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QUESTION 1

**Physiology Of Sleep**

Sleep is a loss of wakefulness. A fundamental function for physical and mental health, it is not loss of conciousness; only a “shift”. It is an unconcious state which can be in part of modified by sensory stimulations. Each cycle can be understood as complete phases of sleep (from stage I to REM phase), and can last between 90 and 120 minutes each.

**Sleep centers**

These are areas causing sleep when stimulated:

1. Raphe nuclei in lower pons and medulla

– Targets (efferents): Reticular formation,

thalamus, neocortex, hypothalamus, limbic

system, dorsal roots of spinal cord

– Neurotransmitter: Serotonin (5HT)

2. “Medullary synchronization area” in nucleus tractus solitarius level:

3. Diencephalic sleep areas:

1. Rostral of hypothalamus, especially the suprachiasmatic area

2. Intralaminar and anterior thalamic nuclei

4. Basal forebrain sleep area:

1. Preoptic area and Brocaʼs diagonal band.

Some factors known to interfere with sleep

1) Adenosine - Inhibits the specific cholinergic neurons of RAS which stimulates the cortex

2) PgD2-Increases tendency to sleep when released from medial preoptic area of hypothalamus

3) PgE2-wakefulness

4) IL-1

5) Δ-sleep inducing factor

6) Muramil Peptide

7) Rythmic stimulation of mechanoreceptors (10 Hz or lower)

**Why do we sleep?**

One of the first theories formulated to understand the dream process was the Passive Theory of Sleep, which Bremmer formulated in 1935. This theory was based on the fact that the excitatory areas of the brainstem were becoming exhausted throughout the day, so When it was time to sleep, they were already tired and deactivated. It would be something similar to your mobile’s battery, taking the fact of charging it as our sleeping process. But after several years and some experiments the theory became obsolete and a different vision began to be seen. Currently the theory that accompanies this process says that sleep is produced by an active inhibition. This means that in the brain there is a small area that causes parts of it to be deactivated during sleep. Something like a vigilante that prevents other brain areas from doing their work while you sleep. But you have to be clear that the brain does not sleep while you do it, but that your way of working changes to be in line with the process. To this day, we still do not know what is the physiological purpose that creates the need of any living being to sleep. As you read above, the dream is considered a priority need, and even the fact of not sleeping for a time can cause disorders and even death although it sounds incredible. People can not sleep without anything for 1 to 2 nights. From the third night without sleep, disorders would appear that little by little would increase in severity and would have serious consequences. This would affect areas such as attention, memory, mood and may even appear hallucinations and convulsions.

Possible mechanisms of sleep-wake cycle

* Wakefulness is caused by excitatory effects of RAS and thalamus. Stimulation of RAS(Reticular Activating System) reinforced by the positive feedback from cortex and peripheral nervous system

RAS gets “tired” during the day.

* Sleep is caused by diminished RAS activity allows sleep centers to inhibit RAS and drowsiness begin...

**Phases of Sleep**

**1. Slow-wave sleep (NonREM):**

• Phase 1-4

2. **Paradoxal/desynchronized sleep (REM- Rapid Eye Movements)**

**Slow-Wave (nonREM) Sleep**

This stage is also known as no-Rem , it comes from the English translation “non-rapid movement of the eye”, this first stage is the first contact with the dream. It is the first state of reverie in which we enter and for most adults it will be the place that occupies 75% of the totality of your dream.

• Entrance to sleep • Takes appr. 90 minutes with 5-20 minutes intervals • Peripheral vessel tone and vegetative body functions decrease • Muscle tone decreases • 10-30% decrease in blood pressure, respiration rate and basal metabolism • Spinal reflexes can be elicited but strech (deep tendon) reflexes are absent. • Dreams cannot be remembered • Theta and delta waves in EEG • Duration and frequency decrease with age

**Phase-1 nonREM**

It is the stage where we feel drowsy or we are asleep. The waking state is disappearing since the Alpha rhythm also does it. At the moment muscle tone does not relax completely. The Beta waves have disappeared.

• Transition period between wakefulness and sleep; takes approximately 1-15 minutes.

• Eyes closed and relaxed...

