Chapter 13

Lecture 9: Circadian Rhythms, Sleep & Dreaming

Origins of Biological Rhythms

- Certain environmental conditions repeat themselves on a regular basis:
  - Earth's rotation about its axis gives us night and day.
  - Earth's rotation around the sun gives us seasons.
- These repetitive events naturally impose certain constraints on organisms:
  - It's not always practical to hunt at night.
  - Food and other resources can be scarce during the winter months.

Adapting with Biorhythms

- It's very adaptive to be able to cope with and exploit these cycles.
  - Animals that evolved in equatorial regions tend to base their behavior around the day/night cycle (circadian rhythm).
  - Animals that evolved in polar regions, where seasons affect survival more than day/night, tend to show seasonal cycles (circannual rhythm).

Biorhythms are Common

- **Cyanobacteria** (blue green algae) are very simple organisms. They are similar to organisms that would have lived billions of years ago.
- Cyanobacteria have adapted to the light/dark cycle by photosynthesizing during the day, and nitrogen fixing at night.
- Cyanobacteria with functioning circadian rhythms out-compete genetic mutants lacking circadian rhythms.

The Variety of Biorhythms

- **Circannual Rhythm**
  - Yearly (e.g., migratory cycles of birds)
- **Infradian Rhythm**
  - Less than a year (e.g., human menstrual cycle)
- **Circadian Rhythm**
  - Daily (e.g., human sleep cycle)
- **Ultradian Rhythm**
  - Less than a day (e.g., eating cycle)

What are Circadian Rhythms?

- Circadian rhythms are biorhythms with a **period** of approximately 24 hours.

Circadian

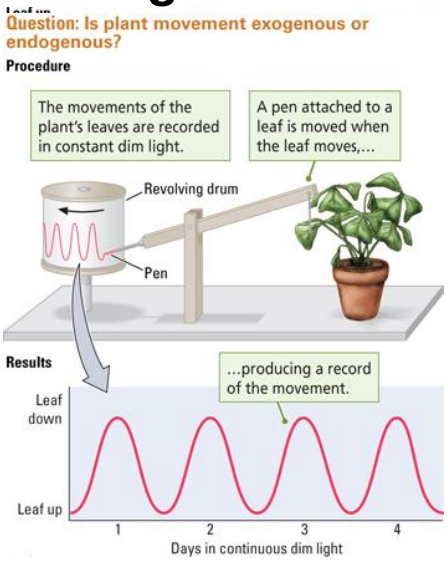
Circa	Dian
Latin for “about”	*Dies*, latin for “day”

Properties of Circadian Rhythms

- 24-hour period
  - Responses that have a circadian rhythm repeat on a 24 hour period.
- Endogenous
  - Rhythmic responses continue even in the absence of stimulation.
- Entrainment
  - Circadian rhythms can be reset or adjusted by exposure to external stimuli such as light, food, and heat.
- Temperature Compensation
  - Temperature can affect metabolism, but proper circadian rhythms maintain a 24h period over a variety of temperatures.*

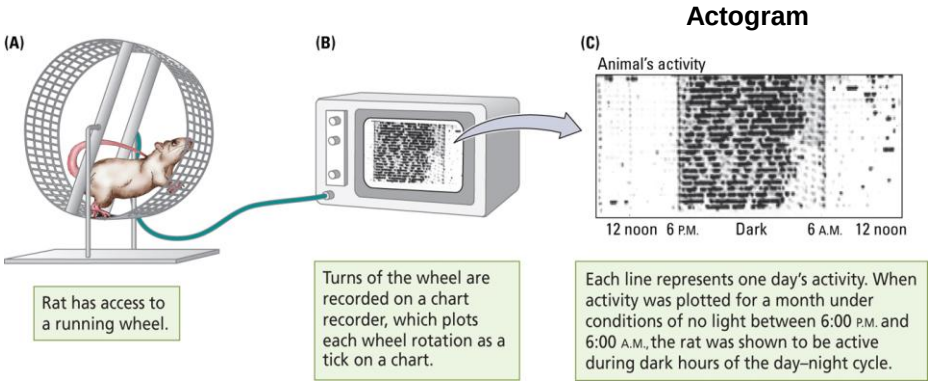
**This property is not particularly relevant to warm-blooded creatures such as ourselves.*

Circadian Rhythms are Endogenous



- Many plants adjust their leaves over the course of the day such that they have more access to sunlight during the day. Is this **endogenous** or is it simply a *response* to sunlight?
- In this example, the plant is placed in a dim room with no light/dark cycle.
  - If leaf movement is a *response* (exogenously caused) then no movement will occur in dim light.
  - If leaf movement has endogenous causes, the 24h cycle of leaf movement will persist in dim light.
- The verdict: **endogenous**!

