Chapter 2: The Need to Sleep

Homeostatic Properties of Sleep

- **Homeostasis**: Regulation by a living organism of its internal environment, with the goal of preventing critical bodily functions or states from reaching dangerous extremes.
  - e.g., body temperature varies by no more than about 2 or 3 degrees F when healthy.

- **Homeostatic Sleep drive**: the desire to sleep that slowly increases over a waking period and is gradually reduced during sleep.

- Analogously to homeostatic body temperature regulation, homeostatic sleep regulation prevents sleep drive from becoming too high (causing sleep deprivation) and promotes wakefulness when there has been sufficient sleep to reduce sleep drive to a low level.

A bit of neuron/cellular biology
A candidate cellular mechanism for homeostatic sleep drive

- Cell groups throughout the body use a molecule known as adenosine triphosphate (ATP) for energy. As phosphate components break off, energy is released and energy potential of the molecule is depleted.
- The depleted molecule, known as adenosine, binds to receptors on the cell body (for some cell types). The more bindings, the less cellular activity, apparently promoting sleep.
- During sleep, there is less activity and less use of ATP, allowing the bloodstream to carry away the built-up adenosine.
- This adenosine binding effect is prominent in the basal forebrain, which is known to be a trigger location for sleep onset.
- The above is a candidate neuro-chemical mechanism for homeostatic sleep.
- In support, caffeine prevents adenosine from binding and adenosine supplement promotes sleepiness.

Unusually high homeostatic drive (too long awake) results in sleep deprivation effects:

- **Subjective / emotional**: lethargy, loss of pleasure, depression, irritability, paranoia.
- **Behaviors**: decreases in humor and socialization, disorientation, slowed reaction time and novelty management, micro-sleeps.
- **Mental / cognitive**: difficulty concentrating, hallucinations; decreased short-term memory, reasoning, thinking, creativity, and vigilance.
- **Biological / physiological**: palpitations, < body temp., tremor, weight gain.
- **Electrophysiology**: leaves beta waves unchanged but reduces alpha wave amplitude.

Deprivation can result in micro-sleeps

- Brief loss of attention/consciousness typically lasting a few seconds (often without subsequent awareness).
- Occurs usually after sleep deprivation while doing monotonous tasks.
- Presents with head snapping, abnormal blinking patterns, theta waves, pupil contraction. Eyes can remain open.
- Auto companies working on warning systems.
Behaviors not substantially affected by moderate sleep deprivation

- Physical strength in brief bursts
- Very low mental effort physical activities (e.g., word naming)
- Brief non-timed repetitive activities.

So, sleep deprivation apparently does not cause a global worsening of performance, but exceptions prove the rule.

Fighting effects of sleep deprivation

- Bright light
- Good posture
- Cool temperature
- High motivation level for ongoing activity
- Some drugs (caffeine; stimulants; modafinil)
- Sleep! Only way to resolve homeostatic sleep pressure.

Recovery from full night sleep deprivation

- Ultimately, only sleep can compensate for lack of sleep.
- Full behavioral recovery from one night of deprivation requires at least two nights of recovery sleep.
- SWS has “priority” during recovery sleep. Later in the first night, or during subsequent nights, REM sleep recovers.

Selective REM sleep deprivation

- If dreams are psychologically critical (Freud), REM deprivation should cause severe mental problems.
- Tested by waking subjects whenever the polysomnograph indicates REM sleep.
- Difficult to achieve: Deprivation from REM results in more attempts to enter REM. (e.g., 17, 42, and 68 awakenings over three consecutive nights).
- Symptoms: hallucinations, emotional changes, increased liveliness, memory problems, increased appetite and interest in sex.
- In rats, appears to suppress neurogenesis in basal forebrain and hippocampus.
A problem for interpretation of results: Any combination of three factors could be causing the deprivation effects in these experiments: REMS deprivation, theta wave deprivation, and sleep fragmentation. Generally, when factors other than the variable of interest could be the cause of a result, the experiment is to be confounded.

Another problem: some anti-depressants suppress REM without any observed negative effects.

Selective SWS deprivation

- Problem: Waking from SWS will also disrupt REM.
- Solution: When subject enters SWS, sound a tone just loud enough to raise them to stage 2 NREM sleep.

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- Problem: Waking from SWS will also disrupt REM.
- Solution: When subject enters SWS, sound a tone just loud enough to raise them to stage 2 NREM sleep.
- SWS deprivation results in increasing attempts to enter SWS.
- Does not result in any large behavioral (observational) deficits, although subjects do appear subdued and withdrawn. Some reports of lethargy and muscle aches.
- But, it appears to result in a decrease in insulin sensitivity similar to that of people at risk for 2 diabetes.

