*Pathophysiology of Epilepsy

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*Objectives

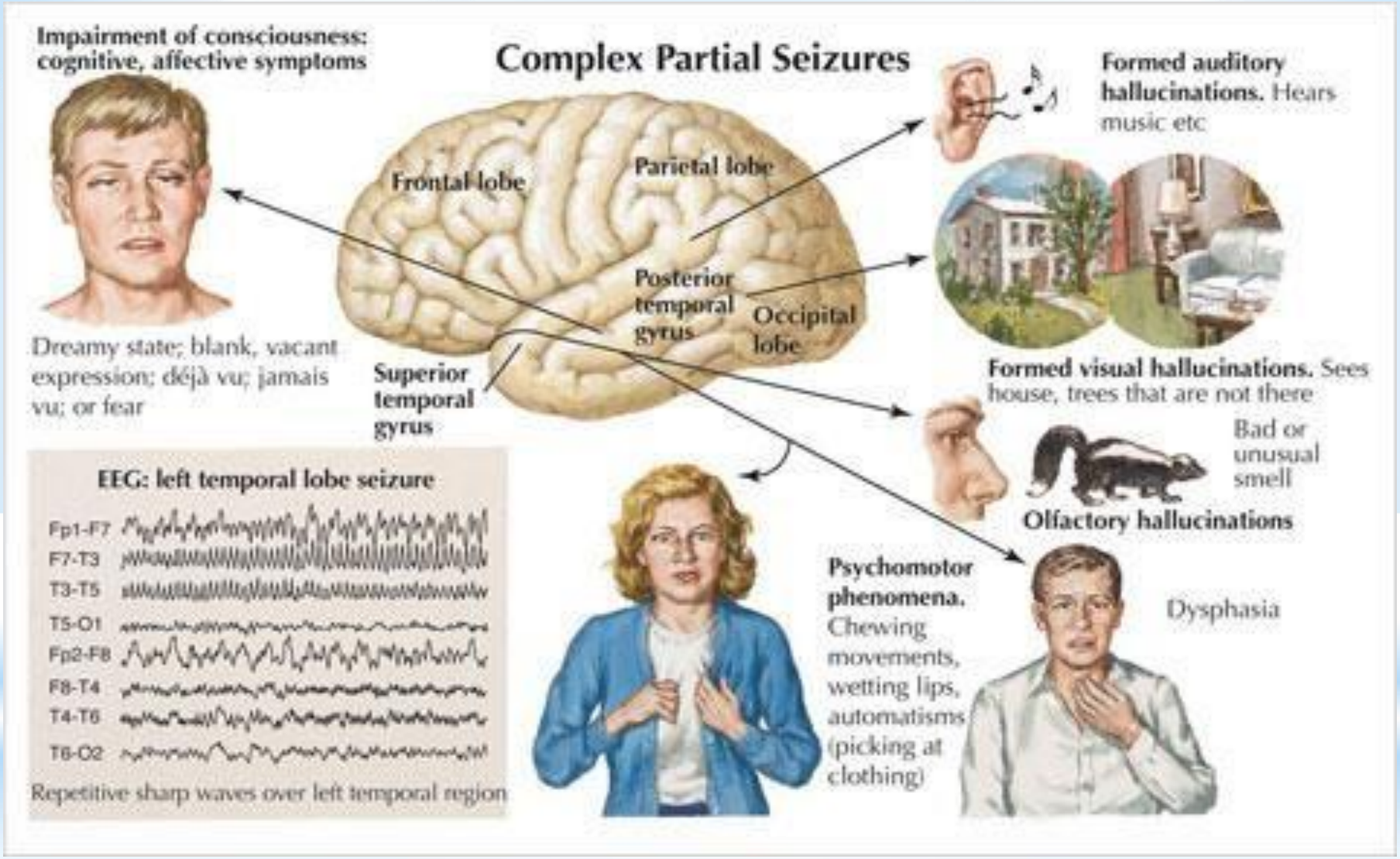
*At the end of this lecture the students should be able to:-

1. Define Epilepsy
2. Etio-pathology of Epilepsy
3. Types of Epilepsy
4. Role of Genetic in Epilepsy
5. Clinical Features
6. Role of Electro Physiological tests in the diagnosis of Epilepsy