How are Circadian Rhythms Studied in Mammals?



Principles similar to this can be employed in testing human subjects under controlled conditions

Circadian Rhythms are Entrainable

Light Status

12h lights on/12h lights off

Constant Darkness

Circadian Rhythms are Entrainable

- Daily activity is normal when a 24h light/dark cycle is present.
- When placed in constant darkness, the animal still shows a regular pattern of activity.
- But because the animal's circadian clock runs a little slow, the pattern of activity gradually drifts into almost a complete inversion.

Zeitgebers Entrain Biorhythms

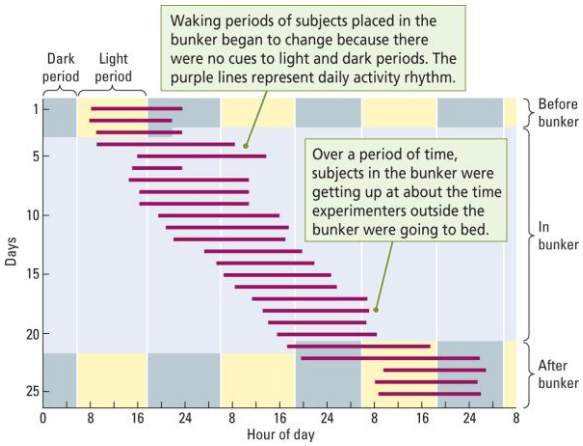
- In this experiment, it seems that light is necessary to keep proper time. Endogenous rhythms are not accurate enough on their own to be relied upon.
- Light is a **Zeitgeber,** it acts to 'reset' the circadian clock, and helps to maintain its correspondence to the outside world.
- A circadian clock that is properly reset by a zeitgeber is said to be **entrained.**

Zeit-geber *(German)*

Time Giver

Free-running Rhythms

- In the absence of zeitgebers, an animal's circadian rhythm may be a little more or less than 24h. This is called the **free-running rhythm.**



- **Aschoff & Weber's study:**
- When isolated (underground) from the sun, people's free-running rhythm tended to be longer than 24h.
- Every night they tend to go to bed later than the night before. Ultimately the sleep/wake cycle is completely reversed.

Review. Circadian Rhythms are…

Endogenous

- Cycles continue even when environmental stimuli are withdrawn.

Entrainable

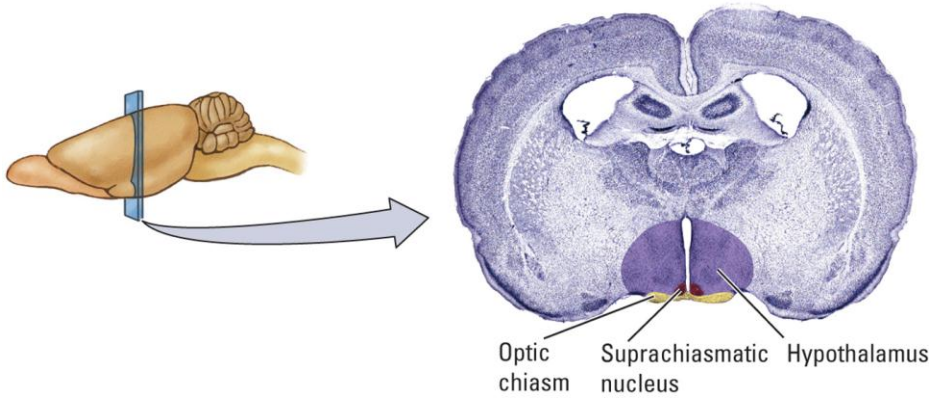
- Cycles can be reset or adjusted by daily exposure to a regular stimulus (a zeitgeber).

