



Lecture:



والله Khalleedd ✓

Disorders of the Motor Cortex “Convulsions and Epilepsy”

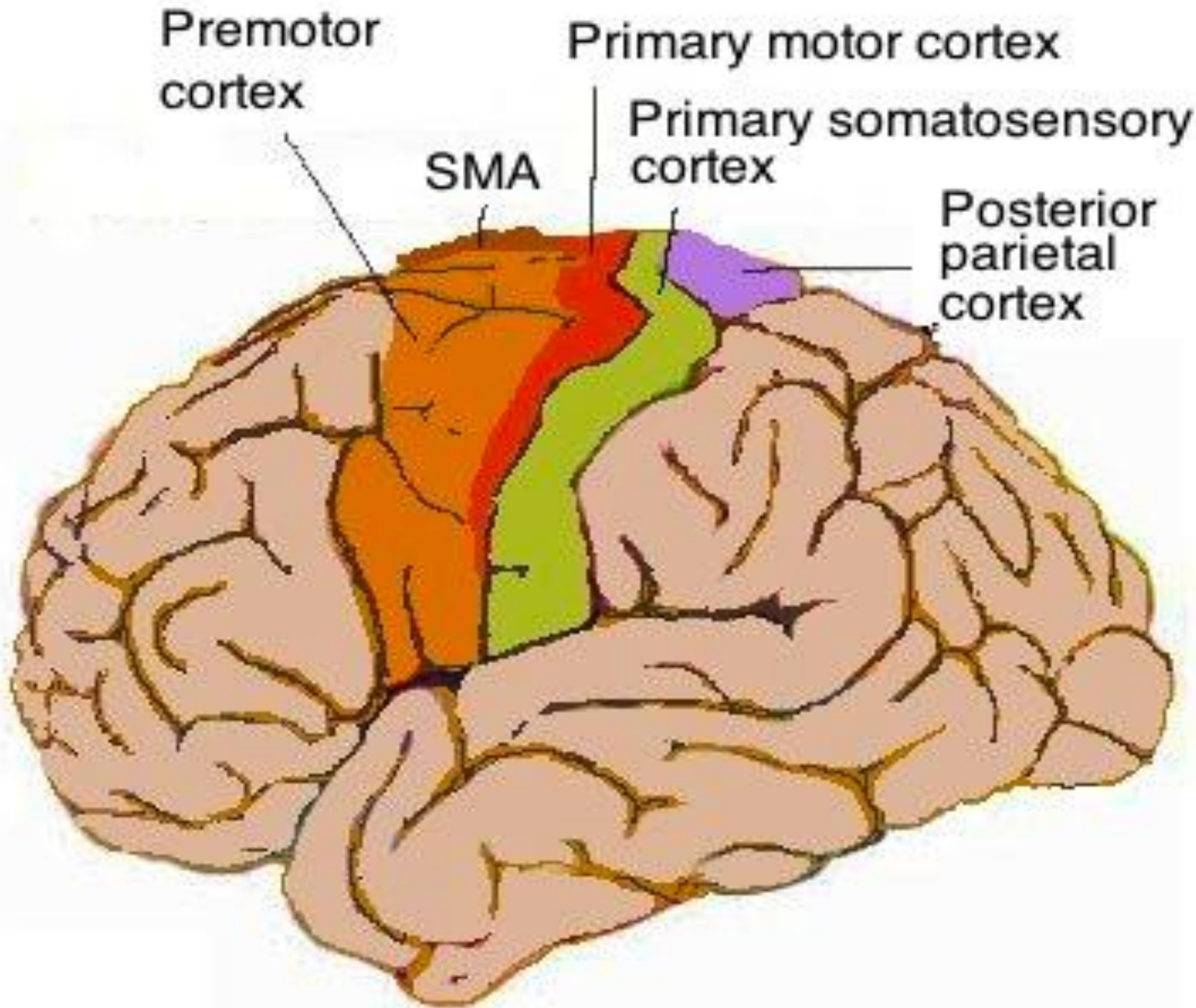
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The Motor Cortex

The responsible lobe for motor cortex is the frontal lobe → primary motor cortex located in precentral gyrus, area (4) = between central sulcus and precentral sulcus

- **The motor cortex located** anterior to the central cortical sulcus, occupying the posterior one third of the frontal lobes.
In front of central sulcus
- **The motor cortex** is divided into three areas:
 - ✓ **The primary motor cortex,** Area 4
Behind it primary somatosensory cortex = area 1,2,3
Located in the posterior of the frontal lobe
 - ✓ **The premotor area,**
Located in the anterior of the parietal lobe
 - ✓ **The supplementary motor area.** SMA
In between primary motor and sensory gyrus there is central sulcus



Levels of the Central Nervous System Function

1. The spinal cord level. Like spinal reflexes or stretch reflexes
2. The lower brain or subcortical and brain stem levels.
Like respiratory center, cardiovascular centers, micturation and these things
3. The higher brain or cortical level (**Motor Cortex**): 3 parts is
an area of the frontal lobe located immediately anterior
to the central sulcus.

Components of the Motor Cortex

Go next slide ✓

The primary motor take the plan (signal) to start the movement from premotor cortex
Then through corticospinal tract it give signals to motoneuron in AHCs (2nd order neuron)
in spinal cord

Then these motor neuron what ever its type alpha or gamma it will transmit the signal
to skeletal muscle through spinomuscular fibers

1. ^{Area 4} The Primary motor cortex: control the execution of Responsible for movement

movement. Programmed patterns of motoneurons are
activated in the motor cortex.

2+3

2. The premotor cortex and supplementary motor area Responsible for planning

(SMA): are responsible for generating a plan for

movement, which is transferred to the primary motor
cortex for execution. The supplementary motor cortex SMA
programs complex motor sequences.

primary cortical ال upper motor neuron AHCs انما ياتي به ال لذلك أي ليجه يتصل به ال

area لحد م اوصل لل AHCs على أي ليف ← تؤدي إلى UMNL

ال AHCs تخرج الإشارة خلال ال ant. root وتندمج ال post. root وتعمل nerve mixed spinal nerve ويجه
ascending fibers to reach the the voluntary skeletal muscle

Components of the Motor Cortex

The primary motor area (4) take the plan (signal) to start the movement from premotor cortex

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ل قبل توصيل الإشارة للـ AHCs أنا بكمي عنه upper motor neuron لذلك أي ليجه يتوصل منه الـ primary cortical area لحد توصيل

للـ AHCs على أي ليفل ← تؤدي إلى UMNL

منه الـ AHCs من تخرج الإشارة خلال الـ ant. root وتندمج مع الـ post. root وتعمل nerve mixed spinal nerve ويتجه الـ ascending fibers to reach the the voluntary skeletal muscle

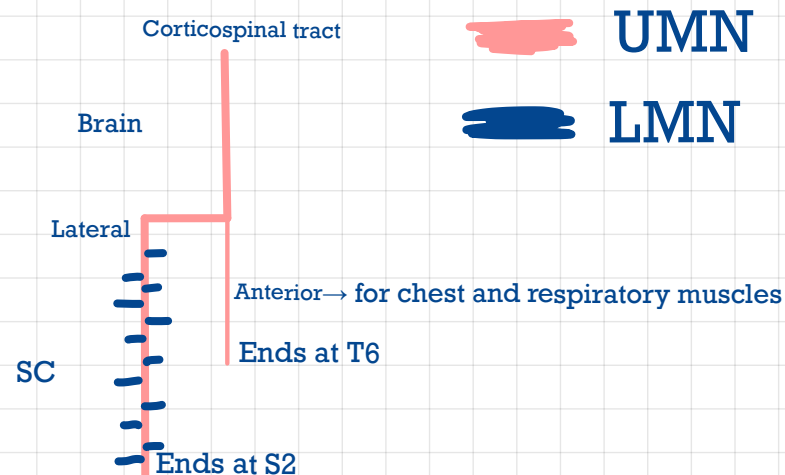
Corticospinal tract decussate at lower part of MO

If the damage in the upper motor neuron UMN → symptoms below the level.

If the damage in the lower motor neuron LMN → symptoms at the level.

In descending tracts if the damage before the decussation or crossing the symptoms at the contralateral side of the body and affect below the level of the lesion

At each spinal cord segment it gives motor fibers like C5 axillary nerve for deltoid muscle
So damage of the ant. horn cells means lower motor neuron and the symptoms ipsilateral at the same level
Even if the anterior horn cells damaged it will cause the same → cause it LMN



The Functions of Motor Part of the Nervous System

- The motor function of the CNS is achieved by controlling:

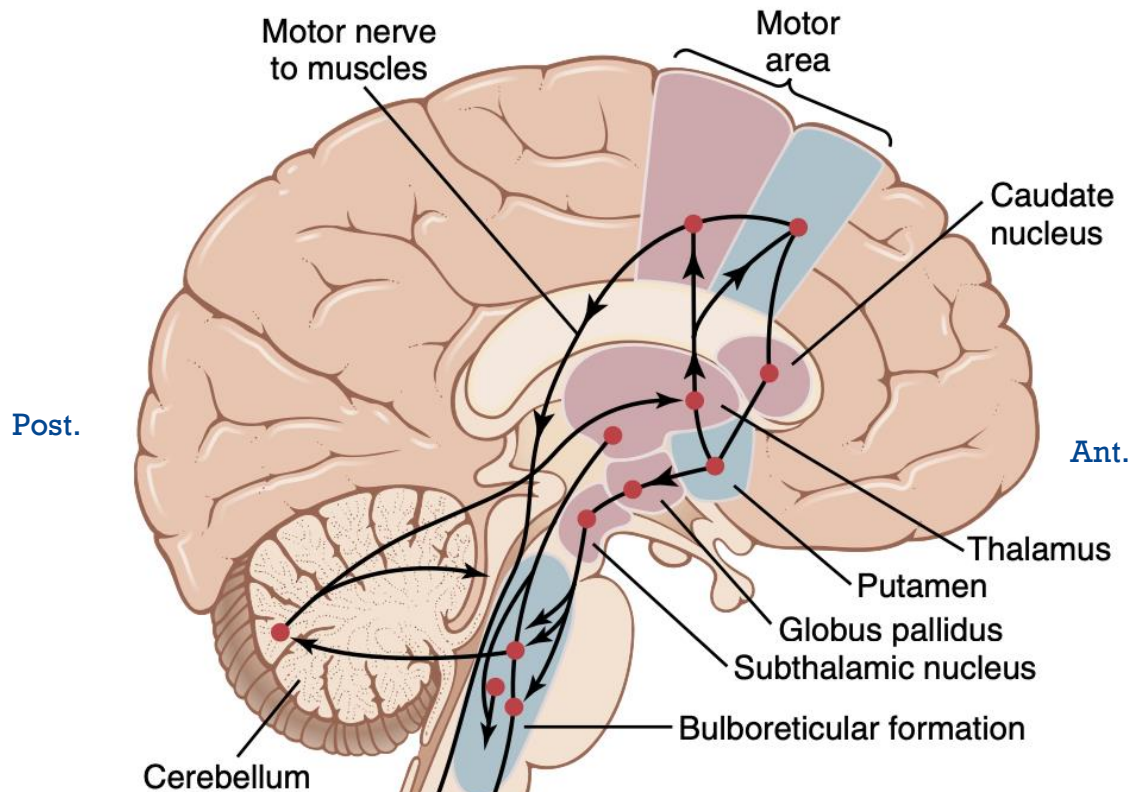
1. Voluntary Contraction of appropriate skeletal muscles of the Somatic body (Somatic Motor nervous system). Either cranial or spinal parts

2. In voluntary Contraction of smooth muscle in the internal organs (Autonomic nervous system).

3. In voluntary Secretion of active chemical substances by both exocrine and endocrine glands in many parts of the body Through a duct then to epithelial surface Direct to bloodstream (Autonomic nervous system).

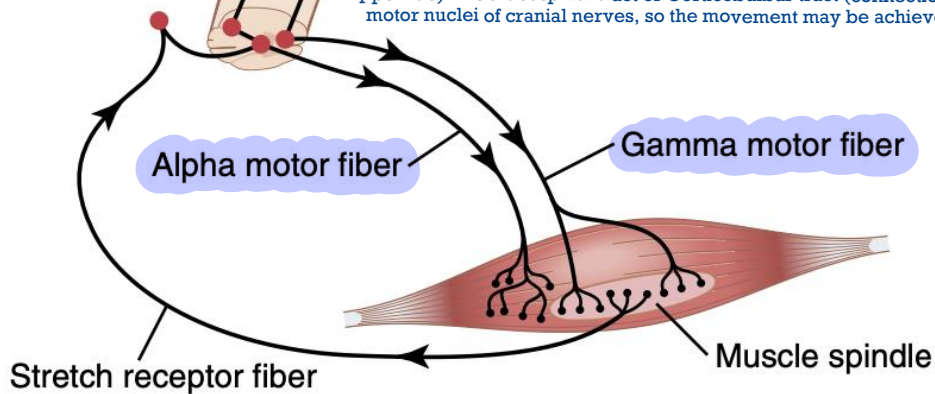
❖ The muscles and glands are called effectors.

يعني بيناتهم بالإشارات المنقولة إليها منه العصب، يعني باختصار هي ال target organ



- كيننا انه ال cortex either primary or secondary كله بياخرهم ال premotor and SMA بعد هيك بتسلم الاشئ ال primary motor
 - cortex بعد هيك تنتقل الإشارة عبر corticospinal tract لغدرم توصلا ال SC في ال AHCs وبنا الحاية بتوصلا عنال voluntary muscles وبعيدك الحركة بتكون دقيقة
 وطبعاً ال voluntary muscles أخذت هه ال alpha and gamma motor neuron ال الوجوده بال AHCs

Premotor and SMA → primary motor cortex (if head and neck it take from lower 1/3, if upper and lower limbs take from upper 2/3) → Corticospinal tract or Corticobulbar tract (connection with brainstem) → then brainstem 2nd order motor nuclei of cranial nerves, so the movement may be achieved by SC(corticospinal) or brainstem(corticobulbar)



The Primary Motor Cortex

- **The primary motor cortex**, lies in the frontal lobes anterior to the central sulcus. This area is the same as **area 4 in Brodmann's**.
- **The primary motor cortex:** The human is inverted
 - Lower 1/3 ✓ Beginning with the face and mouth region near the sylvian fissure, Lateral Sulcus → separate the temporal from parietal and frontal
 - Middle 1/3 ✓ The arm, hand and trunk area, in the midportion of the primary motor cortex,
 - Upper 1/3 ✓ The leg and foot areas, in the upper part of the primary motor cortex that dips into the longitudinal fissure. In the medial surface

If meningioma in the medial surface of frontal lobe

ممكّن ييجي المريض ويكّونه عنده paraparesis والمريض ما يديرّك رجليه ال ٢ يعني bilateral paralyzed وبعد الفحص نلاقي hyperreflexia مع خلال المطرقة تاحت الفحص، وهذا انّشي يبساح
 لانه لو كان areflexia حيثوجه مخي للتفكير SC lesion طب كيف بدّي اعرف اذا المشكلة SC or not
 بروح مباشرة افحص ال sensation لو كان ال sensory level deficit اذنا انا بكمي مع SC أما لو لقبت only motor deficit without sensory يده ييجي في بالي ال falx
 cerebri meningioma الي يتيجي بيّه ال 2cerebral hemisphere بالبداية رح تضغط على الجزء العلوي المسؤول مع ال foot and legs

