SLEEP PHYSIOLOGY& DISORDERS

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Sleep consists of two distinct states: NREM and REM.

NREM: Non−rapid Eye Movement Sleep

a. Divided into 4 stages on the basis of EEG criteria

b. Alternates with REM sleep throughout the sleep period and is characterized by:

   i. Slowing of the EEG rhythms

   ii. Higher muscle tone

   iii. Absence of eye movements

   iv. Absence of "thoughtlike" mental activity

c. Is an idling brain in a movable body.

REM: Rapid Eye Movement Sleep

a. Characterized by:

i. An aroused EEG pattern (sawtooth waves)

ii. Sexual arousal

iii. Saccadic eye movements

iv. Elaborate visual imagery (dreaming)

v. Associated with pons

b. Is an awake brain in a paralyzed body.

Biologic Rhythms

1. The sleep-wake cycle itself is a circadian rhythm, i.e., an endogenous cyclic change occurs in an organism with a periodicity of roughly 24 hours.
2. The cycle is regulated by the superchiasmatic nucleus (SCN).
3. The REM cycle, which is approximately 90 minutes, is an example of an ultradian rhythm, occurring with a periodicity of less than 24 hours.

Sleep Facts

1. Most of NREM Stages 3 and 4 (the deepest sleep levels) occur during the first half of the night.

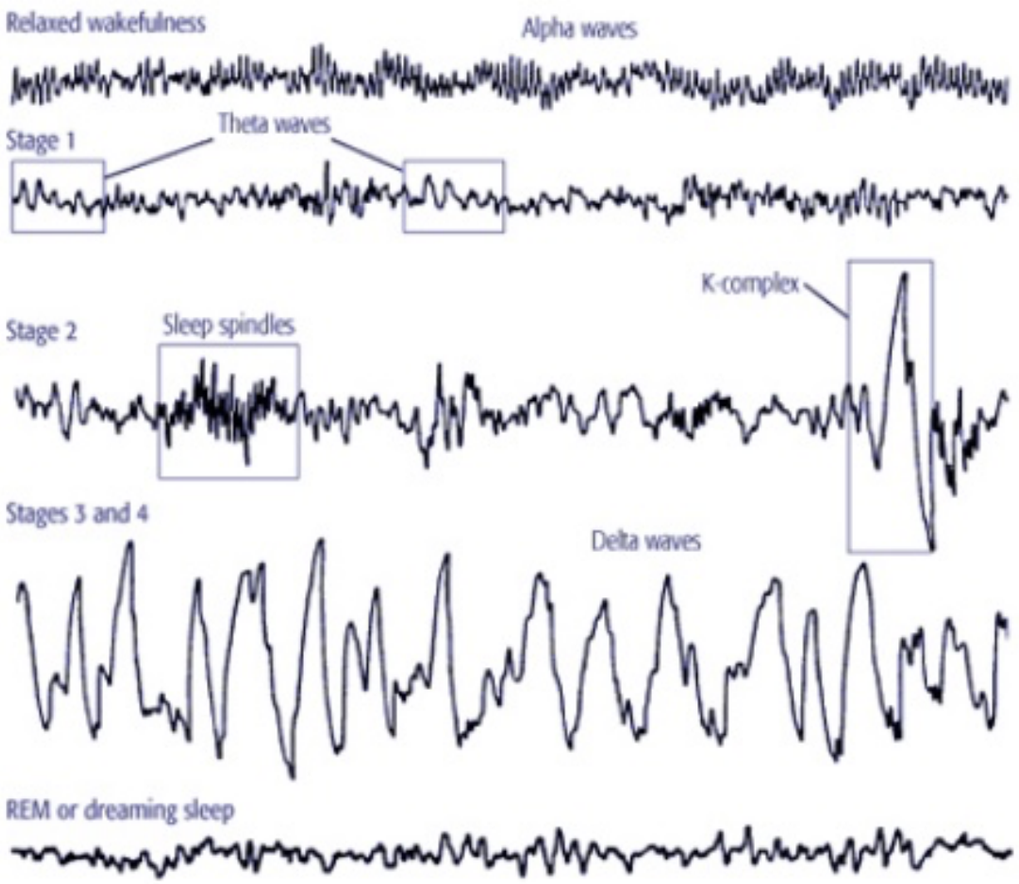
2. Stages 3 and 4 together are referred to as delta sleep or slow-wave sleep.

3. Most REM sleep occurs during the last half of the night. REM sleep gets progressively longer as the night goes on.

4. The average adult spends most sleep time in Stage 2, least in Stage 1. Adults most commonly wake out of REM or Stage 2 sleep.