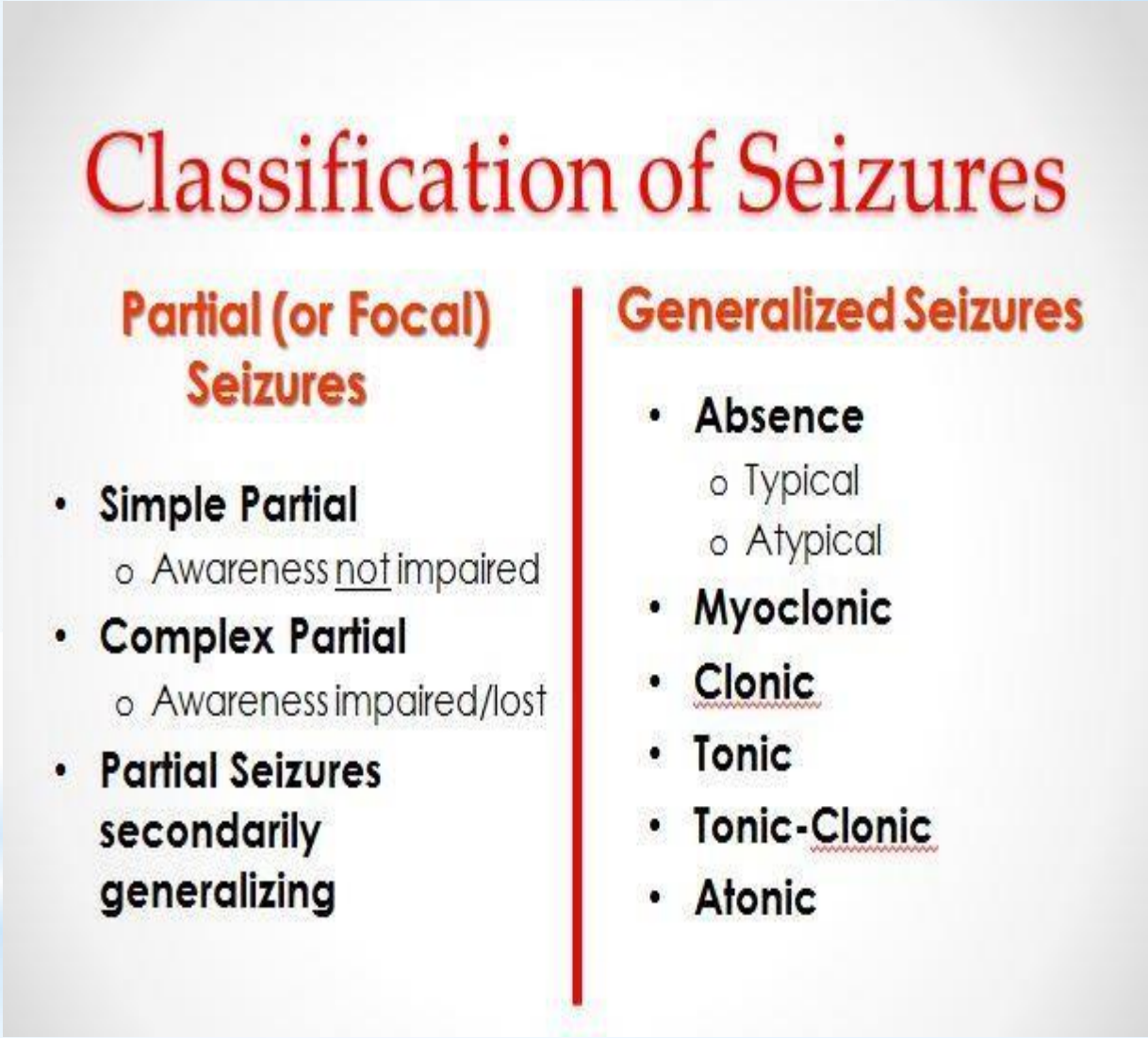
* Definition of seizure and Epilepsy

* Seizures are symptoms of a disturbance in brain function , which can be due to epilepsy or other causes
* A seizure is a sudden surge in electrical activity in the brain that causes an alteration in sensation, behavior, or consciousness

* Abnormal , excessive electrical discharge of a group of neurons within the brain.
* When a person has recurrent (2 or more) , unprovoked seizures → " epileptic ".
* Hence seizures can be a symptom of epilepsy .


