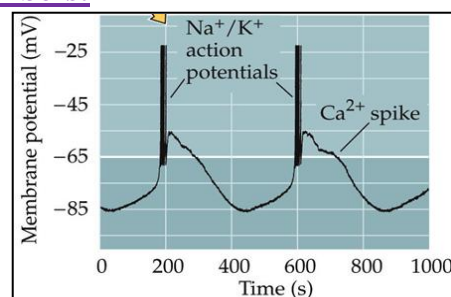




- Fibers from the thalamus to the cortex are known as thalamo-cortical neurons. These fibers cause the opening of Na^+ -channels → therefore, leading to influx of sodium ions (they will enter inside the neurons) → and this is going to create a negative environment outside the neurons → which will result in the generation of a small current that will be recorded by EEG.
- **Source of EEG:** pyramidal cells of the cortex (these pyramidal cells are organized in a specific way and they are parallel to each other thus their electrical activity will be summated).
- When we are awake, information are allowed to reach the cortex.

- **There are two states of activity of thalamo-cortical fibers:**

- **They can be tonically active (desynchronized state):** and this is concerned with alertness and making a person awake.
- **Or they can be in an oscillatory/burning state (synchronized state):** in which there is a hyperpolarization (caused by activation of type T calcium channels) state and then an action potential will arise all of a sudden (see the image). This state represents sleep.



✓ Why do action potentials appear in this sleep state?

- ❖ *Because the thalamus is trying to keep the cortex in connection with although the cortex is isolated from external environment and external stimuli. Therefore, the cortex will not be lost and we don't enter a state of coma.*

- **Brain waves:**

- **Alpha waves:** these are seen in adults who are in an awake state with occipital dominance (if you ask the person to close his eyes → the occipital lobe will not be functioning → therefore, alpha waves will appear).
- **Beta waves:** they refer to anxiety and psychological problems/ issues.
- **Theta waves:** some can be detected normally in the temporal lobe → but excessive theta waves detected in an awake state is abnormal (because normally it should be detected during sleep or when there is less brain activity).
- **Delta waves:** these must not be detected/recorded in an awake person! Because normally it is seen during deep sleep (note that diffuse delta waves are detected in encephalitis because the brain is not functioning properly and has less activity).

- **Terminologies:**

- **Seizure (means: to possess):** it is defined as abnormal electrical activity of the brain.
- **Epilepsy:** when a person has tendency to suffer from recurrent seizures.
- **Epileptogenesis:** when there are changes which convert neurons from normal neurons to epileptogenic neurons.

- **Seizures are classified to:**

- **Partial seizures:** in which only one part of the body is affected (an example is myoclonic epilepsy which is occurring in the hand only). Partial seizures are further classified to:
 - ✓ Simple partial: in which the level of consciousness is not altered (alertness is preserved).
 - ✓ Complex partial: in which the level of consciousness is altered (patient loses his consciousness) and he will experience aura (through which he knows that he will get the attacks).
 - ✓ Partial seizures evolving to tonic-clonic convulsions.
- **General seizures:** in which the whole body is affected (examples include atonic epilepsy or clonic epilepsy). Generalized seizures are further classified to:



- ✓ **Absence seizures:** mostly occurring in children in which they will be isolated from reality for few seconds and then come back (as if nothing happened). In EEG, absence seizure is characterized by domes and spikes. This condition usually resolves when the child grows up.
- ✓ **Myoclonic seizures:** sudden, jerky, violent movements occurring in one group of muscle (on part of the body).
- ✓ **Clonic seizures:** in which the whole body of the patient will be jerking (convulsions).
- ✓ **Tonic seizures:** in which the whole body of the patient stiffens.
- ✓ **Atonic seizures:** in which the whole body of the patient will lose its tone (يصبح الجسم رخو)
- **Partial seizures which can develop into general seizures:** this occurs when the focal abnormal electrical activity spreads and reaches the thalamus.
- **What causes the seizure:**
 - **Hyperexcitability of the neuron:** discharging action potentials easily.
 - ✓ **What causes neuronal hyperexcitability?**
 - ❖ *Changes in ion-channels* (increased sodium or calcium channels will result in hyperexcitability while increased chloride channels will result in hypoexcitability)
 - ❖ *Changes in receptors:* calcium receptors are excitatory (depolarizing) while potassium receptors are inhibitory (hyperpolarizing).
 - ❖ *Neurotransmitters:* in epilepsy the excitatory neurotransmitter glutamate is increased while the inhibitory neurotransmitter GABA is decreased.
 - **Hypersynchrony:** in which group of neurons are discharging their action potentials at the same time and spreading easily.
 - **Propagation:** in which there is ability to transport electrical activity throughout the brain.
- **Role of glial cells:** they are regulating the concentration of potassium in extracellular fluid. Also, they are important in reuptaking neurotransmitters.
- **Pathophysiology of epilepsy:**
 - **The most important structure in the brain involved in epilepsy is the hippocampus (representing 80% of cases with temporal lobe epilepsy).** Normally, hippocampal cells are hyperexcitable allowing us to make memories thus they are susceptible to be excited easily and might release abnormal electrical activities (كأنهم قنبلة موقوتة).
 - ✓ So all memories are made by the hippocampus and then stored in different areas of the cortex.
 - ✓ The hippocampus is a simple structure located deep in the brain and composed of 3 layers and 2 parts (body and tail).
 - **Interictal spikes:** are those spikes which can be detected between epileptic attacks (when recording brain waves by EEG).
 - ✓ **Paroxysmal depolarization shift (PDS):** these types of neurons has no constant resting membrane potential (which mean that they become hyperexcitable neurons) → notice that PDS is recorded normally in the hippocampus but if it is recorded elsewhere in the brain → this is considered abnormal.
 - ❖ Decreased GABA will result in PDS → so PDS is the basic underlying mechanism of focal epilepsy.
 - ❖ Normally, PDS of hippocampus is not recorded because EEG only records superficial electricity of the brain.
 - **Epileptogenesis (how does it occur?)** → an inciting event occurs to the normal brain tissue → so it will become hyperexcitable (has less GABA secretion) → and there will be generation of repeated action potentials resulting from changes in neuronal network stability → eventually resulting in seizure.



