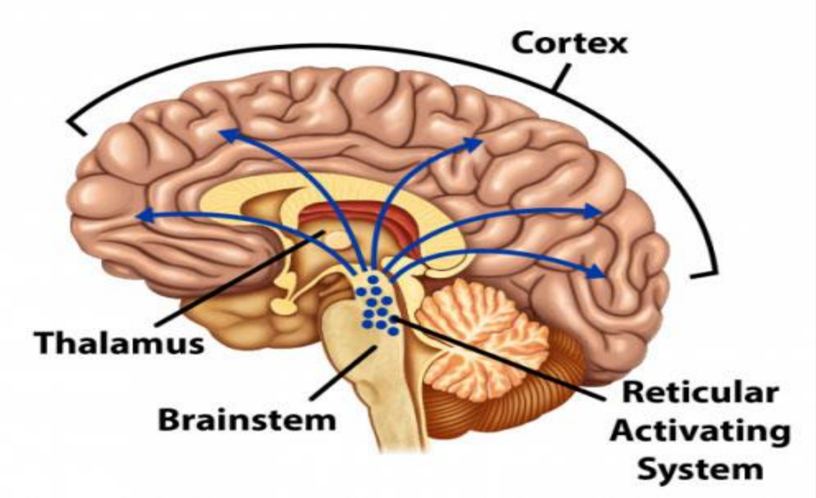
# CNS MODULE
# PHYSIOLOGY (LECTURE 7)
# AROUSAL MECHANISM; RETICULAR ACTIVATING SYSTEM (RAS)

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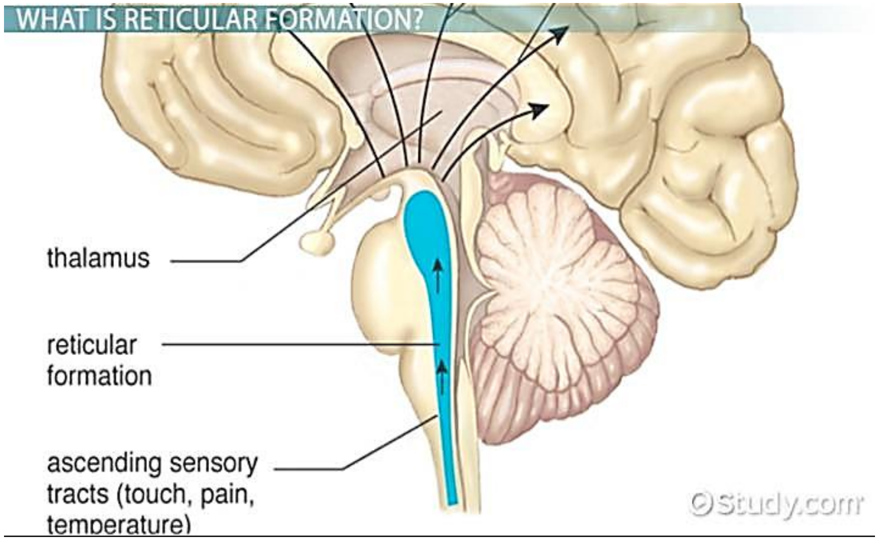
# THE RETICULAR FORMATION

- A network of neurons that connects the **brainstem** with widespread regions of the brain and spinal cord.
- It is primarily an anatomic area made up of various neural clusters and fibers with discrete functions. It contains the **cell bodies and fibers** of many of the **serotonergic, noradrenergic and cholinergic systems**.
- **This network is essential for life** and integrates a large number of physiological functions, including cardiovascular and respiratory control.
- **Some** of the **descending fibers** in it **inhibit transmission in sensory and motor pathways in the spinal cord**.
- It is also involved in **states of consciousness** through **ascending** reticular activating system (**RAS**).