Complex Partial Seizures
Impairment of consciousness: cognitive, affective symptoms
Dreamy state; blank, vacant expression; déjà vu; jamais vu; or fear
Frontal lobe
Parietal lobe
Posterior temporal gyrus
Occipital lobe
Superior temporal gyrus
Formed auditory hallucinations. Hears music etc
Formed visual hallucinations. Sees house, trees that are not there
Bad or unusual smell
Olfactory hallucinations
Psychomotor phenomena. Chewing movements, wetting lips, automatisms (picking at clothing)
Dysphasia
EEG: left temporal lobe seizure
Fp1-F7
F7-T3
T3-T5
T5-O1
Fp2-F8
F8-T4
T4-T6
T6-O2
Repetitive sharp waves over left temporal region

* Seizures
* Partial
* or
* Generalized



*a. Simple partial seizures manifest motor, somatosensory, and psychomotor symptoms without impairment of consciousness(e.g Jaksonian seizures)

*b. Complex partial seizures
impairment of consciousness

Partial psychomotor (temporal lobe) seizure

- Epileptic seizures which originate in the temporal lobe of the brain.
- The seizures involve sensory changes, for example smelling an unusual odour that is not there, and disturbance of memory.
- Visual , auditory , olfactory or visceral hallucinations, déjà vu (over familiatry), feelings of unreality (jamais vu)
- The most common cause is mesial temporal sclerosis

Jacksonian epilepsy

- Focal motor seizures begin in motor areas of cerebral cortex, usually begins with twitching of the thumb or finger , toe or the angle of the mouth.
- Spreading to involve the limbs on the side opposite the epileptic focus.
- Clinical evidence of this spread of activity is called the march of the seizure

- Simple partial seizures can progress to complex partial seizures, and complex partial seizures can secondarily become generalized.

- Seizures affect all ages. Most cases of epilepsy are identified in childhood, and several seizure types are particular to children.

*c. Generalized seizures

*manifest a loss of consciousness
convulsive or non-convulsive
*Generalized seizures include →
*(1) generalized tonic- clonic seizures(GTC)
*(Grand Mal epileptic seizure)
*(2) Absence seizures
(Petit mal epileptic seizures)

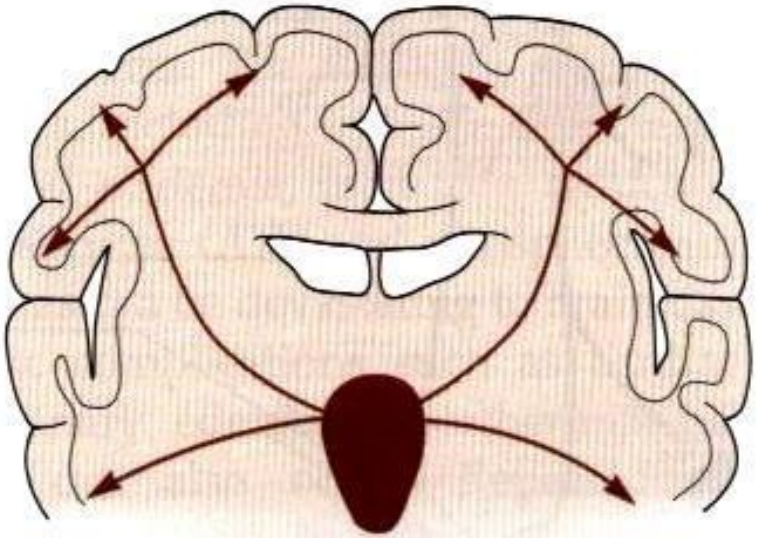
- *GTC are convulsive and Absence are non-convulsive .*

