Unit VIII – Problem 3 – Physiology: Reticular Formation and Sleep

- **Reticular formation**: it is a mixture of grey matter and white matter extending through all the components of the brain stem (these are: midbrain, pons and medulla). It has:
  - **Afferents**: fibers going to reticular formation. These fibers are receiving sensory input from:
    - ✓ All ascending lemnisci: medial, spinal, trigeminal and lateral.
    - ✓ The visual, auditory and olfactory pathways.
    - ✓ The basal ganglia.
    - ✓ The cerebellum.
    - ✓ The cerebral cortex (corticofugal fibers).
    - ✓ The hypothalamus.
    - ✓ The vestibular apparatus.
  - **Efferents**: fibers coming from reticular formation. They are further divided into:
    - ✓ Facilitatory (excitatory) part:
      - ❖ This part is located in pons and midbrain.
      - ❖ It has an ascending branch to the brain which enhances alertness (this is known as the ascending reticular activating system).
      - ❖ It has a descending branch which is stimulating the spinal cord to maintain posture and movement (ventral reticulospinal tract).
        Note: the excitatory part is using acetylcholine as a neurotransmitter.
    - ✓ Inhibitory part:
      - ❖ This part is located in medulla oblongata (lateral reticulospinal tract).
      - ❖ The inhibitory part is using serotonine as a neurotransmitter.
- **What are the functions of reticular formation?**
  - Controlling the level of consciousness (via the ascending reticular activating system).
  - Regulation of the stretch reflex and muscle tone (via reticulospinal tracts).
  - Pain inhibition (by raphe magnus nucleus).
  - Control of sleep (by 2 specific centers).
  - Control of visceral functions (by controlling the spinal lateral horn cells).
- **Arousal (الإثارة – النهوض) and attention:**
  - **This is decided by the parietal lobe of the brain.**
  - **Levels:**
    - ✓ Alertness and arousal: the basic aspects of attention that enables a person to extract information from the environment to select a particular response.
    - ✓ Selective attention: an example of this is when you are sitting in a crowded place where all people are talking together but you have the ability to select one of those people to hear/listen.
    - ✓ Vigilance: it is the ability to sustain alertness.
- **Neural correlates of selection:**
  - **P300 wave (attention: mostly auditory):** in which a person can selectively choose a stimulus.
  - **N400 (recognition: visual):** if you are in a car and someone else is staring or looking at you from the car which is next to you → suddenly you will look to that person (because your brain is recognizing this but ignoring and filtering).
- **Specific attention:**
  - **Early selection theory**: an example on this theory is when you talk to a specific person → in this case you are selecting him and inhibiting all other people who might be talking.
    - ✓ This theory is not 100% true (Why?) → because the brain is filtering and monitoring (which means that your brain is not always ignoring). Example: if one of those people who you are ignoring mentioned a name of a person who you know → you will hear that person and start selecting him.

- **If the area between the midbrain and pons is cut** → a person will enter a state of coma → because there will be a loss of a connection which is between the reticular formation and the cerebral cortex (ARAS).
- **There is an area in the midbrain which will send two projections to the thalamus (both of them are acetylcholinergic):**
  - **One of these fibers will reach the sensory thalamus (in VPL nucleus) and then will reach the cortex.**
  - **The other fiber will terminate in the reticular nucleus of the thalamus which is inhibiting the cortex.**
    - ✓ If a person is exposed to a sensory stimulation:
      - ❖ *Direct*: there will be activation of sensory thalamus.
      - ❖ *Indirect*: there will be inhibition of reticular nucleus in the thalamus (inhibition of inhibition = stimulation).
- **Sleep and dreams:**
  - **Definition of sleep**: it is periodic, natural, reversible loss of consciousness.
  - All animals (and even insects) sleep.
  - We spend 1/3 of our lives sleeping (1/4 of this sleep is dreaming).
  - **Suprachiasmatic nucleus is the main regulator of sleep.**

Biological rhythm	Time frame	Example
Circannual	Yearly	Migratory cycles of birds
Infradian	Less than a year	Human menstrual cycle
Circadian	Daily	Human sleep cycle
Ultradian	Less than a day	Human eating cycles

- **Physiology of sleep (circardian cycle):**
  - Rods and cons in the retina of the eye are stimulated by photons (light) to form a picture.
  - **Retinal ganglion cells are stimulated by light and they contain the photopigment melanopsin. There are axons which are extending from these cells to the hypothalamus forming retino-hypothalamic tract. This tract will give axons which will project to suprachiasmatic nucleus in anterior hypothalamus.**
  - **Melatonin is released from pineal gland at night when no light is present. Functions:**
    - ✓ Induces sleep (by causing drowsiness chemically).
    - ✓ Anti-oxidant and anti-carcinogenic.
    - ✓ Enhances immunity.
    - ✓ Lowering body temperature.
    - ✓ Dreaming.
    - ✓ Anti-ageing? → in elderly, melatonin synthesis decreases and peaks earlier (that is why most elderly sleep early and wake up early).
- **Sleep in needed** → sleep deprivation causes psychosis and eventually results in death!
- **All mammals (and some birds) have Rapid Eye Movement-sleep (REM-sleep) → which is concerned with dreaming.**
  - Dolphins have a genetic modification which makes them sleep with half of their brains (Why?) → so they don't breath under the water and die.

