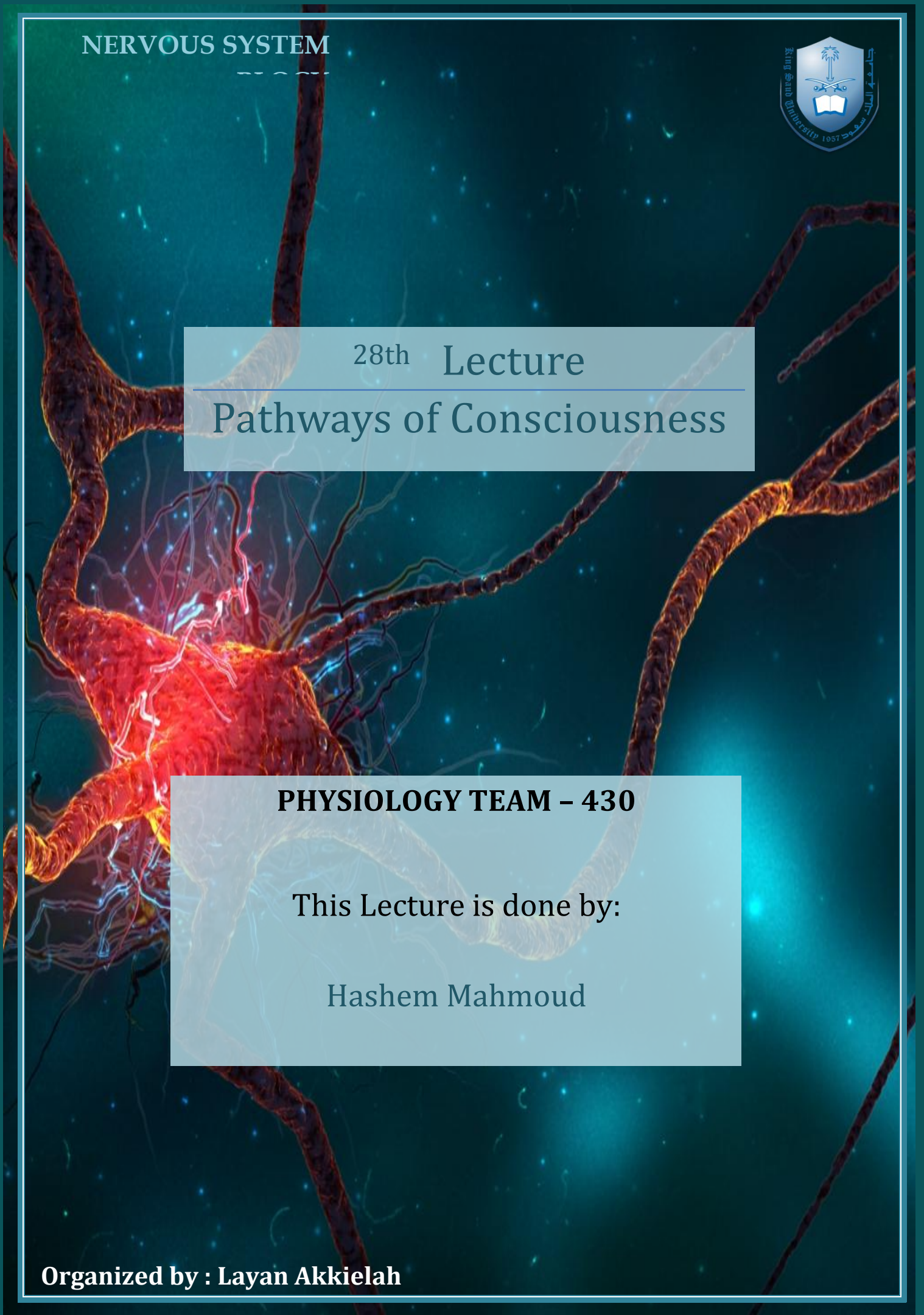
NERVOUS SYSTEM



28th Lecture

Pathways of Consciousness

PHYSIOLOGY TEAM – 430

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❖ What is Consciousness ?

It is the brain state in which a person is being aware of the self and surroundings.
It is a product of electrical activity of the brain
A person with a flat EEG cannot be conscious !

❖ What are the levels of consciousness?