* Seizure Classification & Clinical Manifestations

1. Focal / Partial seizures → their onset (start) is limited to part of the cerebral hemisphere

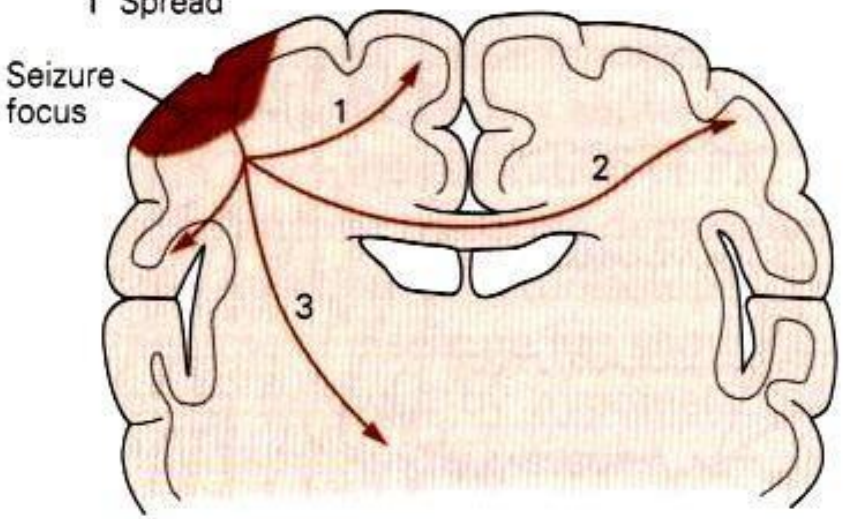
2. Generalized seizures → those that involve the cerebral cortex diffusely (whole of it) from the beginning (*generalized* seizures)

Primary generalized seizure

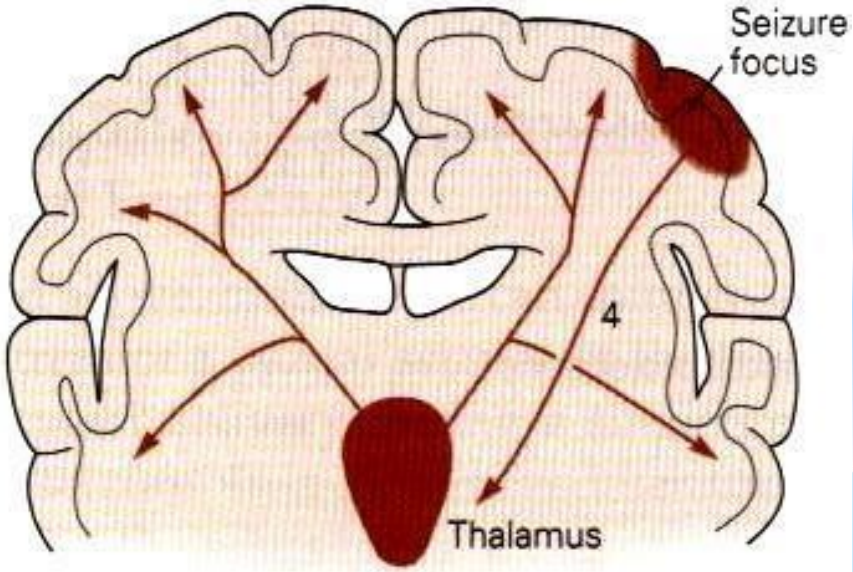


A Partial seizure

1 Spread



2 Secondary generalization



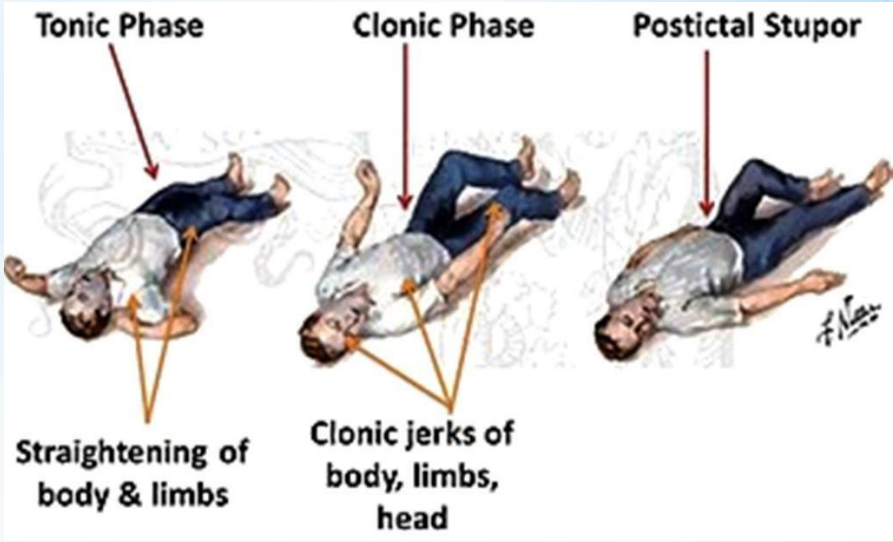
* The onset of a seizures:

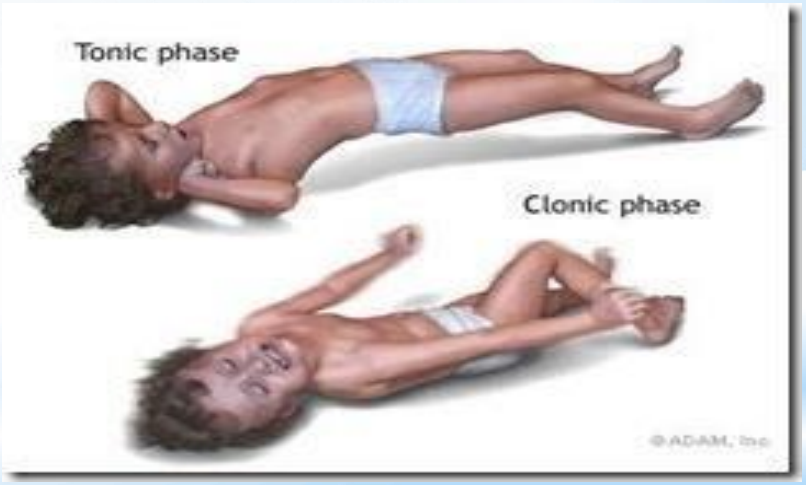
Small group of abnormal neurons undergo prolonged depolarizations

- Rapid firing of repeated action potentials

* Spread to adjacent neurons or neurons with which they are connected into the process.

* A clinical seizure occurs when the electrical discharges of a large number of cells become abnormally linked together, creating a storm of electrical activity in the brain.
* Seizures may then spread to involve adjacent areas of the brain or through established anatomic pathways to other distant areas.





Generalized

1- Generalized tonic-clonic (grand mal) seizure

a. +/- **aura**

(peculiar sensation or dizziness; then sudden onset of seizure with loss of consciousness)

tonic phase :

Rigid muscle contraction in which clenched jaw and hands; eyes open with pupils dilated; lasts 30 to 60 seconds

clonic phase:

Rhythmic, jerky contraction and relaxation of all muscles in with incontinence and frothing at the lips; may bite tongue or cheek, lasts several minutes.

*__ostictal state__:

Sleeping or dazed for up to several hours.

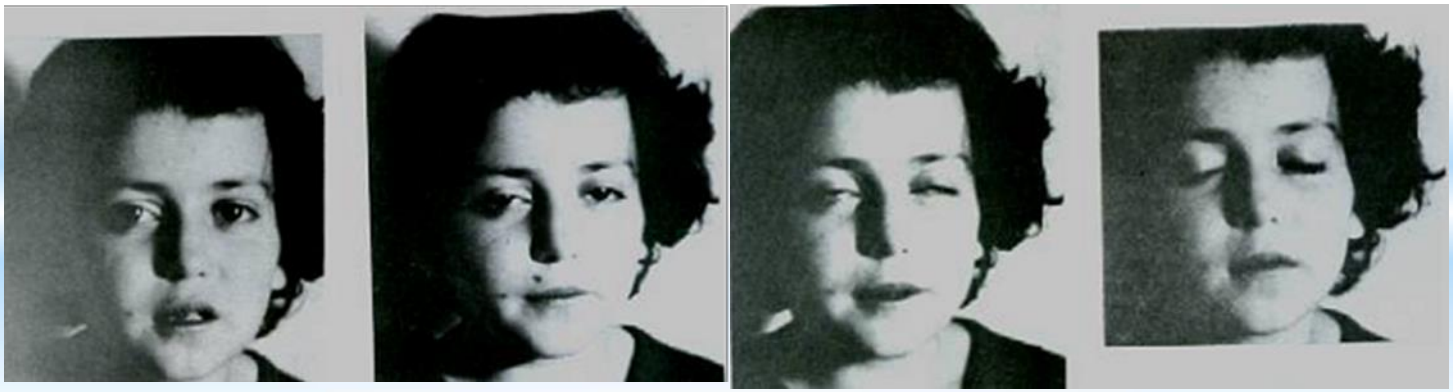
Generalized

2. Absence (petit mal) seizure

a. Loss of contact with environment for 5 to 30 seconds.

b. Appears to be day dreaming or may roll eyes, nod head, move hands, or smack lips.

c. Resumes activity and is not aware of seizure.