5. Duration of delta sleep is 65% inherited.

EEG during sleep & wakefulness



Latency

1. Sleep latency: period between being awake until sleep onset. Insomniacs have long sleep latencies. Typically, 5–15 minutes.

2. REM latency: period between falling asleep until first REM. In the average adult, REM latency is 90 minutes.

Sleep Deprivation

1. The cerebral cortex shows the greatest effects of sleep deprivation but has the capacity to cope with one night's sleep loss.

2. The rest of the body seems relatively unaffected by sleep deprivation. Physical restitution of the body comes from the immobility that is a by- product of sleep, not from sleep itself.

3. If getting 5 hours of sleep or less per night, person functions at level of someone legally drunk!

4. The longer the prior period of wakefulness, the more Stage 4 sleep increases during the first part of the night and the more REM declines.

5. Short sleepers lose the latter part of REM sleep.

Sleep Deprivation

1. In sleep-deprived individuals, the following occurs:

   a. Lymphocyte levels decline. b. Cortisol levels rise c. Blood pressure rises
   d. Glucose tolerance is reduced e. Greater amygdala activation.
   f. Lower prefrontal cortical activity g. Increased negative mood

2. REM sleep appears to increase somewhat in both children and adults after learning, especially the learning of complex material, in the previous waking period.
   a. REM sleep is essential to get the most out of studying. It is when most long-term memories are consolidated by the hippocampus.

3. REM deprivation
   a. Does not impede the performance of simple tasks
   b. Interferes with the performance of more complex tasks
   c. Makes it more difficult to learn complex tasks
   d. Decreases attention to details but not the capacity to deal with crisis situations

4. Delta sleep increases after exercise and seems to be the result of raised cerebral temperature.

Sleep Deprivation

5. Melatonin is not related to sleeping, but rather to feelings of sleepiness:
   a. Produced in the pineal gland and directly in there retinas of the eyes
   b. Sensitive to light via a pathway from the eyes
   c. Release is inhibited by daylight, and, at nighttime, levels rise dramatically
   d. Likely mechanism by which light and dark regulate circadian rhythm
   e. Responsible for "jet lag"
   f. Responsible for seasonal affective disorder (SAD)
   g. Adjust melatonin with bright light therapy, *not* pills

DEVELOPMENTAL ASPECTS OF SLEEP

1. Sleep develops during childhood and adolescence into adult patterns.
2. Infants
   a. Premature infants do not demonstrate a discernible sleep-wake cycle.
   b. EEG demonstrates adult like rhythms of sleep and wakefulness by about 1 year.
   c. Neonatal sleep cycle: starts at 30 to 40 minutes, gradually lengthens to 90 minutes by teens
   d. Mismatch of infant and adult cycles produces "sleep fragmentation" for new parents.