• Light sleep, hallucination-like visions...

• α (alpha) waves weaken, slower θ (delta) waves emerge.

**Phase-2 nonREM**

It is the stage where although we are asleep, the dream is light, the Alpha rhythm disappears more and more, muscle tone continues to exist. We experience the entrance to the theta waves little by little.

• First stage of the real sleep; takes about 20 minutes

• Sleep spindles: 12-14 Hz sharp waves appear for 1-2 seconds...

• Slow eye movements

• Hard to awaken

• Fragments of dreams

**Phase-3 nonREM**

It is the stage where although we are asleep, the dream is light, the Alpha rhythm disappears more and more, muscle tone continues to exist. We experience the entrance to the theta waves little by little.

• Half-way deep sleep

• Body temperature and blood pressure decreases

• Harder to awaken

• Low frequency δ (theta) waves

• Sleep spindles are decreased

• No slow eye movements

**Phase-4 nonREM**

This is the stage of deep sleep, the encephalographic rhythm is very low, muscle tone is maintained or may be greatly diminished. Delta waves appear in our brain. Actually these stages differ in that the muscular atony is gradually increased and brain waves are gradually changing depending on the relaxation of the body.

• Deepest sleep; takes about 30-40 mins.

• δ (theta) waves predominate

• Most reflexes are intact; muscle tone slightly decreased

• Sleep-walking; sleep-talking; snoring andbedwetting generally occurs at this stage.

**REM Sleep**

This is the paradoxical dream phase, since during this phase the brain has an activity that resembles that which occurs when we are awake. Also during this phase rapid eye movements are seen. The body is in atony. What we dream of occurs during this phase. To this day, there is no clear theory of why ocular movement occurs during the REM phase.

• 5-30 minutes with 90 minute-intervals • Active dreaming (dreams are remembered)

• Active body movements • More difficult to wake up with sensory stimulations • Waking up in the morning generally coincides with the last REM period. • Decrease in muscle tone (except respiratory and eye muscles) • Irregularity in heart and respiration rate. • 20% increase in brain metabolism • Atonia in neck muscles • Rapid eye movements • Beta waves in EEG =paradoxal sleep, =desynchronized sleep

**How is sleep organized during the night?**

Adults usually have about 8 hours of sleep per day. If the 8 hours are carried out in a continuous manner, it will take about 4 or 5 cycles. Each cycle can be understood as complete phases of sleep (from stage I to REM phase), and can last between 90 and 120 minutes each. The distribution is usually the following:

Phase I during the cycle would be developing approximately 1.5% of the total cycle. This means that if the cycle lasts 100 minutes, only 1 minute and a half the body would be in phase I.

Phase II during the cycle would be present approximately 25% of the total cycle. In a cycle of 100 minutes, 25 minutes would be the duration of Phase II.

Phase III and IV during the cycle would last 45% of the total cycle. In a 100 minute cycle, these phases would last approximately 45 minutes.

The REM phase, during the cycle would have a duration of 25% of the total cycle. So in a cycle of 100 minutes, only 25 minutes correspond to the paradoxical dream and dreams.

**Possible causes of REM Sleep**

• ACh neurons in rostral reticular formation • Lateral tegmentum> lateral geniculate body> occipital cortex = Ponto-geniculo-occipital spikes in EEG

Waking up

• It is hard to wake up in nonREM Phase 4.

• Spontaneous arousal occurs in REM

• In thalamic neurons: • “Hyperpolarized” phasic firing during sleep • “Depolarized” tonic firing due to sensory input

**Physiological effects of sleep**

• Sleep helps the maintenance of normal activity level of CNS.

• Helps to maintain the “balance” between the different parts of the CNS.

