Sleep Disorders

Chapter 8 (first part)
A Physiological and Behavioral Description of Sleep
I. beta activity  
   A. ~20 Hz  
   B. desynchronized, LVF  
   C. awake and alert  

II. alpha activity  
   A. ~10 Hz  
   B. synchronized, HVS  
   C. resting, inattentive, eyes closed  

III. theta activity (from the cortex)  
   A. ~5 Hz  
   B. synchronized, HVS  
   C. light sleep, extreme boredom  

IV. delta activity  
   A. ~2.5 Hz  
   B. synchronized, HVS  
   C. deep slow-wave sleep (SWS)
REM Sleep: Electrical Signs

I. the EEG - synchronized during SWS; desynchronized during REM

II. the EOG - slow and drifting during SWS; shows rapid eye movements during REM

III. the EMG - reduced activity during SWS; very much reduced or absent activity during REM

IV. PGO waves (recorded from the LGN) - absent during SWS, appear just before the onset of REM

A Typical Night’s Sleep

A typical pattern of the stages of sleep during a single night. The dark blue shading indicates REM sleep.

EEG STAGE:
- W: beta or alpha
- 1: onset of theta
- 2: theta and delta
- 3: over 50% delta
- 4:

Hours:
1 2 3 4 5 6 7 8

Awake
REM sleep
The Sleep Cycle

• wakefulness - alert and vigilant (beta) or resting with eyes closed (alpha)

• stage 1 - theta begins to appear in EEG
  • Oswald considered this an intermediate state - “borderland” or “hypnagogic”
  • thinking distorted with bizarre associations and psychotic-like thought patterns
  • sensory shocks - sudden, momentary sensory and motor phenomena MAY occur
    • falling sensations - due to sudden muscle relaxation
    • auditory hallucinations - bells, guitars, breaking glass, voices
    • unformed visual experiences such as light flashes
  • hypnagogic hallucinations - formed visual dreams that the sleeper is viewing passively (sometimes persist after waking - a particularly scary one is seeing someone standing next to your bed!)

• stage 2 - light sleep
The Sleep Cycle

- stage 3 and 4 - deep SWS sleep
- progression to this state normally takes 15-30 min. after falling asleep (sometimes up to an hour)
- deep sleep - most difficult to awaken, and awaken groggy and unresponsive
- occurs mostly early in the night
- the most restful stages of sleep
- this is where sleepwalking and sleep-talking typically occur
The Sleep Cycle

- REM sleep - in humans, detected by a sudden decrease in muscle tension, the appearance of REMS, and a shift to desynchronized EEG
  - this is when dreaming occurs
  - first episode may last 10 min., but episodes become progressively longer during the night
  - in an average night there will be 4-5 REM periods - we all dream every night, but some of us don’t remember it
  - also called paradoxical sleep (because of the desynchronized EEG)
  - the flaccid paralysis of muscles is only partial in humans, but is more complete in animals, which can become quite floppy
  - sexual arousal - penile erection and vaginal moistening occur
Sleep is Not a State of Brain Shutdown
The Basic Rest-Activity Cycle

• Nathaniel Kleitman

• the 90-min. cycles seen in SWS/REM alternation is also seen throughout the day in activities like eating, drinking, smoking, performance on cognitive tasks, etc.
Changes in Sleep During the Lifespan

- During certain periods of gestation, the brain is in REM 24 hrs/day.
- This may be in the service of brain development, or...
- It may be because the incompletely developed brain is not fully capable of SWS.
Effect of Aging on Sleep Cycles

![Graph showing sleep cycles for young adults and elderly persons.](Image)
Patterns of the stages of sleep of a normal subject and of a patient with major depression. Note the reduced sleep latency, reduced REM latency, reduction in slow-wave sleep (stages 3 and 4), and general fragmentation of sleep (arrows) in the depressed patient.

Mental Activity During Sleep

- Are we really “unconscious” during sleep?
- during REM sleep
  - blood flow is high in the visual association cortex
  - low in the primary visual cortex
  - lots of activity in motor areas as if the person were actually moving - but these impulses are prevented from reaching the muscles (usually)
  - brain mechanisms active during a dream are those that would be active if the events of the dream were actually occurring
- night terrors, as well as sleepwalking and sleep talking, typically occur during SWS
Is the Content of Dreams Symbolic?