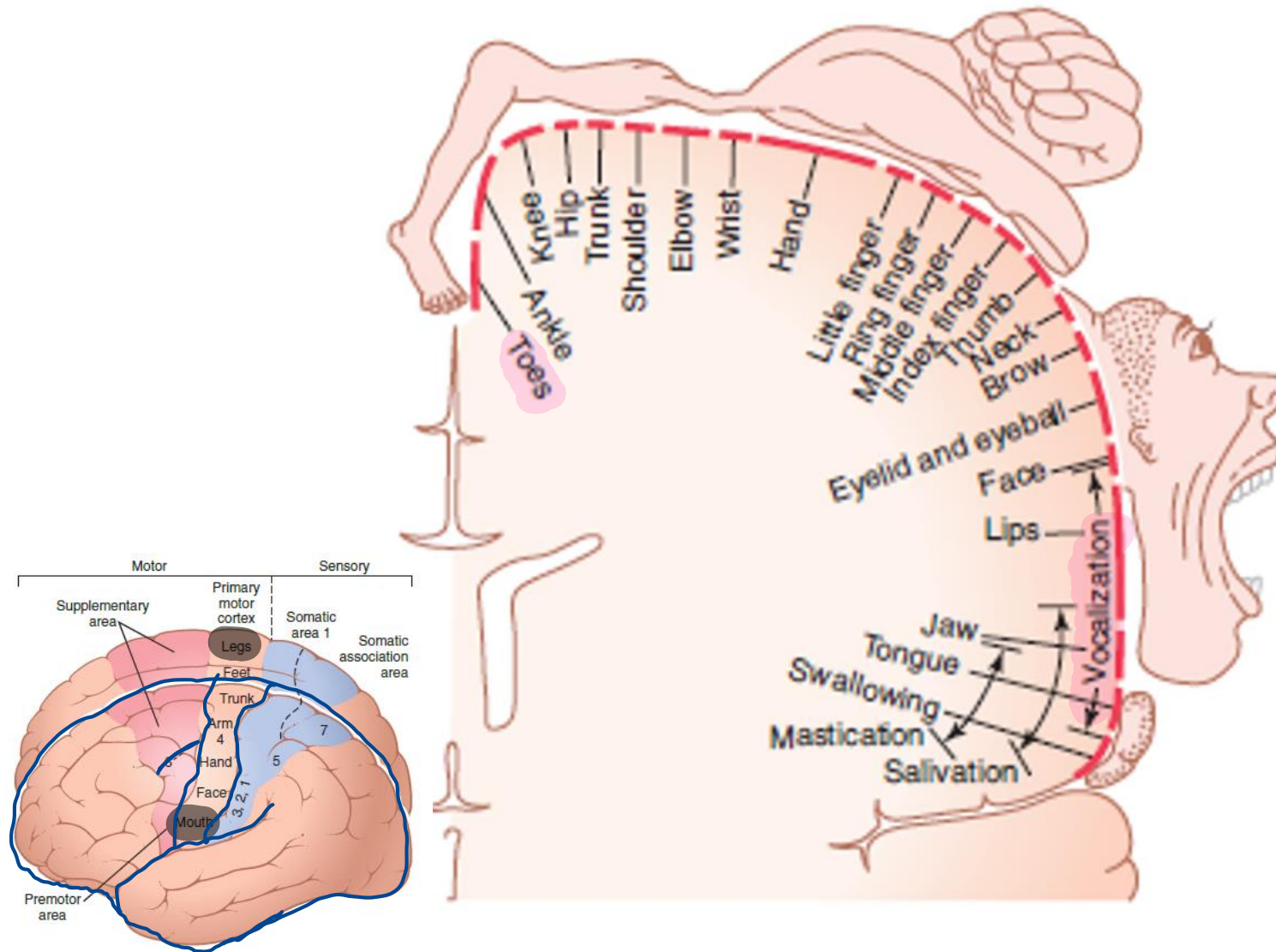
If patient had lower paraplegia, spastic (stiffness), with normal SC examination → it may be falx cerebri lesion and do pressure on upper part of the primary cortex that responsible for leg and foot
 But if there is sensory level deficit → we can confirm that it is SC lesion not cortical lesion

If we do surgical removal to a tumor either it is glioma or benign or it's degree if low grade or moderate or high grade these things contribute to whether the patient will walk after the operation.

The responsible artery for upper superiolateral Cortex (responsible for leg and foot) of the frontal lobe is the ACA = anterior cerebral artery
 While hand and upper limb from MCA = middle cerebral artery

Motor cortex

Motor cortex controls different muscle group



The Premotor Cortex

- The premotor area, lies anterior to the primary motor cortex.
- The posterior part of the premotor cortex sends its signals either:

The net result the signal reach to primary motor cortex. Either direct or indirect.

The primary motor cortex make the movement done either by corticospinal or corticobulbar tracts

✓ Directly to the primary motor cortex.

✓ Indirect By way of the basal ganglia and thalamus back to the primary motor cortex.

Nuclei

- A special class of neurons called **mirror neurons** becomes active when a person performs a specific motor task or when he or she observes the same task performed by others.

هذا الاسم هو يقلد حركة شافها و قريقل حد بنفس الحركة

- The mirror neurons** may be important for understanding the actions of other people and for learning new skills.

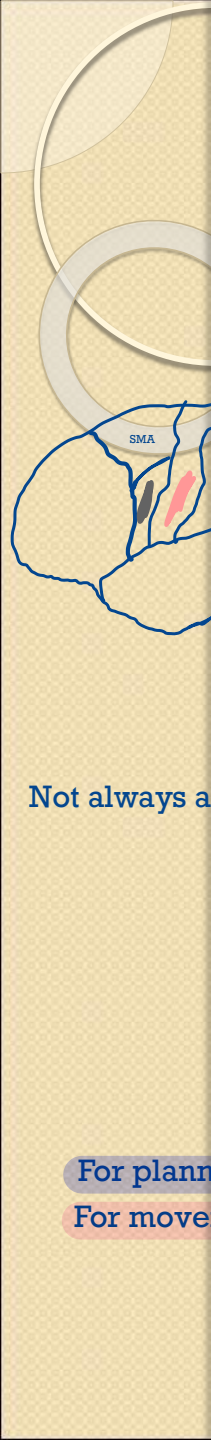
For planning

- The premotor cortex, basal ganglia, thalamus, and primary motor cortex control of complex patterns of coordinated muscle activity.

For planning

For movement

Not always activated



The Supplementary Motor Area (SMA)

Has relation to plan of movement
Bilateral grasping movements

- The SMA lies mainly in the longitudinal fissure but extends in the superior frontal cortex.
- Stimulation frequently leads to bilateral grasping movements of both hands. lesion in SMA يعني أحياناً اليد بعد حدوث الجلطة الدماغية بتصير تسكر بزيادة وهاد عادة بسبب
- In general, this area functions in concert with the premotor area to generating a plan for movement, and programs complex motor sequences.

Other Specialized Motor Areas

To take in consideration that the dominant hemisphere for speech and language is the left in 97% of people

- 1. Broca's Area: area 44** or motor speech area, lying immediately anterior to the primary motor cortex. While Wernik's area is sensory speech area
If damaged it will cause contralateral hemiplegia
If damage in ACA → weakness in lower limb.
If damage in MCA → faciobrachial hemiplegia. Face and upper limb
- 2. Voluntary Conjugate Eye Movement Field: area 8**, lies Both eyes immediately above Broca's area, for controlling voluntary eye movements.
Work in contralateral way → The responsible hemisphere for looking Lt. Is the Rt. one
- 3. Head Rotation Area:** slightly higher in the motor association area, 2+3 mainly works together electrical stimulation leads to head rotation to opposite side. This area is closely associated with the eye movement field.
- 4. Area for Hand Skills:** in the premotor area immediately anterior to the primary motor cortex for the hands and fingers is a region that is important for "hand skills." Its damage leads to **motor apraxia.**
Found in middle frontal
للمهارات الحركية التي تتم باليد

Clinical slide: How to differentiate between rt. and lt. lesions in ②+③ and between destruction lesion and irritative lesion

Everything is contralateral cause the function work to the other side

A patient come with stroke (destruction) in right frontal area and by physical examination he's looking to the right side and his head is deviated to the right → cause the function of the right side is to look left and its disrupts so the dominant hemisphere is the contralateral side = left side

This case is called the patient looking to the lesion

A patient come with tumor (irritation) in the right side it will cause the head to deviate to left and the eyes looking to the left → cause the dominant function is the right and it will works to the contralateral side

Without MRI how can we differs if it is irritation or destruction?

We gonna look to the hemiplegia

Stroke in the Rt. Side

If the eye and head is deviated to right and hemiplegia on the left we can confirm it is destruction

Tumor in the Lt. Side

If the eye and head is deviated to right and the weakness (hemiplegia) on the right we can confirm it is irritative

The conclusion

If destruction → ipsilateral eye and head deviation and contralateral hemiplegia (weakness)

If irritative → contralateral weakness and eye and head deviation

The Important Gyri of Frontal Lobe

Central sulcus and precentral sulcus inbetween there is pre central gyrus area 4

Anterior to precentral sulcus there is 2 horizontal sulci superior and inferior frontal

Lateral sulcus separate temporal from frontal and parietal

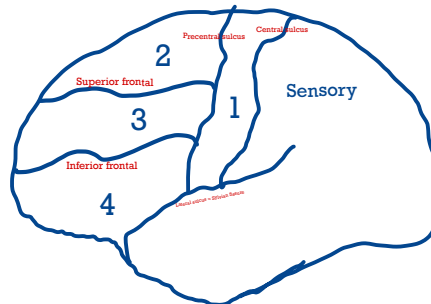
1. **The precentral gyrus:** between the central and
Primary motor cortex = area 4

precentral sulci.

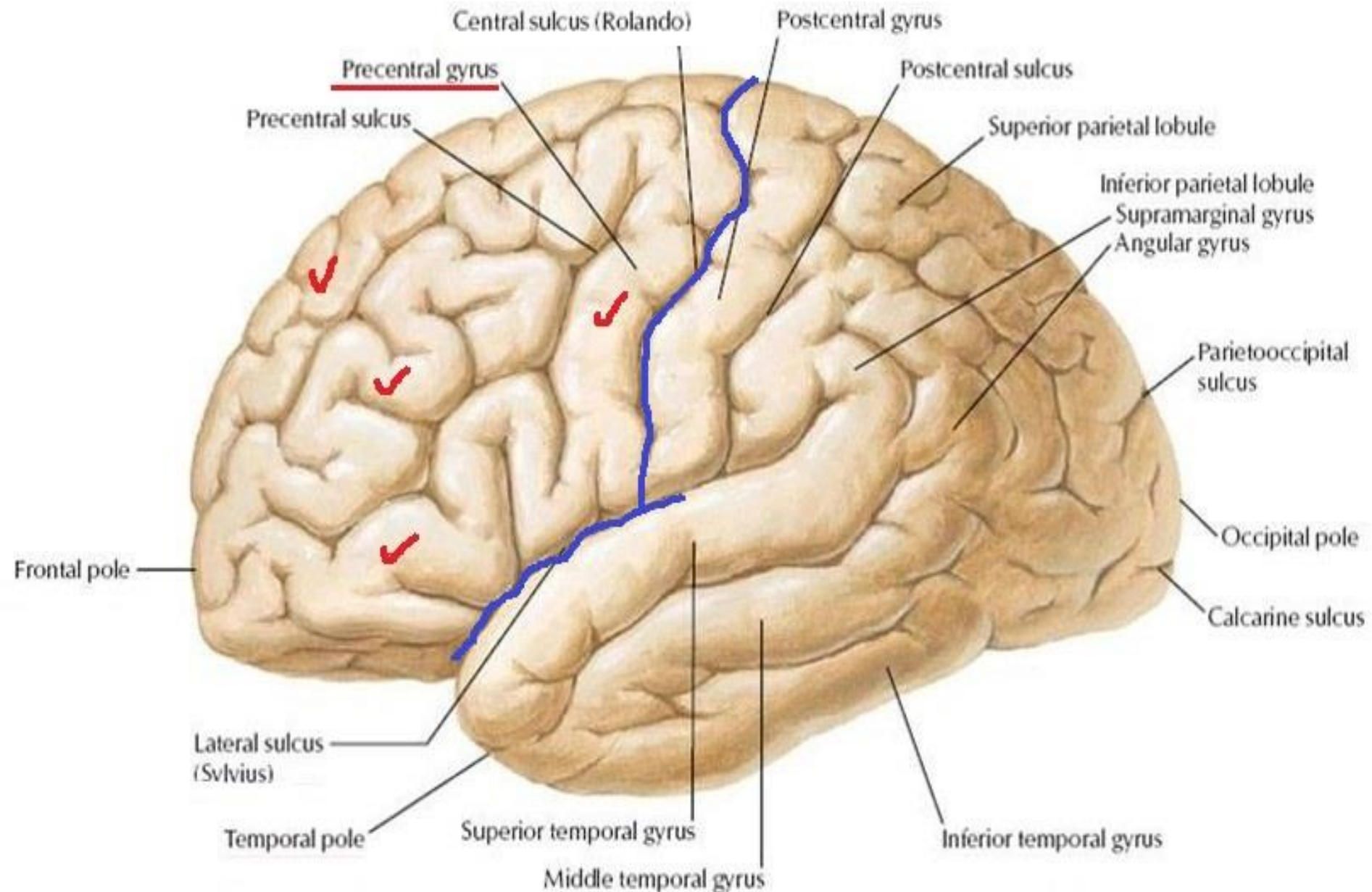
2. **The superior frontal gyrus:** above the superior frontal sulcus.

3. **The middle frontal gyrus:** between the superior and inferior frontal sulci.

4. **The inferior frontal gyrus:** below the inferior frontal sulcus.



The Important Gyri of Frontal Lobe



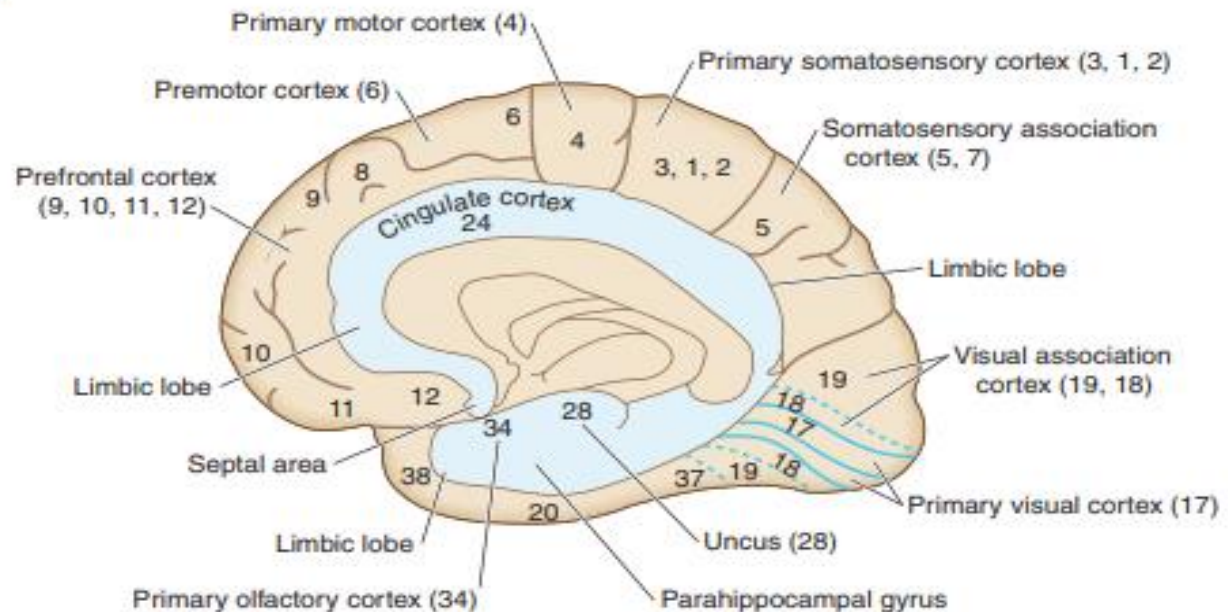
▶ Always corticospinal tract give symptoms to the opposite side either irritative (convulsion) or destructive (paralysis)

The Important Functional Areas of the Frontal Lobe

Areas	Site	Function	Lesion
Primary motor cortex (4)	Precentral gyrus & anterior paracentral lobule	Voluntary motor activity of opposite 1/2 of the body Contralateral	Irritative: contralateral motor Tumor Jacksonian fit Focal epilepsy Destructive: contralateral motor Ischemia paresis. Hemiplegia either complete or partial ACA → dominant in lower limb MCA → faciobrachial
Secondary motor (Premotor) cortex (6)	Anterior part of precentral gyrus in the superior frontal gyrus	Gives extrapyramidal fibers For planning	Contralateral muscle hypertonia & exaggerated deep reflexes +ve plantar reflex Inc. muscle tone and spasticity
Frontal eye conjugate (8) Done ✓ before With head rotation area	Middle frontal gyrus Contralateral	Voluntary conjugate deviation of eyes to opposite side	Irritative: conjugate deviation of eyes to the opposite side Destructive: conjugate deviation of eyes to the same side. Eyes looking to the lesion
Broca's area (44 & 45)	Inferior frontal gyrus in domin. hemisphere	Motor center of speech. And writing If we write with right hand the dominant hemisphere is the left and also there is area in Rt. cerebral hemisphere that supply the left side of the body This achieved by corpus callosum → bind the right and left So if we do disconnection process between 2 cerebral hemispheres we will face apraxia This operation used in medical refractory epilepsy	Motor (Expressive or Broca's) aphasia: the pt. unable to express idea in spoken words Verbal-non fluent jargon aphasia (salad speech) → area 40
Prefrontal Areas (9-12, 32, 46 & 47)	Anterior pole Of frontal lobe	Higher center of memory, orientation, thinking and intelligence ترك	Amnesia (impaired of memory), Dementia, gait apraxia Disorientation, behavior changes Loss of personal hygiene “careless” Sphincters dysfunction,

A

if damaged it will cause jargons aphasia and apraxia the patient will lose all the motor skills



Seizure and Epilepsy

- **A seizure:** ^{نوبة مرض شديدة} is a paroxysmal single event ^{مؤقتة} "Transient disturbance of cerebral function" due to uncontrolled ^{نتيجة لزيادة الشحنات الكهربائية} excessive neuronal activity, that usually results in ^{Change} altered perception or behaviour.
- **Single seizure** ^{Fasting seizure} is not epilepsy but indication for investigation.
^{Acute symptomatic seizure → like a symptom of hypoglycemia} ^{Either DM patient or insulinoma}
- Seizures are symptoms of a disturbance in brain function, which can be due to epilepsy or other causes.
- **Provoked seizures:** ^{By drugs or alcohol} is occur in the setting of acute medical and neurological illnesses in people with no prior history of seizures.
- **NB:** not all people having seizures have epilepsy.
^{Cause it may be symptomatic seizure not epilepsy}
- **5-10%** of the population will have a seizure at some point in their lifetime. ^{Just 1%} of them enters the epilepsy state

It may be caused by a tumor like meningioma (benign), 67% of the people having meningioma will face seizure → cause it is cortical and cause irritation in cortex and the neurons are in the cortex

What is Epilepsy?

