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DEPARTMENT: MEDICINE & SURGERY

COURSE: PHS 305 (NEUROPHYSIOLOGY)

- 1.) Discuss the physiology of sleep.
- 2.) Discuss the role of basal ganglia in coordinating movement.

Answers

1.) SLEEP ARCHITECTURE

Sleep architecture refers to the basic structural organization of normal sleep. There are two types of sleep, non-rapid eye-movement (NREM) sleep and rapid eye-movement (REM) sleep. NREM sleep is divided into stages 1, 2, 3, and 4, representing a continuum of relative depth. Each has unique characteristics including variations in brain wave patterns, eye movements, and muscle tone. Sleep cycles and stages were uncovered with the use of electroencephalographic (EEG) recordings that trace the electrical patterns of brain activity.

NREM and REM Sleep Cycles

A sleep episode begins with a short period of NREM stage 1 progressing through stage 2, followed by stages 3 and 4 and finally to REM. However, individuals do not remain in REM sleep the remainder of the night but, rather, cycle between stages of NREM and REM throughout the night. NREM sleep constitutes about 75 to 80 percent of total time spent in sleep, and REM sleep constitutes the remaining 20 to 25 percent. The average length of the first NREM-REM sleep cycle is 70 to 100 minutes. The second, and later, cycles are longer lasting—approximately 90 to 120 minutes. In normal adults, REM sleep increases as the night progresses and is longest in the last one-third of the sleep episode. As the sleep episode progresses, stage 2 begins to account for the majority of NREM sleep, and stages 3 and 4 may sometimes altogether disappear.

Four Stages of NREM Sleep

The four stages of NREM sleep are each associated with distinct brain activity and physiology.

Stage 1 Sleep

NREM stage 1 sleep serves a transitional role in sleep-stage cycling. Aside from newborns and those with narcolepsy and other specific neurological disorders, the average individual's sleep

episode begins in NREM stage 1. This stage usually lasts 1 to 7 minutes in the initial cycle, constituting 2 to 5 percent of total sleep, and is easily interrupted by a disruptive noise. Brain activity on the EEG in stage 1 transitions from wakefulness (marked by rhythmic alpha waves) to low-voltage, mixed-frequency waves. Alpha waves are associated with a wakeful relaxation state and are characterized by a frequency of 8 to 13 cycles per second.

Stage 2 Sleep

Stage 2 sleep lasts approximately 10 to 25 minutes in the initial cycle and lengthens with each successive cycle, eventually constituting between 45 to 55 percent of the total sleep episode. An individual in stage 2 sleep requires more intense stimuli than in stage 1 to awaken. Brain activity on an EEG shows relatively low-voltage, mixed-frequency activity characterized by the presence of sleep spindles and K-complexes. It is hypothesized that sleep spindles are important for memory consolidation. Individuals who learn a new task have a significantly higher density of sleep spindles than those in a control group.

Stages 3 and 4, Slow-Wave Sleep

Sleep stages 3 and 4 are collectively referred to as slow-wave sleep (SWS), most of which occurs during the first third of the night. Each has distinguishing characteristics. Stage 3 lasts only a few minutes and constitutes about 3 to 8 percent of sleep. The EEG shows increased high-voltage, slow-wave activity.

The last NREM stage is stage 4, which lasts approximately 20 to 40 minutes in the first cycle and makes up about 10 to 15 percent of sleep. The arousal threshold is highest for all NREM stages in stage 4. This stage is characterized by increased amounts of high-voltage, slow-wave activity on the EEG.

REM Sleep

REM sleep is defined by the presence of desynchronized (low-voltage, mixed-frequency) brain wave activity, muscle atonia, and bursts of rapid eye movements. “Sawtooth” wave forms, theta activity (3 to 7 counts per second), and slow alpha activity also characterize REM sleep. During the initial cycle, the REM period may last only 1 to 5 minutes; however, it becomes progressively prolonged as the sleep episode progresses.

Dreaming is most often associated with REM sleep. Loss of muscle tone and reflexes likely serves an important function because it prevents an individual from “acting out” their dreams or nightmares while sleeping. Approximately 80 percent of vivid dream recall results after arousal from this stage of sleep. REM sleep may also be important for memory consolidation.

Physiology During Sleep

There are body system changes that occur during sleep. Generally, these changes are well tolerated in healthy individuals, but they may compromise the sometimes fragile balance of individuals with vulnerable systems, such as those with cardiovascular diseases. Physiological changes also occur in the following systems:

- Cardiovascular: Changes in blood pressure and heart rate occur during sleep and are primarily determined by autonomic nervous system activity. For instance, brief increases in blood pressure and heart rate occur with K-complexes, arousals, and large body movement. Further, there is an increased risk of myocardial infarction in the morning due to the sharp increases in heart rate and blood pressure that accompany awakening.
- Sympathetic-nerve activity: Sympathetic-nerve activity decreases as NREM sleep deepens; however, there is a burst of sympathetic-nerve activity during NREM sleep due to the brief increase in blood pressure and heart rate that follows K-complexes. Compared to wakefulness, there is a rise in activity during REM sleep.
- Respiratory: Ventilation and respiratory flow change during sleep and become increasingly faster and more erratic, specifically during REM sleep. Ventilation data during REM sleep are somewhat unclear, but they suggest that hypoventilation (deficient ventilation of the lungs that results in reduction in the oxygen content or increase in the carbon dioxide content of the blood or both) occurs in a similar way as during NREM sleep. Several factors contribute to hypoventilation during NREM, and possibly REM, sleep such as reduced pharyngeal muscle tone.
- Renal: There is a decreased excretion of sodium, potassium, chloride, and calcium during sleep that allows for more concentrated and reduced urine flow. The changes that occur during sleep in renal function are complex and include changes in renal blood flow, glomerular filtration, hormone secretion, and sympathetic neural stimulation.
- Endocrine: Endocrine functions such as growth hormone, thyroid hormone, and melatonin secretion are influenced by sleep. Growth hormone secretion typically takes place during the first few hours after sleep onset and generally occurs during SWS, while thyroid hormone secretion takes place in the late evening. Melatonin, which induces sleepiness, likely by reducing an alerting effect from the suprachiasmatic nucleus, is influenced by the light-dark cycle and is suppressed by light.