* **Clinical Manifestation of Seizure:**
* The clinical manifestations of a seizure reflect the area of the brain from which the seizure begins (i.e., seizure focus) and the spread of the electrical discharge.

* Clinical manifestations accompanying a seizure are numerous and varied, including →
* (1) indescribable bodily sensations,
* (2) "pins and needles" sensations,
* (3) smells or sounds,
* (4) fear or depression,
* (5) hallucinations,
* (6) momentary jerks or head nods,
* (7) staring with loss of awareness, and
* (8) **Convulsions** → i.e., involuntary muscle contractions) lasting seconds to minutes.

Aetiology of seizures

- Epileptic
  - Idiopathic (70-80%)
  - Cerebral tumour
  - Neurodegenerative disorders
    (Alzheimer, Multiple sclerosis)
  - Secondary to
    - Cerebral damage: e.g. congenital infections, intraventricular haemorrhage
    - Cerebral dysgenesis/malformation: e.g. hydrocephalus

- **Non-epileptic**
  - Febrile convulsions
  - Metabolic
    - Hypoglycemia
    - HypoCa, HypoMg, HyperNa, HypoNa
  - Head trauma
  - Meningitis
  - Encephalitis
  - Poisons/toxins

Pathophysiology of Epilepsy (at molecular level)

- Cortical cell membrane level

➢ Hypersensitive neurons with lowered thresholds for firing and firing excessively , related to →

- (1) Excess of Excitatory (acetylcholine- or Glutamate – related activity)
- (2) Decreased inhibitory (GABA –related activity)

➢ Together and/or (2) above → leading to instability of cell-membrane & lowered threshold for excitation → excessive polarization, hypopolarization allowing the cell to be more susceptible to activation spontaneously or by any ionic imbalances in the immediate chemical environment of neurons

*Genetic & Epilepsy:

* Some types linked to genes (run in families)
* Genetic abnormalities >>>> increasing a person's susceptibility to seizures_that are triggered by an environmental factor
* Several types of epilepsy have now been linked to defective genes for **ion channels, the "gates"** that control the flow of ions in to and out of cells and that regulate neuron signaling.

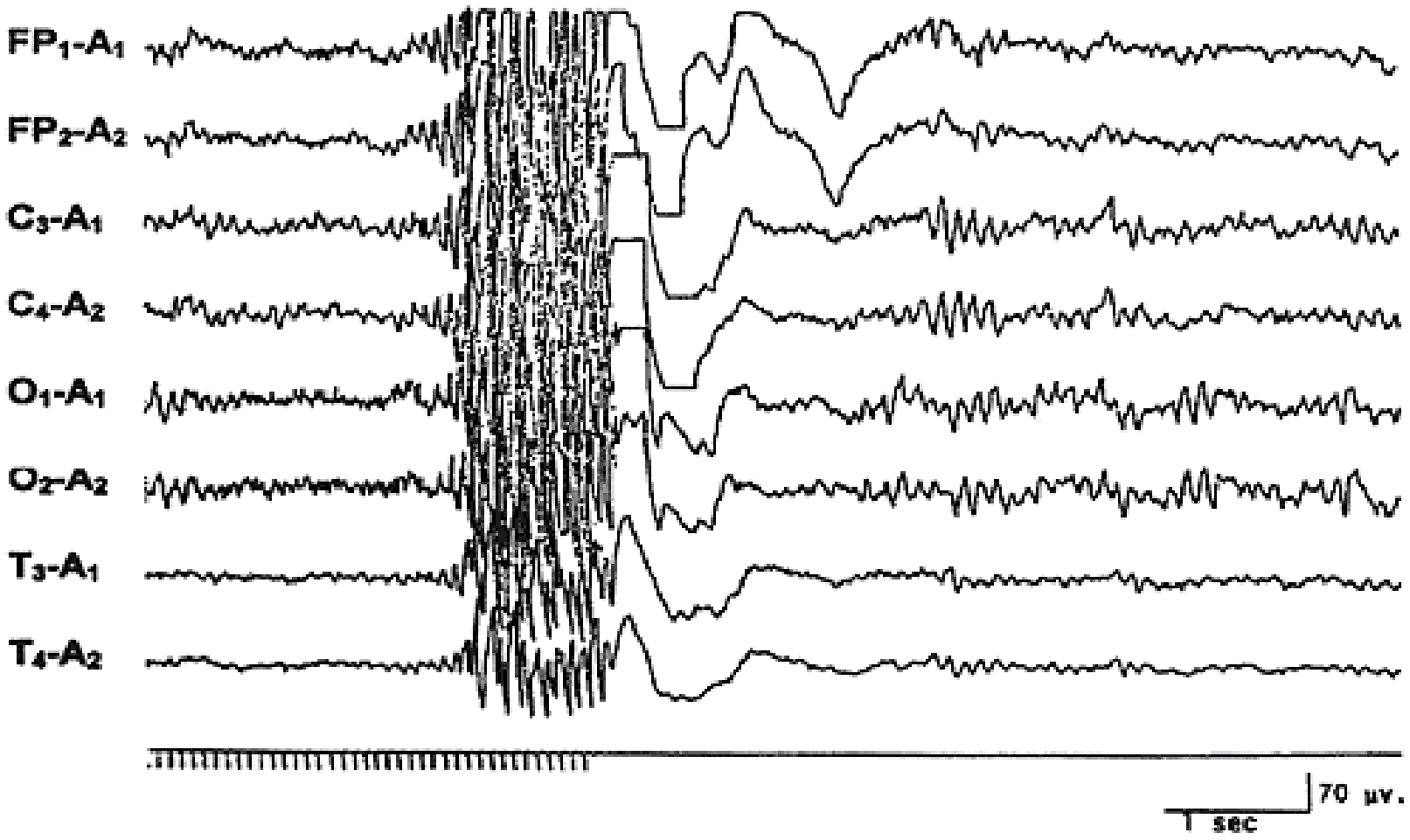
- Example : Lafora's disease, has been linked to a gene that helps to break down carbohydrates.