Neural Basis of the Circadian Clock

- Given that circadian rhythms manifest mostly as behavioral, cognitive, and hormonal changes, it is reasonable to suspect that circadian clocks reside somewhere in the brain.

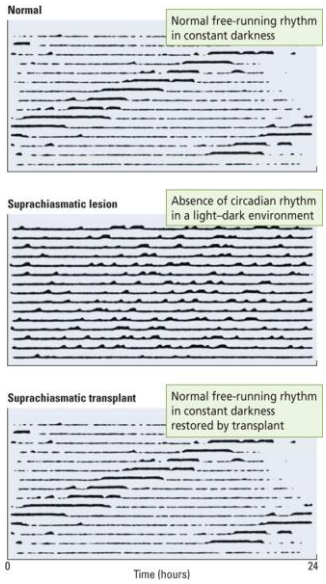
- Prior to its characterization by Richter in the early 20thC, the exact location of this clock was not known (it wasn't even known how many clocks there were).

The Suprachiasmatic Nucleus

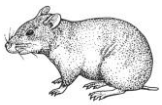


The suprachiasmatic nucleus (SCN) is a region of the hypothalamus located directly above the optic chiasm.

The Suprachiasmatic Nucleus

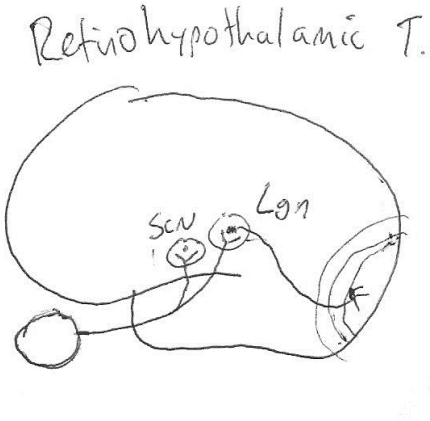


- If the **suprachiasmatic nucleus** (SCN) is lesioned, animals continue to sleep about the same amount, however the distribution of this sleep is completely random.
- If neurons from embryonic suprachiasmatic nuclei are transplanted, the circadian rhythm re-appears. This suggests that endogenous rhythm is not learned.



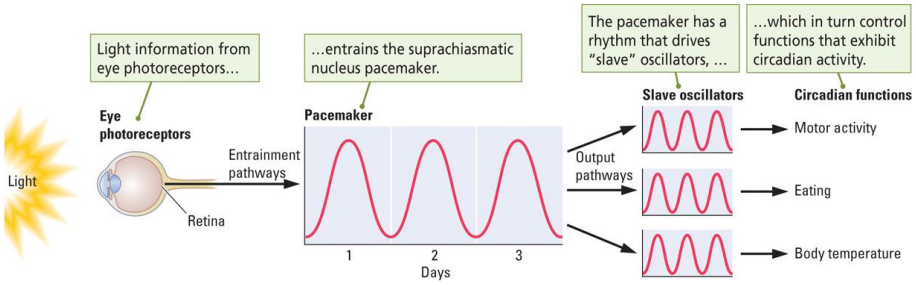
Hamster

The Retinohypothalamic Tract



- The **retinohypothalamic tract** is, as the name suggests, a visual pathway leading from cells in the retina to the hypothalamus (in particular, the suprachiasmatic nucleus). This is in contrast to the ordinary visual pathway that arrives in the visual cortex via the thalamus.
- The retinohypothalamic tract is critical for light based entrainment of circadian rhythms. Since it uses a third type of photosensor (not rods or cones), it is dissociable from ordinary vision.

The Retinohypothalamic Tract



- Light entrains the SCN pacemaker
- SCN pacemaker drives a number of "slave oscillators," each of which controls the rhythmic occurrence of one behavior (e.g., body temperature)
- SCN pacemaker may drive the slave oscillators via hormones, proteins, or neurotransmitters

The Pineal Gland & Melatonin

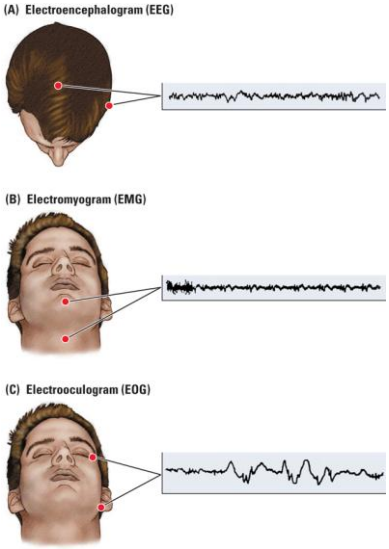
- Melatonin is secreted by the pineal gland, a small structure posterior to the thalamus.
- Melatonin is released during the dark phase of the light/dark cycle.
  - This is true in both nocturnal and diurnal animals.