لأنه neurons يكونون على القشرة الخارجية في الشيء لما يكون deep يكون أقل عرضة أنه يسبب epilepsy

- **Epilepsy:** is a chronic condition of ^{Not single} **recurrent**

By hypoglycemia or
drug or febrile seizures
By hyperthermia

unprovoked seizures caused by sudden excessive

We must make sure it is not secondary to something else

changes in the electrical function of the brain.

- 1% of the population currently has epilepsy.
- **Status Epilepticus:** a continuous seizure lasting more

If more than 30 mins it is called medical refractory status epilepticus and the patient needs ICU and intubation and general anesthesia

than 5 mins.

We called it epilepsy if:
2 or more seizures
Unprovoked

Epilepsy is ^{غير معدوي} **not contagious**

ليس مرض عقلي
it is **not a mental illness**

ليست إعاقة معرفية
or **a cognitive disability.**

أحياناً ممكن أبلش أحياناً anti epilepsy من النوبة الأولى وأتعالج مع المريض كانه epilepsy في حالة لو المريض كانه high risk for recurrence

What do we mean by high risk people!

- If the patient comes with severe dense seizure with shoulder dislocation or urine or stool incontinence
- If the patient has history of neuro surgical operations on brain
- If the patient has any focal damage on the brain → stroke, trauma, abscess
- If he has seizures during sleep

If seizures come during sleep we should start treatment
While sleeping we can confirm it is true convulsion not pseudo not psychogenic
May through sleeping previous seizures happened and not noticed
Electrical activity through sleeping is low so if he has it during sleeping he will probably face it through awake

Acute Symptomatic Seizures

As a 2ndry result to an disease or state

- **Not all seizures imply epilepsy "for example, seizures during:**
 - ✓ Hypoglycemia,
 - ✓ Acute CVA,
 - ✓ SAH, Subarachnoid hemorrhage
 - ✓ Acute electrolyte disorders, Electrical disturbance Hypo or hyper Ca, Mg, Na
 - ✓ Drugs (e.g., cocaine and tramadol),
 - ✓ Eclampsia, While pregnancy
 - ✓ Kidney and hepatic failure,
 - ✓ Hypertensive encephalopathy,
 - ✓ Meningitis. Meningoencephalitis

Seizures Terminology

- **Ictal** = seizure. النوبة نفسها

- **Post-ictal** = symptoms following seizure. May be disoriented confused and may face vomiting headache psychosis or even Todd's paralysis (شلل لليد والرجل لـ ٢٤ ساعة ويعود ليرجع طبيعي)

- **Aura** = abnormal sensation preceding the seizure. ما قبل النوبة
May smell or see hallucinations or depressed

- **Automatisms** = nonsensical involuntary movements.

- **Tonic** = tonic contraction producing extension and arching. Hyper extension

- **Clonic** = alternating muscle contraction-relaxation Jerking movements
Flexion and extension

- **Complex** = consciousness impaired Unconscious

- **Simple** = consciousness unimpaired Normal Conscious

- **Partial** = focal region involved

- **Generalized** = whole brain Diffused bilateral

- **Convulsions** = shaking or twitching

- **Grand mal and petite mal** = for convulsive and non-convulsive seizure respectively Non convulsive absence
Convulsive generalized

Seizure may be convulsive (motor) or non convulsive (non motor)

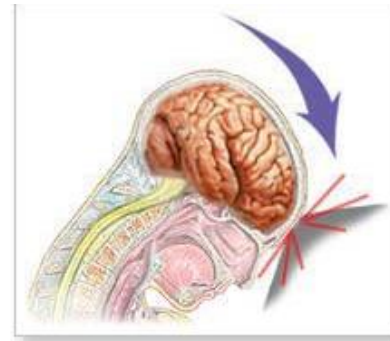
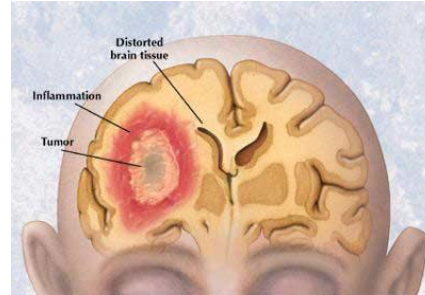
Epilepsy: Epidemiology

- There is about 50 million epileptic patients in the world.
- About 1-8 new cases per 1000 population each year.
- Over two-thirds of all epileptic seizures begin in childhood^{2/3} (most in the first year of the life).
- 5% of the population suffer a single seizure at some time.
- 1% of the population affected by epilepsy.
- All ages affected.
- 70% well controlled with drugs (prolonged remissions).
- 30% epilepsy at least resistant to treatments = **Intractable**
Refractory

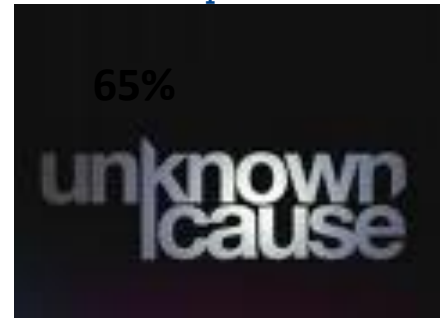
Epilepsy. May need surgical intervention like vagus nerve stimulation

Risk Factors for Epilepsy

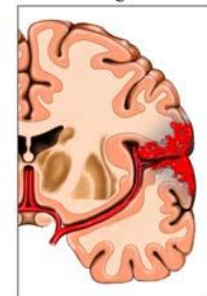
- Febrile convulsion,
Hyperthermia = fever
- Perinatal insult,
- CNS infection,
- CNS mass lesion,
Tumor abscess AV malformation aneurism
- Family history of epilepsy,
- Head injury,
 - Abnormal gestation or delivery,
- Developmental delay,
- Stroke (ischemic or hemorrhagic).



Idiopathic

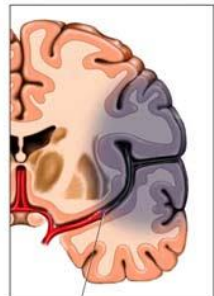


Hemorrhagic Stroke



Hemorrhage/blood leaks into brain tissue

Ischemic Stroke

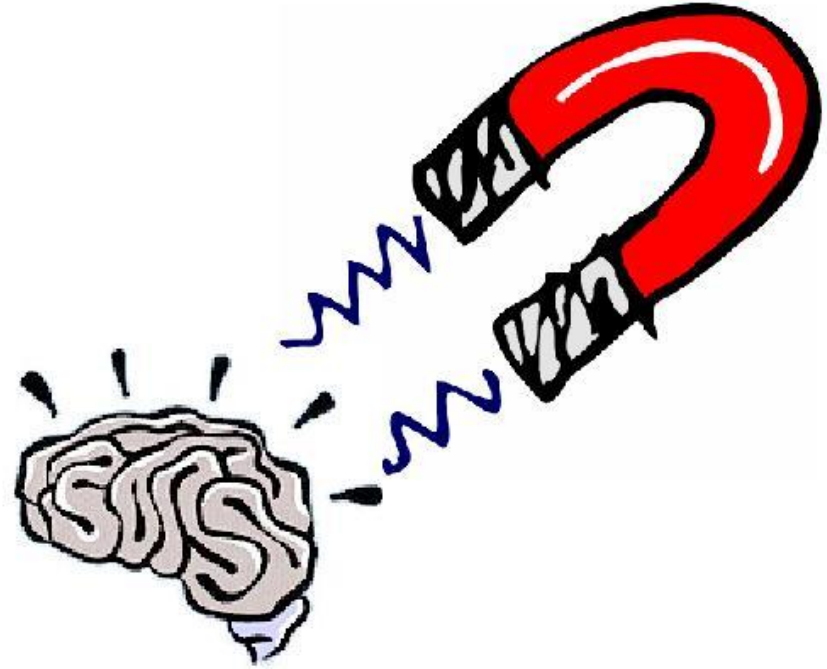


Clot stops blood supply to an area of the brain

Triggers for Seizures

Cause may the patient take anti epileptic and still face seizures

- Poor compliance,
- Sleep deprivation, الحرمه منه النوم
- Stress,
- Photo stimulation, لذلك يجب الامتناع عنه الجوال لفترة طويلة
- Hyperventilation,
- Alcohol,
- Infection,
- Menstrual cycle.



Etiology of Seizures

• Epileptic:

- ✓ Idiopathic (70%),
- ✓ Genetic factors,
- ✓ Brain tumors,
- ✓ Neurodegenerative disorders: Alzheimer
بعد سنه الخمسينه بتزيد فرصه حدوث الحالة بسبب زيادة ال neurodegeneration state
disease,
- ✓ Cerebral stroke,
- ✓ Cerebral dysgenesis/malformation.
- ✓ Hippocampal sclerosis. If u wanna google it

Etiology of Seizures

- **Non-epileptic:** Considered as acute symptomatic seizures
2ndry No need for anti epileptic

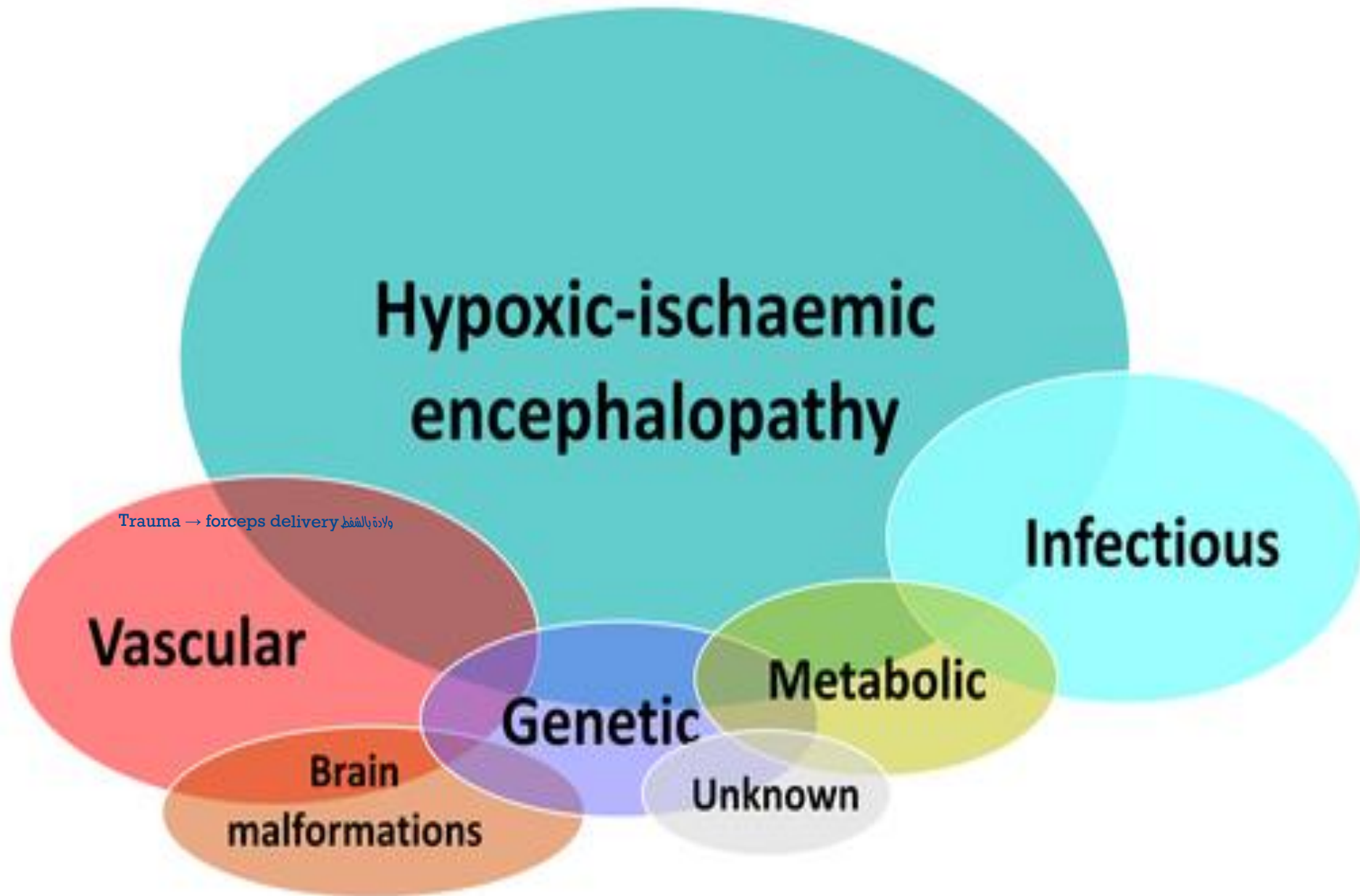
- ✓ Electrolyte disbalance, K, Ca, Na, Mg
- ✓ Head trauma,
- ✓ Meningitis,
- ✓ Encephalitis,
- ✓ Poisoning / toxins.
- ✓ Febrile convulsions,
Fever
- ✓ Metabolic,
 ✓ Hypoglycemia or hyperglycemia,
 Generalized Focal

Genetic & Epilepsy

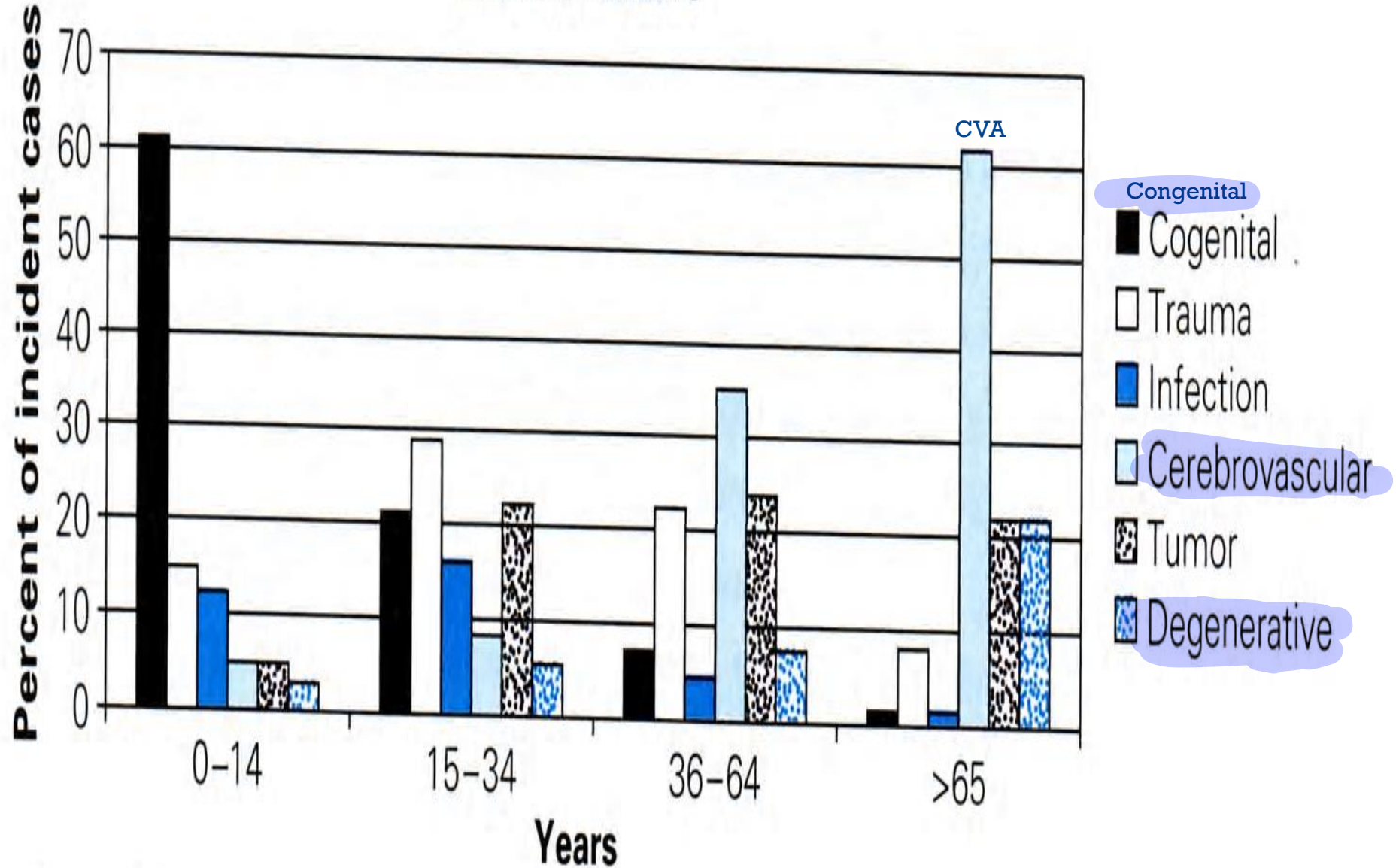
بعض الحالات تم ربطها بالجينات والوراثة

- Some types linked to genes called familial epilepsy.
- Several types of epilepsy have now been linked to defective genes for ion channels, that control the flow of ions in to and out of cells and that regulate neuron signaling.
- **Examples:** Most types has relation to genetic factors and need gene study
These genes related to ion channel activation → Na Ca ...
 - ✓ Benign familial neonatal seizure.
 - ✓ Autosomal dominant nocturnal frontal lobe epilepsy.
 - ✓ Progressive myoclonic epilepsy syndrome.