1) Normal Consciousness (state of normal arousal , being fully awake and aware of the self and surroundings
2) Clouded consciousness : person conscious but mentally confused (e.g., in cases of drug or alcohol intoxication , high fever associated with malaria or septicemia , dementia , etc) .
3) Sleep : person unconscious (in relation to the external world & surroundings) but is arousable (can be aroused) .
4) Coma : person unconscious and not arousable.

❖ Structures involved, Consciousness depends upon interactions between :

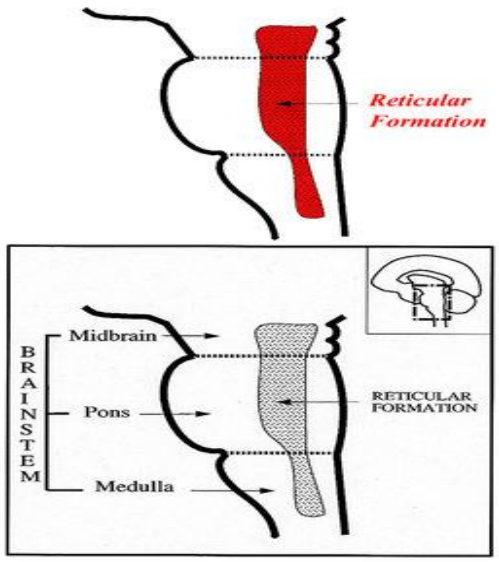
- **Reticular Formation (RF)**
- **Thalamus**
- **Cortical Association areas.**

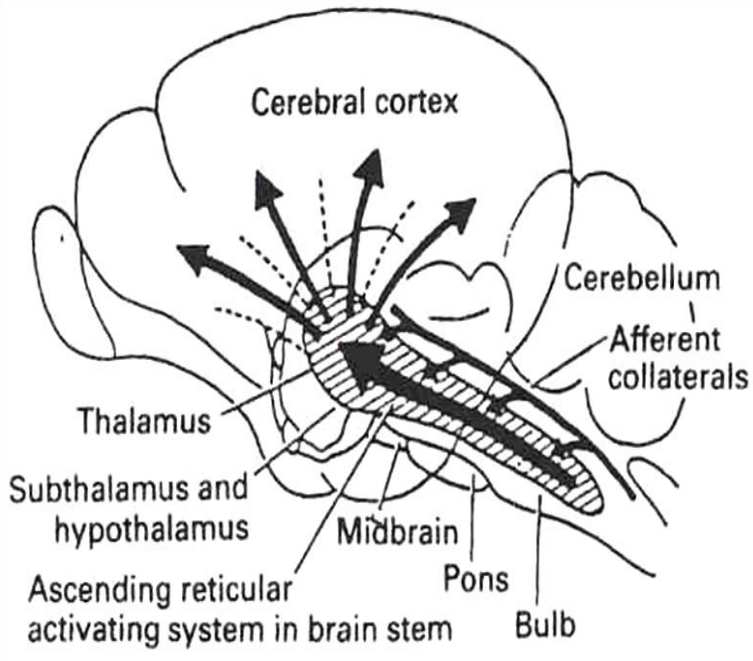
❖ Functions of reticular formation:

1. **Somatic motor control** - maintaining tone, balance, and posture during body movement.
2. **Cardiovascular control** - The reticular formation includes the cardiac and vasomotor centers of the medulla oblongata.
3. **Pain modulation** - The reticular formation is one means by which pain signals from the lower body reach the cerebral cortex. It is also the origin of the descending analgesic pathways. The nerve fibers in these pathways act in the spinal cord to block the transmission of some pain signals to the brain.
4. **Sleep and consciousness** - The reticular formation has projections to the thalamus and cerebral cortex . It plays a central role in states of consciousness like alertness and sleep. **Injury to the reticular formation can result in irreversible coma.**
5. **Habituation** - This is a process in which the brain learns to ignore repetitive, meaningless stimuli while remaining sensitive to others. A good example of this is when a person can sleep through loud traffic in a large city, but is awakened promptly due to the sound of an alarm .

❖ Reticular Activating System

- In 1945 , the Italian neurophysiologist Moruzzi and his colleagues foun that a lesion in the mid-pons makes the animal spends the rest of its life unconscious .
- They concluded that the areas in the upper pons and midbrain are essential for wakefulness , and called it the Bulboreticular Facilitory (Excitatory) Area of the reticular formation .
- (This Bulboreticular Facilitory Area is also called by some scientists Th Brainstem Ascending Reticular Activating System).
- The Bulboreticular Facilitory (Excitatory) Area sends excitatory signals into Thalamus . As a result , the thalamus excites almost all areas of the cortex .
- The Bulboreticular Facilitory (Excitatory) Area + Thalamus together constitute the Reticular Activating System (RAS) .
- The RAS is the system which keeps our cortex awake and conscious .