Introducing Sleep

Introducing Sleep

- There is a great deal of variability in people's sleep-wake behavior.
  - This varies over the course of the lifespan, infants sleep up to 16h per day, the elderly around 6.
  - This also varies between people, people have somewhat different sleep requirements. The average is 7-8h per night.

Measuring Sleep in Humans

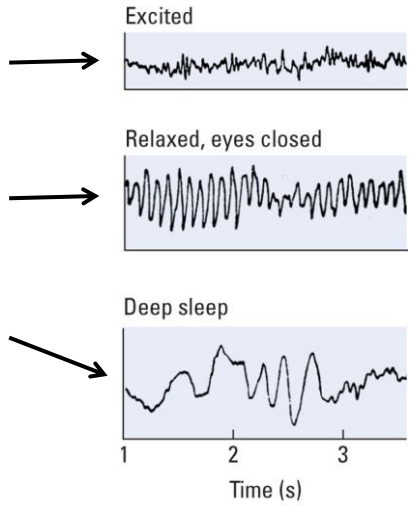


- A polygraph is used to measure the electrical activity of the brain and body (***polysomnography***).

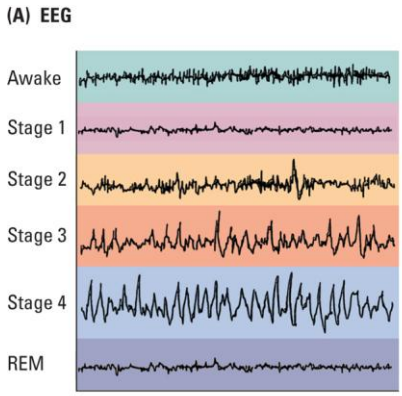
- Electroencephalogram (**EEG**)
  - Record of brain-wave activity
- Electromyogram (**EMG**)
  - Record of muscle activity
- Electrooculogram (**EOG**)
  - Record of eye movements

Stages of Sleep

- **Beta Rhythm** (Waking State)
  - Fast brain-wave activity (15 to 30 Hz) pattern associated with a waking EEG.
- **Alpha Rhythm** (Drowsy State)
  - Large, extremely regular brain waves (7 to 11 Hz) associated with drowsiness.
- **Delta Rhythm** (Sleeping State)
  - Slow brain-wave activity (1 to 3 Hz) pattern associated with deep sleep (**NREM sleep**).
- **REM Sleep** (Dreaming State)
  - Fast brain-wave pattern displayed by the neocortical EEG record during sleep

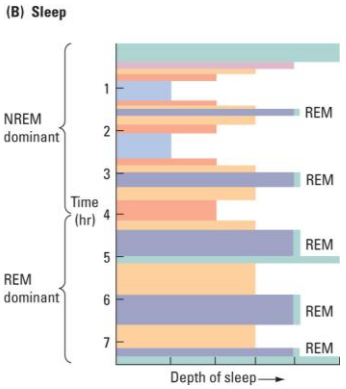


The Stages of Sleep

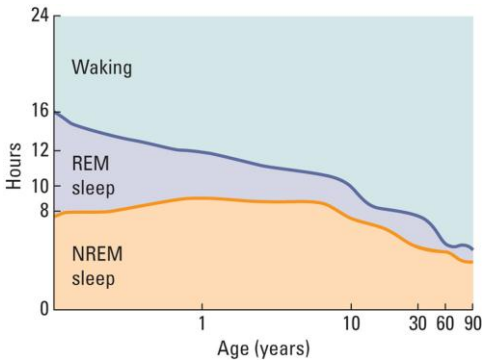


- **Four Stages of Non-REM (NREM) Sleep**
  - *Stage 1* ***Shallow***
  - *Stage 2*
  - *Stage 3*
  - *Stage 4* ***Deep***
- Stages 3-4 are referred to as "slow-wave sleep". These stages are difficult to awaken from.
- ***Sleep inertia*** refers to the groggy, impaired feeling that follows being woken up from deep sleep.