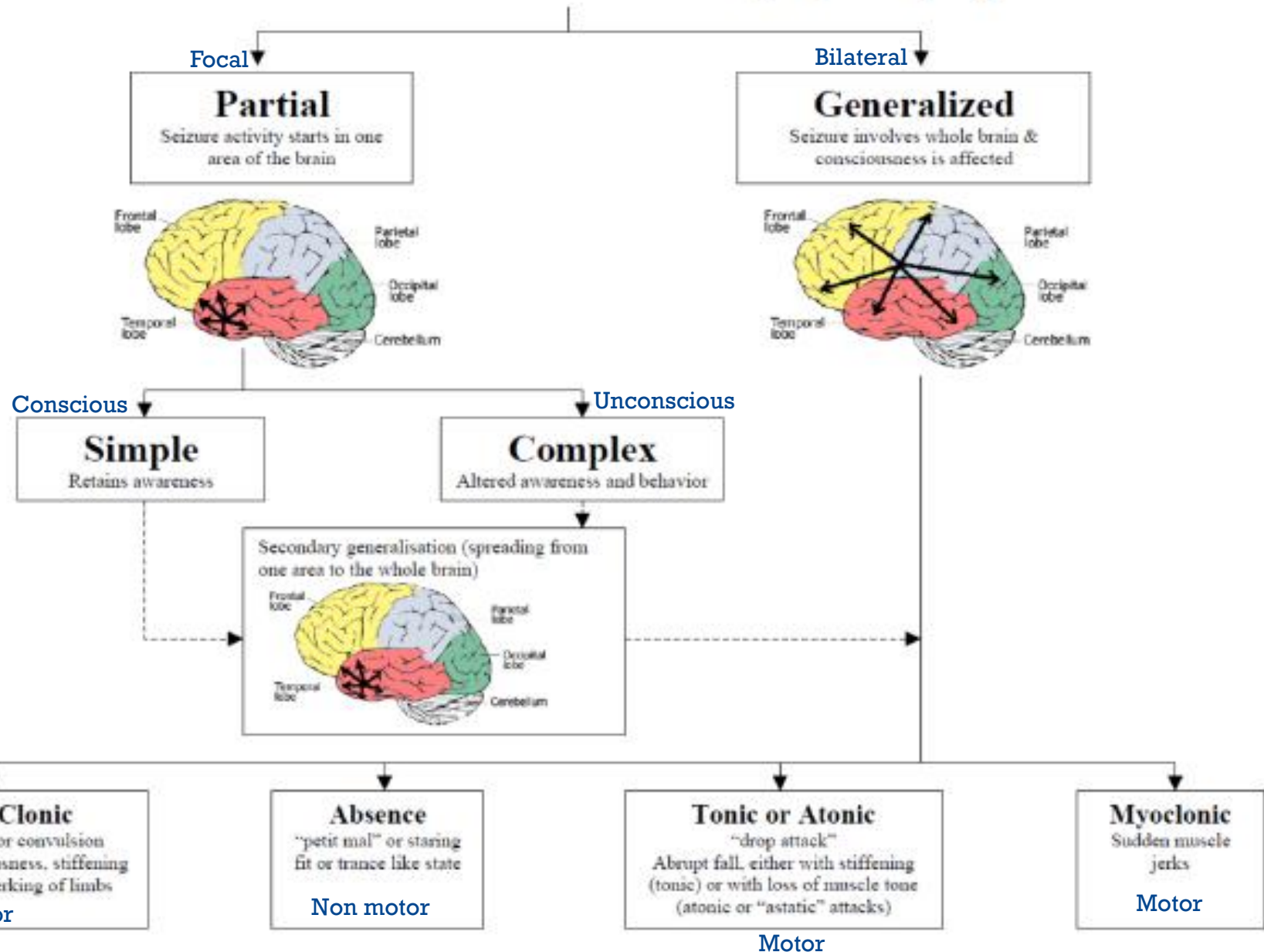
Relative Occurrences of Common Etiologies of Neonatal Seizures



Cause of seizure



Classification of Seizures/Epilepsy



ILAE 2017 Classification of Seizure Types

Focal may cause secondary generalized
When it start focal and become bilateral

FOCAL

Awareness/Impaired Awareness

Motor Onset

- Automatism
- Atonic
- Clonic
- Epileptic Spasm
- Hyperkinetic
- Myoclonic
- Tonic

Non-Motor Onset

- Autonomic
- Behavior Arrest
- Cognitive
- Emotional
- Sensory

Focal to Bilateral Tonic Clonic

GENERALIZED

Motor

- Tonic-Clonic
- Clonic
- Tonic
- Myoclonic
- Myoclonic Tonic-Clonic
- Myoclonic Atonic
- Atonic
- Epileptic Spasm

Non-Motor (Absence)

- Typical
- Atypical
- Myoclonic
- Eyelid Myoclonia

Absence seizure generalized non motor

UNKNOWN

Motor

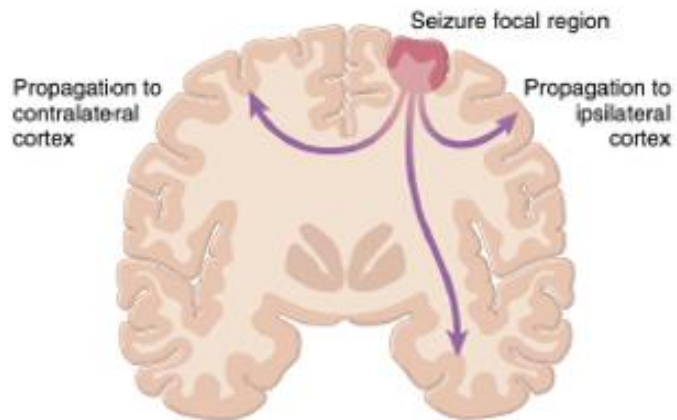
- Tonic-Clonic
- Epileptic Spasm

Non-Motor

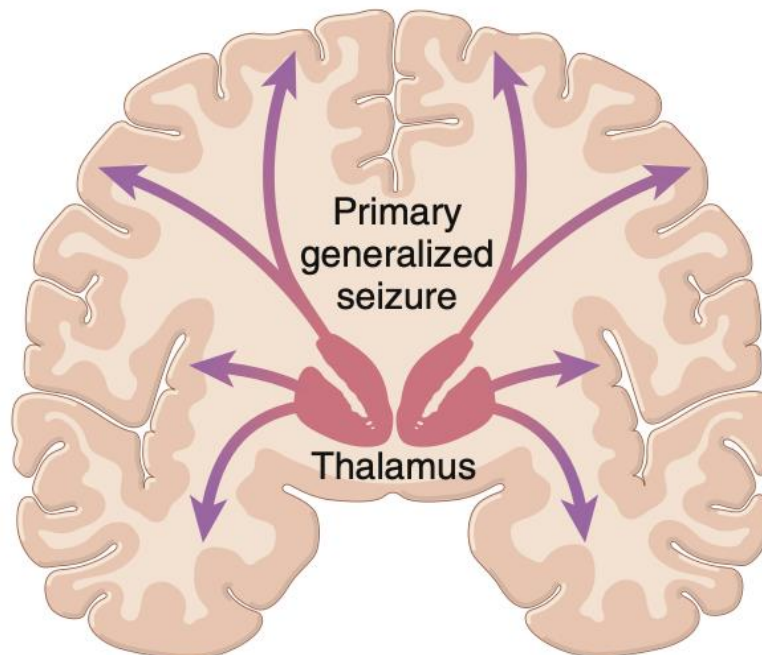
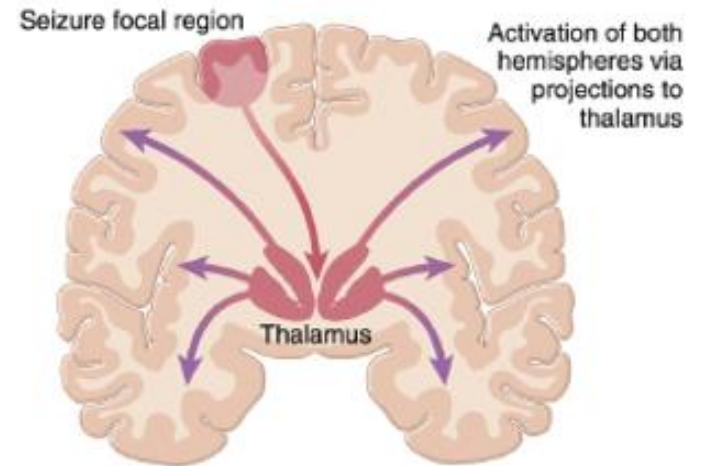
- Behavior Arrest

Unclassified

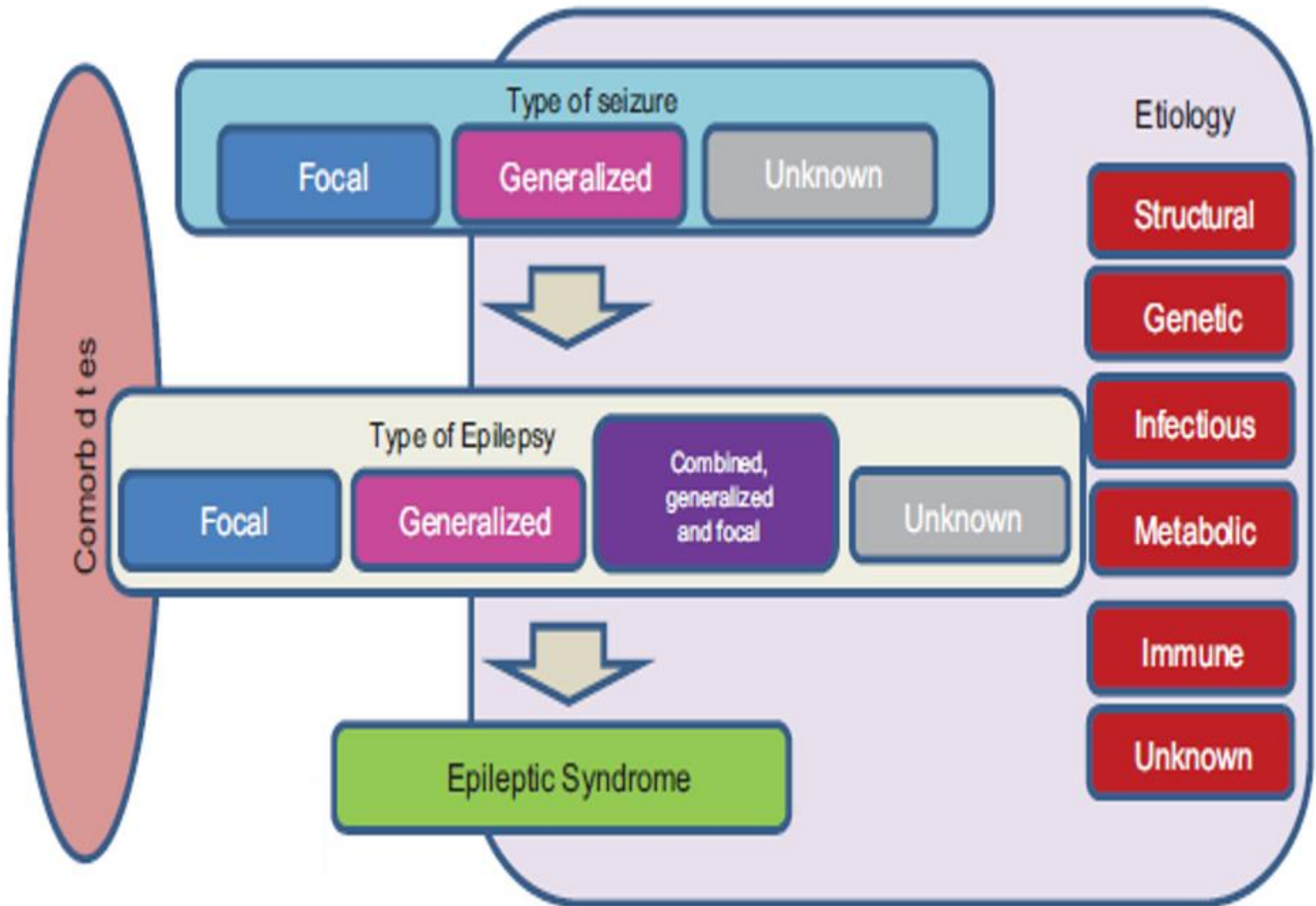
Propagation of seizures



Secondary generalization of a focal seizure



ILAE 2017 Classification of Seizure Types



Absence → generalized non motor

hyperventillation يتكرر كثيرها في الحالات عند الأطفال خلال اليوم وهذه ال triggers تعونها هو ال

==<https://www.instagram.com/reel/CvhdF32BMnt/?igshid=MzRIODBiNWFlZA>

<https://youtu.be/M3ulV9eJKQQ>

Generalized tonic conic

It was called previously grand mal

الفرق بينه الحالات هي مرحلة ال post ictal كل شخص يفوت بحالة مختلفة في ناسه بتنعس وناسه بتدوخ وهكذا

<https://youtu.be/gWZGMABBFYo>

Myoclonic seizure

flexion and extesion وكأنه الشخص بينقرو تسمى الحركة jerking movement وهما سببها انو بيدحن بشكل مفاجئ

حصل معنا كلنا تقريباً اقل مثال بعد حمام بارد بالشتا بنصير نرجف

<https://youtu.be/zPNVYFRhthg>

Pathophysiology of Epilepsy

Excessive excitation (glutamate + Ach)
Decrease inhibition (GABA)

So in the treatment either we increase (GABA) or inhibits (glutamate + Ach)
To decrease paroxysmal brain activity

- Small group of abnormal neurons undergo:
 - ✓ Prolonged depolarization.
 - ✓ Rapid firing of repeated action potentials.
- The action potential then spreads to adjacent neurons.
- A clinical seizure occurs when the electrical discharges of a large number of cells become abnormally.
- Seizures may then spread to involve adjacent areas of the brain or through established anatomic pathways to other distant areas.

- 
- Instability of cell membrane at the cortical level leads to susceptible cell membrane to polarization abnormalities (lower threshold) that **any ionic imbalance** in the immediate chemical environment of the neurons will spontaneously result in:

- ✓ Excessive excitation (Ach., Glutamate).
- ✓ Decreased inhibition (GABA).

At the Molecular Level

- Instability of cell membrane at the cortical level leads to susceptible cell membrane to polarization abnormalities (lower threshold) that **any ionic imbalance** in the immediate chemical environment of the neurons will spontaneously result in:
 - ✓ Excessive excitation (Ach., Glutamate).
 - ✓ Decreased inhibition (GABA).

Pathophysiology of Epilepsy (Molecular Level)

- **Cortical cells membrane level:** Related to the neuron
- Instability of the cortical cells membrane → Polarization abnormalities (excessive polarization), allowing the cell to be more susceptible to activation → Hypersensitive neurons with lowered thresholds for firing and firing excessively, related to:
 - 1. Excess of Excitatory (acetylcholine - or Glutamate).
 - 2. Decreased inhibitory (GABA).



