



Sleep



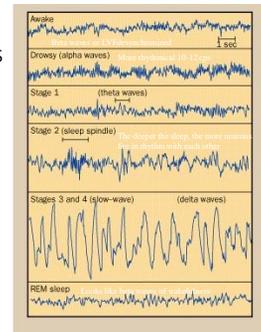
Polysomnogram ("multiple sleep recordings")



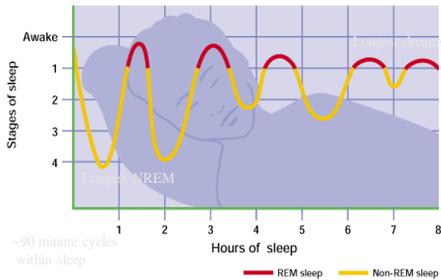
- EEG (electroencephalogram)
- EOG (electrooculogram)
- EMG (electromyogram)
- Sometimes additional measures like respiration, BP, etc.



EEG Wave Patterns



A Typical Night's Sleep



2 Main Types of Sleep

- Non-REM (Stages 1-4)(about 80% of night)
- REM sleep (20% of night)

Non-REM or NREM Sleep (Stages 1-4)

- gradual decrease in movements, breathing, heart rate
- change in brain activity from LVF to high voltage slow, rhythmical brain waves ("delta waves")
- the deepest stages often called "slow wave sleep"
- hard to wake up
- sleep-thinking more common than dreaming

REM Sleep

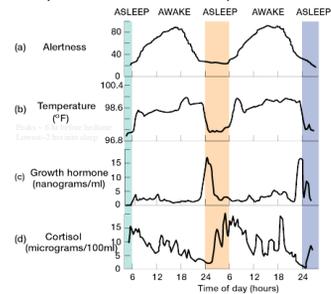


- very active LVF irregular similar to waking
- rapid jerky eye movements
- total loss of tone in most muscles
- breathing, heart rate unpredictable
- 80-90% chance of vivid dream report
- erection; vaginal lubrication
- Most often missing REM → REM rebound

Biological (Endogenous) Rhythms:

- Regular, periodic cycles of physiological/psychological functioning
- Rhythms are **endogenous** (generated internally, by biological clocks) but are influenced or "reset" by external stimuli.
- Most common: **circadian rhythms**: ~24 hr cycles in many bio processes & behaviors (e.g. sleep/waking, temp., hormones, urination, sensitivity to drugs)
- Rhythms keep our internal workings in phase with the outside world

2 Day Circadian Examples



How do we know they are endogenous?

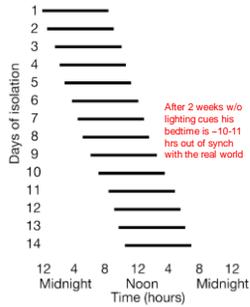
- There are also biorhythms of other lengths:
- Circannual rhythms (yearly cycle)
 - Examples: Birds' migratory patterns, animals storing food for the winter or hibernating, annual mating.
- Circalunar rhythm (monthly cycle)
 - Menstrual rhythm
- 90 minute rhythm within sleep

- If deprived of time of day signals, our circadian biorhythms continue to run on their own internal clock: "free-running rhythms" – often with a cycle of slightly over 24 hr (average = 24.3-24.4 and averaging 24.5 in some blind persons)

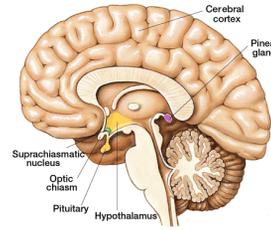
- Example of research that revealed these free-running rhythms:
- <http://www.youtube.com/watch?v=aF24ZmPwzB0> (GO TO 2:55)

“Free-Running Rhythm”

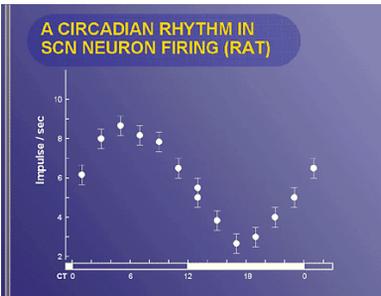
Sleep hours of someone without environmental indicators of time (very similar to Fig. 9.1 of a flying squirrel's rhythms without outside cues)



Key Internal Clock: Suprachiasmatic Nucleus of Hypothalamus (SCN)

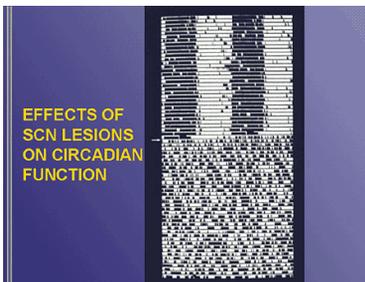


Isolated SCN neurons show circadian rhythm of firing activity



- **SCN lesions** disrupt activity, sleep, eating, & hormone rhythms.
- SCN transplants can change an animal's natural biorhythm to that of donor.