So the RAS is composed of (bulboreticular facilitory area + thalamus), the Reticular Formation includes the bulboreticular facilitory area, which is located in the upper pons and mid-brain. Another name for bulboreticular facilitory area brainstem ascending RAS.

❖ Anatomical components:

- The RAS is composed of several neuronal circuits connecting the brainstem to the cortex . These pathways originate in the upper brainstem reticular core and project through synaptic relays in the rostral intralaminar and thalamic nuclei to the cerebral cortex. As a result, individuals with bilateral lesions of thalamic intralaminar nuclei are lethargic or somnolent.
- Several areas traditionally included in the RAS are:
- Midbrain Reticular Formation.
- Mesencephalic Nucleus (mesencephalon)
- Thalamic Intralaminar nucleus
- Dorsal Hypothalamus.
- Tegmentum.

❖ Neurotransmitters in RAS and regulation of consciousness:

The awakening action of the RAS is mediated by fibers **secreting Acetylcholine** (ACh) and **Norepinephrine** (NE)

- The RAS provides the main drive that maintains effective cortical excitability level & interruption of this ascending pathway (e.g., by a tumor or hemorrhage) causes the subject to go into coma .
- The level of consciousness is largely influenced by :

1) peripheral sensory inputs
2) Thalamocortical sectors .

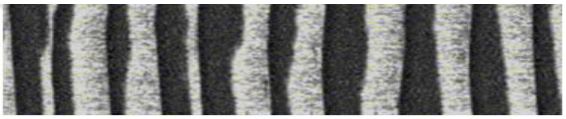
- **Peripheral Sensory Inputs Increase the Level of Excitation of the Bulboreticular Faciltatory Area :**

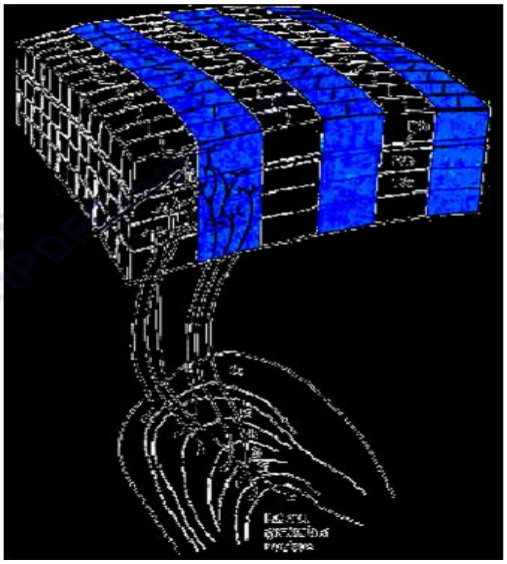
  - The level of activity of the Bulboreticular Facilitatory Area and , consequently , the level of alertness and arousal is largely determined by the number and type of sensory (afferen) signals that enter the CNS from the periphery .
  - Pain signals , in particular , increase activity in this excitatory area and therefore strongly excite the brain to attention .

- **Role of Thalamo-Cortical Sectors :**

  - Not only do excitatory signals pass to the cerebral cortex from the RAS , but feedback signals also return from the cortex back to the Thalamus (which is part of the RAS)

- ✓ Almost every area of the cerebral cortex connects with its own highly specific area in the thalamus .
- ✓ These functional segments are called Thalamocortical Sectors
- ✓ They are made of → Thalamo-cortical (TC) fibers and feedback Cortico-thalamic (CT) fibers .
- ✓ These neural circuits between the thalamus & cortex are essential for determining the level of consciousness .





❖ Neurotransmitters (details):

The neuronal circuits of the RAS are modulated by complex interactions between a few main neurotransmitters. **The RAS contains both cholinergic and adrenergic** components, which exhibit synergic as well as competitive actions to regulate thalamocortical activity and the corresponding behavioral state.