PATHOPHYSIOLOGY

Paroxysmal discharges in cortical neurons

A seizure originates from grey matter of any cortical or subcortical area



Abnormal firing of neurons



Breakdown of normal membrane conductance & inhibitory synaptic currents



Locally



widely



Focal seizure



Generalized seizure

- Abnormality of Potassium conductance
- Defect in voltage sensitive ion channels
- Deficiency in membrane ATPase

Neurone membrane instability

seizures

GABA **Deficiency of inhibitory neurotransmitters**

Glutamate+Ach **Increase in excitatory neurotransmitters**

promotes

Abnormal neuronal activity

Seizure

Either focal or generalized

Cellular Mechanisms of Seizure Generation

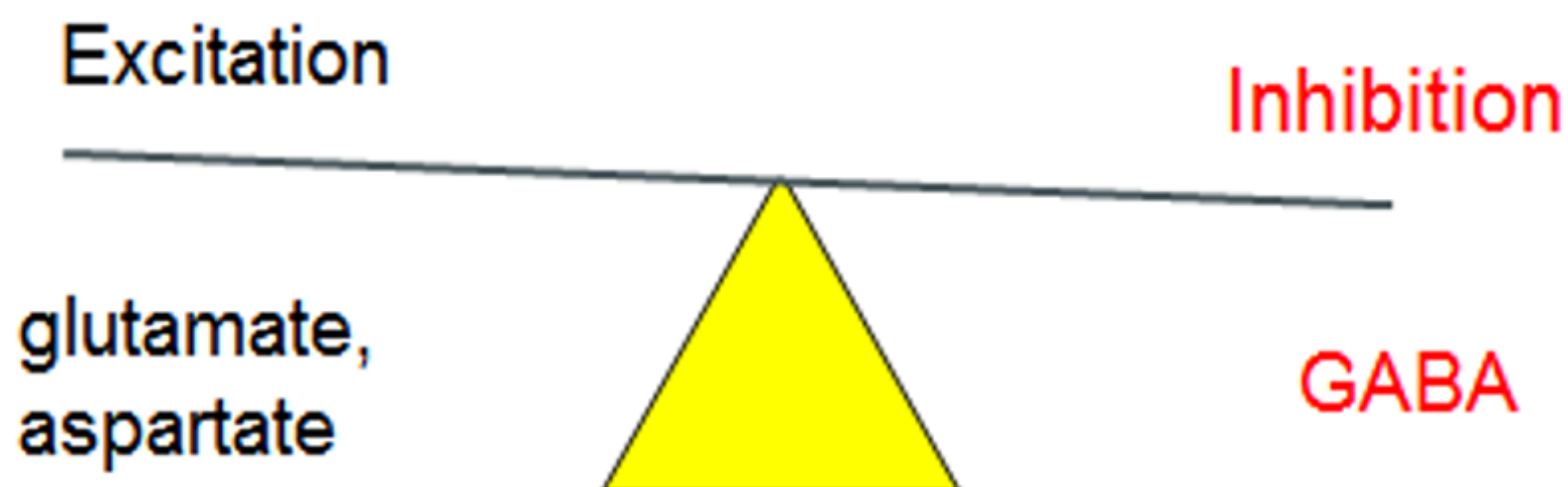
♦ Excitation (too much)

- Ionic—inward Na^+ , Ca^{++} currents
- Neurotransmitter—glutamate, aspartate

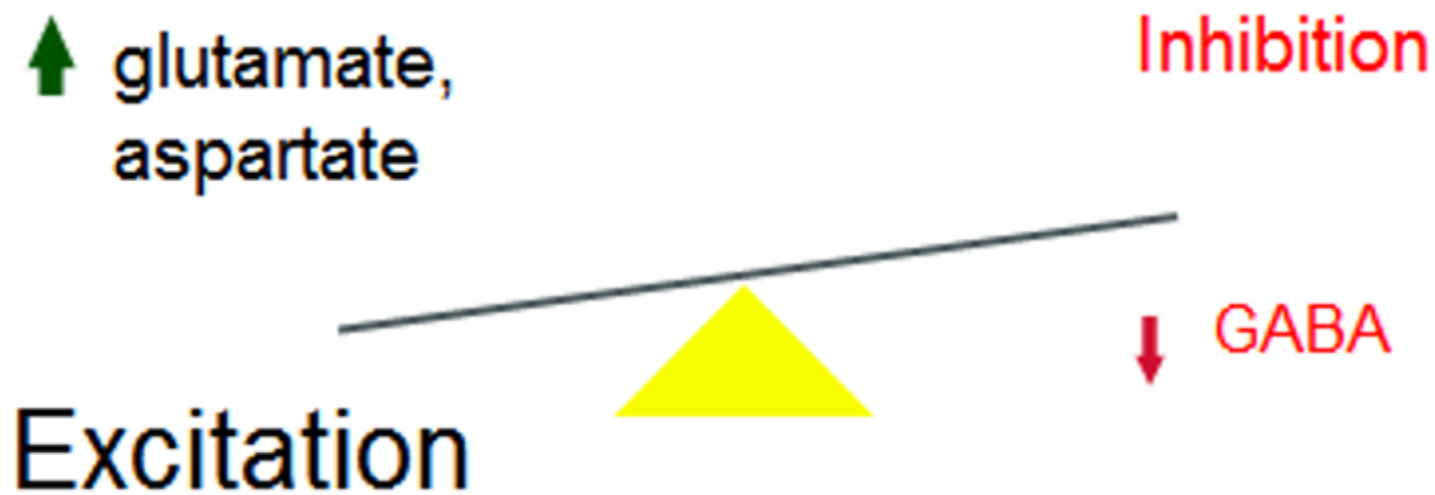
♦ Inhibition (too little)

- Ionic—inward Cl^- , outward K^+ currents
- Neurotransmitter—GABA

Normal CNS Function



Hyperexcitability reflects both increased excitation and decreased inhibition



Partial Epilepsy

Focal epilepsy

Mainly as a result to focal brain damage → tumor, abscess and so on

- Partial seizures may arise from any disease of the brain.
- The presence of partial seizures signifies the presence of focal cerebral pathology.

Case: Parasthesia and numbness in right side of the body then general fatigue

- **Divided into:**

without convulsion → normal brain MRI, EEG shows high electrical

We start treatment with (carbamazepine)= anti epileptic drug

The diagnosis is simple partial epilepsy (sensory)

1. **Simple partial seizures:** manifest motor, somatosensory,
Conscious

and psychomotor symptoms without impairment of

consciousness (e.g. Jacksonian seizures).

May be motor or sensory

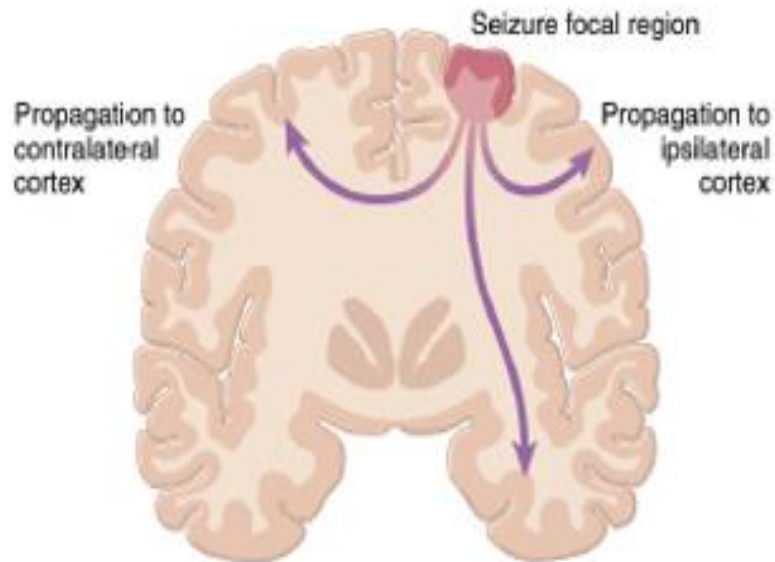
2. **Complex partial seizures:** impairment of consciousness
Unconscious

and strange repetitive movements (automatisms).

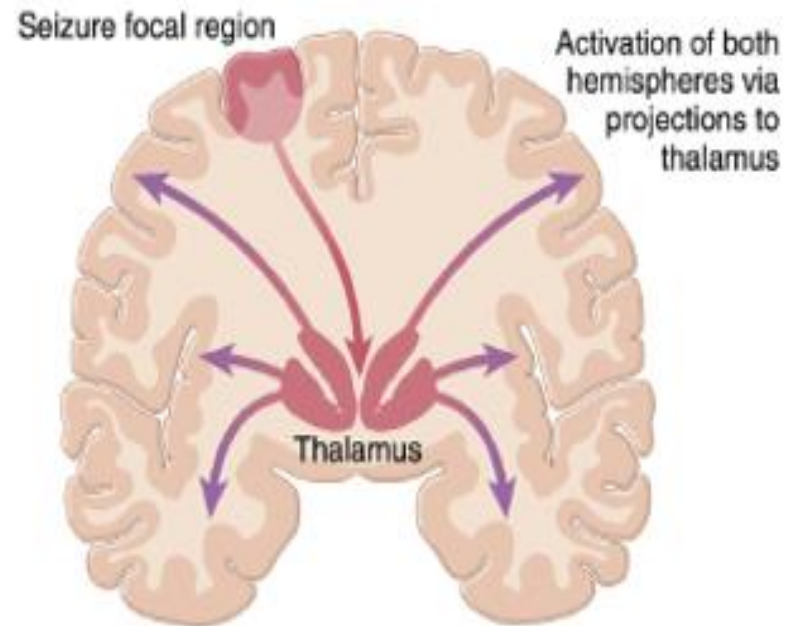
The most defecult type is temporal lobe epilepsy

كيف ممكنه الحالة تتطور وتنشئ لمناطق تانية منه ال brain

Propagation of seizures



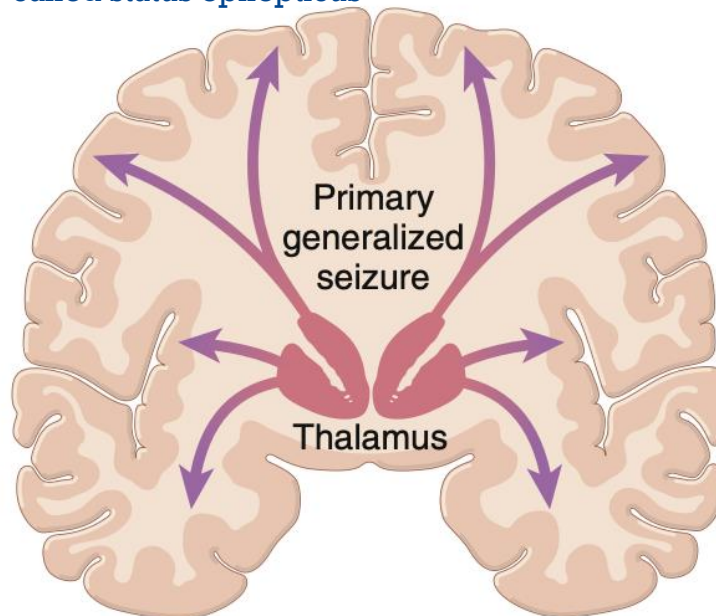
Secondary generalization of a focal seizure



Generalized Seizures

Bilateral symptoms as a result of bilateral excessive brain discharge

- **Generalized tonic-clonic (grand mal) seizure**, characterized by diffuse, excessive, and uncontrolled neuronal discharges that at the outset spread rapidly and simultaneously to both cerebral hemispheres through interconnections between the thalamus and cortex.
- Lasts from a few seconds to 3 to 4 minutes.
More than 5 mins → called status epilepticus



Tonic-Clonic Seizures

Follow the generalized motor

(Grand-Mal Seizures Or Generalized Major Convulsions)

Characterized by 3 stages:

- Preictal stage (aura). شعورها قبل النوبة
- Ictal stage (seizure). النوبة نفسها
- Postictal stage. بعد النوبة

1. Preictal stage (aura):

يُكُون حاسساً انه النوبة جاية

- It is a warning sign for the coming attack.
- May be somatic (fatigue), psychic (depression), autonomic (nausea, vomiting). See or smell hallucination

2. Ictal stage (seizure): 3 stages

a. Sudden loss of consciousness: فقدان وعي مفاجئ بالكامل

b. Tonic phase:

- The body becomes rigid.
- Extended limbs. Hyperextension
- The patient utters a cry (spasm of vocal cord) and falls.
- Rolling of eye upwards.
- Cyanotic face. ازرقاق الوجه Bluish purple face because of hypoxia
- Tongue is usually bitten.
- Urine incontinence. Stole
- Frothing. زبد الفم

c. Clonic phase:

- Generalized convulsion with frothing at the mouth.
- Rhythmic jerking of muscles (contract and relax repeatedly and rapidly). This lasts from a few seconds to several minutes in status epilepticus“.

More than 5 mins

الفرق بين ال tonic وال clonic هو انه الأول يكون hyperextension
والثاني يكون flexion and extension

3. Postictal stage:

As a result to muscle contraction and lactic acid accumulation that stimulate pain receptors

a. Somatic: generalized fatigue, sleepiness or coma, aphasia, Todd's paralysis (paralysis not more 24 hrs).

We mentioned it

b. Autonomic: Inc. ICP headache, dizziness, vomiting.

c. Psychic: confusion.

Phases of Tonic-Clonic Seizures

Aura

It varies from person to another, but may include peculiar¹ sensation, dizziness, strange smell or feeling of numbness, followed by the sudden onset of the seizures with loss of consciousness.

Tonic Phase

Straightening of body and limbs due to the rigid muscle contraction, manifested by clenched jaw and hands, open eyes with dilated pupils. Lasts from 30 to 60 sec.

Clonic Phase

Rhythmic, jerky contraction and relaxation of all muscles.

Incontinence, frothing at the lips and some may bite tongue or cheeks during this phase. Lasts several mins.

Postictal State

A period of disorientation follows the grand mal seizures.

Is a neural depression leave the individual sleepy and fatigue for several hours.



Absence Epilepsy (Petit Mal Epilepsy)

Follow the generalized non motor

- Also called **generalized nonconvulsive seizures**.
 - Onset usually in childhood between **4-12** years of age.
 - Family history in 40% of patients.
 - 15% to 20% of epilepsy cases in children.
 - The seizures consist of multiple brief staring **episodes** with behavioral arrest.
 - The absence may occur many times a day within a duration of **5-15** seconds.
 - Attacks may be induced by **hyperventilation**.
 - They are associated with generalized **3-hertz spike and slow wave** discharges on EEG.
- Diagnostic examination

Temporal Lobe Epilepsy (TLE)

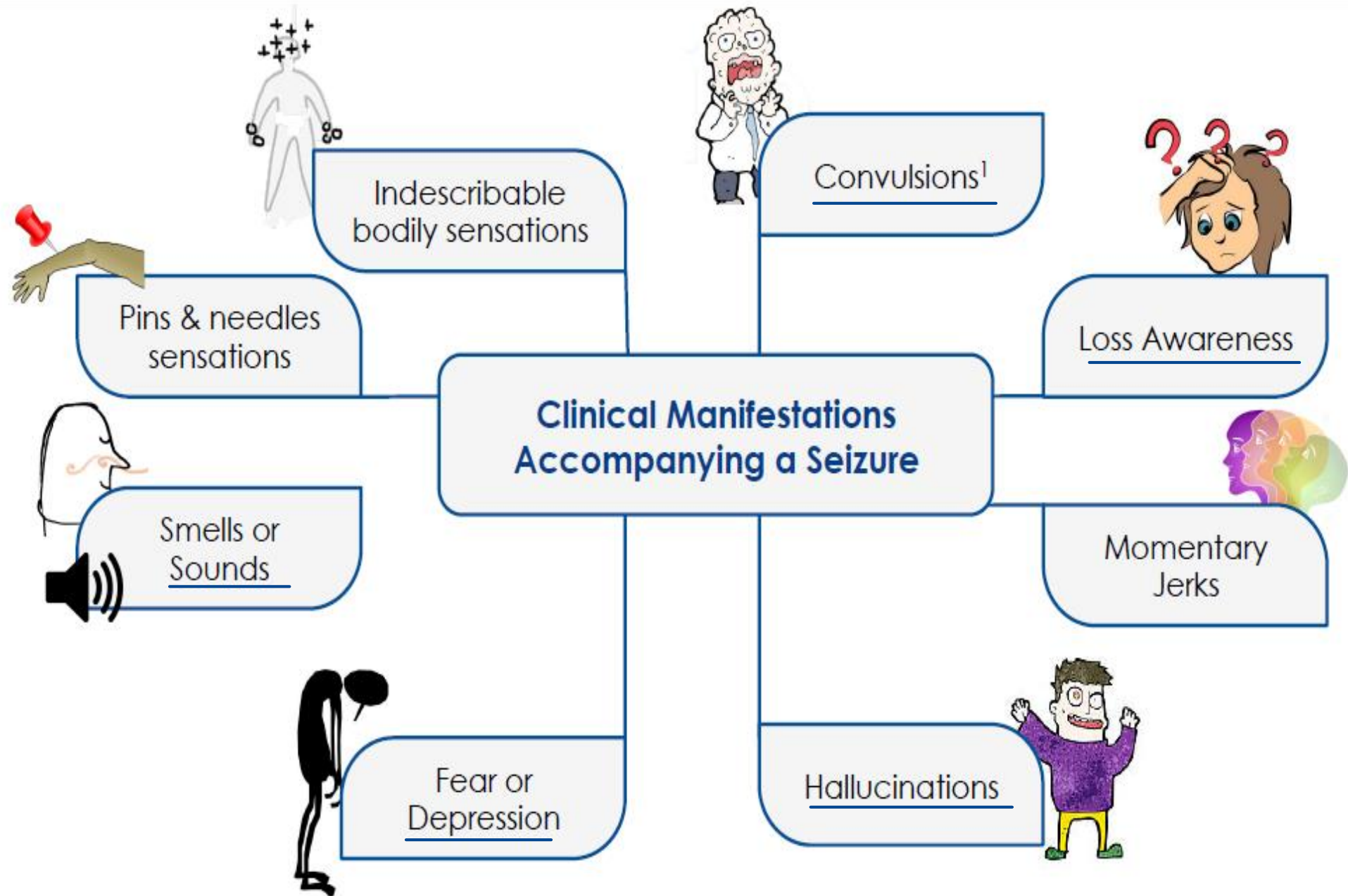
Most difficult type of complex partial epilepsy

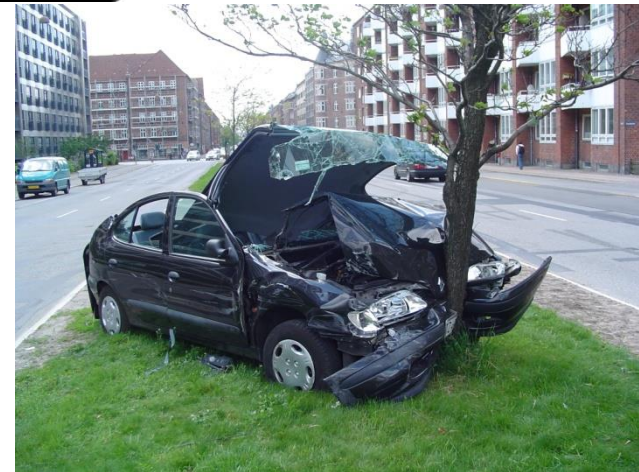
- TLE is the most common manifestation of **complex partial seizures**.
- **Hippocampal sclerosis** is the most common underlying cause of TLE 81%.
Hiippocampus in temporal lobe
- About one-third of patients have secondary generalized tonic-clonic seizures in addition to complex partial seizure. TLE
- A seizure aura with sensory symptoms (abdominal pain) and psychic such as **deja vu, jamais vu**.
These patients face heterogenous symptoms
Cause the Insulla is close to the temporal lobe and may cause intestinal cramp.