# Functions of Reticular Formation

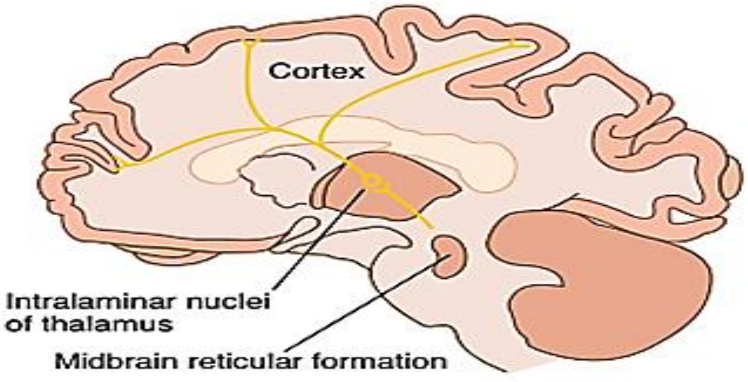
1. Cardiovascular and respiratory control.
2. Control of the level of consciousness via the ascending reticular activating system (RAS).
3. Regulation of the stretch reflex and muscle tone via the ventral and lateral reticulospinal tracts:

- **Pontine reticular nuclei** send projections through the pontine reticulospinal tract of the anterior column of the spinal cord **(ventral reticulospinal tract)**, with **excitatory** synapses on motor neurons innervating axial muscles involved in posture and support of the body against gravity.
- **Medullary reticular nuclei**, through projections descending in the medullary reticulospinal tract of the lateral column of the spinal cord, **(lateral reticulospinal tract) inhibits** motor neurons that innervate axial muscles.

4. Pain inhibition by the raphe magnus nucleus.

# RETICULAR ACTIVATING SYSTEM (RAS)

- **The RAS is a complex polysynaptic pathway arising from the brain stem reticular formation with projections to the non-specific (midline and intralaminar) nuclei of the thalamus which, in turn, project diffusely and nonspecifically to wide regions of the cortex (reticulo-thalamo-cortical pathway).**
- Collaterals funnel into it not only from the long ascending sensory tracts but also from the auditory, visual, and olfactory systems.
- The system is therefore **nonspecific**, whereas the classic sensory pathways are specific in that the fibers in them are activated by only one type of sensory stimulation.
- Varying activation and inhibition of these neurons mediate transitions between waking and sleeping states.



- The **awake state** is characterized by **widespread activation of the cortex and thalamus by ascending pathways of the RAS**.
- Neurons originating in the **brainstem** release the **monoaminergic neurotransmitters** (**norepinephrine and serotonin)**. Their nerve terminals are distributed widely throughout the brain, where they enhance **excitatory** synaptic activity.
- Neuropeptides called **orexins** (a name meaning “to stimulate appetite”) also play an important role in maintaining the **awake state**.
- They are produced by neurons in the **hypothalamus** that have widespread **projections throughout the cortex and thalamus**.

- **Orexin-secreting neurons also densely innervate and stimulate action potential firing by the monoaminergic neurons of the RAS.**
- Experimental animals and humans that lack orexins or their receptors suffer from narcolepsy (a condition characterized by sudden attacks of sleepiness that unpredictably occur during the normal wakeful period).
- Loss of orexinergic neurons that occurs with age may explain why older people sometimes have difficulty sleeping.

- Sleep is characterized by a markedly different pattern of neuronal activity and neurotransmitter release.
- The active firing of neurons in the **"sleep center,"** a group of neurons in the **preoptic nucleus of the hypothalamus**. These neurons release the inhibitory neurotransmitter **GABA** (gammaaminobutyric acid) onto neurons throughout the brainstem and hypothalamus, including those that secrete monoamines and orexins.
- Inhibition of these regions reduces the levels of orexins, norepinephrine, and serotonin throughout the brain. Each of these substances has been associated with alertness and arousal; therefore, inhibition of their secretion by GABA tends to promote sleep.
- This accounts for the sleep-inducing effects of benzodiazepines such as diazepam (Valium) and alprazolam (Xanax), which are GABA agonists and are used to treat anxiety and insomnia in some people.

