bodily functions linked to day length Light/dark cycle important determinant.
- How does light/dark information affect body systems?



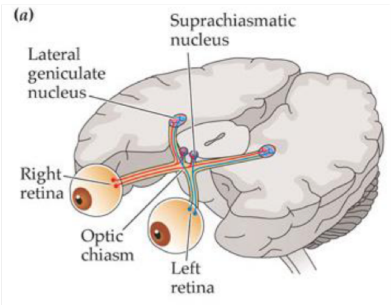

❖ Optic tract lesion

- Circadian rhythm maintained, even in constant light
- Periodicity changed

❖ Suprachiasmatic nucleus lesion

- Circadian rhythm abolished
- No periodicity

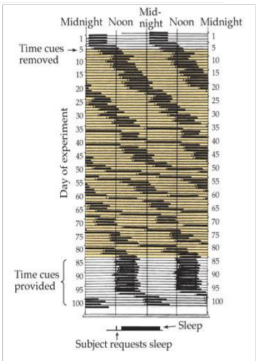
Therefore suprachiasmatic nucleus important for circadian rhythm

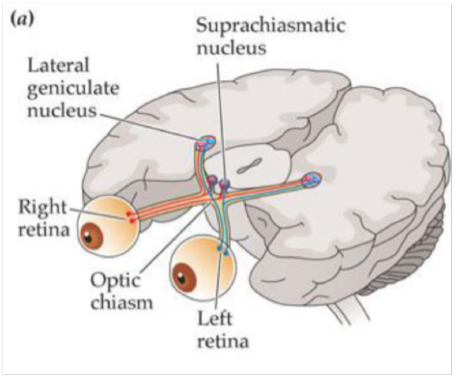



## Suprachiasmatic nucleus (SCN)

❖ Located in hypothalamus, just above optic chiasm
❖ Cells in SCN show oscillations of activity

- Related to circadian rhythm
- Believed to form the 'biological clock'
- Many functions (e.g. sleep wake cycle) are maintained in constant light or constant dark .
- Periodicity may not be 24 hours
- In normal light/dark cycle SCN rhythm is 'phase locked' to light dark






## How does light information reach SCN

❖ Many non-mammalian species have photoreceptors outside the eye.

• e.g. amphibians and reptiles – pineal gland is light sensitive

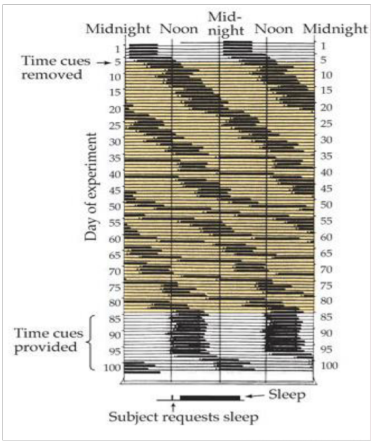
❖ In mammals a direct pathway from eyes to SCN has been identified

- Carries light information to SCN
- Rods and cones do influence SCN function
- Light sensitive information still reached SCN in the absence of rods and cones
- Therefore other light receptors also present in eye.

## Circadian rhythms in action: sleep

'Free running' sleep rhythm about 25 hrs

Entrainment to light dark cycle maintains a 24 hr periodicity , Mediated through SCN activity




### Jet-lag

- Rapid shifts in light dark cycle
- Takes a few days for endogenous rhythm to re-entrain

## Passive onset of sleep

### Bremer (1930)

- Surgically separated midbrain from forebrain in cats
- Animals remained permanently asleep
- Proposed that in the absence of sensory input the cortex became quiescent (i.e. sleep)

### Moruzzi & Magoun

- Electrical stimulation of the midbrain woke sleeping animals
- Lesions to this area caused persistent sleep
- Activating system in the midbrain, which activates the cortex
- Lack of tonic activating influence of midbrain causes cortical neurones to cease firing, and sleep to ensue.

## Normal Sleep

- Normal sleep consists of 1-4 series of phases of increasing depth(Non REM) and REM phases.
- Each phase has a characteristic EEG.
- There is a decrease with age in sleep length.