انوا البيشنت بيرحم انه شايف الشخص منه قبل وهيك

- The patients are generally unaware and unresponsive during attack.
- Automatisms are common. فصيلة أو غياب عنه الواقع
ممكته تؤدي صينية الأكل للحمام بدال المطبخ وهذا
- Chewing, lip smacking.
- Less commonly observed behaviors associated with TLE include: crying, and walking or running away.
- Postictal confusion usually lasts minutes, but may be complicated by psychosis.

Clinical Manifestations of Seizure

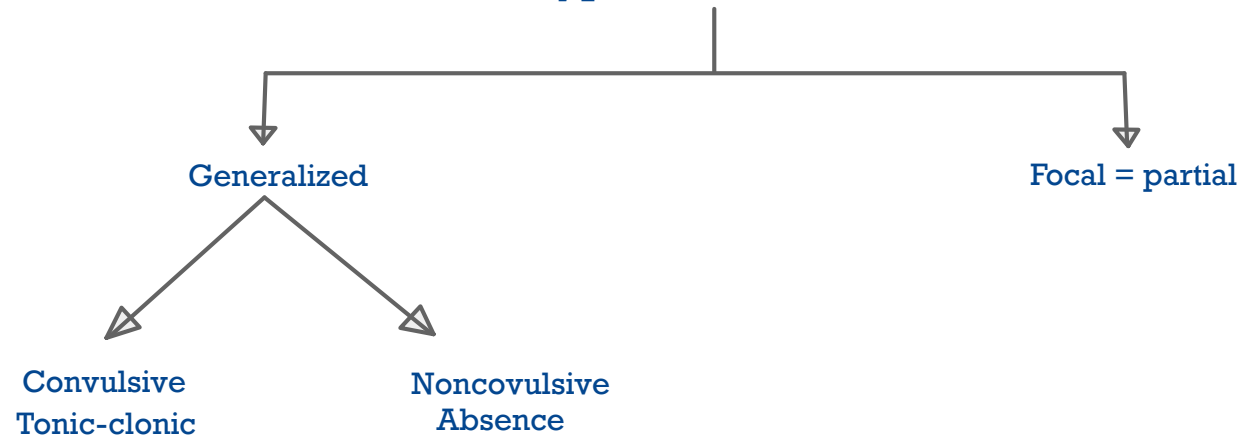




Status Epilepticus

SUDDEN
DEATH

Type of seizures



Status Epilepticus “SE”

- **Serial Epilepsy:** repeated seizures with brief periods of recovery.
- **Status Epilepticus:**
 - ✓ SE is a state of continuous seizures “prolonged seizure $\geq$ 5 min duration” or having more than 1 seizure within a 5 minutes period, without returning to a normal level of consciousness between episodes is **called status epilepticus**.
 - ✓ This is a medical emergency that may lead to permanent brain damage or death.

Types of Status Epilepticus

- **Types of status epilepticus:**

- ✓ **Generalized convulsive status:** tonic-clonic status, tonic status, clonic status, and myoclonic status.
- ✓ **Generalized nonconvulsive status:** absence status.
- ✓ **Partial status.**

المرضى هاد بييجي ن coma as a result of nonconvulsive seizure ويكول صعية بالتشخيص ولازم
ناخذ هسستوري صدمه الأهل عشان نربط بيه ال coma الي انا المريض بسببها المستشفى وال absence epilepsy

We used EEG in diagnosis
3-hertz spike and slow wave

In these cases we give empiric therapy anti-epileptic drug
and the patient wakes up from the coma

- **Complications of SE:**

- ✓ **Cardiorespiratory failure.**
- ✓ **Irreversible brain damage.**
Due to prolonged hypoxia
- ✓ **Rhabdomyolysis.** Acute kidney injury AKI
As a result to harmful proteins produced in
the blood that is nephrotoxic and cardiotoxic

Died from these complications

- **Status epilepticus has a mortality of 10-15%.**

So we must deal with it as emergency

In children as a result of fever or hyperthermia
Febrile Seizures
Follow the generalized convulsive

No need for anti-epileptic drug we should treat the fever
We should treat the cause if infection → antibiotic, if fever → antipyretic

When we should give the patient anti epileptic
drugs→ if it comes again with no trigger (fever)

- Affect 3% of children, have a genetic predisposition.
- Occur in children before 6 years of age. بتستمر لهذا السبب، ف يتعامل معهم أخصائيي الأطفال
- Are usually, generalized tonic-clonic seizures occurring with a rapid rise in fever.
- If a bacterial infection, especially meningitis, is present, it needs to be identified and treated.
- **If simple**, does not affect intellectual performance or risk of developing epilepsy, and AEDs not indicated.
- **If complex**, 4-12% risk of subsequent epilepsy.

Pseudoseizures

- The fit usually occurs in the presence of other people to gain their sympathy. شغل نساوي
- The patient alert with generalized convulsion. In pseudo
In true seizure the patient not alert and can't talk about what happened
- Eyes often closed during attack.
- It never occurs during sleep. Just during the day
- The patient never hurts himself (by tongue-biting or body injury).
- Autonomic signs during attack uncommon. In true may face → Tachy or brady cardia, cyanosis, HTN
- Urine incontinence never occur.
- EEG is normal and AED contraindication.
Anti-epileptic drugs
- Normal prolactin level after attack.

The Electroencephalogram (EEG) تخطيط الدماغ

- The EEG is a recording of the electrical activity of the brain from the scalp.
- The first recordings were made by **German Psychiatrist Hans Berger** in 1924.^{1st time}

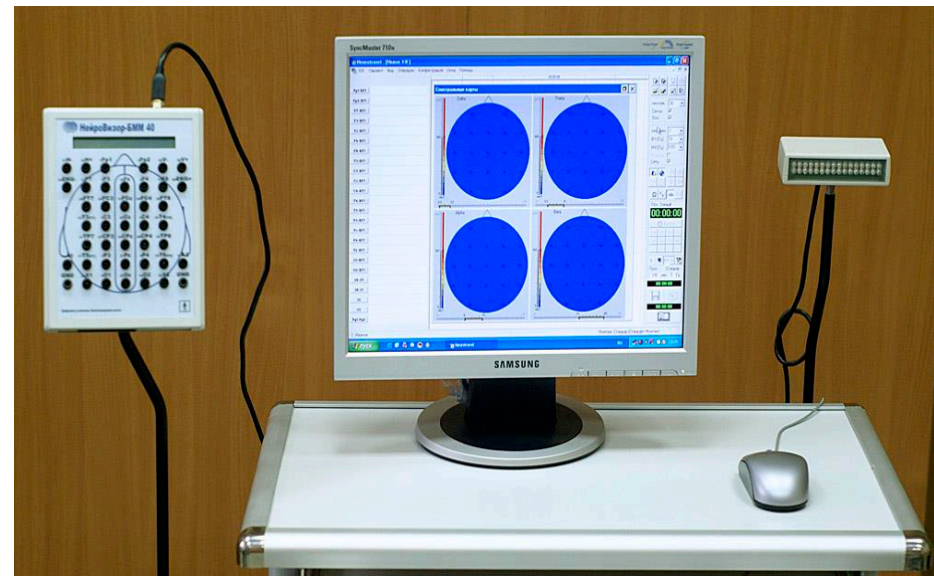
EEG Electrodes



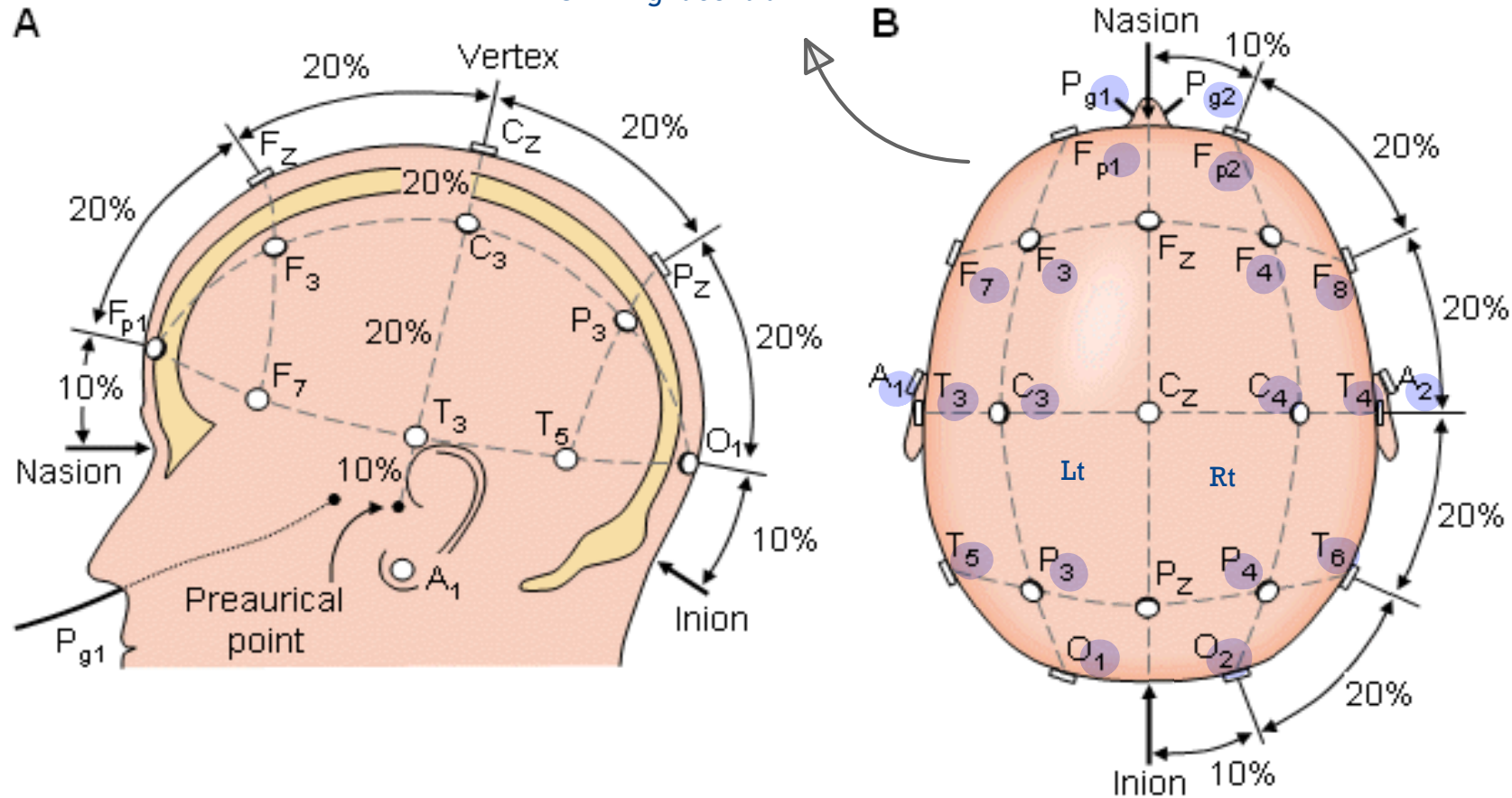
Sliver Electrodes



Electrodes Cap



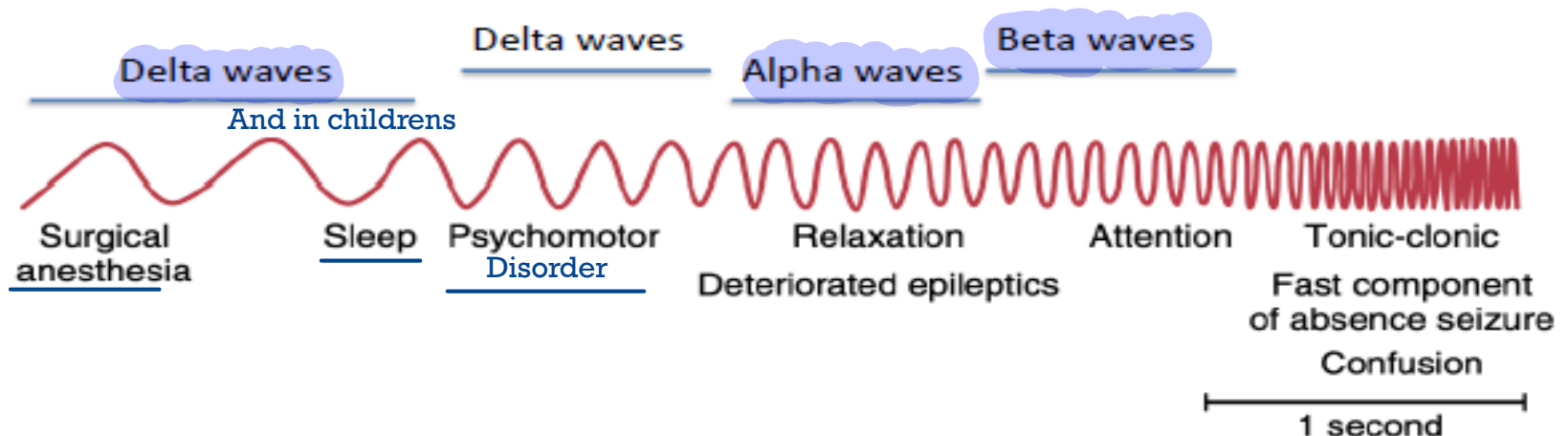
Fp1 → left frontoparietal
O1 → left occipital
T3 → left temporal
C4 → right central



Brain Waves

- Electrical recordings from the surface of the brain or even from the outer surface of the head demonstrate that there is continuous electrical activity in the brain.
- The recorded electrical potentials, are called ^{الاشي الي يتم قرائته} **brain waves**, and the record is called an ^{الخطط الكهربائي} **electroencephalogram (EEG)**.