– ***Cholinergic:***

- Are two ascending mesopontine tegmental pathways. These pathways involve cholinergic neurons of the posterior midbrain, the pedunculopontine nucleus (PPN) and the laterodorsal tegmental nucleus (LDT), which are active during waking and REM sleep.
- **Cholinergic projections descend throughout the reticular formation and ascend to the substantia nigra, basal forebrain, thalamus, and cerebellum.**

– ***Adrenergic:***

- The adrenergic component of the reticular activating system is closely associated with the noradrenergic neurons of the locus coeruleus.

Extra: "the blue spot", a name derived from its bright blue appearance in unstained brain tissue. The color is due to light scattering from melanin in noradrenergic nerve cell bodies. Located in the brainstem, it is involved to physiological responses to stress and panic.

- There are ascending projections directly to the cerebral cortex and descending projections to the spinal cord.
- The adrenergic neurons are active during waking and slow wave sleep.

❖ **Function of RAS in regulating sleep-wake transition:**

- The main function of the RAS is to modify and potentiate thalamic and cortical functio resulting in(EEG) desynchronization**.**
- There are distinct differences in the brain's electrical activity during periods of wakefulness and sleep: Low voltage fast burst brain waves (EEG desynchronization) are associated with wakefulness and REM sleep , large voltage slow waves are found during non-REM sleep.
- **Stimulation of the RAS produces EEG desynchronization by suppressing slow cortical waves.**
- **The physiological change from a state of deep sleep to wakefulness is reversible and mediated by the RAS.**
- Inhibitory influence from the brain is active at sleep onset, likely coming from the preoptic area (POA) of the hypothalamus. During sleep, neurons in the RAS will have a much lower firing rate; conversely, they will have a higher activity level during the waking state**.**
- **In order that the brain may sleep, there must be a reduction in ascending afferent activity reaching the cortex by suppression of the RAS.**

Also note:

The reticular activating system also helps mediate transitions from relaxed wakefulness to periods of high attention. There is increased regional blood flow (presumably indicating an increased measure of neuronal activity) in the midbrain reticular formation (MRF) and thalamic intralaminar nuclei during tasks requiring increased alertness and attention.

❖ RAS and learning:

- The RAS is the center of balance for the other systems involved in learning, self-control or inhibition, and motivation.
- When functioning normally, it provides the neural connections that are needed for the processing and learning of information, and the ability to pay attention to the correct task.
- **If the RAS doesn't excite the neurons of the cortex as much as it ought to, then we see the results of an under-aroused cortex, such as difficulty learning, poor memory, little self-control, and so on. In fact, if RAS failed to activate the cortex at all one would see a lack of consciousness or even coma.**
- What would happen if the RAS was too excited, and aroused the cortex or other systems of the brain too much?

  "Then we would see individuals with excessive startle responses, hyper-vigilance, touching everything, talking too much, restless, and hyperactive"
- So the Reticular Activating System must be activated to normal levels for the rest of the brain to function as it should.

❖ Indices of Level of Consciousness:

- **Appearance & Behavior :**

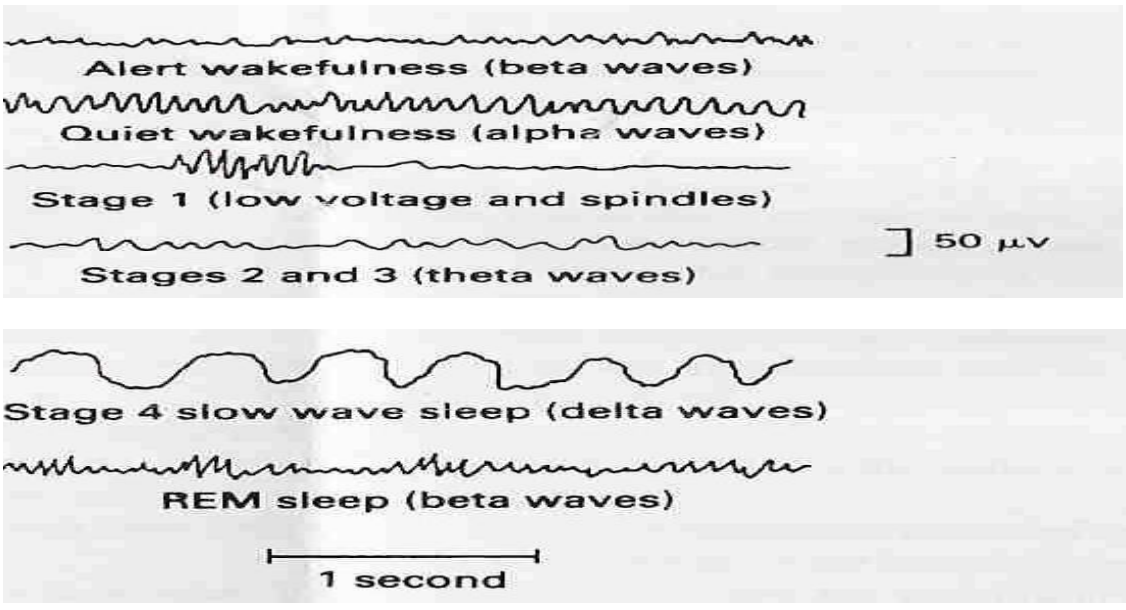
  posture (sitting , standing ?) , open eyes ? Facial expression ? , responds to stimuli (including the examiner's questions about name , orientation in time & place ? & other general Qs like who is the president ?)
- **Vital signs :**
  pulse , BP, respiration , pupils , reflexes , particularly brainstem reflexes , etc
- **EEG** →
  Each of these states (wakefulness , sleep , coma and death) has specific EEG patterns .
- **Evoked potentials** (in cases of Brain Death).