• Increased sympathetic activity and muscle tone during the awake period decreases with sleep

• Body temperature drops, energy loss decreases

• Growth hormone and cortisol secretion

• Phosphate excretion from kidneys increase

• Melatonin secretion increases

• Skin and tissue repair

**Sleep disorders**

• Insomnia • Disturbances in sleep onset or maintenance • Fatal Familial Insomnia • Unable to sleep, emotional instability, hallucinations, stupor- coma and death

**Sleep deprivation**

• Prolonged wakefulness may result in irritability, confusion and psychotic symptoms

• Fatigue, prostration, depression • Unability to direct attention • Hypersensitivity to pain

• Visceral problems including anorexia and distruption of excretion • Defects in skin repair

• Collagen fibres loose their flexibility and may display color changes

**REM sleep deprivation**

• Confusion • Paranoia • Affective disorders • Decrease in motor performance • Memory consolidation impairments • Loss of balance • Decreased immune efficiency • Parasomnias • Sleep walking (somnanbulism), talking, etc • Behavioral disorders in REM sleep • Excess motor activity in REM. • Narcolepsy • Restless leg syndrome • Reccurrent leg movements like shaking or withdrawal extension • Sleep paralysis • Unable to move for a couple of minutes right after sleep onset or after waking up.

**Sleep disorders**

• Obstructive Sleep Apnea Syndrome • Collapse in the upper airways, interruption of

respiration, snoring • May cause restlesness and day sleep

**QUESTION 2**

**What is the role of the basal ganglia in coordinating movement.**

The basal ganglia or basal nuclei are clumps of gray mass located below the cortex in the depth of both cerebral hemispheres (1). These nuclei can have different shapes and are involved in the control of movement.

The basal ganglia are surrounded by a white mass of the cerebral hemisphere, and the individual nuclei that enter into their composition build the walls of the lateral cerebral chamber.

The basal ganglia include: i) corpus striatum ii) claustrum iii) the amygdala iv) substantia nigra v)subthalamic sails

We can classify these nuclei into the following groups:

1. Input nuclei: corpus striatum(caudate, putamen)
2. Intermediary nuclei: Globus Pallidus Externa, Nigra substance, and Subthalamic Nucleus.
3. Output nuclei: Substantia Nigra and Globus Pallidus

**Functions of the basal ganglia**

In order to understand the functions of the basal ganglia, we must mention the extrapyramidal system. This system is the part of the brain and brain stem that participates in motor control except for the corticospinal (pyramid) system.

It includes: i) Basal ganglia and their pathways. ii)Portions of the cerebral cortex that give projections to the basal ganglia. iii)Parts of the cerebellum that give projections to the basal ganglia. iv) Parts of the reticular formation that are connected to the basal ganglia and cerebral cortex. v)Thalamus nuclei associated with the basal ganglia and reticular formation.

**The role of the extrapyramidal system is to control automatic movements, skeletal muscle tone, and maintenance of postural reflexes.**

The basal ganglia exert their role in motor control through constant interaction with the cerebral cortex and the corticospinal pathway. They get information mainly from the cerebral cortex and send out information.

Almost all the motor and sensory nerve fibers that connect the cerebral cortex to the spinal cord pass between the major masses of the basal ganglia (nucleus caudatus and putamen) and are called the internal brain capsule.

The connections of the motor cortex, the thalamus and the joint circuits of the brain stem and cerebellum are very important. Namely, the main circuit of the basal ganglia system involves a huge number of connections between the basal ganglia themselves, as well as numerous entry and exit pathways between the motor regions of the brain and the basal ganglia.

The most prominent functions of the basal ganglia include:

1. Represents the accessory motor system. Mediates between neocortical motor centers and the "elderly" motor areas of the brainstem Selects the purposeful and desired motor activity and suppresses unwanted movements.
2. Acts by modifying ongoing neural activity in motor projections
3. Delivers an inhibitory role in motor control
4. Inhibits muscle tone (balance of excitatory and inbound input signals according to PMN terminating on skeletal muscle)
5. Monitor and adjust slow and continuous contractions (equilibrium, body position, etc.)
6. Regulates attention and individual cognitive processes
7. Participates in motor planning and learning
8. Assisting the cerebral cortex in making subconscious, learned movements
9. Temporal pattern of movement and gradation of the intensity of movement (2).

One of the major roles of the basal ganglia is to participate in the control of complex patterns of motor activity such as: letter writing, cutting paper with scissors, throwing a ball into a basket, adding the ball in football, many aspects of vocalization, controlled eye movements, or literally all our other skilled movements.