Effect of Varying Levels of Cerebral Activity on the Frequency of the EEG



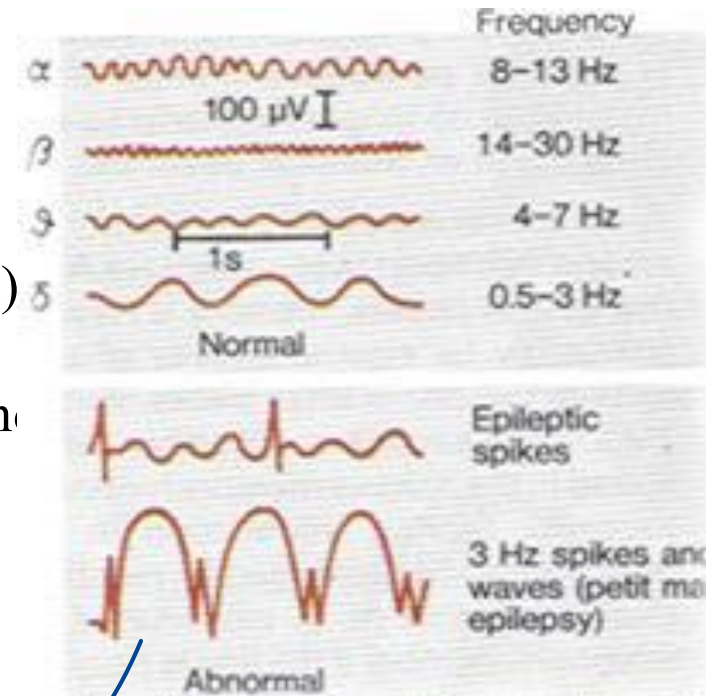
EEG Frequencies

- **Alpha Rhythm** (8-13 Hz – cycles/second)
- **Beta Rhythm** (> 13 Hz – cycles/second)
The fastest
- **Delta Rhythm** (< 4 Hz – cycles/second).
The slowest
- **Theta Rhythm** (4-7 Hz – cycles/second):

If we saw spikes it means there's paroxysmal epileptic and brain activity

We used EEG in diagnosis
3-hertz spike and slow wave

Means → Absence epilepsy, generalized non convulsive seizure



In children's mainly

Different Types of Brain Waves in Normal EEG

Rhythm	Frequency (Hz)	Amplitude (miclovolte)	Recording & Location
Alpha(α)	8 - 13	50 – 100	• Adults, rest, eyes closed. • Occipital region
Beta(β)	> 13 Hz	20	• Adult, mental activity • Frontal region
Theta(θ)	4 – 7	Above 50	• Children, drowsy adult, emotional distress • Occipital
Delta(δ)	< 4	Above 50	• Children in sleep

If a doctor give the patient antiepileptic whenever the paroxysmal activity is recorded maybe psychological problems and migraine and these problems is not epileptic

القاعدة تقول تخطيط الدماغ يُثبت ولا ينفى، وينفى ولا يُثبت

EEG in Epilepsy

هنا التخطيط ينفى ولا يُثبت

We shouldn't give the patient anti epileptic unless there is clinical symptoms and manifestations

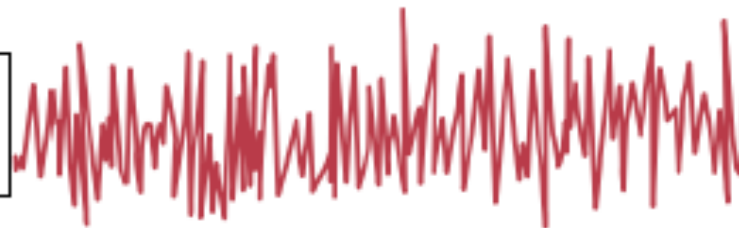
- In combination with appropriate clinical findings, epileptiform EEG spikes or sharp waves strongly support a diagnosis of epilepsy, classifying seizures correctly, and making therapeutic decisions.
- EEG evidence of seizures activity is shown typically by focal cortical or generalized spike-and-wave activity.
- A normal EEG between attacks (interictal) does not in any way exclude epilepsy. يُثبت ولا ينفى → We shouldn't stop anti epileptic drugs
- Many people with epilepsy have normal interictal EEG. True seizures المرضى لا يزال يشهدون له بكونه ال EEG نوسل بين النوبات
- 3 Hz spike-and-waves activity occurs specifically in petit mal epilepsy. Slow Diagnostic for absence (generalized non convulsive) epilepsy
- If the routine EEG findings are normal, a sleep-deprived EEG and video-EEG should be performed. نستأتي بديل عن ال EEG العادي With photostimulation → increase electricity With hyperventilation

Changes of EEG in Epilepsy

- EEG is used to **diagnosis and classifying seizures**, and depending on it the therapeutic decisions are made !
- Epileptiform patterns on EEG shows **Spikes or Sharp waves**.
- Generalized tonic-clonic seizures shows ^{High amplitude} **high voltage** & ^{Fast waves = sharp} **high frequency patterns “Spikes”**,
- ^{Generalized non convulsive} Absence epilepsy shows brief period of **slow & spiky waves “3 Hz spike-and-waves activity”**.
^{Slow}

Electroencephalogram (EEG)

high-voltage, high-frequency discharges occur over the entire cortex



100 μ V

Generalized tonic-clonic seizure

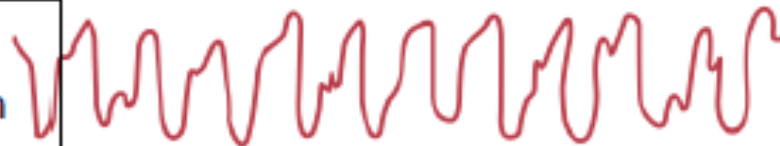
spike and dome pattern



50 μ V

Absence seizure

low- frequency rectangular wave with a frequency between 2 and 4/sec and with occasional superimposed 14/sec waves



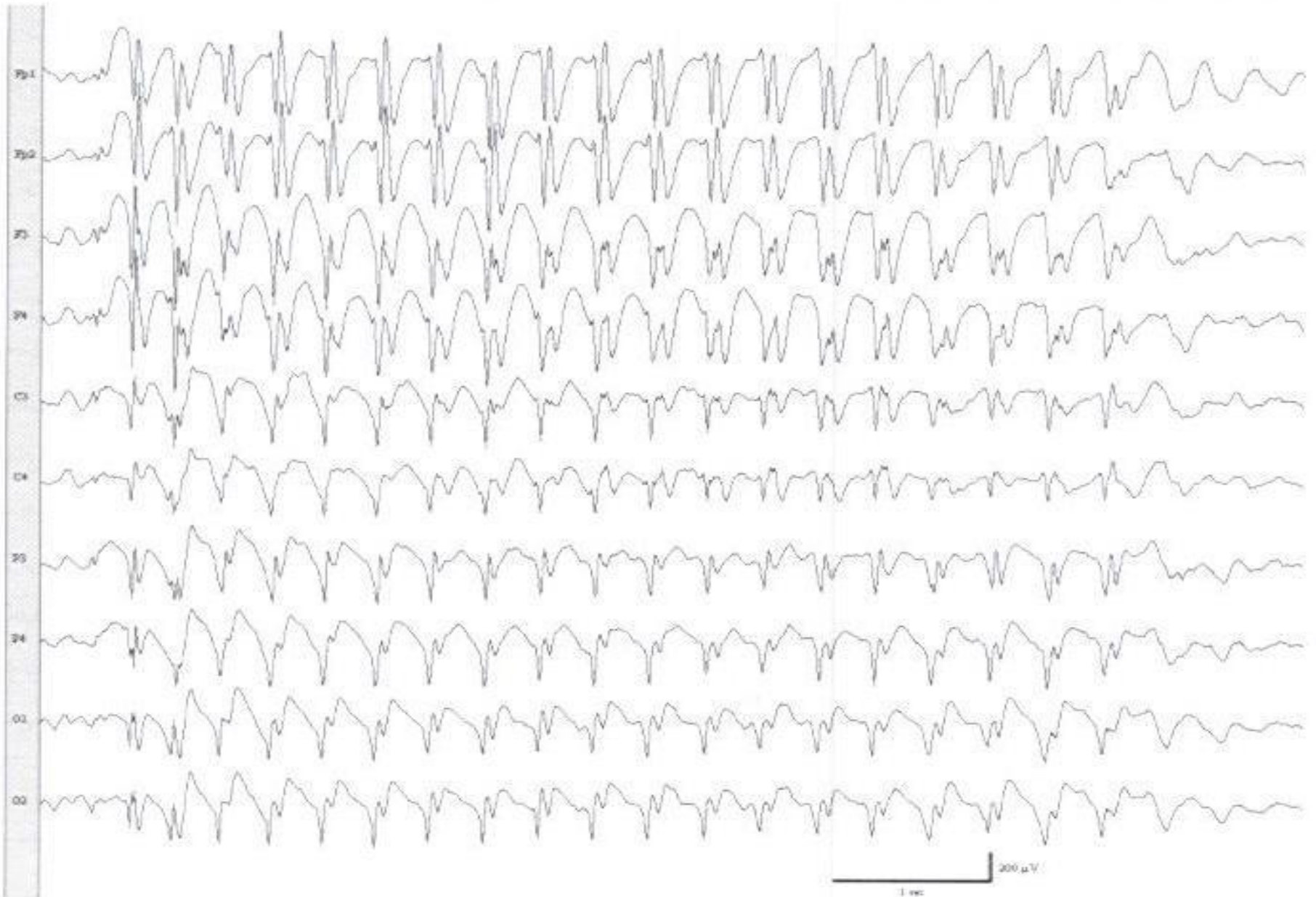
50 μ V

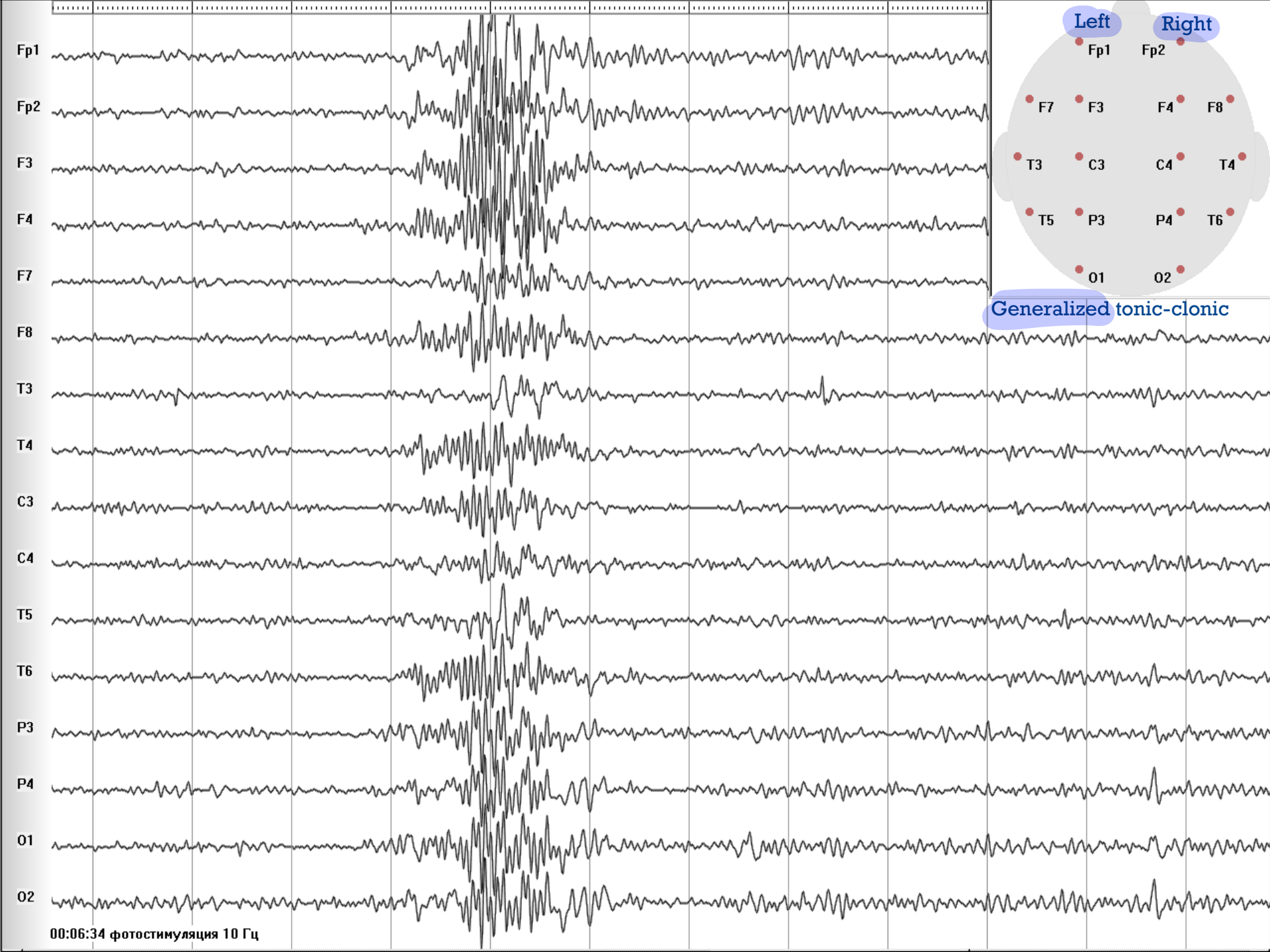
Psychomotor
Disorder

We diagnose it by taking history
and see irregular slow wave

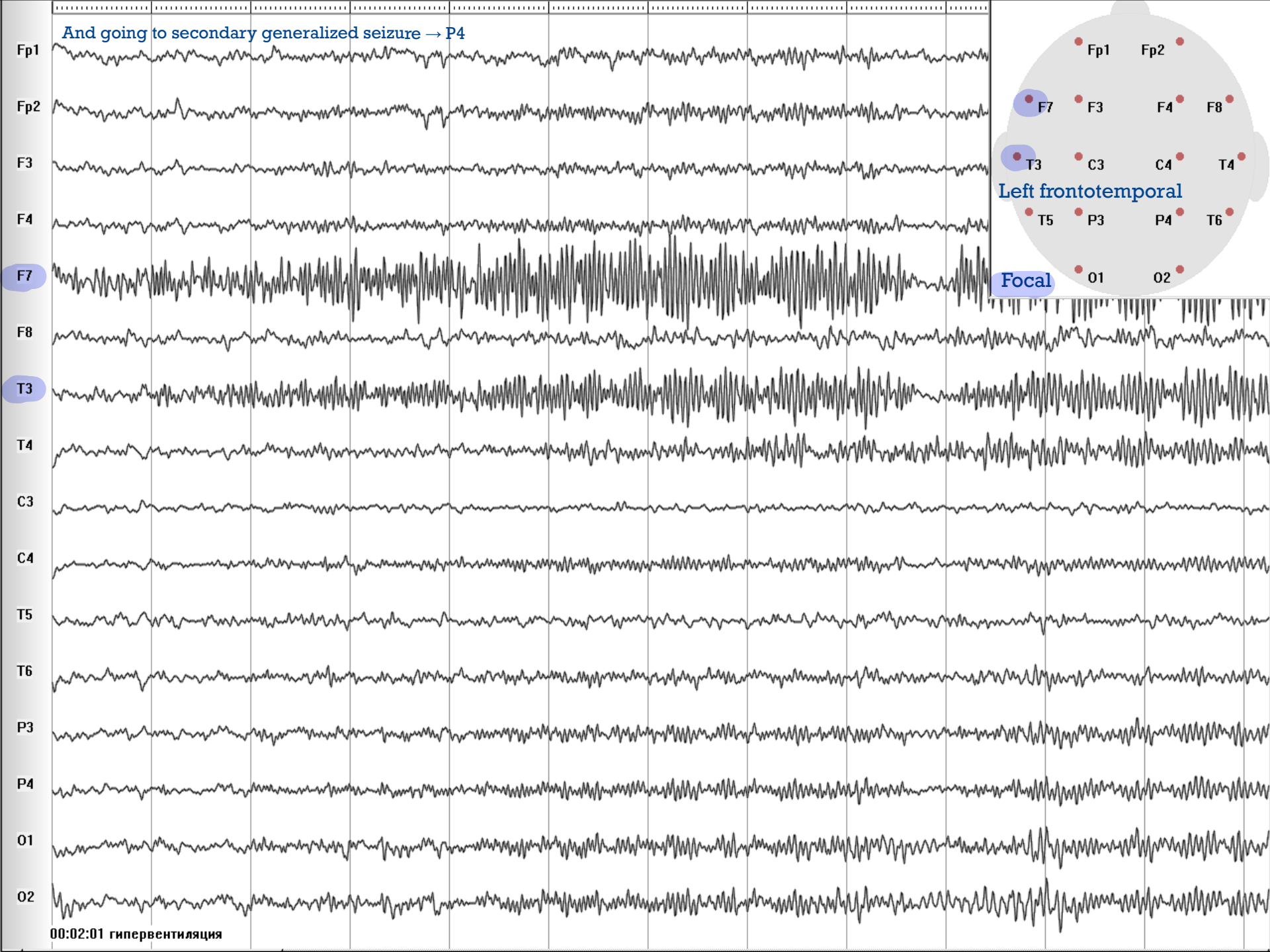
Generalized → لأنها موجودة بالزوجي والفردى
Bilateral → 3- hertz spike slow waves → non convulsive = absence