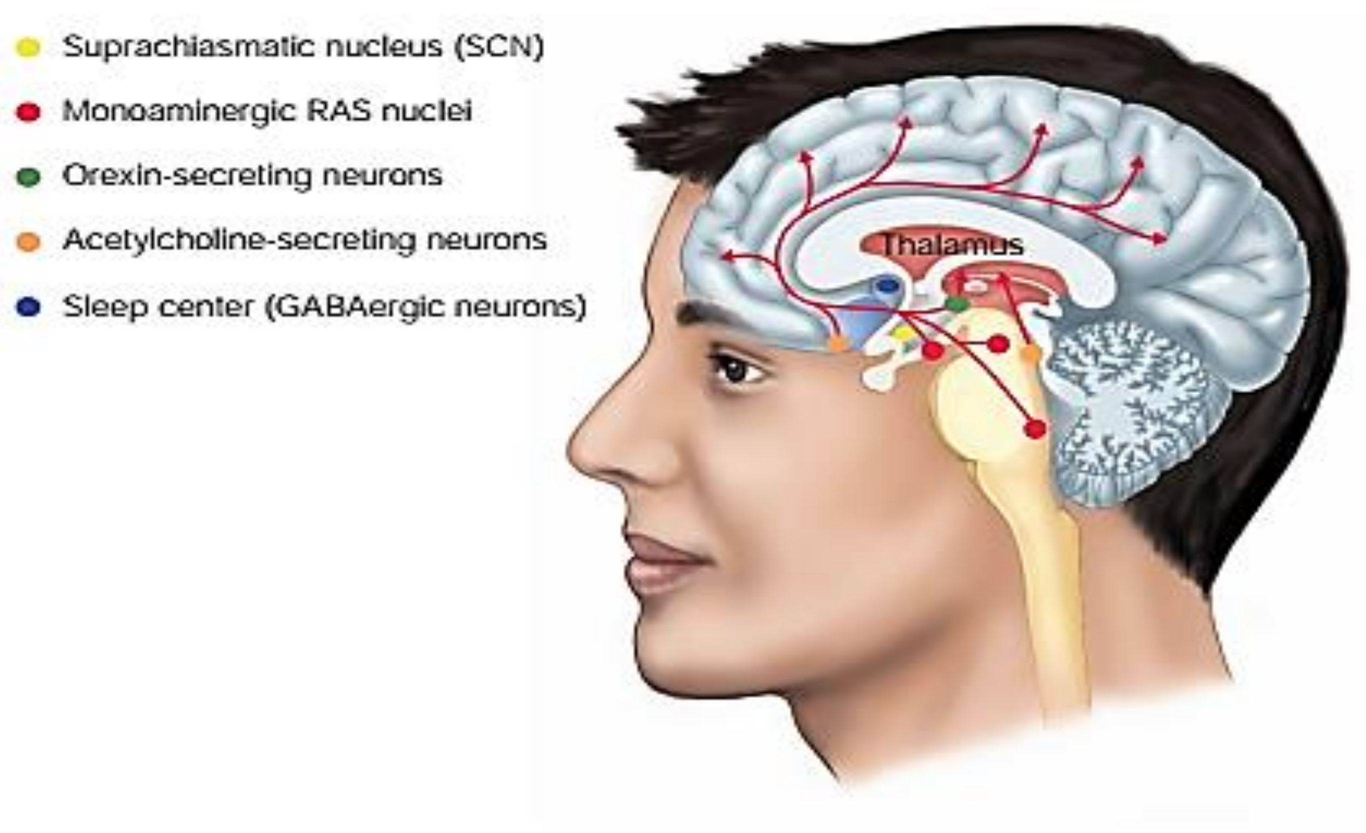



**Figure 8.6** APR Brain regions involved in regulating states of consciousness. Red arrows indicate principal pathways of ascending activation of the thalamus and cortex by the reticular activating system (RAS) during the awake state. Additional pathways not shown that are important in maintaining cortical arousal include excitatory inputs to the monoaminergic RAS nuclei from orexinergic neurons, and inhibitory inputs to the sleep center from the monoaminergic RAS nuclei. Monoamines from the RAS nuclei include histamine, norepinephrine, and serotonin. Orexin neurons and GABAergic neurons of the sleep center are hypothalamic nuclei, and the acetylcholine neurons are in the basal forebrain and pons.