- latent vs. manifest content (Freud)
- or is it inherently meaningless random brain activity that the brain then attempts to give some meaning to
  - Hobson’s activation-synthesis theory
  - dream interpretation may be like a Rorschach test
- the content of most dreams is mundane
Sleep Disorders
How Much is Enough

- there are large individual differences
- a few people do fine with 5 hrs. (rarely less)
- other people need 9 or even 10 hrs.
- people who get about 7 hrs/night seem to live the longest (this does NOT mean you should force yourself to get 7 hrs.)
- signs of insufficient or poor quality sleep
  - difficulty waking up
  - poor concentration and attention
  - urge to sleep during the day
  - feelings of moodiness or depression
Sleep Disorders: Insomnia

- incidence: 25% occasionally and 9% regularly

- forms of insomnia
  - sleep onset insomnia
  - sleep maintenance insomnia
  - early awakening insomnia
  - pseudoinomnia
  - sleep apnea
  - fatal familial insomnia - a genetic disease (next)
Fatal Familial Insomnia

- autosomal dominant gene
- found in probably less than 100 families in the world
- it’s a prion disease related to CJD
- average age of onset of symptoms is 50 yrs.
- always progresses to a fatal outcome within 1-2 yrs.

http://virtualaboratory.net/Biofundamentals/lectureNotes/Topic3-3_Proteins.htm

The schematic of the brain on the left is from a person with familial fatal insomnia (FFI).

FFI is due to the inheritance of a mutation in the PRNP gene; this mutation changes the normal aspartic acid 178 to an asparagine.

The squares mark brain regions affected; the lower section reveals the presence of aberrant protein aggregates in these regions.

When combined with a second mutation at position 129, the FFI mutation leads to Creutzfeld-Jacob disease (CJD).
Causes of Insomnia

• irregular sleeping habits
• stress, worry
• psychological disorders such as depression and anxiety disorders
• pain, discomfort, physical ailments
• drug dependency insomnia - withdrawal from sleeping medications (iatrogenic)
• sleep apnea - throat muscle atonia or obstruction of the throat (usually)
Sleep Disorders: Narcolepsy

- diagnosed incidence - 1 in 1500-2000 people (maybe 3X that many cases undiagnosed)

- a neurological disorder characterized by sleep, or some of its phenomena, at inappropriate times

  - sleep attacks - an overwhelming urge to sleep, usually in monotonous situations, and resulting in 2-5 minutes of normal sleep

  - cataplexy - person collapses into a flaccid paralysis, usually during emotionally arousing situations, but remains aware of his surroundings

  - sleep paralysis - intrusion of REM paralysis into waking just before or after sleep

  - hypnagogic hallucinations - intrusion of visual dreaming into waking, usually during episodes of sleep paralysis
During the intensely hot summer of 1825, I experienced an attack of this affection. Immediately after dining, I threw myself on my back upon a sofa, and, before I was aware, was seized with difficult respiration, extreme dread, and utter incapability of motion or speech. I could neither move nor cry, while the breath came from my chest in broken and suffocating paroxysms. During all this time I was perfectly awake; I saw the light glaring in at the windows in broad sultry streams; I felt the intense heat of the day pervading my frame; and heard distinctly the different noises in the street, and even the ticking of my own watch, which I had placed on the cushion beside me; I had, at the same time, the consciousness of flies buzzing around, and settling with annoying pertinacity on my face. During the whole fit, judgment was never for a moment suspended. I felt assured that I labored under incubus. I even endeavored to reason myself out of the feeling of dread which filled my mind, and longed, with insufferable ardour, for some one to open the door, and dissolve the spell which bound me in its fetters. The fit did not continue above five minutes: by degrees I recovered the use of sense and motion; and, as soon as they were so far restored as to enable me to call out and move my limbs, it wore insensibly away. (Binns, 1852, p. 156)

from Carlson, 2e, p.467
Causes of Narcolepsy

• in the lateral hypothalamus there is a nucleus of neurons that use a peptide neurotransmitter called hypocretin or orexin - hypocretinergic or orexinergic cells

• these cells are activated by environmental events and psychological factors that motivate wakefulness and interfere with sleep

• they activate brainstem areas that maintain wakefulness

• narcolepsy is due to a deficiency of orexin receptors or of orexin-secreting neurons - probably due to a genetic disorder, perhaps autoimmune

• onset is usually during adolescence, which is when the immune system begins attacking these cells

• treatment

  • Ritalin or similar stimulants for sleep attacks

  • antidepressants that are both 5-HT and NE agonists are used to treat the REM sleep symptoms
Narcolepsy and Hypocretin (Orexin)

A schematic diagram of the effect of activation of the hypocretinergic system of neurons of the lateral hypothalamus on the sleep/waking flip-flop. Motivation to remain awake or events that disturb sleep activate the hypocretinergic neurons.