Activity cycles (black) of rats before (top) and after (bottom) SCN lesions



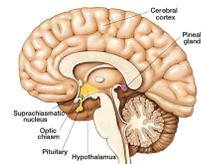
What Resets the Clock?

- **Daylight** is key external “zeitgeber” (“timegiver”), **resetting** our biological clock & keeping it “entrained” with the cycle of where we are living. (Other less effective zeitgebers: exercise/activity, noise, environmental temperature, meals.)

- Light resets the SCN via direct connection from the retina: *retinohypothalamic path*.
- Comes from a special group of ganglion cells that have their own photopigment called *melanopsin*.
 - These cells respond directly to light and do not require any input from the rods or cones.
 - Respond slowly to ambient lighting
 - Most sensitive to short (blue) wavelengths

- SCN very sensitive, very adaptive – this allows “re-setting” of our biological clock when we travel to different time zones
- But unfortunately our modern devices emit lots of blue wavelengths and night time use may reset your clock and delay your sleep cycle!

- Retinal blindness can disturb resetting if it affects these ganglion cells
- Some blind individuals have “free-running rhythms” for this reason.
- But under normal conditions our internal clock itself is very resistant to disruption.



- The SCN regulates the **pineal gland** located posterior to the thalamus.
- The pineal gland secretes **melatonin**, a hormone that increases sleepiness, normally beginning a couple hrs before your bedtime.
- <http://www.youtube.com/watch?v=KnJkMfmea28&feature=related>

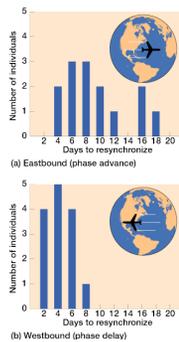
Melatonin

The hormone of darkness

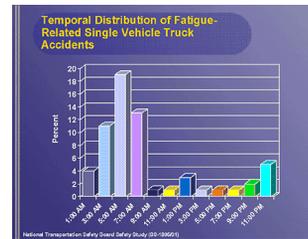


- Melatonin (~.3mg) in the afternoon may make you sleepy earlier; melatonin after midnight may help you adjust to sleeping later.
- SCN has melatonin receptors (allows feedback)
- SCN control of rhythms shows some deterioration with aging

- **Jet lag**: mismatch between circadian rhythms & outside world due to crossing time zones.
 - Sleepiness & impaired functioning during the day and sleeplessness at night until clock re-synchronizes with new environment
 - Traveling west = “phase-delay”, traveling east= “phase-advance”. Phase delays are easier for your clock to adjust to.
- **Shift-work sleep disorder**, similarly, is related to trying to work when your circadian clock is telling you to sleep and trying to sleep when your SCN is telling you it is time to be awake.



Desynchronization of work cycle and circadian cycle correlated with accidents



Knowing how to best handle jetlag and shiftwork is of importance to a huge number of businesses & international interactions.

Shifting Your Biorhythms

- You must control your environment to provide the right cues to your SCN
- For several days before your shift in cycle:
 - Expose yourself to **bright light** beginning at the time of your "new morning"
 - Dim or no lights at time of new "night-time"
 - May take melatonin a few hours before new bedtime for phase advances
 - Match mealtimes, exercise times to new cycle
 - Maintain exposure to "correct" stimuli to keep new biorhythms entrained
- It is easier to delay your clock (go to bed later, wake up later) than it is to advance your clock (go to sleep earlier, wake up earlier).

Multiple Genes Influence the Clock

Researchers have discovered several rhythm related genes which influence our biological clocks. For example 3 of these genes are involved in the production of proteins which accumulate over the day & eventually make you sleepy. Light increases production; production stops during night.

Differences in these genes are responsible for inborn differences in circadian rhythms, both normal and extreme.

- <http://www.youtube.com/watch?v=17L5S7Kk7Cc>

Why Do We Sleep?

- Repair/restoration theory: sleep allows the body/brain to repair and replenish itself.
- Most likely to be associated with NREM slow wave sleep
- Critical for many immune and endocrine functions; neurotransmitter synthesis
- Amount of deep sleep tends to stay constant even if sleep time is shortened.
- If we miss a night of sleep we make up for almost all of the deep sleep
- Short sleepers & long sleepers have same amount of deep sleep.
- Loss of deep sleep → sleepiness; loss of REM sleep does not make you sleepy

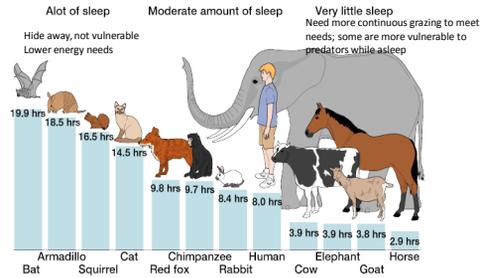
Why Do We Sleep?