# ELECTRICAL ACTIVITY OF THE BRAIN

The brain has a marked electric activity and 2 types of potentials can be recorded: Evoked potentials and spontaneous potentials (EEG).

## (1) Evoked Cortical Potentials (EP)

- Definition: These are the potential changes that occur in the cerebral cortex after stimulation of a sensory receptor.
- Recording:

The subject is anesthetized and the exploring electrode is applied over the excited cortical area.

- 2 types of these potentials are recorded:

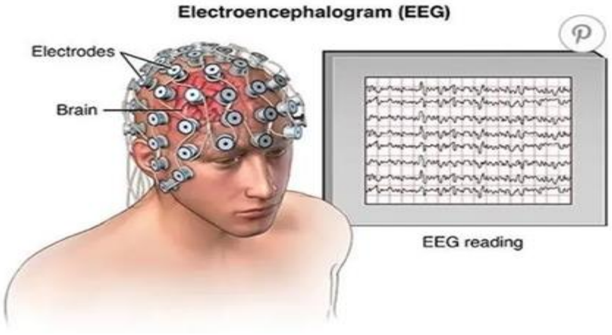
**A. Primary evoked potential.**

**B. Secondary evoked potential (diffuse secondary response).**

# (2) Spontaneous Cortical Potentials Electroencephalogram (EEG) OR Brain Waves

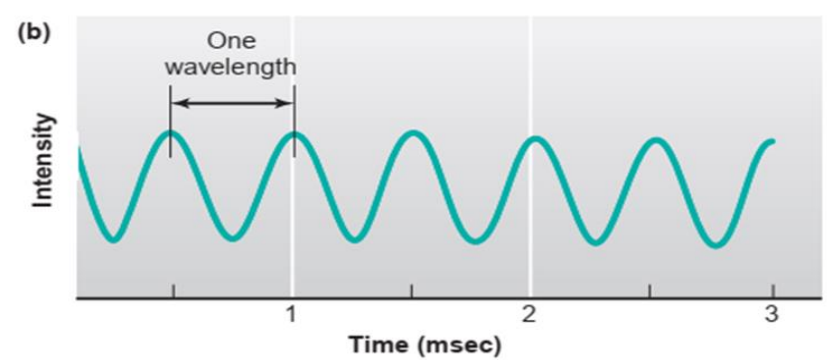
**Electroencephalogram (EEG):**

- The electroencephalogram (EEG) records electrical activity of the cerebral cortex via electrodes placed on the skull.
- Electrodes, which are wires attached to the head pick up electrical signals generated in the brain and transmit them to a machine that records them as the EEG.
- Electrodes are not positioned to detect individual action potentials but they can detect simultaneous action potentials in large number of neurons.
- EEG patterns are detected as **wavelike patterns** known as **brain waves. Their intensity (amplitude) and frequency differ according to state of brain activity.**



- ✓ There is large variations in both amplitude and frequency of brain waves.
- ✓ The wave's amplitude is measured in microvolts (μV).
- ✓ A large amplitude indicates that many neurons are being activated simultaneously. In other words, it indicates the degree of synchronous firing of the neurons that are generating the synaptic activity.
- ✓ On the other hand, a small amplitude indicates that these neurons are less activated or are firing asynchronously.
- ✓ The amplitude may range from 0.5 to 100 μV.