Hypocretin Neurons (controls vs narcoleptics)

Thannickal et al. (2000) Neuron, v. 27, p. 469

Other Sleep Disorders

- REM sleep behavior disorder - aka REM without atonia
  - results in dreams being acted out
  - presumably due to disruption of functioning of a nucleus in the medulla called the nucleus magnocellularis
  - this is the nucleus that keeps the muscles turned off during REM sleep
  - so now all that motor activity visible on the scans can be expressed in behavior!
- similar disorders can be produced in experimental animals by lesioning this nucleus
- absence of REM sleep - at least one person has been discovered who has no REM sleep (doesn’t seem to have any ill effects)
Other Sleep Disorders

• disorders associated with SWS
• sleepwalking and sleep-talking
• night (sleep) terrors
• bed wetting
• sleep-related bruxism
• sleep-related eating disorder
What Are the Effects of Too Little Sleep?
Sleep Deprivation Experiments

- some early experiments (1950s) on sleep deprivation (esp. REM deprivation) suggested that prolonged wakefulness could make you psychotic
- this doesn’t actually seem to be the case
Pete Tripp, a DJ at WMGM (AM) radio in NYC, agreed to stay awake for 201 hrs. to raise money for the March of Dimes. He ended up hallucinating and delusional.

67 hrs. in

1959

199 hrs. 50 mins.

being walked by a nurse to keep him awake

being put to bed afterwards
But Pete is reported to have taken amphetamine to help keep himself awake during the ordeal!

Prolonged ingestion of amphetamine can cause hallucinations and delusions by itself.
1964

Randy Gardner, a 17-yr-old high school student in San Diego, CA, stayed awake for 264 hrs. with the help of friends, TV reporters, and a basketball. He suffered no ill effects.

Note: The Guinness Book no longer includes this as a record category.
The REM Rebound

REM deprivation results in a "pressure to dream"

An increasing number of awakenings are required to keep the subject deprived...

and when allowed to sleep normally, the subject shows a rebound in REM...

however, SWS is recovered first!

The two effects of REM-sleep deprivation.

Number of Times Subjects Were Awakened to Enforce REM-Sleep Deprivation

The number of awakenings required to deprive a subject of REM sleep increases as the period of deprivation ensues.

Percent of Total Sleep Time Spent in REM Sleep

After a period of REM-sleep deprivation, subjects spend a greater than usual portion of their sleep time in REM sleep.
Sleep Deprivation (cont.)

• more recent studies have suggested that the primary effect of sleep deprivation is profound sleepiness

• visual effects - visual distortions and “hallucinations” (fog, cobwebs, etc.)

• failure of concentration

• no serious deterioration in simple mental capabilities - highly motivated subjects do as well as non-sleep-deprived subjects

• when people are aroused from SWS, they act groggy and confused, as if the cortex had been shut down and was taking some time to start up again - maybe the function of SWS is to allow the cortex to rest

• there is a direct relationship between how much beta an area of cortex displays during wakefulness and how much delta it displays during SWS - “the harder it works, the harder it rests”
Sleep Deprivation (cont.)

72 Hours of Total Sleep Deprivation: Effect on Arithmetic Task Performance

Some Effects of Sleep Deprivation

Turner-Fairbank HYSIM Driving Simulator Performance under Sleep Deprivation

Fig 2. Localization of epileptiform graphoelements on EEG 1 (routine EEG) and 2 (sleep-deprived EEG). GBD, generalized bilateral discharges; GBD>R, generalized bilateral discharges, predominant to the right; GBD>L, generalized bilateral discharges, predominant to the left; LF, left frontal; RF, right frontal; LT/RT, left/right temporal; MRF, median right frontal.
Changes in Brain Activity After Sleep Deprivation

rested

deprived

fMRIs showing activation during an arithmetic task

FIG1: Activation during the arithmetic task after a normal night of sleep (top) and following sleep deprivation (bottom). Significant activation in color is overlaid onto the mean Talairach anatomical image averaged across all 13 subjects. Yellow represents the most intense activation, red the least intense. Slices are the following distances from the center point: 41 mm superior (axial), 25 mm right (sagitta) and 29 mm anterior (coronal). Axial and coronal slices are in radiological orientation (left and right are reversed). From the December 1999 issue of NeuroReport
The End of Sleep