Generalized absence seizure





And going to secondary generalized seizure → P4



00:02:01 гипервентиляция

Cause it may be secondary epilepsy not primary idiopathic

Neurological Imaging Studies in Epilepsy

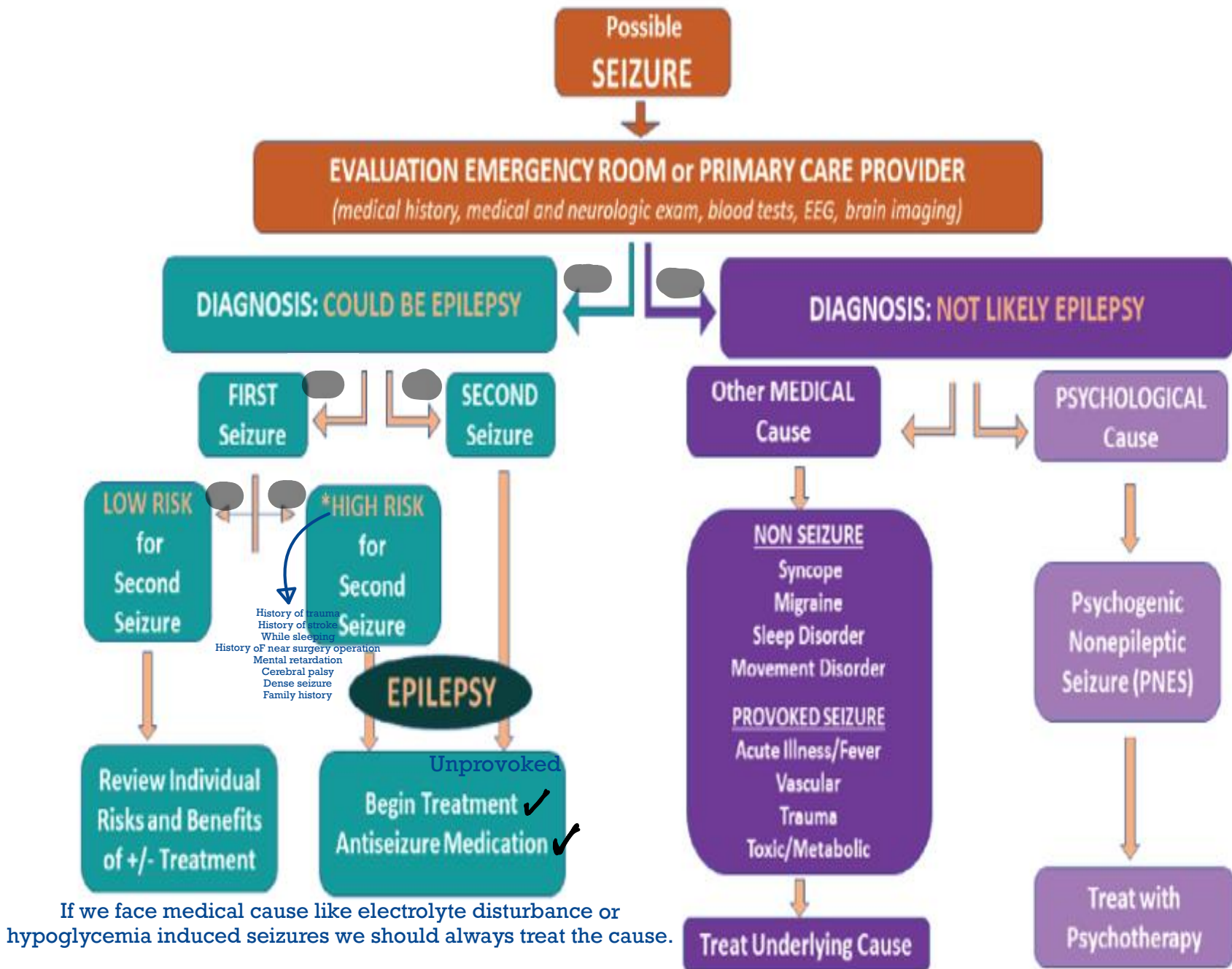
So we must exclude the organic causes like tumors or AV malformation

CT
CTA
MRI
MRIA
PET
SPECT

Magnetic Resonance Imaging (MRI).

- Functional MRI (fMRI).
- Computed Tomography (CT).
- Positron emission tomography (PET).
- Single-photon emission computerized tomography (SPECT).





Guidelines for Anticonvulsant Therapy

Our goal is → complete seizure control with minimum side effects

1. Start one first line drug.
2. Start with low dose. To avoid the side effects like ataxia, dizziness, teratogenicity in pregnancy.
3. Gradually increase dose to effective control of seizures or side effect "use serum drug level".
4. If first drug failed "seizures continue or side effects", start second-line drug whilst gradually withdrawing first.
5. Try ^{3 monotherapy} three singly drugs before using combination. To avoid the side effects from this combination
6. Do not use more than three drugs in combination.
7. The goal of therapy should be complete seizures control with a single drug and without side effects. If young female patient and wanna get pregnant we should take the less teratogenic drug (valproic acid) Or if she's taking OCP we should avoid carbamazepine cause it will decrease its efficiency

When to start treatment after the first seizure?

Which patients are at highest risk for recurrent seizures?

High risk for recurrence and we should start the treatment from the 1st seizure

Seizure recurrence is more likely if the patient has:

- ❖ Focal neurologic deficit.
- ❖ Mental retardation.
- ❖ EEG demonstrates severe epileptiform abnormalities.
- ❖ Structural brain lesion.
- ❖ An initial high density of seizure. نوبة كبيرة قوية
- ❖ Positive family history.
- ❖ Seizure during sleep

When should antiepileptic treatment be stopped?

ممر ٣ سنوات بدون أي نوبة ويعمل تخطيط دماغه ويكُون نوبلاً بقرأ وقف العلاج بالتدريج خلال ٦ أشهر
وبنية المريض أنو تلت الحالات وهو قاهر بيخفف الدواء أو يوقفه ممكنه نرجح النوبة ووقفها بدي ارجح العلاج مع تاتي

- 70-80% will eventually become seizure free, it is common practice to consider drug withdrawal after becoming seizure free for 2-3 years.
- Withdrawal should be undertaken slowly, reducing the drug dose gradually over 6 months.
- Recent studies suggest that approximately **33% of adult** patients and **25% of children** who are seizure free fore 2 years well relapse after termination of AED.

ويوصي المريض انو يتجنب كل ال triggers الي ممكنه تفوته بالنوبة مع سهر كثير، إعطاءة محالية زي الجولات،
Any thing related to the recurrence

Refractory Epilepsy

We may call it resistant to treatment

عشان احكي عنها medical refractory لازم يتحقق شرطيه
الأول : يكون مانشي على ٣ أدوية أو أكثر مده ال AED
الثاني : يحصل معك أكثر مده ٤ نوبات خلال الشهر

- There is no unifying definition of refractory epilepsy.
- “Failed” 3 or more AEDs.
- More than 4 seizures /month.
- 20-30% of epilepsy are ^{Resistant} intractable to medical therapy.
- Intractable epilepsy accounts for 60-75% of total cost of epilepsy care.

Clinical Uses of Antiepileptic Drugs

- ^{Generalized convulsive} **Tonic-clonic (grand mal) seizures:** ^{Valproic acid} valproate, phenytoin or ^{Tegretol} carbamazepin. Use of single drug is preferred when possible, because of risk of pharmacokinetic interactions and side effect.
- **Partial (focal) seizures:** carbamazepine, valproate, clonazepam or phenytoin.
- ^{Generalized non convulsive} **Absence seizures:** ethosuximide, valproate or ^{Lamictal} lamotrigine.
 Gradual increase of the dose. To avoid steven-jonson syndrome
 Carbamazepine is contraindicated وعلى العكس يتروود النوبات
- **Myoclonic seizures:** valproate, clonazepam or phenobarbital.
 Valproate is contraindicated for female planning to get pregnant → cause of its teratogeneity

If overweight patient we give it topirmate for migraine and epilepsy

Mechanism of Antiepileptic Drugs In Parma

Our goal in treatment of epilepsy

By understanding the pathophysiology

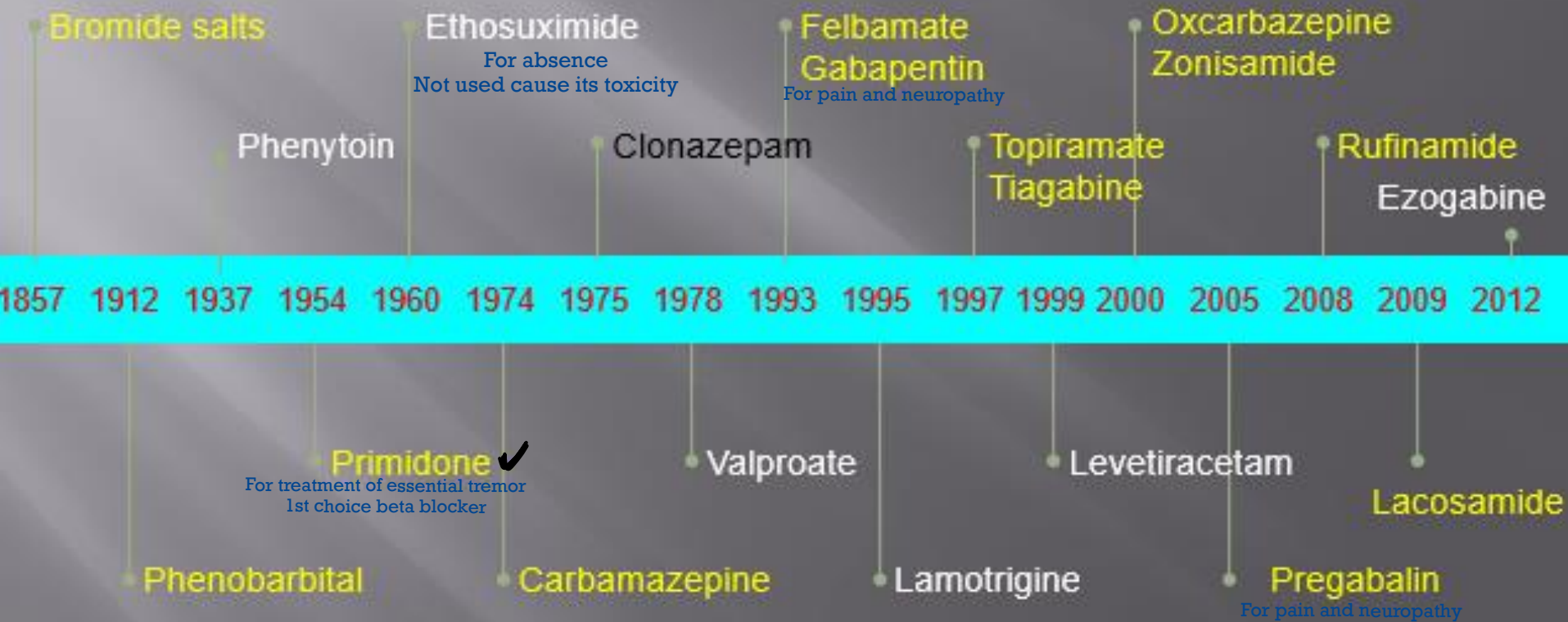
Antiepileptic drugs include the following:

- 1. Block of voltage-dependent sodium channels:** e.g., carbamazepine and phenytoin.
- 2. Altered calcium currents:** e.g., ethosuximide.
- 3. Increase in ^{Inhibitory} GABA activity:** e.g., phenobarbital and benzodiazepines.
- 4. Inhibition of receptors for ^{Excitatory} glutamate:** the most prevalent excitatory neurotransmitter, e.g., perampanel.
- 5. Multiple mechanisms of action:** e.g., valproate and topiramate, which block of voltage-dependent sodium channels and increase GABA activity in the brain.

Common Antiepileptic Drugs

Generic Name	Trade Name
• Valproic acid May cause loss of hair weight gain	➤ Depakin
• Phenytoin May cause gingival hyperplasia	➤ Epanutin In status epilepticus IV
• Carbamazepin May cause pancytopenia Hyponatremia Low levels of 3 blood cell types	➤ Tegretol
• Phenobarbital	➤ Luminal
• Topiramate	➤ Topamax
• Vigabatrin May cause visual field defect	➤ Sabrin
• Gabapentin	➤ Neurontin
• Levetiracetam منه أحسنهم وأقلهم تأثير جانبي	➤ Keppra Even in liver failure patient
• Clonazepam	➤ Clonex
• Lamotrigine May cause Steven-Johnson syndrome Related to skin	➤ Lamictal
• Diazepam	➤ Assival, Valium
• Lorazepam	➤ Loracare
• Midazolam	➤ Dormicum
• Propofol	➤ Diprivan
• ACTH In treatment of west syndrome(epileptic/infantile spasm)	➤ ACTH Adrenocorticotrophic hormone

Epilepsy Drug Development



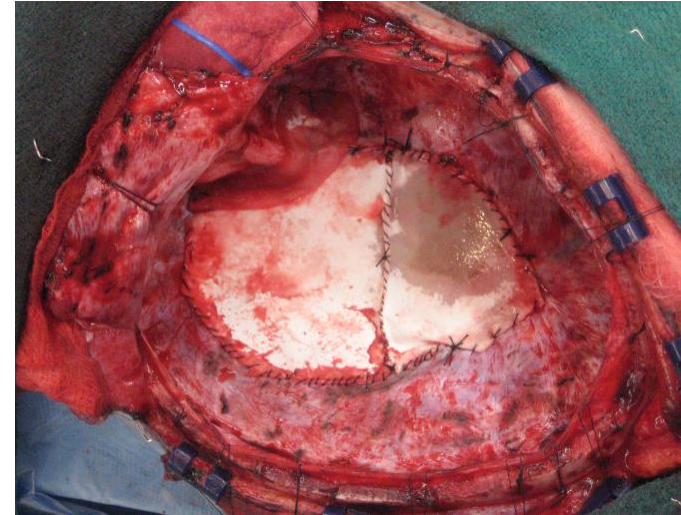
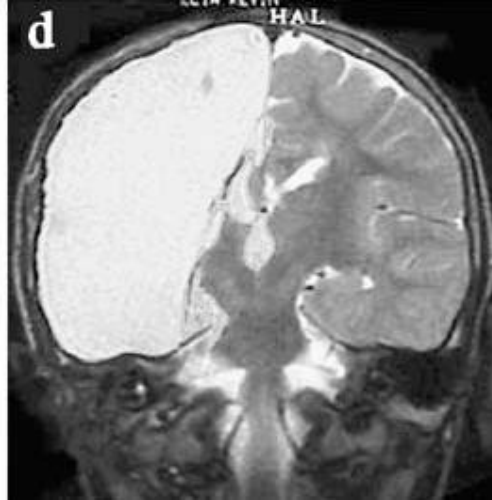
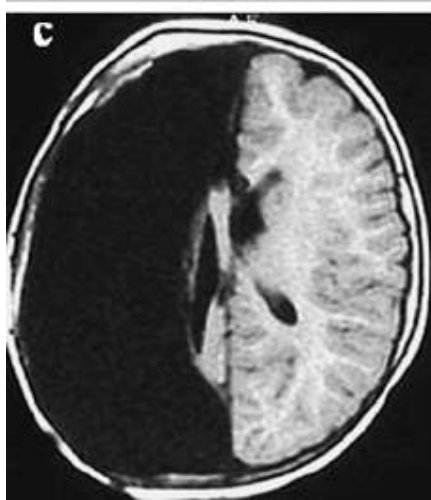
Surgical Treatment

❖ For medical refractory epilepsy. Focal brain resection is the most common type of epilepsy surgery:

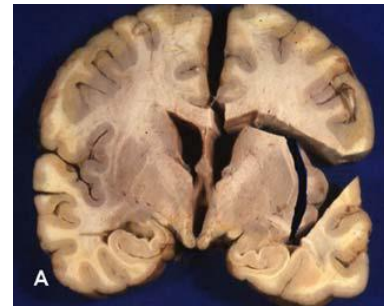
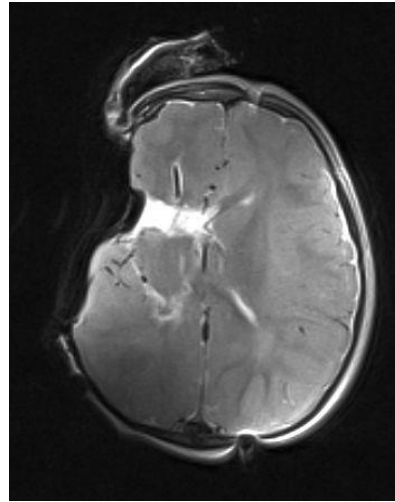
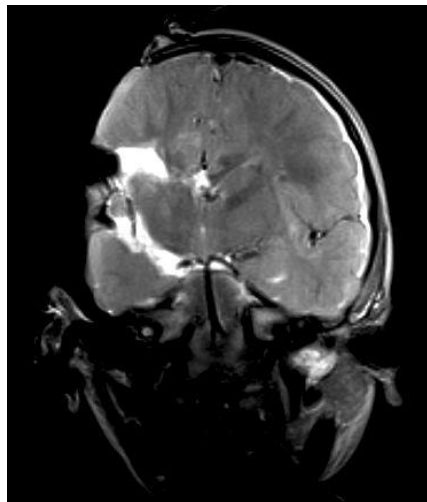
1. Hemispherectomy.
2. Anterior temporal lobe resection.
3. Lesionectomy: epileptogenic structural lesion
With PET and SPECT scan
resection. Or by gamma knife destruction
4. Vagus nerve stimulation.

Corpus callosum disconnection between the right and the left cerebral hemisphere

- Hemispherectomy



- Hemispherotomy



Vagus Nerve Stimulation



Thank You