- ✓ The frequency of the wave is measured in hertz (Hz, or cycles per second) and may vary from 0.5 to 40 Hz or higher.
- ✓ There is a general **correlation between level of cerebral activity and average frequency of the EEG rhythm**, the average frequency increasing progressively with higher degrees of activity.
- ✓ In general, lower EEG frequencies indicate less responsive states, such as sleep, whereas higher frequencies indicate increased alertness (Meanwhile, one stage of sleep is an exception to this general relationship).
- ✓ Recording of the human EEG showed **4 main types of waves** that define different states of consciousness.

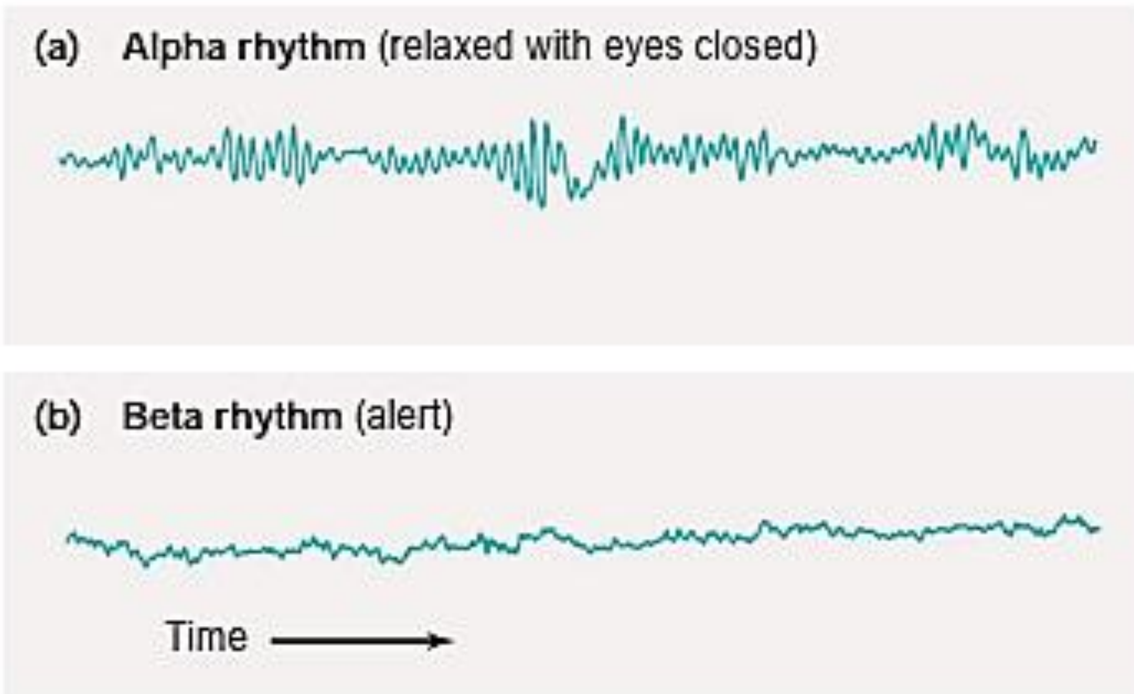


## Alpha waves:

- These waves are the dominant waves recorded in **awake adults during rest, while they are relaxed and their eyes closed**.
- Their **voltage is about 50 μV**.
- The **frequency** of alpha rhythm is **8-13 Hz**.
- It is most marked in the **occipital regions (also recorded from parietal and frontal).**

## Beta waves:

- They are recorded **in awake adults during brain activity (alert) with opened eyes and also in adults during REM sleep**.
- These waves have the **lowest voltage (20 μV)**.
- The **frequency** of beta rhythm is **13-30 Hz**.
- It is most marked in the **frontal region (also recorded from parietal region)**.


(a) **Alpha rhythm** (relaxed with eyes closed)
(b) **Beta rhythm** (alert)
Time

## Theta waves:

- They are recorded in **children and in adults during light sleep**.
- These waves have a **higher voltage than the alpha waves**.
- The **frequency** of theta rhythm is **4-7 Hz**.
- It is most marked in the **parietal and temporal regions**.