❖ EEG:

An electroencephalogram (EEG) is a test used to detect abnormalities related to electrical activity of the brain. This procedure tracks and records brain wave patterns. Small metal discs with thin wires (electrodes) are placed on the scalp, and then send signals to a machine to record the results. Normal electrical activity in the brain makes a recognizable pattern.

– Alpha Rhythm :

- **Observed in awake , relaxed adult humans witheyes closed**
- **Frequency = 8- 13 Hz**
- Most prominent in the Parieto-Occipital region , though it is sometimes observed in other locations When attention is focused on something the alpha rhythm becomes replaced by irregular lowvoltage activity This phenomenon is known as Alpha Block
- This replacement of alpha by irregular low-voltage activity is also called It is also called Desynchronization & Alerting Response
- It is due to activity of RAS
- However , the rapid EEG activity seen in the alert state is also synchronized , but at a higher rate . Theefore , the term " desynchronization " is misleading

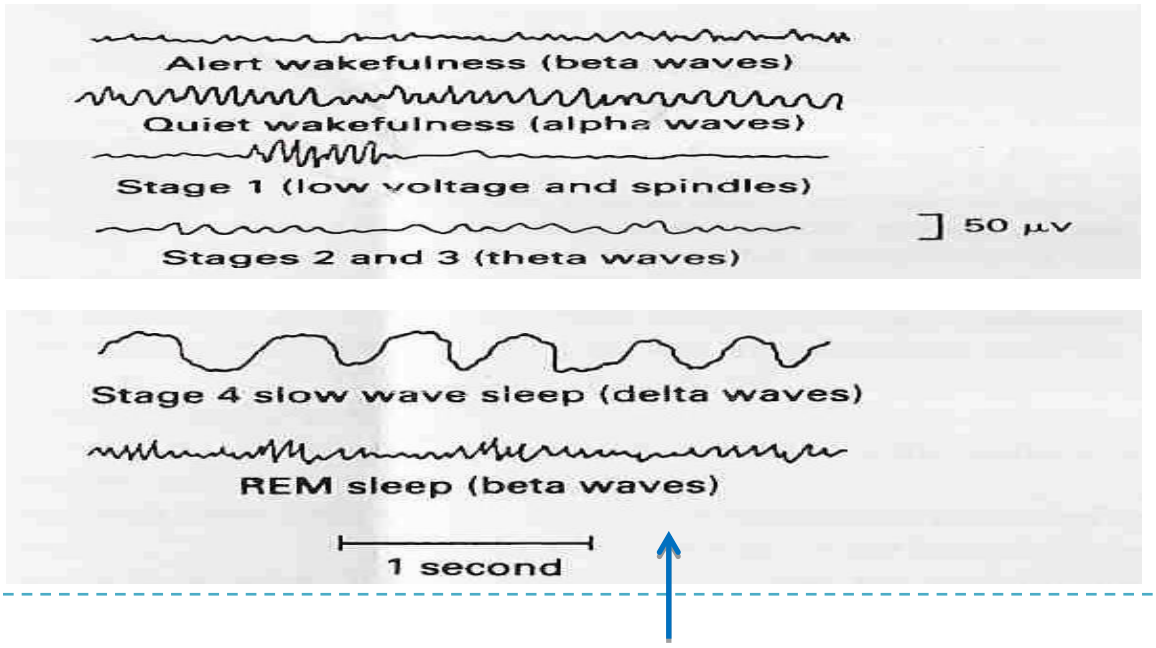


– Beta Waves (a fast rhythm) :

- 14- 30 Hz , lower amplitude than alpha .
- In fully awake person
- In frontal regions .

