17/mhs01/260
Medicine and surgery
300 level
Neurophysiology

1. Discuss the physiology of sleep

Sleep influences all of the body's major physiologic systems, including thermoregulatory, musculoskeletal, endocrine, respiratory, cardiovascular, gastrointestinal, and immune systems. Sleep also impacts individual's weight, mental health, and overall quality of life.

All of these relationships are bi-directional: in other words, many of these physiologic systems also influence an individual's sleep. Partial or total lack of sleep, disturbed sleep, and poor quality sleep can all drastically change an individual's thinking and behavior and negatively impact his or her physical, mental, and emotional health.

The physiology of sleep-thermoregulation&sleep

Core body temperature is regulated by circadian rhythm.

Our body temperature is higher during the day and declines at night. In normal sleepers and normal conditions, sleep onset occurs as a person's body temperature falls and his or her heat loss increases — these changes also prompt the maintenance of sleep. (This is why exercise should ideally occur four to six hours before bedtime, in order to ensure that the person's core temperature is not elevated when they try to go to sleep.)

Body temperature continues to decline during sleep until about 4:00 AM, when it starts to rise again. People usually wake up during this rising part of the circadian rhythm, as the body warms up and stops losing heat.

The Musculoskeletal system & sleep

Physiologically, most muscles relax during non-rapid eye movement (NREM) sleep and become atonic (i.e., exhibiting a lack of muscle tone similar to paralysis) during rapid eye movement (REM) sleep, except for the ocular muscles and the diaphragm. This atonia prevents us from moving around and hurting ourselves or bed partners during sleep, but it can also contribute to the etiology of certain sleep disorders, such as narcolepsy.

Musculoskeletal disorders of the bones, joints, and muscles — like arthritis, fibromyalgia, or chronic back pain — can result in pain that leads to microarousals with movement and interferes with the ability to sleep. This problem with sleep leads to fatigue, interferes with the person's quality of life, and can make their pain worse. Treating such pain and insomnia concurrently — rather than sequentially — yields better outcomes for both conditions, compared to maximizing treatment for one condition and subsequently adding treatment for the second.

The Endocrine System & Sleep

The endocrine system (the collection of glands that secrete hormones into the circulatory system and are carried to another organ) has a complex response to sleep. The secretion of some hormones increases during sleep (e.g., growth hormone, prolactin, and luteinizing hormone), while the secretion of other hormones is inhibited (e.g., thyroid stimulating hormone and cortisol).

Some hormones are tied directly to a particularly sleep stage. Growth hormone is typically secreted in the first few hours after the onset of sleep and generally is released during slow-wave

sleep (SWS). Cortisol is tied to the circadian rhythm, and peaks in late afternoon, regardless of the person's sleep status or the darkness/light cycle. Melatonin is released in the dark and is suppressed by light58. Thyroid hormone secretion occurs in the late evening.

Considerable research has linked endocrine dysfunction and sleep dysfunction (specifically insomnia). It has been proposed that over-activity (or hyper-drive) of the "hypothalamic-pituitary-adrenal" (HPA) axis, the over-activation of hormonal interaction between a part of the brain and the adrenal gland, can impact sleep function — perhaps in response to stress — and subsequently increase secretion of cortisol and norepinephrine, thus promoting wakefulness.

Diabetes is a specific disease that affects the endocrine system's ability to produce the hormone insulin and is, in turn, affected by sleep. Adults who report getting 5 or fewer hours of sleep a night were 2.5 times more likely to have diabetes, compared to people who sleep 7 - 8 hours per night. People who slept 6 hours/night were 1.7 times more likely to have diabetes than their peers who sleep longer. Interestingly, people who sleep for 9 or more hours also have higher rates of diabetes, so perhaps both insufficient sleep and too much sleep are both unhealthy when it comes to insulin and the development of diabetes. Orexin plays an important role in glucose metabolism (including through its involvement in the production of a circadian glucose rhythm), preventing or promoting insulin resistance.

The Respiratory System & sleep

Sleep has a large impact on the respiratory system, and vice versa. Ventilation (entry and exit of air into the lungs) and respiration (transportation of oxygen into circulation in the lungs, and of carbon dioxide in the opposite direction) both change while a person sleeps. Specifically, they

become faster and more erratic during rapid eye movement (REM) sleep. The cough reflex is also suppressed during REM and NREM sleep.

In people with sleep-disordered breathing, respiration pauses often occur during sleep due to the airways either completely or partially collapsing. Obstructive sleep apnea (OSA, in which no ventilation occurs) and hypopneas (reduced ventilation due to partial airway obstruction) lead to intermittent and abrupt reduction in blood oxygen levels. These bring individuals to a more awake stage of sleep and can wake them up. Sleep-disordered breathing symptoms include snorting, snoring, gasping, and choking in one's sleep (often these occur without the sleeper's awareness). They result in excessive daytime sleepiness (or "tiredness"); often, the individual has no idea whey they are so tired.

This respiratory system interruption also has other, negative, long-term results, including increased activation of the adrenalin-secreting sympathetic nervous system, inflammation, and hormonal changes. These, in turn, can increase the risk of hypertension, coronary artery disease (blocked heart arteries and heart attacks), abnormal heart rhythms (like atrial fibrillation), stroke, a rise in blood sugars (glucose intolerance) to the point of diabetes, obesity, mood problems (such as depression, memory problems), and other issues. In fact, OSA significantly increased the risk of death from any cause — independent of other variables

The Cardiovascular System & sleep

Blood pressure and heart rates both change during sleep. There are brief increases in the person's blood pressure and heart rate during K-complexes, sleep arousals, and large body movements. In the few hours before a person wakes up, and as the person wakes up in the morning, there is an

increase in both heart rate and blood pressure (this may contribute to the higher risk of having a heart attack in the early morning and soon after awakening.