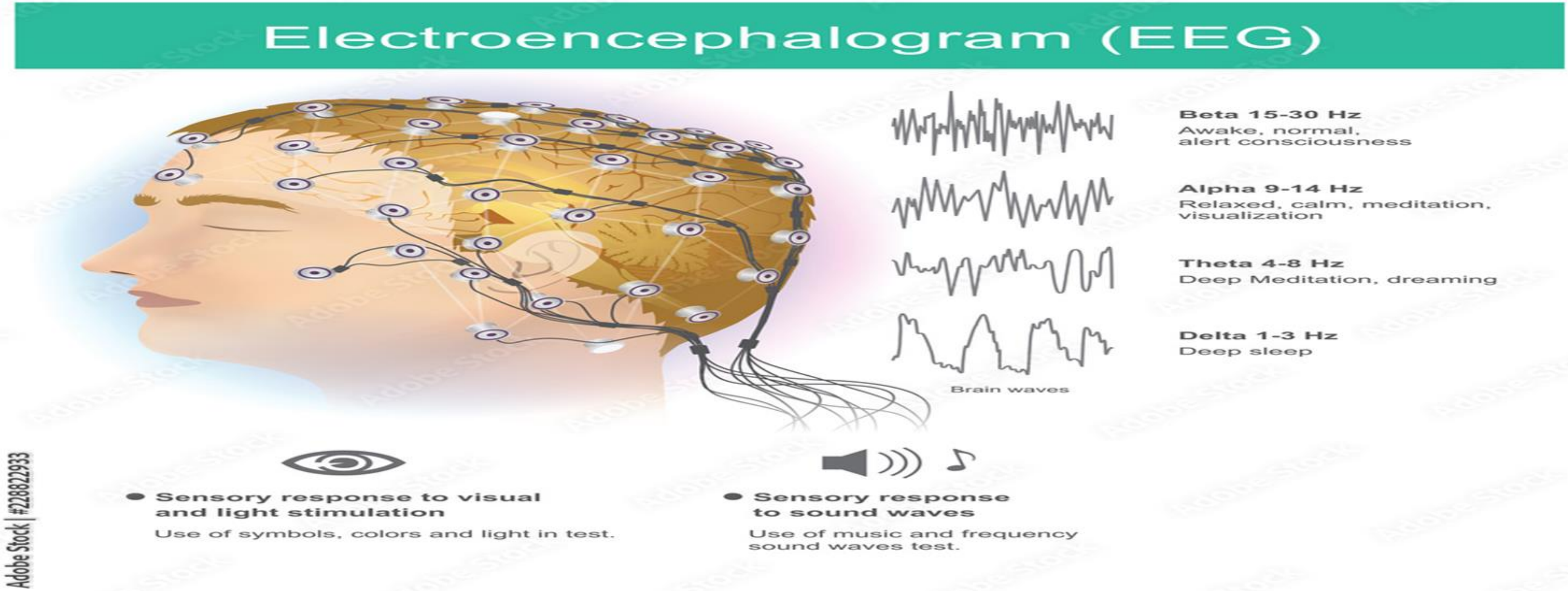
## Delta waves:

- They are recorded in **infants and in adults during deep sleep**.
- These waves have the **highest voltage (100 µV)** and lowest **frequency (1-3 Hz)**.

N.B. The frequency of waves is generally inversely proportionate to their amplitude (voltage).

| | Alpha | Beta | Theta | Delta |
|---|---|---|---|---|
| **1. Frequency** | 8-13 Hz | 13-30 Hz | 4-7 Hz | 1-3 Hz |
| **2. Amplitude** | 50 µV | 20 µV | Higher than alpha | 100 µV |
| **3. Age and State of the person** | Adult:<br>Awake<br>relaxed<br>Closed eyes | Adult:<br>Awake<br>Alert<br>Opened eyes<br>(During brain activity)<br>REM sleep | Children<br>Or<br>in<br>Adults: during light sleep | Infants<br>Or<br>in<br>Adults: during deep sleep |
| **4. Recorded at** | Mainly Occipital Region<br>(also recorded from parietal and frontal) | Mainly Frontal and parietal regions | Parietal-Temporal regions | |

N.B. Other waves may be recorded in certain conditions e.g. Gamma waves: Fastest (30-100 Hz, 10 µV) – during intense brain activity (cognitive function, memory & learning).