Distribution of Sleep Phases



The amount of time spent in REM sleep varies over the course of the night.



The amount of time spent in REM sleep also varies over the lifespan.

Non-REM Sleep

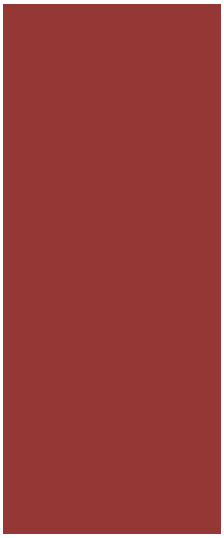
- Large range of activities take place.
  - Examples: decrease in body temperature and increase in growth hormone release
- Dreaming does occur in NREM sleep, but dreams are not as vivid as in REM sleep.
- Sleeptalking (**Somniloquy**)
- Sleepwalking (**Sonambulism**)
- Night terrors
  - Brief, very frightening dreams
  - May be experienced by children
  - Occur in NREM sleep

Dreaming During REM Sleep

- Vivid dreams occur during REM sleep.
  - Everyone dreams a number of times each night.
  - Normally these dreams are forgotten. However if an individual is awoken during REM sleep, they will almost always report having been in the middle of a dream.
  - Dreams appear to take place in real time, dream sessions get longer throughout a sleep session.
- Muscle tone is lost during REM sleep (**atonia**)

Sleep Paralysis

- Because muscle tone is suppressed during REM sleep, it can be quite disturbing to partially awaken during this phase.
- Typically individuals will be partly awake, yet frozen in place and unable to move in bed.
- This is accompanied by an overwhelming feeling of dread, and the sense of a monstrous presence in the room.
- There is often a sense of pressure or weight on the chest, if the individual is supine.



Why we Dream: Psychoanalytic Theories

- Sigmund Freud
  - Dreams are the symbolic fulfillment of unconscious wishes
  - Manifest Content: The content of the dream as it appears (taken at face value).
  - Latent Content: The true meaning of the dream.
- Carl Jung
  - Dreams are expressions of our “collective unconscious” (history of the human race).

Why we Dream: Activation Synthesis Theory

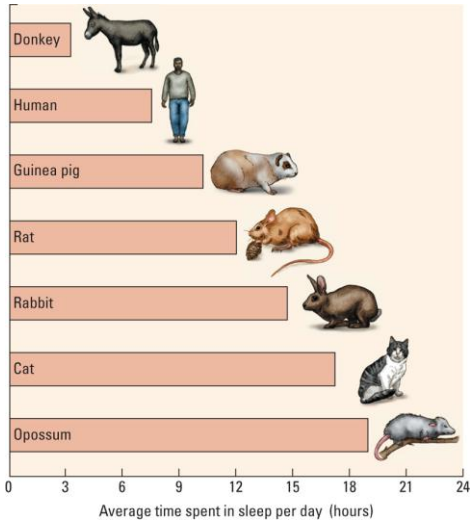
- Theory: Dreams are meaningless brain activity (*epiphenomena*).
- J. Allan Hobson: Activation-Synthesis
  - During REM sleep, the brain is active in a way that very much resembles the waking state. The cortex receives more or less random signals from the brainstem during this time.
  - In what is presumably an effort to make sense of these signals, the cortex generates images, actions and emotions.
  - Because these responses draw from personal experiences, they have a vague relationship to our waking lives. However, since the signals that give rise to them are random, the dreams are essentially meaningless.

Why we Dream: An Evolutionary Theory

- Antti Revonsuo
  - Dreams are organized and somewhat coherent, and very biased toward danger and threatening images.
  - Dream content may incorporate the ongoing emotional problems of the dreamer.
  - Because dreams aren't real, they can act as "training scenarios" that may prepare the individual for improved performance in waking life.
  - This ability is evolutionarily adaptive, particularly for our ancestors who were in near perpetual danger.