– Gamma Waves (a fast activity) :

- 30 - 80 Hz .
- Effect of "Focused Attention"&/or " alert Wakefulness , even if eyes are closed " : Often seen in a subject who is , on being aroused , focuses his attention on something (a particular object/person/ animal ,etc)..



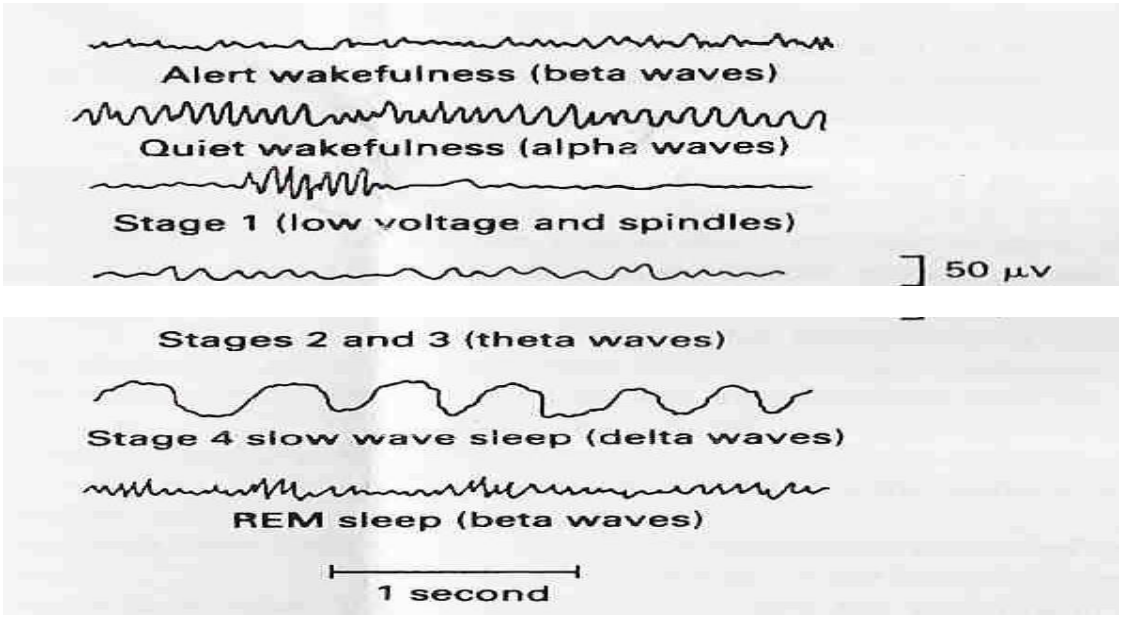
Slow-wave sleep is divided into four stages. In the first stage, a stage of very light sleep, the voltage of the EEG waves becomes very low; this is broken by "sleep spindles," that is, short spindle-shaped bursts of alpha waves that occur periodically. In stages 2, 3, and 4 of slow-wave sleep, the frequency of the EEG becomes progressively slower until it reaches a frequency of only 1 to 3 waves per second in stage 4; these are delta waves. (Guyton)

– **Theta Waves :**

- Large amplitude , regular , 4-7 Hz activity
- Occurs in children .

– **Delta Waves :**

- Large amplitude , < 4 Hz waves
- In deep sleep and coma .