Electroencephalogram (EEG)
Beta 15-30 Hz
Awake, normal, alert consciousness
Alpha 9-14 Hz
Relaxed, calm, meditation, visualization
Theta 4-8 Hz
Deep Meditation, dreaming
Delta 1-3 Hz
Deep sleep
Brain waves
Sensory response to visual and light stimulation
Use of symbols, colors and light in test.
Sensory response to sound waves
Use of music and frequency sound waves test.
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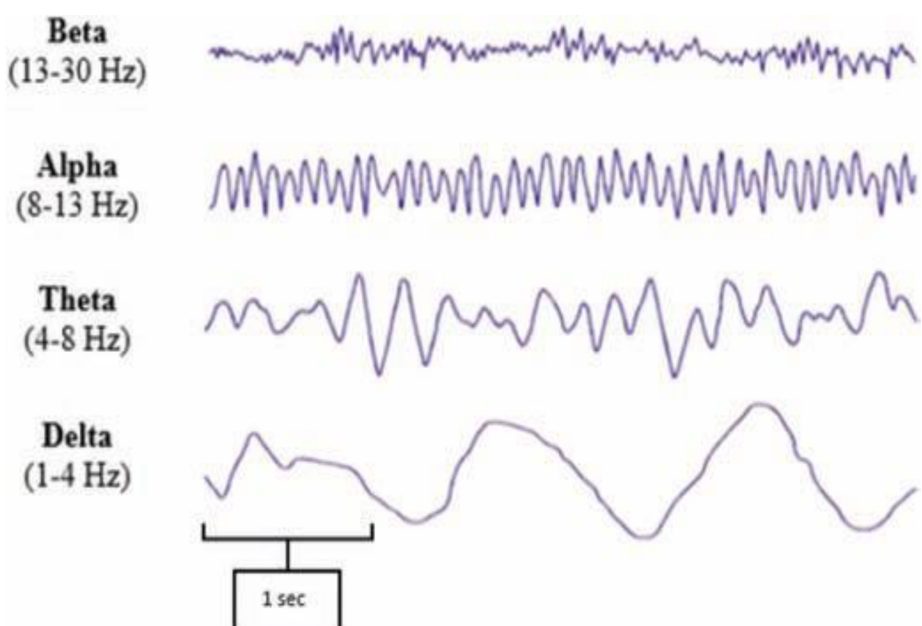
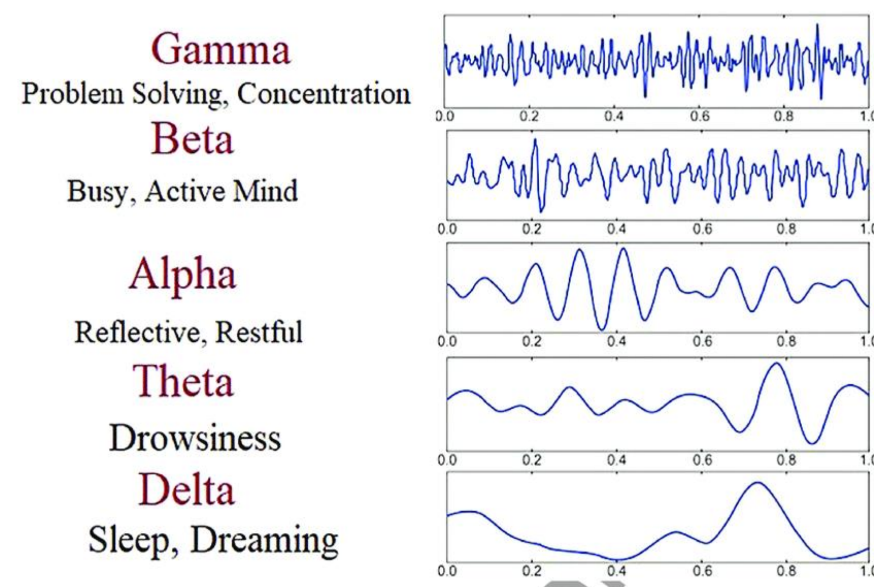