Cognitive control of motor activity in which the nucleus caudatus plays a major role is another important function of the basal ganglia. Likewise, planning which movement patterns will be used together, or in what order in order to achieve a complex goal, is another role of the basal ganglia.

**Basal Ganglia Neurotransmitter Systems**

This advanced system consists of several important segments or systems. Those are:

A system of dopamine neurons located in the substantia nigra, and give projections to the nucleus caudatus and putamen.

A system of GABA-containing neurons located in nucleus caudatus and putamen, and give projections in substance nigra.

A system of acetylcholine neurons located in the cerebral cortex, and they give the projections to the nucleus caudatus and the putamen.

Noradrenergic, serotonin and other neuronal systems are located outside the basal ganglia system, and yield projections into this system.

**Striatum**

Corpus striatum builds up the lentiformis and caudatus cores/nuclei. Nucleus lentiformis consists of putamen and globus pallidus. The globus palidus is the inner layer, while the putamen is located on the outside. The striped body is divided into dorsal and ventral parts. The dorsal part is associated with the somatosensory and somatomotoric systems, and the ventral one is associated with the limbic system. All information aimed at the basal ganglia goes through the striatum. The dorsal part of the striatum is built by a repatriate and lenticular nucleus. The lens juxtaposes a layer of white mass on the outside - a putamen and the globus palidus that is inside. These two elements are separated by fibers of the inner capsule, but in some places, they are connected by cellular bridges. The putamen, together with the nucleus caudatus, builds the neostriatum, and the globus palidus forms paleostriatum.

**Nucleus caudatus**

The nucleus caudatus has a shape of letter C. It consists of the head, body and tail. With its structures, it participates in the construction of the lateral brain chamber. On the inside of the nucleus caudatus, there is the thalamus. Between this nucleus and the thalamus, is the stria terminalis, and above it is positioned the vein of the thalamostriata. The corpus callosum is positioned above the nucleus caudatus.

At the tip of it, we can locate a very important brain element, the amygdala. The anterior limb of the inner medulla separates the nucleus caudatus from the nucleus lentiformis.

**Nucleus Lentiformis**

Nucleus lentiformis is located medially from the insula cortex (2). Between these two segments, from the outside to the inside, we can locate the capsula extrema, claustrum, and the element called capsula externa.

As mentioned earlier, the lentiformis nucleus builds the inner part of the globe pallidus and the outer putamen. They are separated by a layer of white mass. The globe palidus consists of an inner and an outer part.

The ventral portion of the striatum is smaller. It is located below the front commissure. It consists of a basal nucleus, nucleus accumbens, and segment called tuberculum olfactorium. A significant loss of large neurons in the basal nucleus was observed in patients with Alzheimer's disease.

Nucleus accumbens is located at the junction of the putamen and the tail of the nucleus caudatus. The nucleus accumbens integrates and reconciles information from the extrapyramidal and limbic systems.

The role of the scent element scientifically called tuberculum olfactorium has not yet been fully clarified. However, these basal ganglia play a very important role in the central nervous system.

**Claustrum (rampart) Basal Ganglia**

The claustrum is a layer of graymass that lies between the end capsule (capsula extrema) and the outer capsule(capsula externa). It is separated from the putamen by the outer capsule. Thefunction of the ramparts has not yet been sufficiently researched.

**The Amygdala**

Some authors describe the amygdala solely within the limbic system. As the human brain is still incompletely explored, we do not have the full insight into the interconnectedness of certain brain structures. The amygdala is probably part of the limbic system and belongs to the basal ganglia.

**Nigral complex (substantia nigra)**

This complex is composed of the so-called "black substance" and the ventral tegmental nuclei. The black substance is found in the midbrain. It consists of a reticular and compact part. The reticular part contains cells that are similar to cells of the globe palidus. These two structures are separated by an inner capsule. The compact section contains dark-colored dopaminergic neurons. The loss of these neurons occurs in Parkinson's disease.

**Sub-thalamic nucleus**

This nucleus is located below the thalamus. It's a cigarette-shaped brain segment. The subthalamic nucleus receives information from the globus palidus, the cerebral cortex, the substantia nigra, and the mesh substance of the pons.