- BUT restoration probably not the whole story:
 - Length of sleep of species not strongly correlated with exertion/activity (including humans).
 - Sleep deprivation causes less disruption than expected; we don't make up for *all* the sleep we miss
 - Some individuals routinely sleep only 1-3 hrs, many with only 5 hr.
- Adaptation Theory
 - Sleep evolved as an adaptation that increased survival by:
 - Conserving energy at times when food-seeking was inefficient
 - Protecting species during dangerous time of the day/night cycle

Adaptation Theory of Sleep

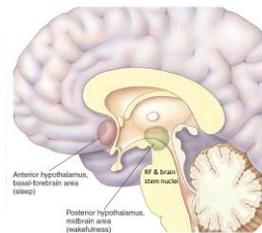
- Sleep was “selected for” in the process of evolution - it has survival value beyond restoration of the body. It allows conservation of energy and safety at a time when food-seeking is inefficient or unsafe.
 - Sleep time is negatively correlated with exposure/vulnerability during sleep and and negatively correlated with the time needed to meet energy needs.
 - “Biological clock” triggers periodic changes in arousal independent from need for restoration – kind of like a furnace that has been programmed to conserve energy each night.

Species Differences



Four Areas of the Brain Involved in Sleep

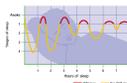
- **Posterior hypothalamus & reticular formation – wakefulness**
- **Anterior hypothalamus & brainstem nuclei (pons & medulla)– sleep**



What happens if something goes wrong in these sleep control circuits?

Let's start with NREM related disorders.

NREM Sleep “Disorders”



- Very common in kids; tend to run in families. Most outgrow them. A much smaller # of adults continue to have NREM disorders, most often when stressed.
- Night terrors (partial arousal associated with intense anxiety during 1st few hrs of sleep; no memory of it next morning)
- Sleepwalking – stereotypical actions done without full awareness (again usually in the 1st few hrs of sleep & no memory of it)
- Recall our discussion of how the sleep system can inhibit or put some areas of the brain asleep, while others are still active/awake. Prefrontal cortex is asleep but cingulate and thalamus active during somnambulism.

Narcolepsy (1/2000 people)

- Typically begins in late teens/twenties
- Persistent daytime sleepiness & irresistible REM sleep attacks (but may not sleep well at night)
- Cataplexy (sudden loss of muscle tone while still awake), often triggered by laughter, anger, embarrassment, sex, exertion, or talking to strangers.
- Sleep paralysis when falling asleep or waking
- Hypnagogic hallucinations (dreams begin while awake)

Narcolepsy continued

- Genetically based in dogs and some humans, but only 25% concordance in identical twins so environmental factors must also be involved.
- Associated with absence of orexin neurons in hypothalamus.
- May be due to autoimmune action, at least in some narcoleptics.
- Narcoleptic dogs lack orexin receptors. Mice without orexin also look narcoleptic..

Another REM related disorder: REM Behavior Disorder (or "REM without atonia")

- Deterioration of cells in pons which normally send messages to the spinal cord to inhibit muscle tone/movement during REM
- Vigorous movements occur during dreaming
- Most common in older men; may precede or accompany Parkinson's disease or Lewy Body dementia or Multiple System Atrophy
- Has been produced in animals by experimental brain lesions in this region
- <http://www.youtube.com/watch?v=rFXYRQ9xPUA>

Other Sleep Disorders

- Many different causes/types of insomnia, e.g.
 - "Onset" insomnia (trouble falling asleep)(may be associated with phase-delayed temp cycle)
 - "Termination" insomnia (waking too early) (often associated with phase-advanced temp cycle)
 - Depression: early REM & termination insomnia
 - Insomnia may also be related to "restless legs syndrome" which delays sleep or involuntary leg movements during sleep ("periodic limb movement disorder") which can disrupt sleep & make it less restful
 - Insomnia/disrupted sleep cycle due to sleep apnea
 - Insomnia due to drug use or drug withdrawal

Treatment of Narcolepsy

- Excessive sleepiness treated with stimulants like Dexedrine (d-amphetamine) or Ritalin (methylphenidate) or the newer Provigil (modafinil).
- Abnormal REM symptoms treated with antidepressants which suppress REM & often have an anti-ACh action
- Newest approach: Xyrem (sodium oxybate or GHB) both improves nighttime sleep and suppresses REM symptoms like cataplexy.



Exp. brain lesions in the region of the pons that is necessary for the loss of muscle tone in REM leave this cat able to move during REM, seemingly acting out its dreams.

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- **Sleep apnea** is a sleep disorder characterized by abnormal lapses in breathing during sleep.
- Causes daytime sleepiness, impaired attention, & possible heart problems & brain damage.
- Cognitive impairment may result from loss of neurons due to insufficient oxygen levels.
- Causes can be "mechanical" or neurological, and include obesity, use of drugs/meds that increase muscle relaxation, genetics, old age, and deterioration of the brain mechanisms that control breathing.
- Related to SIDs