Sleep	
Non-REM	**REM**
Brain is resting but body is capable of moving	Brain is active but body is paralyzed
Increased parasympathetic tone	Increased sympathetic stimulation
Less brain energy is utilized	High oxygen consumption in brain
No structural complex dreams	There are structural complex dreams
75% of sleep	25% of sleep

- **Why do we sleep?**
  - **Restorative function**: restoring the body so it can work again when we are awake.
  - **Adaptation**: to keep ourselves apart from problems or to conserve energy.

- **REM function:**
  - There is no known function of dream.
  - When a person is REM-deprived → he is still capable of dreaming.
  - **Freud theory**: he said that our brain is divided into:
    - ✓ Conscious brain.
    - ✓ Unconscious brain: which contains our prevented desires (animal desires: sex, killing, eating… etc) → this will be activated during sleep when the connection between consciousness and unconsciousness is very weak.
      Note: as the person wakes up, the cortex will remove those scenes in our dreams which represented our animal desires.
  - **Activation-synthesis hypothesis**: when the stage of REM starts during sleep → the pons will produce spikes (action potentials) → some of these action potentials will move to the cortex where fragments of our memory will get randomly activated → the cortex will link between these fragments to generate a random story.
  - **Consolidation of memory**: there is no evidence proving it.
- **Sleep and brain waves:**
  - **The brain activity can be:**
    - ✓ Fast: this appears when a person is awake and active (due to desynchronization: impulses are many and cancelling each other to produce small but fast waves).
    - ✓ Slow: due to synchronization (this occurs during sleeping when impulses will merge together to generate high amplitudes with low frequency waves).
- **Stages of sleep:**
  - **When a person is awake** → his brain shows waves which are high in frequency but have decreased amplitude (the characteristic of these waves will start to reverse when sleep begins).
  - **There are 2 types of sleep waves:**
    - ✓ Rapid-wave sleep (occur during REM): in this stage, EEG will show similar waves to an awake person (Why?) → because in this stage the eye is moving and the brain is very active. In addition sympathetic activity is increased in this stage (leading to tachycardia, sweating, erection increased respiration… etc).
      - ❖ *So REM-sleep is occurring in pons and locus coeruleus.*
    - ✓ Slow-wave sleep: this is occurring during stages I, II and III (sleep stages).
      - ❖ *So slow-wave sleep is occurring in basal forebrain.*
- **EEG during sleep stages:**
  - **An awake person will show** → β-waves which have high frequency (15-60 Hz) and small amplitude. Note that (Hz) is equal to waves per second (waves/sec).
  - **Stage I (hypnagogic):** frequency will start to reduce while the amplitude will start becoming bigger. Note that hallucinations occur in this stage before falling asleep.
  - **Stage II:** characterized by sleep-spindles and K-complexes.
  - **Stage III:** delta waves.
  - **Stage IV:** it has the lowest frequency (2-4 Hz) and the biggest amplitude. Waves in this stage are delta-waves.
  - **After passing through these 4 stages, the person will pass again briefly through stages II and III → eventually entering the REM-sleep.**
- **We start sleeping with more slow-sleep and less REM-sleep** → then, the proportion of REM-sleep will start increasing while we are sleeping until it reaches its peak in the morning so we become awake at this time (it is easy to wake up because the brain activity is very high during REM-sleep).
  - A person is detecting the stimuli from the external environment during REM-sleep (which is a dreaming stage) → therefore, some stimuli which might not be enough to

wake the person will interfere with his dreams! (e.g. listening to a music in the dream and when waking up finding the music is actually playing).