* Electroencephalogram (EEG)

- EEG is helpful for establishing the diagnosis, classifying seizures correctly, and making therapeutic decisions
- In combination with appropriate clinical findings, epileptiform EEG patterns termed **spikes** or **sharp waves** strongly support a diagnosis of epilepsy
- EEG in patients with seizures :
  - focal epileptiform discharges indicate focal epilepsy
  - generalized epileptiform activity indicates a generalized form of epilepsy.

- Most EEGs are obtained between seizures, and interictal abnormalities alone can never prove or eliminate a diagnosis of epilepsy
- Epilepsy can be definitely established only by recording a characteristic ictal discharge during a clinical attack.
- 3Hz spike-and-wave (spike and dome pattern) activity occurs specifically in petitmal

15 Yr. M.



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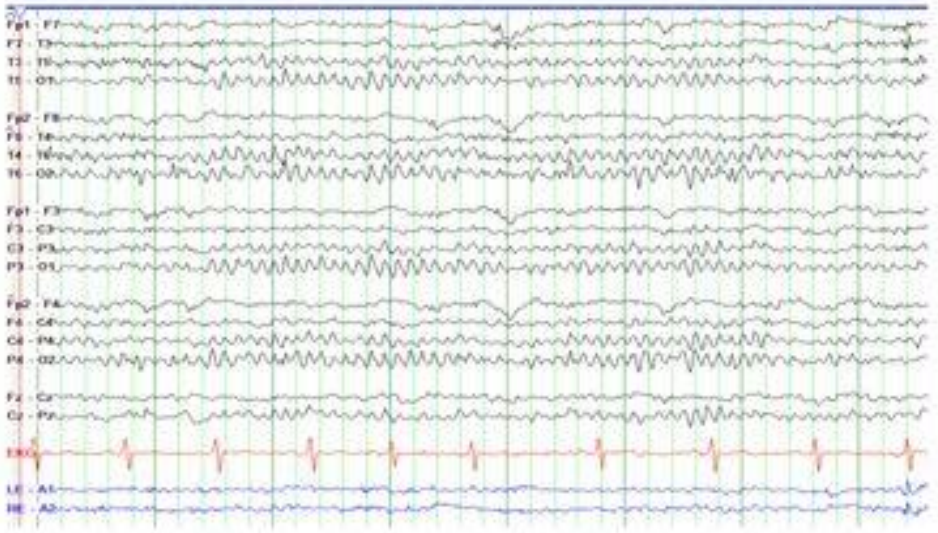
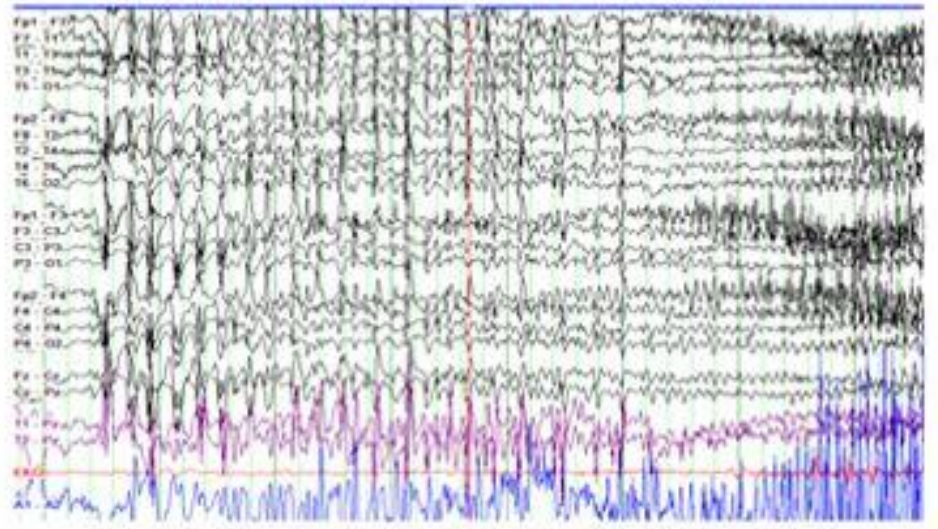
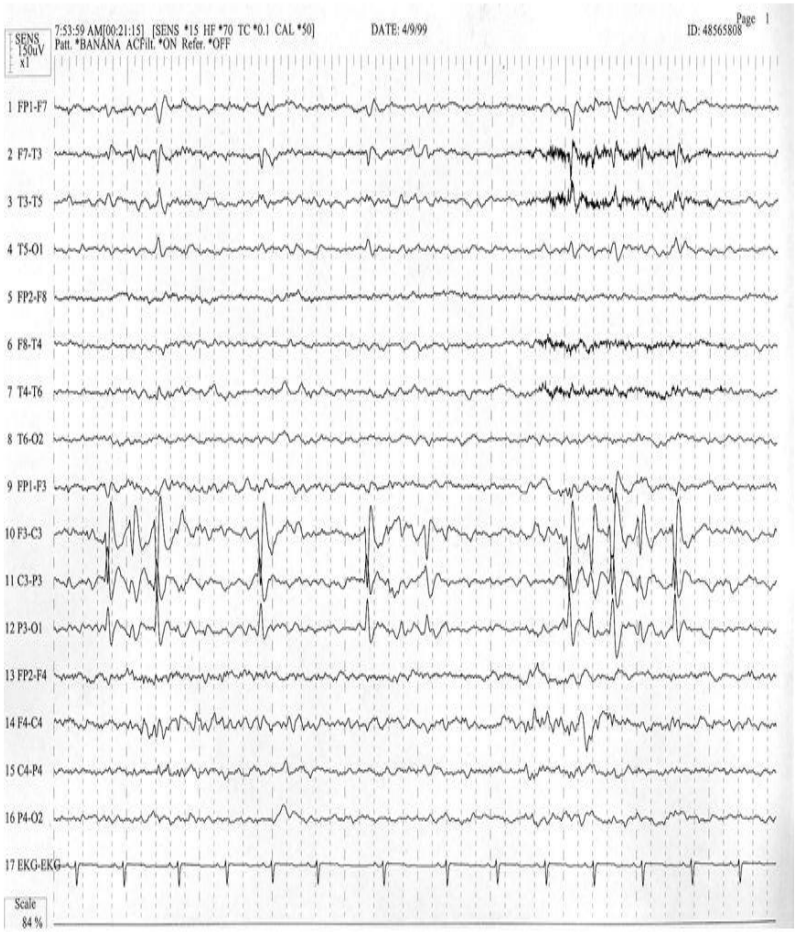
Normal EEG Awake



Generalized Tonic Clonic



EEG: Partial Seizures



Thank you