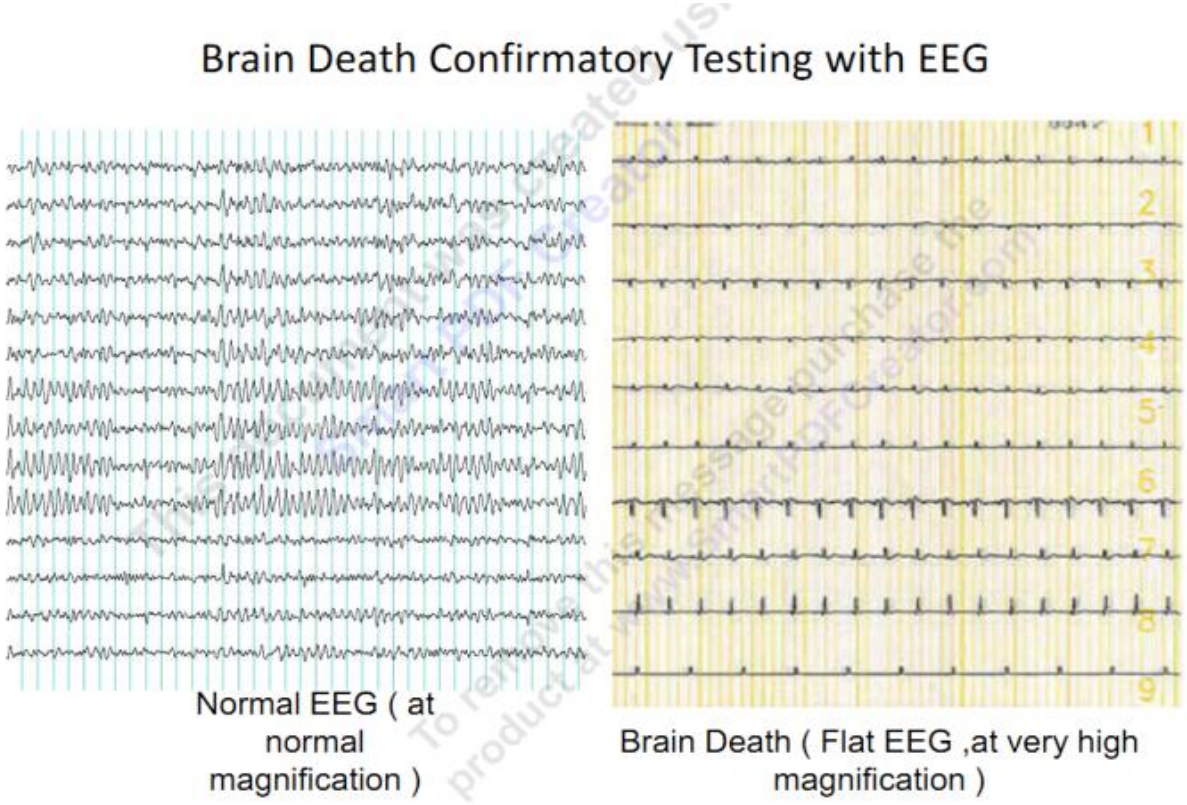


Note, in theta waves: it is **normal** in occur in:

- Awake children.
- All people in stage 2 and 3 sleep.

– The Normal EEG is Largely Age-Dependent :

- The EEG shows special features in different age groups of normal subjects .
- For example : EEG of premature babies is different from that of full-term newborn (even different grades of prematurity have different special EEG features ,depending on the intrauterine age).
- During childhood the occipital rhythm changes from the delta range (0.5-2.0 Hz) in the newborn and gradually increases until it gets established at the alpha range.
- The age-dependent changes in childhood EEG are used as landmarks to indicate the degree of the child's cerebral growth & maturation.
- EEGs of early childhood , late childhood , adolescence , middle age and old age also have some differences .
- **In cases of coma EEG may be dominated by delta waves**
- **In case brain death the EEG is flat, even at very high magnification (where only machine timing artefacts maybe seen).**



❖ Brain Death Confirmatory Testing with Somatosensory Evoked Potentials

Stimulation of a sense organ can evoke a cortical response that can be recorded by scalp electrode over the primary receiving cortical area for that particular sense.

When the full clinical examination, including both assessments of brain stem reflexes and the apnea test, is conclusively performed, no additional testing is required to determine brain death. In some patients, skull or cervical injuries, cardiovascular instability, or other factors may make it impossible to complete parts of the assessment safely. In such circumstances, other brain death confirmatory test in necessary, one of which is somatosensory evoked potential.

In this test, brain death occurs when there is a bilateral absence of certain responses produced by stimulating specific nerves and areas.

Note: This procedure is not an EEG, however, it uses the same concept (placing electrodes and recording electrical impulses etc.). let's say a patient is pricked, this evokes an electrical signal (potential) in the brain the that the machine catches via the electrodes. Sometimes, it is used to test sensory tracts (dorsal column especially).