Medical Neuroscience | Tutorial Notes

Sleep and Wakefulness

MAP TO NEUROSCIENCE CORE CONCEPTS[1]

NCC2.   Neurons communicate using both electrical and chemical signals.

NCC3.   Genetically determined circuits are the foundation of the nervous system.

NCC8.   Fundamental discoveries promote healthy living and treatment of disease.

LEARNING OBJECTIVES

After study of the assigned learning materials, the student will:

1.   Discuss circadian rhythms in homeostatic functions and overt behaviors.

2.   Discuss the underlying neural systems that account for circadian rhythmicity.

3.   Describe the basis of "brain waves" (electroencephalographic activity).

4.   Characterize the stages of non-REM and REM sleep.

5.   Describe the functional states of the thalamocortical projection neurons in non-REM sleep and waking states.

TUTORIAL OUTLINE

I.   Introduction

    A.   human sleep patterns

        1.   how much is enough? (see **Figure 28.1A**[2])

        2.   age matters (see **Figure 28.1B**)

    B.   sleep essentials

        1.   why do we sleep?

        2.   sleep is essential for optimal health status (see **Figure 28.3**)

II   Circadian cycles

    A.   diverse physiological (homeostatic) functions and overt patterns of behavior cycle with a period of approximately 24 hours (see **Figures 28.2** and **28.4**)

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[1]   Visit **BrainFacts.org** for *Neuroscience Core Concepts* (©2012 Society for Neuroscience) that offer fundamental principles about the brain and nervous system, the most complex living structure known in the universe.

[2]   Figure references to Purves et al., *Neuroscience, 5th Ed.*, Sinauer Assoc., Inc., 2012. [click here]

1.   oxidative metabolism and core body temperature decline during (or just prior to) the onset of sleep

2.   certain hormones (e.g., cortisol, growth hormone) "spike" in relation to intervals of nightly sleep

3.   daily cycles of activity and sleep:

   a.   average 24.0 hours

   b.   if isolated from external cues, daily cycles "free-run" with a period of just longer 24 hours

   c.   indicates that circadian rhythms are generated internally, but entrained to environmental cycles of day and night

B.   **Suprachiasmatic nucleus** (SCN) and photoentrainment

1.   the SCN is located in the periventricular zone of the anterior hypothalamus, just above the optic chiasm (see **Box 21A**)

2.   SCN neurons maintain an intrinsic circadian rhythm (see **Box 28B**)

   a.   SCN lesions abolish circadian rhythms of sleep and wakefulness

   b.   isolated SCN neurons show circadian rhythms

      view an online animation that accompanies *Neuroscience*, 5th. *Ed.*, Chapter 28: **Animation 28.01 A Molecular Clock** [click here]

3.   neural mechanism of photo-entrainment (see **Figure 28.5**)

   a.   SCN receives retinal input via the retino-hypothalamic tract from newly discovered, photosensitive ganglion cells

   b.   SCN activates projection neurons in the paraventricular nucleus (medial hypothalamus) that innervate sympathetic preganglionic neurons in the intermediolateral cell column

   c.   sympathetic postganglionic neurons in the superior cervical ganglion innervate the pineal body (gland), which synthesizes and secretes the sleep promoting hormone, **melatonin**

   d.   melatonin modulates the activity of hypothalamic and reticular formation centers that, in turn, regulate the sleep-wake cycle

III.   Sleep stages

A.   sleep comprises a series of successive stages that occur in a characteristic sequence and cycle during a normal night's sleep (see below)

B.   first, a primer on **electroencephalography** (EEG) (see **Box 28C**)

1.   electrical activity generated by the billions of neurons and their synaptic connections within the cerebral cortex is reflected in the electrical potentials that can be recorded from the surface of the scalp

2.   the amplitude and frequency of the surface EEG ("brain waves") is a function of:

        a.   the number of active neurons that underlie any electrode

        b.   the firing rate of the active neurons

        c.   the **synchrony** of the active population (see **Box 28C**, **Figure C**)