Why do we Sleep? – Four Theories

- The amount of hours engaged in sleep has no clear relationship with physiological measures like body size or metabolic rate, or even psychological measures for that matter.
- This makes it difficult to resort to common-sense explanations for why we sleep.



1. Sleep as a Restorative Process

- The idea that sleep is for rest has intuitive appeal, and our day to day experience attests to it.
- Chemical events within our cells may need "downtime" in order to maintain optimal function.
- However, this theory runs into trouble in the face of certain realities.
  - Sleep deprivation or restriction is not ideal, but it is not directly lethal (like oxygen or water restriction).
  - **There is a huge variety of sleep schedule and styles across the animal kingdom. Since all animals are built roughly the same way, sleep can't serve a purely physiological function.**

Studies of Sleep Deprivation & Restriction

- Sleep Deprivation
  - When subjects are forced to stay awake for long periods.
  - No marked physiological effects within the periods that have been tested (~18 days).
  - *Microsleeps* are small moments of sleep that begin to occur after long periods without sleep. They make it difficult to study true sleep deprivation.
- Sleep Restriction
  - Long-term reduction of sleep does not appear to cause any obvious changes in mortality in and of itself.
  - However, reduced sleep duration is associated with diabetes, obesity, hypertension, and other problems.

2. Sleep as a Passive Process

- Early explanation that sleep is a passive process that takes place as a result of a decrease in sensory stimulation.
- Does not account for the complexity of sleep.
- No direct evidence
  - Sensory deprivation research has shown that people actually sleep less, not more, when placed in isolated environments (contrary to what one would expect).

3. Sleep as a Biological Adaptation

- Sleep may be an energy-conserving strategy
  - Gather food at optimal times and sleep to conserve energy the rest of the time
  - Animals with nutrient-rich diets spend less time foraging for food and more time sleeping
- Animals that are predators sleep more than animals that are prey
- Nocturnal or diurnal animals will sleep during those times in which they cannot travel easily
  - Example: humans cannot see well at night
  - This seems a bit circular, however, since diurnal animals *by definition* sleep at night, and it's hard to say which is an adaptation to which.

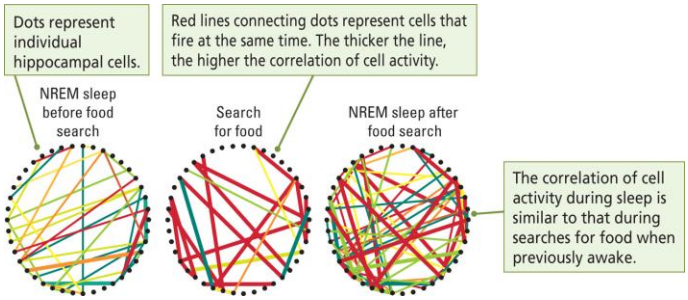
3. Sleep as a Biological Adaptation

- Patterns of sleep differ widely among vertebrates.
- Marine mammals like the walrus, seal, and and killer whale can suspend their sleep cycle and remain awake for days at a time.
  - Dolphins show uni-lateral changes in brain activity that somewhat resemble sleep. However they remain in motion and are able to react to stimuli.
  - The eared seal can switch between ordinary (bilateral) sleep on land, and unilateral sleep while swimming.
- Ultimately the only factor that seems to have any relationship with sleep is the animal's lifestyle. Sleep may therefore represent a period of forced dormancy, similar in function to other dormant periods seen in other forms of life.

Siegel, J. (2009). Sleep viewed as a state of adaptive inactivity. *Nature Reviews Neuroscience, 10,* 747–753.

4. Sleep and Memory Storage

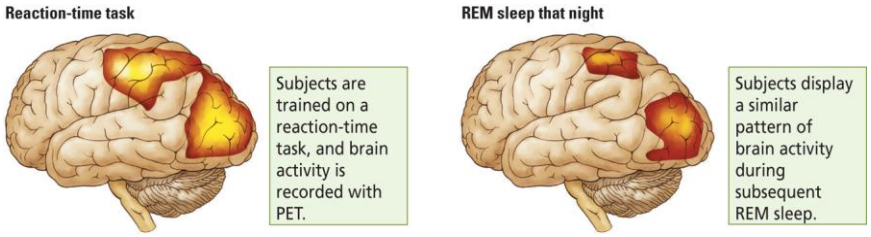
- Allowing yourself time to sleep after learning a new task or piece of information is a very wise practice. Could the purpose of sleep be to help consolidate new memories?