- **As adults, we need 6.5-8.5 hours of sleep**. Students who are sleep-deprived will have reduced cognitive, emotional and physical well-being → this is compensated by sleeping/naps during day-time.
- **REM-sleep is known as paradoxical sleep:** which means that all muscles will be paralyzed although the brain is very active. The percentage of REM-sleep is very high in infants → because it is important in brain maturation, reorganizing the brain chemistry and consolidation of memories.
- **What happens during REM-sleep?**
  - **Once REM-sleep is started** → the pons will begin producing PGO spikes → which will stimulate GABAergic neurons → that through a lot of process will lead eventually in the release of glycine (inhibiting lower motor neurons in the spinal cord leading to paralysis of muscles.
    - ✓ During spinal shock: there is release of glycine which will result in hyperpolarization (paralysis of muscles).
    - ✓ GABA is also inhibiting the medulla resulting in loss of sensations.
  - **Ponto-geniculo-occipital (PGO) complex**: pontine spikes are carried also to lateral geniculate nucleus in the thalamus → reaching eventually the occipital cortex (enabling us to see/visualize) our dreams.
  - **In addition, pontine spikes are transmitted to pontine reticular formation** → superior colliculus → paramedian pontine reticular formation → terminating in ocular cranial nerves (causing eye movement).
  - **In REM-sleep: amygdala (limbic system), parahippocampus and anterior cingulate cortex activities are increased** (concerned with emotions which are more effective during sleeping explaining why a patient might wake up feeling depressed after having a bad dream even if he does not remember it!).
  - **Prefrontal and posterior cingulate activities decrease** → explaining why there is no logic in our dreams (e.g. dreaming that you can fly!).
  - **Melatonin supplement must not be used in a patient who is having depression.**
- **Physiology of sleep:**
  - **What are the causes of wakefulness?**
    - ✓ Cholinergic neurons: in pons-midbrain region.
    - ✓ NE: from locus cerulous.
    - ✓ Serotonine: from Raphe nucleus.
    - ✓ Histamine: from tuberomamillary nucleus.

      Note: orexin is enhancing wakefulness through stimulation of locus cerulous and Raphe nucleus. People suffering from narcolepsy (irrisisted desire to sleep for 30s-30min) have too little orexin.
  - **What is the cause of sleep?**
    - ✓ Ventrolateral preoptic area (VLPO): GABAergic neurons in the hypothalamus suppressing alertness and promoting sleep.
  - **Basal forebrain (for thinking):** is enhancing alertness and inhibiting sleep.
  - **When there is increased activity in the brain and it fatigues → adenosine will be produced → enhancing sleep (note that adenosine is inhibited by caffeine).**
- **Types of dreams:**
  - **Lucid dreams:**
    - ✓ It occurs when you realize that you are dreaming (thus the dreamer can manipulate the dream and direct it toward happy endings).
    - ✓ PGO is present but has less effect in prefrontal lobe (it is not totally depressed) → logic is still working and you realize that the dream cannot be true at all.
  - **Signal dreams**: help you solve problems or make decisions in your waking life.

- **Epic dreams**: they are so huge and vivid (مشرق وقوي) that you cannot ignore them. The details of such dreams remain with you for years as if you dreamed it last night (e.g. the best dream you have ever had).
- **Prophetic dreams**: foretell the future! Unconscious mind knows what is coming before we consciously piece together the same information.
- **Recurrent dreams**: they recur because the person has a problem which remains unsolved or ignored.
- **Nightmare**: disturbing dream which causes the dreamer to wake up feeling anxious and frightened. Nightmare may be a response to real life trauma and situations

- **Sleep disorders:**
  - **Insomnia**: this term includes:
    - ✓ Difficulty in sleeping (not sleeping immediately: taking more than 20 minutes to fall asleep).
    - ✓ Frequently waking up at night while sleeping.
    - ✓ Waking up at night and being unable to sleep again.
  - **Restless leg syndrome**: unpleasant tingling sensation in legs and urge to move them to obtain relief.
  - **Cataplexy (sleep paralysis: ياثوم):** this happens when a person is REM-deprived → so when he comes to sleep → he will pass directly from the stage of awakeness to the REM-sleep (passing very rapidly through the four stages of sleep) → therefore, muscles will be paralyzes while the person is still awake!
  - **Somnambulism (sleep walking):**
    - ✓ Mostly occurring in children (10-15 years).
    - ✓ Occurring during slow-wave sleep.
    - ✓ There is difficulty to awaken the child because there is no REM stage.
    - ✓ The best thing to do is to guide the child back to his bed.
  - **Somniloquy (sleep talking):** everyone may have it. The speech is non-sensical.
  - **REM behavior disorder:** there is loss of muscle paralysis during REM-sleep. This disorder is usually associated with violent acts.
  - **Sleep apnea (الاختناق أثناء النوم):** it can be:
    - ✓ Central: brainstem breathing signals to respiratory muscles decrease a lot.
    - ✓ Obstructive: airway compressed (as in obesity) → the pharynx collapse leading to reflex inspiration which awakens the patient. This type is treated with positive air pressure mask which is used by the patient at night otherwise his condition will result in hypertension, hypoxia and other diseases.
  - **Ondine's curse (congenital central hypoventilation syndrome):**
    - ✓ In which automacity of brainstem is lost (there is no involuntary breathing when a person is asleep).

- **Difference between night terrors and nightmares:**
  - **Night terrors:**
    - ✓ Occurring in children.
    - ✓ Occurring early during sleep.
    - ✓ The child wakes up with tachycardia, sweating, crying and increased sympathetic activity → he forgets all of this in the next morning.
  - **Nightmares:**
    - ✓ Occurring in adults.
    - ✓ Occurring toward the morning during REM-sleep.