## Characteristics of sleep

### Slow-wave sleep(NON REM)

- Progressive decrease in spinal reflexes
- Progressive reduction in heart rate and breathing rat
- Reduced brain temperature and cerebral blood flow
- Increased hormone secretion (e.g. growth hormone)
- Synchronised cortical activity

### REM sleep

- Spinal reflexes absent
- Rapid eye movements behind closed eyelids
- Increased body temperature and cerebral blood flow
- Desynchronised cortical activity
- Dreams

## Dreams

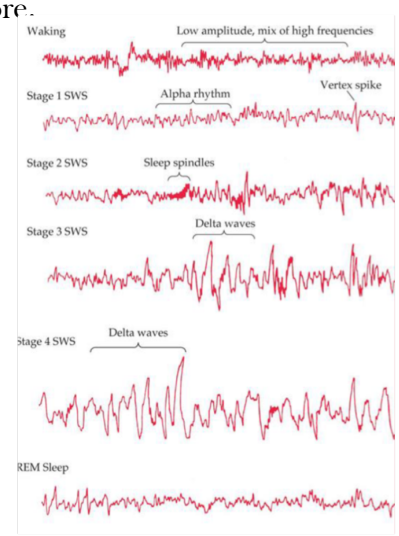
- REM sleep dreams : sexual, clear, sleep paralysis, connected to external stimuli easy to be recalled.
- Nightmares
- Non REM sleep dreams : No story and no recall(Night terrors).

## Normal night Sleep

- In the first cycle:
- 15-20 minutes to fall a sleep.
- Over the next 45 min. one descends to stage 3 & 4(Non REM)
- After 45 min. after stage 4 reaches the first REM stage. (REM latency = 45 + 45 = 90 min.)

## Normal sleep

- As the night progresses:
- * Each REM period gets longer.
- * And stage 3+4 gets shorter until they disappear.
- * Further into the night sleep becomes lighter and dreams become more.



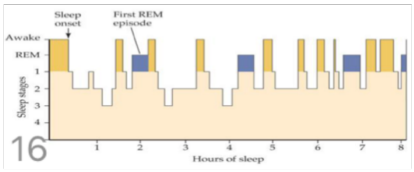

## Brain activity during sleep

**Awake**
Low amplitude high frequency EEG

**Light sleep**
Increasing amplitude decreasing freq. EEG

**Deep sleep**
High amplitude low frequency EEG

**Rapid eye movement (REM)sleep**
Low amplitude high frequency EEG




## Sleep as an active process

Electroencephalographic (EEG) recordings showed abundant neuronal activity in cortex during sleep

- Therefore not passive neuronal quiescence Pattern of the EEG was very different in sleep than in waking
- Waves of activity, indicating synchronous firing of cortical neurones
- Synchronising stimulus coming from sub-cortical areas
- Reticular formation still seen as important Several different levels of sleep
- Sleep is a complex combination of different aspects

## Characteristics of sleep

### Slow-wave sleep(NON REM)

- Progressive decrease in spinal reflexes
- Progressive reduction in heart rate and breathing rate
- Reduced brain temperature and cerebral blood flow
- Increased hormone secretion (e.g. growth hormone)
- Synchronised cortical activity

### REM sleep

- Spinal reflexes absent
- Rapid eye movements behind closed eyelids
- Increased body temperature and cerebral blood flow
- Desynchronised cortical activity
- Dreams

## Neuronal circuitry controlling sleep

Cortex “kept awake” by ascending activation from midbrain

5HT inputs inhibit midbrain ‘activating system’ areas

• therefore promotes sleep

Stimulation of area surrounding SCN induces slow wave sleep • mechanism unclear: Probably involves SCN

No one stimulation site can promote REM sleep
• but lesions to specific brainstem areas abolish REM sleep.

## Neurochemistry of sleep

### Neurotransmitters

- 5HT - promotes slow wave sleep – inhibition of 'activating system'
- Noradrenaline - ? inhibition of muscle tone during REM sleep
- Dopamine - general arousal
- Acetylcholine - induces REM sleep
- Also 'sleep-promoting substances'
- Factor S, DSIP (delta-sleep inducing peptide), melatonin
- Not much known about their action
- May modulate circadian rhythmicity rather than sleep *per se*

### Disorders of sleep

- **Insomnia** - reduction or absence of sleep - transient or persistent
- **Hypersomnia (narcolepsy)** - excessive drowsiness and falling asleep.
- **Sleep-wake schedule disturbance** - transient or persistent
- **Partial arousal** - e.g. sleep-walking, nightmares
- Often associated with anxiety, psychological disturbance or drug taking
- Little known about causes
- Limited capacity for pharmacological treatment of sleep disorders

## Summary

### Homeostasis

- Maintenance of constant conditions
- e.g. hunger / satiety system

### Circadian rhythms

- Biological rhythms with 24 hour periodicity
- Role of SCN as circadian clock: entrainment to light/dark cycle

### Sleep

- Sleep as an active process – EEGs in different stages of sleep
- Characteristics of slow wave sleep and REM sleep
- Disorders of sleep