- In the above study, rats showed patterns of hippocampal activity *during* a search for food and after that search during NREM sleep. This suggests that connections acquired while awake are re-played, strengthened or otherwise refined during sleep.

4. Sleep and Memory Storage

- Maquet et al., (2000). Used PET imaging to record brain activity while humans performed a serial reaction time task.

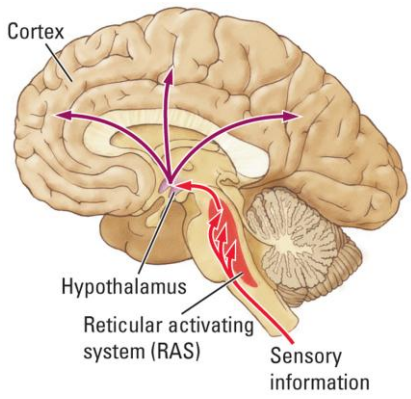


- PET imaging showed that the brain regions activated by the task were also active during REM sleep. Perhaps this represents the subjects dreaming about the task.

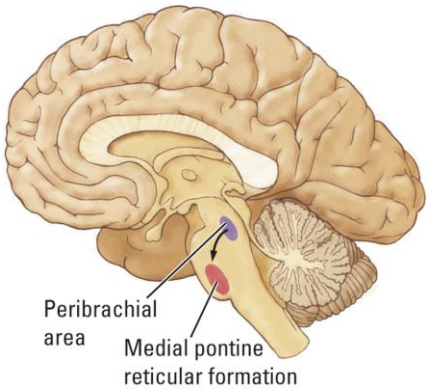
The Neural Bases of Sleep

The Reticular Activating System

- Moruzzi & Magoun (1949) discovered that electrically stimulating the **reticular formation (RF**) in the brainstem produced cortical EEG patterns resembling wakefulness in anesthetized cats.
- Cutting the brainstem *above* (*cerveau isolé*) the RF produces coma, cutting *below* (*encephale isolé*) does not.
- The RF projects widely through the cortex, and itself innervated by collaterals arising from ascending sensory pathways.



Neural Basis of REM Sleep



- Legions of the **peribrachial area** cause a drastic reduction in REM sleep.
- The **peribrachial area** innervates the **medial pontine reticular formation** with acetylcholine.
- Lesions of the **medial pontine reticular formation** also inhibit REM sleep.
  - This region projects to various other brainstem nuclei to bring about REM sleep.

Disorders of Non-REM Sleep

- Narcolepsy
  - Slow-wave sleep disorder in which a person uncontrollably falls asleep at inappropriate times.
  - May be due to mutations in the gene that produces hypocretin/orexin peptides.
- Sleep Apnea
  - Inability to breathe during sleep; person has to wake up to breathe. This results in a fitful and unrefreshing sleep.

Disorders of Non-REM Sleep

- Insomnia
  - Disorder of slow-wave sleep resulting in prolonged inability to sleep
  - Multiple causes
- Drug-Dependency Insomnia (iatrogenic insomia)
  - Condition resulting from continuous use of ***hypnotic drugs*** **(sleeping pills)**; drug tolerance also results in deprivation of either REM or NREM sleep, leading the user to increase the drug dosage.

Some Common Sleep Aids

- Ethanol (alcohol)
  - Well known sedative-hypnotic effects. Leads to poor quality sleep.
- Zolpidem (Ambien)
  - Nonbenzodiazepine $GABA_A$ receptor agonist. It has a short half-life, meaning it doesn't lead to drowsiness the following morning.
- Alprazolam (Xanax)
  - Benzodiazepine $GABA_A$ receptor agonist.
- Diphenhydramine (Nytol, Gravol, Benedryl etc.)
  - Antihistamine that also produces drowsiness. Most commonly available OTC sleep aid.
- Melatonin
  - One of only two hormones available OTC. Good evidence that it can modify circadian rhythms in humans, mixed evidence that it helps with sleep.