SLEEP-WAKE REGULATION

The Two-Process Model

The sleep-wake system is thought to be regulated by the interplay of two major processes, one that promotes sleep (process S) and one that maintains wakefulness (process C). Process S is the homeostatic drive for sleep. The need for sleep (process S) accumulates across the day, peaks just before bedtime at night and dissipates throughout the night.

Process C is wake promoting and is regulated by the circadian system. Process C builds across the day, serving to counteract process S and promote wakefulness and alertness. However, this wake-promoting system begins to decline at bedtime, serving to enhance sleep consolidation as the need for sleep dissipates across the night. With an adequate night's rest, the homeostatic drive for sleep is reduced, the circadian waking drive begins to increase, and the cycle starts over. In the absence of process C, total sleep time remains the same, but it is randomly distributed over the day and night; therefore, process C also works to consolidate sleep and wake into fairly distinct episodes. Importantly, through synchronization of the circadian system, process C assists in keeping sleep-wakefulness cycles coordinated with environmental light-dark cycles.

Sleep-Generating Systems in the Brainstem

Sleep process S is regulated by neurons that shut down the arousal systems, thus allowing the brain to fall asleep. Many of these neurons are found in the preoptic area of the hypothalamus. These neurons, containing molecules that inhibit neuronal communication, turn off the arousal systems during sleep. Loss of these nerve cells causes profound insomnia. Inputs from other regions of the brain also greatly influence the sleep system. These include inputs from the lower brainstem that relay information about the state of the body (e.g., a full stomach is conducive to falling asleep), as well as from emotional and cognitive areas of the forebrain. In addition, as described further in the next section, there are inputs from the circadian system that allow the wake-sleep system to synchronize with the external day-night cycle, but also to override this cycle when it is necessitated by environmental needs.

The sleep-generating system also includes neurons in the pons that intermittently switch from NREM to REM sleep over the course of the night. These neurons send outputs to the lower brainstem and spinal cord that cause muscle atonia, REMs, and chaotic autonomic activity that characterize REM sleep. Other outputs are sent to the forebrain, including activation of the cholinergic pathways to the thalamus to activate the EEG.

CIRCADIAN RHYTHMS, THE 24-HOUR CLOCK

Circadian rhythms refer, collectively, to the daily rhythms in physiology and behavior. They control the sleep-wake cycle, modulate physical activity and food consumption, and over the course of the day regulate body temperature, heart rate, muscle tone, and hormone secretion. The rhythms are generated by neural structures in the hypothalamus that function as a biological clock. Animals and plants possess endogenous clocks to organize daily behavioral and physiological rhythms in accord with the external day-night cycle. The basis for these clocks is believed to be a series of molecular pathways involving “clock” genes that are expressed in a nearly 24-hour rhythm.

In mammals, two proteins, Clock and Bmal1, bind together and move into the nucleus of the cell, where they bind to specific sites in the DNA that activate specific genes (Figure 2-4). Among the genes that they activate are Period and Cryptochrome. The products of these genes also move back into the nucleus, where they disrupt the binding of Clock and Bmal1 to the DNA, thus inhibiting their own synthesis. This results in a rising and falling pattern of expression of the Period and Cryptochrome gene products with a periodicity that is very close to 24 hours.

Sleep and Thermoregulation

Body temperature regulation is subject to circadian system influence. An individual’s body temperature is higher during the day than at night. At night there is a gradual decline in body temperature, a decrease in heat production (called the falling phase of the body temperature rhythm), and an increase in heat loss, all which promote sleep onset and maintenance, as well as EEG slow-wave activity. Conversely, there is a gradual increase in body temperature several hours before waking. The brain sends signals to other parts of the body that increase heat production and conservation in order to disrupt sleep and promote waking.

2.) ROLE OF BASAL GANGLIA IN COORDINATING MOVEMENT

The basal ganglia or basal nuclei are large masses of grey matter located within the central core of white matter of the cerebral hemispheres. The basal ganglia is composed of the following grey nuclei:

- Caudate nucleus
- Lentiform nucleus
- Amygdaloid nuclear complex (or Amygdala)
- Claustrum
- Substantia nigra (within the midbrain)
- Subthalamic nucleus

Role in eye movements

One intensively studied function of the basal ganglia is its role in controlling eye movements. Eye movement is influenced by an extensive network of brain regions that converges on a midbrain area called the superior colliculus (SC). The SC is a layered structure whose layers form two-dimensional retinotopic maps of visual space. A "bump" of neural activity in the deep layers of the SC drives an eye movement directed toward the corresponding point in space.

The SC receives a strong inhibitory projection from the basal ganglia, originating in the substantia nigra pars reticulata (SNr). Neurons in the SNr usually fire continuously at high rates, but at the onset of an eye movement they "pause", thereby releasing the SC from inhibition. Eye movements of all types are associated with "pausing" in the SNr; however, individual SNr neurons may be more strongly associated with some types of movements than others. Neurons in some parts of the caudate nucleus also show activity related to eye movements. Since the great majority of caudate cells fire at very low rates, this activity almost always shows up as an increase in firing rate. Thus, eye movements begin with activation in the caudate nucleus, which inhibits the SNr via the direct GABAergic projections, which in turn disinhibits the SC.