Sleep inertia

- Sleep inertia refers to the gradual onset of fully awake performance levels after awakening. Worst for awakening from SWS, then REM, then NREM 1 and 2.
- Cognitive laboratory tasks show pronounced impaired performance for the first several minutes after awakening (similar in nature to alcohol intoxication), and to some extent for up to 2 hours after awakening.
- Increased accident rates documented.
Circadian Rhythms

- All animals have biological clocks that control physiological functions rhythmically.
- The clock allows for adaptation for day/night cycles through its cyclic (i.e., rhythmic) control of multiple body functions, including temperature, heart rate, activity level, hormone and neurotransmitter levels and many others.
- In humans this clock tends to run a bit slow (~24.2 hr; "day").
- But it is synchronized (reset) daily to a 24-hour day by environmental cues, particularly light. These cues are referred to as zeitgebers.

Evidence for a (slightly slow) clock

- “Free-running” sleep studies in humans (e.g., cave studies)
  - 24.2 hour “subjective day” (average)
- Free running sleep studies in golden hamsters.
  - Reliable daily on-off rhythm for wheel running.
  - Starting at dusk, running for about 8 hours.
  - But, if kept in dark with no other day/night cues, start time for running is progressively later each day by about ½ hour.

Master clock is in the Suprachiasmatic Nucleus (SCN) of the hypothalamus.

- Live SCN cells in Petri dish exhibit rhythmic firings
- When SCN is lesioned, body rhythms disappear.
- When SCN connections are cut, SCN still exhibits rhythmic neural firings.
- SCN tissue transplant into lesioned SCN resurrects rhythms.
- SCN tissue transplant from mutant rats changes normal rat clock timing.

Evidence that SCN is the master circadian clock
Circadian phase response curve: A representation of how sensitive the clock is to light pulses (light zeitgebers) experienced at different points across the nychthemeron.

Circadian phase response curve summary

- Pulses between subjective mid-day and mid-night delay the clock.
- Pulses between subjective mid-night and mid-day advance the clock.
- At exactly subjective mid-day (or mid-night), light pulses have no effect on the clock.

Some rhythms controlled by the circadian clock

- Body temperature
- Heart rate
- Activity level
- Melatonin level
- Eating and urination “drive”
- Neurotransmitter activity (serotonin, acetylcholine, dopamine, epinephrine, histamine)
- Hormone level (dopamine, epinephrine, hypocretin, cortisol)
No strong causal link between any specific rhythm and sleep drive.

In combination, however, these rhythmic changes clearly do affect sleep drive (direct evidence for this discussed next).

Melatonin once thought most critical for sleepiness
- But at dose that tweaks normal levels no sedative effect.
- People with no pineal glands (that produce melatonin) sleep just fine.
- A very large supplement of melatonin has only a mild sedative effect.
- So, just one of many circadian rhythms that affect sleep drive.

How do these rhythms affect sleep drive?

CSD increases at night, working in concert with homeostatic SD.

CSD decreases quickly in the morning (facilitating awakening) and stays low most of the day.

CSD for some people increases briefly in the early afternoon, yielding a tendency for siestas. For those people there are two circadian cycles per nychthemeron.

Circadian Rhythm of Sleepiness

Question: Does sleep drive vary as a function of circadian time when homeostatic effects are held constant?

Experiment:
- Subjects required to maintain 28-hour wake-sleep cycle over multiple days.
- One-third of time (9.33 hrs.) they were resting in dark and asked to sleep.
- Sleep pressure (combined homeostatic and circadian sleep drive) was measured each night by sleep onset latency. Circadian time was approximated using body temperature.
- This design allows the effect of circadian rhythms to be measured independently of the effects of homeostatic sleep drive, i.e., with homeostatic sleep drive at bedtime held constant.
Result: sleep onset latency varied systematically with circadian time, even though homeostatic sleep drive was at the same level at each bed time.

Thus, circadian time clearly does influence sleep pressure.

Subjective Sleepiness: Putting homeostatic, circadian, and other factors together

• **Sleep pressure (SP)** is a function of both homeostatic (H) sleep drive and circadian (C) sleep drive
  
  \[ SP = f(H, C) \]
  
  • Exact function unknown, but we can think of them as operating in a roughly additive way.

• **Subjective Sleepiness** is the combined affect of SP (H and C combined) and other factors such as motivation to stay awake, emotional state, drugs, and other environmental and ID factors.