Beta
(13-30 Hz)
Alpha
(8-13 Hz)
Theta
(4-8 Hz)
Delta
(1-4 Hz)
1 sec


Gamma
Problem Solving, Concentration
Beta
Busy, Active Mind
Alpha
Reflective, Restful
Theta
Drowsiness
Delta
Sleep, Dreaming
0.0
0.2
0.4
0.6
0.8
1.0

# EEG Variations

**(1) Effect of age:**

- In young infants, slow delta waves are recorded.
- During childhood, the delta waves are replaced by theta waves, then the adult alpha rhythm gradually appears during adolescence.

**(2) Effect of sleep.**

# The arousal or alerting response

- This is an EEG response that occurs when the subject becomes alert (e.g. on opening his eyes or when solving a mathematical problem).
- The synchronized alpha rhythm is replaced by rapid low-voltage beta waves.
- It represents breaking up of the synchronized neuronal alpha activity, so it is also called **alpha block**.
- Such response is **reversible** (so if the eyes are closed again, the alpha rhythm is resumed).
- It is due to stimulation of the reticular activating system (RAS).

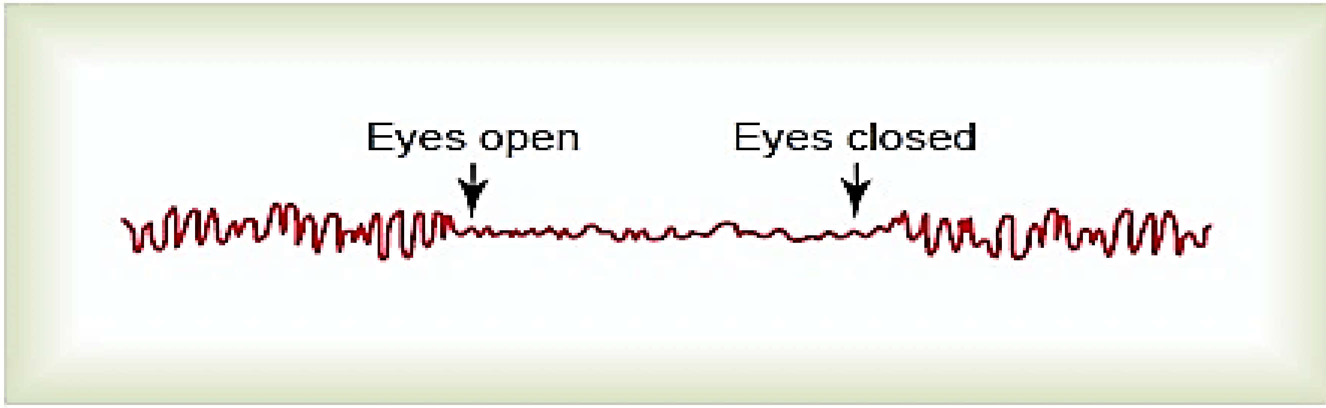



**Figure 59–2**

Replacement of the *alpha* rhythm by an asynchronous, low-voltage *beta* rhythm when the eyes are opened.

# Clinical significance of the EEG

**The EEG is useful clinically in:**

- ✓ The diagnosis of certain brain diseases as epilepsy.
- ✓ It was formerly also used in the detection of brain areas damaged by tumors, blood clots, or hemorrhage. However, the much greater spatial resolution of modern imaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) make them far superior for detecting and localizing damaged brain areas in such cases.


Thank You