Lack of sleep and disordered sleep are also associated with heart attacks and, possibly, stroke. Arrhythmias occur very commonly during sleep and are influenced by the circadian rhythm. They may be significantly increased in those with obstructive sleep apnea and other sleep disorders. These may lead to cardiac events including sudden death.68 69 Just one night of acute sleep loss (3.6 hours of sleep) resulted in increased blood pressure in otherwise healthy young men. One large study found that getting 5 or fewer hours of sleep per night was associated with a 45 percent increase in the risk of heart attack (the researchers controlled for age, weight, smoking, and snoring). Interestingly, higher risk was also found among those who slept for 9 or more hours per night.

The Gastrointestinal System

Gastrointestinal reflux disease (GERD) is a common ailment in which the stomach contents of food and acid back up into the esophagus and disrupt the person's sleep. According to NSF's 2001 Sleep in America poll, people who experience nighttime GERD are more likely to have sleep problems like insomnia, obstructive sleep apnea, daytime sleepiness, and restless legs syndrome, compared to people without nighttime GERD.

Fortunately, there are a number of ways to minimize GERD and its associated sleep problems, including:

- Raise the head of your bed by putting 6- to 9-inch blocks under the legs at the head of your bed
- Do not eat or drink two to three hours before you go to bed

- Quit smoking
- Don’t overeat (especially at dinner)
- Avoid food and drinks that cause heartburn, like alcohol, coffee, and chocolate
- Eat high-protein, low-fat meal

Obesity & Weight

Lack of sleep is associated with an increased risk of obesity: the shorter length of time a person sleeps, the greater their risk of being obese, based on the Body Mass Index (BMI).

Adults who sleep less than 7.7 hours a night are more likely to have a high BMI. One longitudinal study of 500 adults found that, by age 27, those who slept less than 6 hours per night were 7.5 times more likely to have a higher BMI (the researchers controlled for family history, physical activity, and demographic factors).

This association seems to be caused by a lack of sleep decreasing a person’s levels of leptin (a hormone that suppresses appetite), and increasing levels of ghrelin (a peptide that stimulates appetite). These are influenced by orexin and may be altered by changes in sleep and circadian processes. Hence, lack of sleep appears to result in lower leptin and higher ghrelin levels, both of which make you eat more and gain weight.

Obesity is also a risk factor for obstructive sleep apnea (OSA) in middle-aged adults, perhaps because one’s airways become more fleshy and narrower as one gains weight. (OSA also occurs in individuals who are not overweight, and is more common as we age.) Obesity can lead to OSA, and it can result from OSA. The two conditions reinforce and compound each other:

obesity can lead to OSA, which results in excessive sleepiness and fatigue, which inhibits the person from exercising, which further contributes to obesity.

Mental Health

Sleep and mood have a bidirectional relationship: Mental health is both impacted by and impacts how well a person sleeps. Lack of sleep can be caused by other mental health (i.e., psychiatric) conditions that a person is experiencing, and can, in turn, impact those conditions. Sleep disturbance is, in fact, a diagnostic criteria for some mental health disorders, including depression.

A variety of mental health conditions involve insomnia, including substance abuse; eating disorders; and mood, anxiety, and psychotic disorders. It is not known precisely why insomnia is such a common symptom among these illnesses. Possible mechanisms include neurotransmitter (brain chemical) imbalance; circadian phase advance; hypothalamic-pituitaryadrenal axis dysregulation; and decreased activity levels of the frontal, parietal, and temporal cortex compared to healthy individuals.

Sleep and mental health disorders may cause or contribute to the other, or may both be symptoms of an underlying problem For example, patients with persistent, untreated insomnia have up to a ten-fold higher risk of depression compared to people who sleep well. Depressed people may suffer from a range of insomnia symptoms, including difficulty falling asleep and/or staying asleep, unrefreshing sleep, and excessive daytime sleepiness., There is also evidence that insomnia is a risk factor for the development and/or recurrence of anxiety disorders, bipolar disorders, and substance abuse. Post-traumatic Stress Disorder (PTSD) is frequently characterized by nightmares that lead to disturbed sleep .

Individuals with mental health disorders may benefit from targeted insomnia treatment, particularly when treatment for a co-occurring mental health disorder interferes with sleep. As with pain treatment, patients experience better outcomes when insomnia and depression are treated concurrently from the start (compared to initially treating of depression and then subsequently addressing the insomnia if it has not been resolved).

The Immune System & Sleep

There is considerable bidirectional interaction between sleep and the immune system.

Sleep disorders are a challenge to the proper functioning of the body's defense systems — especially sleep loss, due to its contribution to acute stress., Both total sleep time (TST) and slow-wave sleep (SWS) increase during acute infection. Conversely, severe illnesses, discomfort, and pain can inhibit SWS and, therefore, delay healing.

Many factors that regulate the immune response have also been shown to modulate sleep, especially non-rapid eye movement (NREM) sleep. The best data clearly document bidirectional interaction between NREM sleep and both interleukin-1β (IL-1) and tumor necrosis factor-α (TNF), but many similar interactions occur between factors of the immune system and parts of the sleep architecture.

2. Discuss the role of basal ganglia in coordinating movement

The **basal ganglia** (or **basal nuclei**) are a group of subcortical nuclei, of varied origin, in the brains of vertebrates, including humans, which are situated at the base of the forebrain and top of the midbrain. There are some differences in the basal ganglia of primates. Basal ganglia are strongly interconnected with the cerebral cortex, thalamus, and brainstem, as well as several

other brain areas. The basal ganglia are associated with a variety of functions, including control of voluntary motor movements, 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.