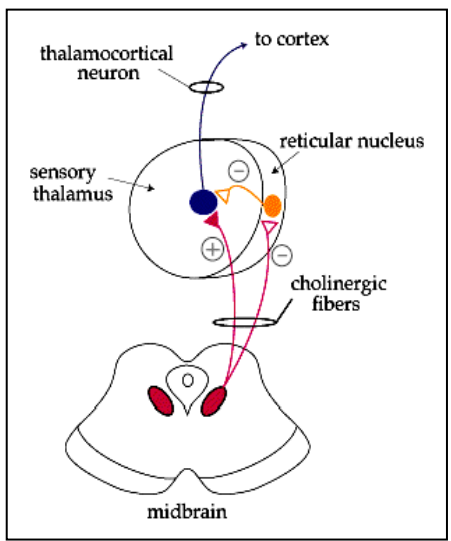
- ✓ The inciting event to the tissue can be:
 - ❖ *Acquired:* trauma, stroke, tumor or infection.
 - ❖ *Genetic:* cell-signaling molecules, neurotransmitter receptor subunits and uptake site, ion channels.

- **Generalized seizure:**

- **One type of generalized seizure is absence seizure** in which the EEG is characterized by the presence of “spikes and dome” at a frequency of 3/sec.

✓ In normal subjects, what happens during day-time and sleep?

- ❖ *In day-time:* reticular nucleus is inhibited and thalamic neurons are tonically active (no hyperpolarization, no stimulation of calcium-channels).
- ❖ *During sleep:* reticular nucleus is not inhibited and thus it causes hyperpolarization of thalamic neurons and there will be stimulation of T-type calcium-channels.



✓ So what happens in those patients with absence seizure?

- ❖ There will be spontaneous firing of (inhibitor reticular nucleus) which will cause inhibition of thalamic neurons and generation of calcium spikes (therefore, isolating the cortex from stimuli of external environment).
- ❖ Another mechanism of absence seizure might be overexpression of calcium-channels in thalamo-cortical neurons.

✓ Absence seizure is treated by “ethosuximide” which acting through blockade of calcium-channels.

- **Tonic-clonic seizure: pathophysiology can be:**

- ✓ Hypoxia during delivery of a baby causing general death of neurons in the brain and resulting in this type of seizure.
- ✓ Or due to genetics.

- **Focal/partial seizure:** in which the cause is the presence of focal structural abnormality in the brain and it may progress to generalized seizure if the focal abnormal electrical activity spreads throughout the brain to reach the thalamus.

- Focal epilepsy might be simple (in which consciousness is not altered) or complex (in which consciousness is altered).
- In focal epilepsy the patient might also experience aura based on the location of the focus in the brain:

FOCUS	Aura
•Somaesthetic cortex (area 3,1,2)	•Paraesthesia in corresponding area
•Motor cortex (area 4)	•Myoclonic twitching
•Temporal lobe	•Auditory or Visual hallucination
•Temporal lobe (Uncus)	•Unpleasant odour
•Temporal lobe (Amygdala)	•Fear
•Hippocampus	•Psychic disturbance, <i>déjà vu, jamais vu</i>

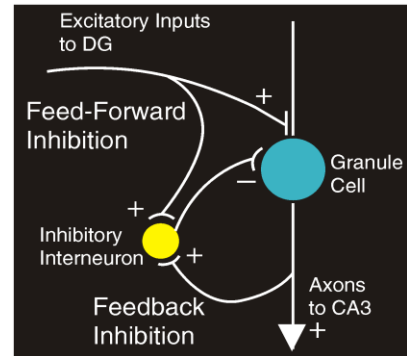
- Notice that you also localize the focus using EEG or MRI.



- **Basic mechanisms to limit excitation:**

- **Whenever a neuron is excited → it should be inhibited immediately after. This is achieved through:**

- ✓ **Feedback:** in which the same neuron will send a branch to inhibit itself whenever it is excited.
- ✓ **Feed-forward:** in which neuron (A) will excite neuron (B) and will also excite an inhibitory interneuron which is going to inhibit neuron (B).



- **Propagation of partial/focal seizure:**

- **Intrahemispheric:** in which the abnormal electrical activity will spread in the same hemisphere but to a different area than the focus.
- **Homotopic contralateral cortex:** in which the abnormal electrical activity will spread to the same area of the focus but in the opposite cortex/hemisphere.
- **Subcortical center:** in which the abnormal electrical activity is reaching thalami and converted to generalized seizure.

- **Vagus nerve stimulator:**

- Applied as a treatment when there is no effect with antiepileptic drugs.
- Approved for partial onset seizure.