3.   EEG activity is conventionally recognized in one of several frequency bands that have characteristic amplitudes:

        a.   delta rhythms = 1-4 Hz, high amplitude (slow-wave sleep)

        b.   theta rhythms = 4-7 Hz, moderate amplitude (active exploration)

        c.   alpha rhythms = 8-12 Hz, moderate-to-high amplitude (quiet rest)

        d.   beta rhythms = 12-60 Hz, low amplitude (attentive, concentrating)

4.   EEG recordings are used to diagnosis normal (e.g., sleep, wakeful conscious) and pathological (e.g., seizure, coma, persistent vegetative) brain states (see **table**)

C.   electroencephalographic and physiological stages of sleep (see **Figure 28.6** & **28.7**)

1.   **stage 1**: primarily characterized by feelings and behaviors associated with extreme drowsiness and EEG rhythms that are slightly slower in frequency and greater in amplitude than those observed in most waking states

2.   **stage 2**: next deeper stage of sleep

        a.   further decrease in EEG frequency and further increase in amplitude

        b.   this "baseline" rhythm is interrupted intermittently by brief, high-frequency clusters of spike activity called **sleep spindles**

3.   **stage 3**: moderate to deep levels of sleep, characterize by a cessation of sleep spindles and still further decreases in EEG frequency and further increase in amplitude

4.   **stage 4**: also called "slow-wave sleep"; this is the deepest level sleep and it is characterize by prominent, high amplitude delta waves

5.   **REM** (= rapid eye movement) **sleep** (also called "paradoxical sleep")

        a.   following stage 4 sleep, the cycles reverse through stage 2 sleep when abrupt transitions to an episode of REM sleep ensues

        b.   paradoxically, EEG activity in REM sleep resembles the waking state

        c.   most (but not all) dreaming occurs in REM sleep (see below)

        d.   certain cortical regions are less active ("executive function" sectors of the prefrontal cortex), while other cortical regions are more active (limbic forebrain structures) (see **Figure 28.10**)

           i.   evidently, this helps explains why dreams typically are characterized by heightened emotionality and, sometimes, by inappropriate social content

        d.   during REM sleep, a number of physiological functions are modulated (see **Figure 28.7**)

      i.   rapid eye movements are expressed

      ii.   but most large skeletal muscles (except for respiration musculature) are actively hypotonic

      iii.   certain visceral motor activities (cardiac output, respiration, blood pressure) are increased

      iv.   thermoregulation ceases

      v.   in men, penile erection occurs; in women, vaginal lubrication occurs

    e.   a normal night's sleep involves multiple cycles through deeper stages of sleep, back "out" to REM sleep, and back into deeper stages, with progressive increases in the duration of REM sleep through the night

    f.   although sleep is essential for life, REM sleep is not

    g.   however, the prevalence of dreams in REM sleep suggests that its overall functions may relate to the occurrence of dreams (see below)

  D.   dreams : why? (no consensus)

    1.   Freud: "ego" relaxes its hold on the "id"

    2.   maintenance: rehearse less common behaviors that are not often activated in waking states (e.g., intense emotional states, aggression)

    3.   unlearning: erases non-adaptive (unwanted) memories

    4.   learning: consolidates learning and memory (synaptic plasticity)

    5.   epiphenomenon: REM important, but not dreams per se

IV.   Neural circuits governing sleep

  A.   transitions of brain state from one stage of sleep to another involve a complex interplay of multiple neurochemical systems in the hypothalamus and the brainstem reticular formation (see **Figure 28.8, 28.11,** and **Table 28.1**)