DEVELOPMENTAL ASPECTS OF SLEEP

3. Adults
   a. Initial REM cycle: approximately 90 minutes. Subsequent cycles across the evening are shorter.

   b. REM: 20% of sleep time

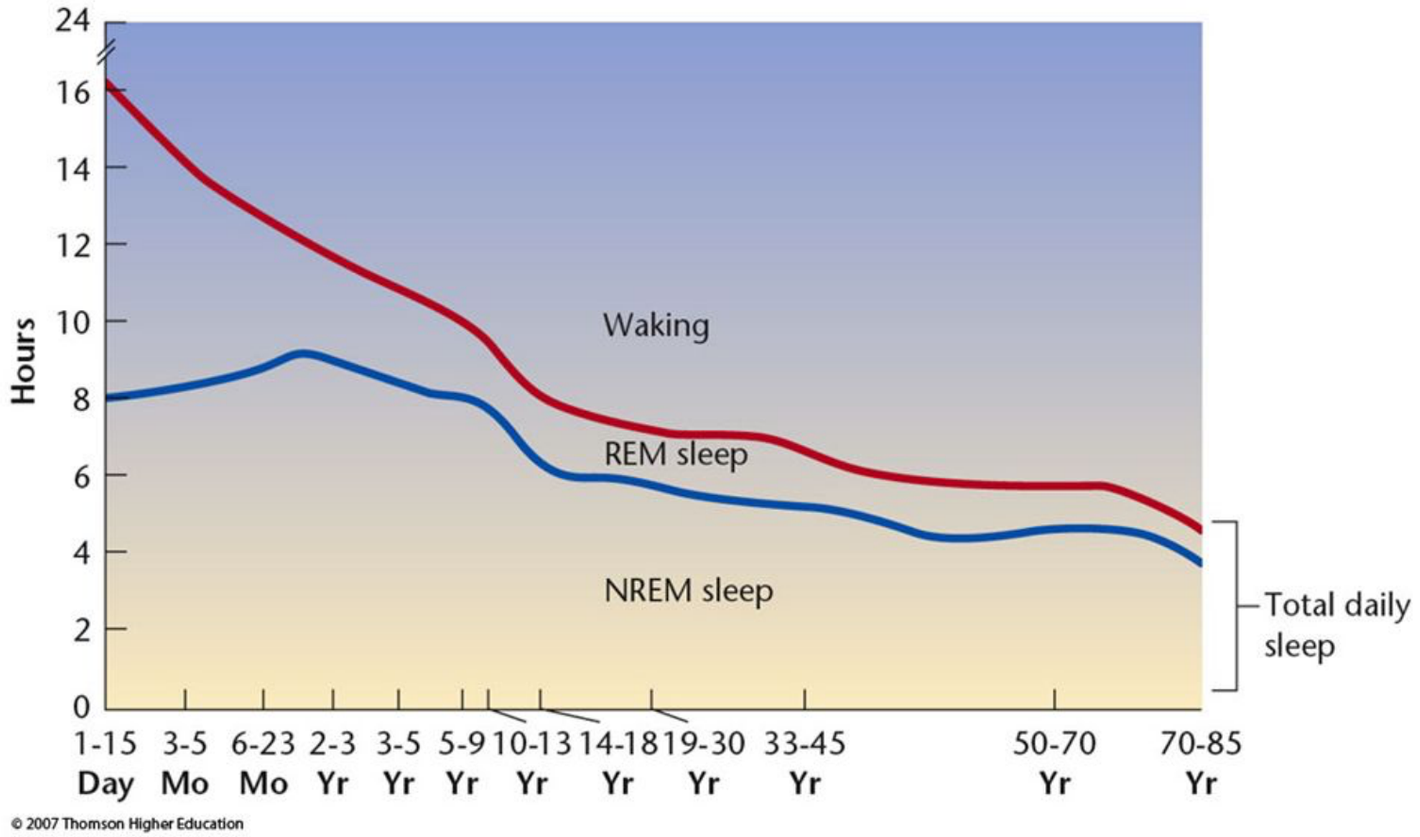
   c. Total sleep time/24-hour period decreases gradually with age.

4. Elderly
   a. Total sleep time continues to decline.

   b. REM percentage remains constant (20%) up to around 80 years of age, then declines further.

   c. Stage 4, then Stage 3 NREM (delta sleep) vanish. Elderly often complain that they don't feel as rested as they used to feel.

REM Sleep and Development



Chemical and Psychiatric Correlates of Sleep

1. Dopamine

a. Any pharmacology that increases dopamine increases wakefulness.

b. Dopamine blockers (e.g., antipsychotics) increase sleep somewhat.

2. Benzodiazepines

a. are associated with reduced REM sleep and delta sleep.

b. Little rebound effect c. Chronic use increases sleep latency.

3. Alcohol consumption

a. Moderate

i. Early sleep onset ii. Increased wakefulness during the second half of the night

b. Intoxication

i. Decreases REM. ii. REM rebound (with nightmares) during withdrawal

4. Major depression

a. Increases REM

b. Decreases REM latency (45 rather than 90 minutes)

c. Decreases Stages 4 and 3 sleep

d. Increased sleep in multiple periods over 24 hours

e. Early morning waking

Neurotransmitters Associated with Sleep: "SANDman"

1. **S**erotonin: helps initiate sleep

2. **A**cetylcholine (ACh): higher during REM sleep (associated with erections in men)

3. **N**orepinephrine (NE): lower during REM sleep
   a. Ratio of ACh and NE is the biochemical trigger for REM sleep.
   b. NE pathway begins in the pons, which regulates REM sleep.

4. **D**opamine: produces arousal and wakefulness. Rises with waking

SLEEP DISORDERS

CLASSIFICATION OF SLEEP DISORDERS

A. Dyssomnias are characterized by problems in the timing, quality, or amount of sleep. They include insomnia, breathing-related sleep disorder (sleep apnea), and narcolepsy, as well as circadian rhythm sleep disorder, nocturnal myoclonus, restless legs syndrome, and the primary hypersomnias (e.g., Kleine–Levin syndrome).

B. Parasomnias are characterized by abnormalities in physiology or in behavior associated with sleep. They include bruxism (tooth grinding) and sleepwalking, as well as sleep terror, REM sleep behavior, and nightmare disorders.

Narcolepsy

A condition characterized by the brain's inability to control sleep-wake cycle.