    1.   waking and REM sleep states are promoted by the **activation** of cholinergic and noradrenergic systems in the brainstem

      a.   these systems, in turn, activate other diffusely projecting neurotransmitter systems in the reticular formation and hypothalamus

      b.   when waking up, cholinergic, aminergic, serotonergic, histaminergic, and orexinergic neurotransmitter systems activate (directly and indirectly) widespread regions of the CNS (see **Figure 28.11**)

      c.   when transitioning from non-REM to REM sleep:

        i.   cholinergic input from the brainstem increases, but serotonergic and noradrenergic input decreases

ii. in REM sleep, descending inhibitory (GABAergic and glycinergic) projections inhibit alpha motor neuron activity in the ventral horn of the spinal cord (see **Figure 28.8**)

2. non-REM sleep stages are induced by the **suppression** of these activating systems by inhibitory neurons in the preoptic region of the hypothalamus, which in turn are activated by the basal forebrain

   a. sleep is promoted by the accumulation of extracellular **adenosine** in certain basal forebrain nuclei

      i. adenosine builds up in cells during active periods when energy utilization is high and ATP is being consumed

      ii. excess adenosine is released (non-synaptically) by facilitated transport/passive diffusion and binds to specific receptors on neurons and glia

      iii. thus, extracellular adenosine is a "signal" reflecting neuronal energy stores and recent levels of neuronal activity

      iv. in the basal forebrain, adenosine levels increase when awake and decline while sleeping

      v. evidently, caffeine and theophylline are stimulants because they antagonize adenosine receptors

   b. basal forebrain nuclei activate the ventrolateral preoptic nucleus (VLPO), which inhibit the hypothalamic histaminergic system (tuberomammillary nucleus) and the activating systems of the brainstem

B. thalamocortical interactions during wakefulness/REM sleep and non-REM sleep

   1. thalamocortical projection neurons show bi-stable functional states: *oscillatory* and *tonically active* (see **Figure 27.12**)

      a. oscillatory, bursting state

         i. neurons in this state display short bursts of action potentials that ride upon prolonged calcium spikes

         ii. between burst events, the membrane potential is hyperpolarized

         iii. hyperpolarized state is induced by:

             - withdrawal of brainstem cholinergic and noradrenergic stimulation

             - interactions of specific relay neurons and inhibitory neurons of the thalamic reticular nucleus (see **Figure 27.13**)

         iv. in this state, thalamocortical neurons do not respond to afferent input; thus transmission of sensory signals is impeded

        and sensory cortical areas are "disconnected" from the outside (and internal) world

     v.   typically, this firing state dominates in non-REM sleep

   b.   tonically active, firing state

     i.   neurons in this state are relatively depolarized and capable of entering tonic modes of firing

     ii.   depolarized state is induced by the activation of cholinergic and noradrenergic systems

     iii.   in this state, sensory signals are transmitted to sensory cortex and perception (generated by sensory experience or by the partial reactivation of stored experience) is possible

     iv.   typically, this firing state dominates in both waking states and REM sleep

V.   Sleep disorders

   A.   **insomnia**

     1.   impairment associated with the inability to fall asleep, stay asleep, or experience restoration from sleep given adequate opportunity to sleep

     2.   affects about 15% of the population

   B.   **circadian rhythm disorders**

     1.   misalignment between a person's sleep pattern and the desired or societal norm sleep pattern

   C.   **sleep apnea**

     1.   mechanical obstruction is the most common and clinically important cause

     2.   predisposing factors: obesity, retrognathia, large tonsils, deviated septum

   D.   **narcolepsy** ("sleep attacks")

     1.   inappropriate intrusion into waking state of <u>fragments</u> of REM sleep

       a.   cataplexy: partial or complete paralysis induced by strong emotion

       b.   residual paralysis while awake around sleep/wake transition

       c.   hallucinations around sleep/wake transition

     2.   attributable to a defect in hypocretin/orexin type-2 receptor gene and/or abnormally low hypocretin/orexin activity

   E.   **restless leg syndrome**

     1.   unpleasant sensations in the legs that produce an urge to move them to obtain relief

     2.   associated with insufficient Fe in substantia nigra, pars reticulata, suggesting possibility of dopamine dysfunction in putamen