1. The narcoleptic tetrad:
    a. Sleep attacks and excessive daytime sleepiness (EDS)
    b. Cataplexy (pathognomonic sign)
    c. Sleep paralysis
    d. Hypnagogic hallucinations (hypnopompic can occur, but not pathognomonic)
        i. Hypnagogic: while falling asleep ii. Hypnopompic: while waking up

2. Narcolepsy is a disorder of REM sleep: onset of REM within 10 minutes.

3. Linked to deficiency in hypocretin when cataplexy is present. Loss of hypocretin results in an inability to regulate sleep.

Narcolepsy

4. Treatment
    a. Modafinil or psychostimulants for excessive daytime sleepiness
        i. inhibits DA reuptake
        ii. activates glutamate; inhibits GABA

    b. Antidepressants (TCA, SNRI)

    c. Gamma hydroxybutyrate (GHB) to reduce daytime sleepiness and cataplexy

Sleep Apnea

Types:

a. Obstructive (upper airway) sleep apnea

i. Middle-aged ii. Overweight iii. Rasping snoring

b. Central (diaphragmatic) sleep apnea

i. Elderly ii. Overweight

iii. Cheyne-Stokes (60-second hyperventilation, followed by apnea)

c. Mixed sleep apnea

Sleep Apnea

2. Clinical presentation and features:

a. High risk of sudden death during sleep, development of severe nocturnal hypoxemia, pulmonary and systemic hypertension (with elevated diastolic pressure)

b. Nocturnal cardiac arrhythmias (potentially life-threatening)

c. Bradycardia, then tachycardia

d. Males outnumber females by 8 to 1

e. EDS and insomnia often reported

f. Heavy snoring with frequent pauses

g. Kicking, punching of sleeping partner

h. Obesity is often part of the clinical picture, but not always

Sleep Apnea

Treatment :

a. Weight loss (if applicable)

b. Behavioral conditioning to change sleep position

c. Continuous positive airway pressure (CPAP). Most likely medical intervention.

d. For severe obstructive and mixed apnea: tonsillectomy or tracheostomy

Insomnia

1. Possible causes:
    a. Secondary to hypnotic medication abuse
        i. Development of tolerance to sedative hypnotics is common and leads to escalating doses
        ii. Sleep architecture becomes disrupted and sleep fragmentation occurs.
    b. Emotional problems, especially anxiety, depression, mania
    c. Conditioned poor sleep: sleep cycle is so disrupted that habit of sleep is lost
    d. Withdrawal from drugs or alcohol

Insomnia

2. When working up an insomniac, examine for medical explanations such as apnea and drug use (prescription or illicit), as well as psychiatric factors such as depression, anxiety, and schizophrenia

3. 50% of insomnia in sleep labs is due to psychological factors.

4. Insomniacs may have GABA levels 30% lower than normal.

Insomnia Treatment

a. Sleep hygiene

b. Behavior therapy still is best (most effective).

i. Muscle relaxation ii. Stimulus control

c. Drugs

i. Action on GABA receptors
Zaleplon, Zolpidem, Eszopiclone

ii. Ramelteon
Melatonin receptor agonist (MT1, MT2)

Low chance of dependence

No hangover or rebound

Enuresis (Bed-wetting)

1. Most seen in Stages 3 and 4 sleep, but can occur in all stages.

2. Boys twice as likely as girls. At age 5, 7% of boys, 3% of girls

3. Boys cease wetting later.

4. Often history with same-sex parent

5. Common after change or new sibling born. Defense mechanism of regression

6. Treat with desmopressin, imipramine or bell pad technique.

Somnambulism (Sleep-walking)

1. Repetitive walking around during sleep
2. No memory of the episode on awakening
3. Begins in childhood (usually 4–8 yrs of age)
4. Occurs during delta sleep
5. If wakened, the person is confused and disoriented.
6. Treat with benzodiazepines

Bruxism (Teeth-grinding)

1. Tooth grinding during sleep (stage 2)
2. Can lead to tooth damage and jaw pain
3. Treat with dental appliance worn at night or corrective orthodontia

Night Terrors versus Nightmare

Sleep stage	Night Terrors Stage 4 (delta sleep)	Nightmares REM
Physiologic arousal	Extreme	Elevated
Recall upon waking	No	Yes
Waking time anxiety	Yes, usually unidentified	Yes, often unidentified
Other issues	Runs in families More common in boys Can be a precursor to temporal lobe epilepsy	Common from ages 3 to 7 If chronic, likelihood of serious pathology Desensitization behavior therapy provides marked improvement

The End