

جامعة
الملك سعود
King Saud University



EPILEPSY

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Objectives

- By the end of this lecture you should be able to know:
 - Definition of epileptic seizure, provoked seizure and epilepsy.
 - Status epilepticus.
 - Frequent causes of seizure and risk factors.
 - Triggers of seizures in epileptic patient.
 - Epilepsy classification and seizure semiology.
 - DDX of SZ
 - Seizure vs syncope
 - Approach to seizure disorder (Hx, Ex, inx)
 - Medical and surgical management of epilepsy.
 - How to select antiepileptic medications.
 - When to stop antiepileptic medications.



History

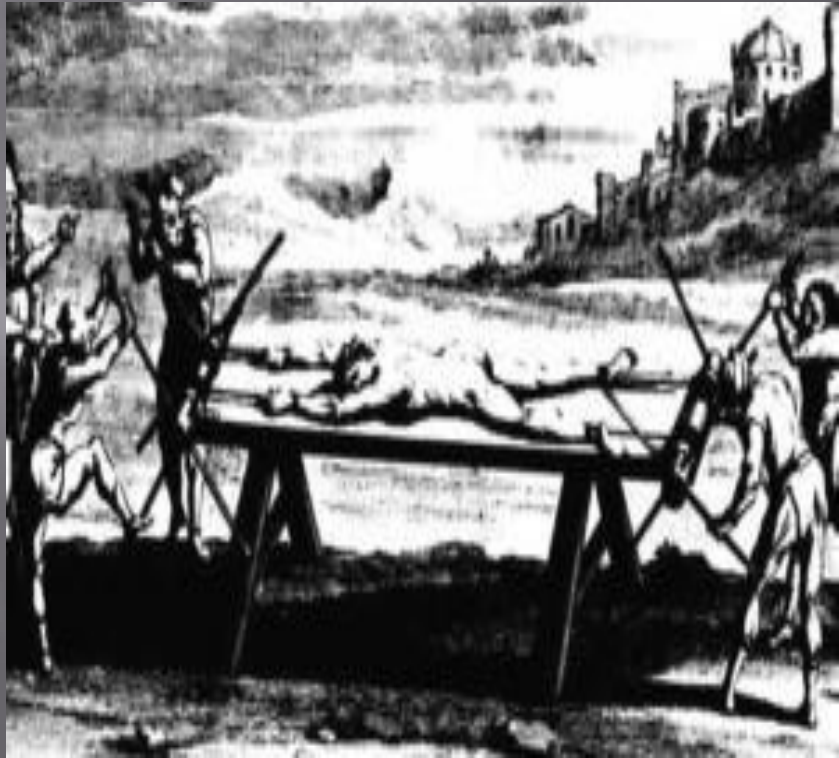
- ▣ One of the earliest descriptions of a secondarily generalized tonic-clonic seizure was recorded over 3000 years ago in Mesopotamia.
- ▣ The seizure was attributed to the god of the moon.
- ▣ Epileptic seizures were described in ancient cultures, including those of China, Egypt, and India.



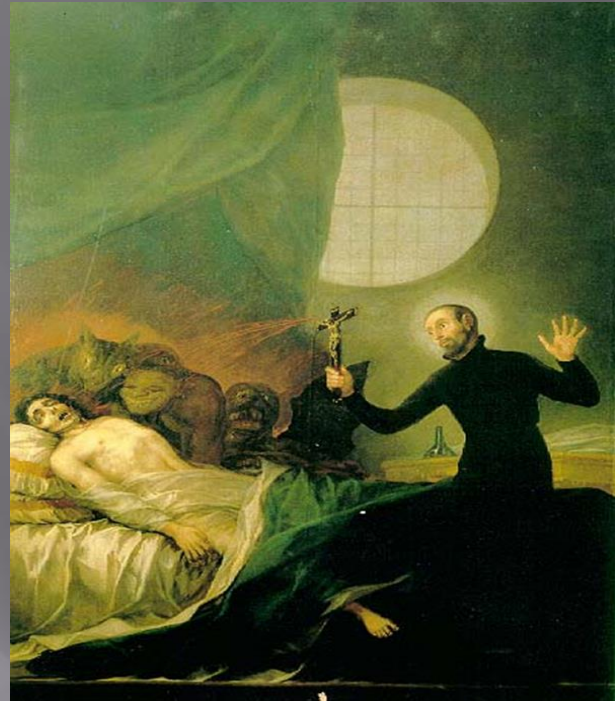
History

- ▣ Hippocrates wrote the first book about epilepsy almost 2500 years ago.
- ▣ Hippocrates in his book *On Sacred Disease* described the first neurosurgery procedure referring that craniotomy should be performed at the opposite side of the brain of the seizures, in order to spare patients from “phlegma” that caused the disease.





- In 18th and 19th century, medicine made important advances and research on epilepsy was emancipated from religious superstitions such as the fact that epilepsy was a divine punishment



What is epilepsy?

- ▣ **Epileptic seizure:** transient occurrence of signs and symptoms of sudden changes in neurological function due to abnormal excessive ,synchronous discharge of cortical neurons ..
- ▣ **Provoked seizures:** is occur in the setting of acute medical and neurological illnesses in people with no prior history of seizures
- ▣ **Epilepsy:** recurrent (two or more) unprovoked seizures.
- ▣ Seizure is a symptom of epilepsy.



Status Epilepticus

- ▣ **Status epilepticus (SE):** defined as recurrent convulsions that last for more than 30 minutes (5 min in the last update) and are interrupted by only brief periods of partial relief.
- ▣ **(SE):** is a serious, potentially life-threatening.
- ▣ Any type of seizure can lead to SE, the most serious form of status epilepticus is the generalized tonic-clonic type.



Emergency



Epidemiology



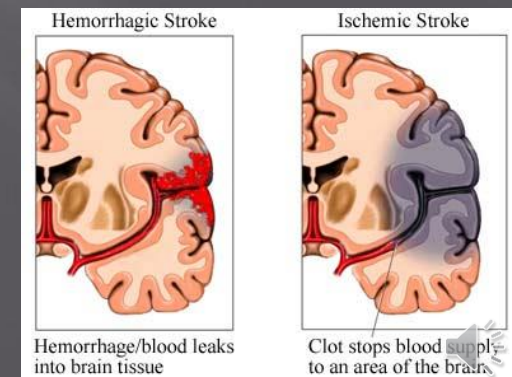
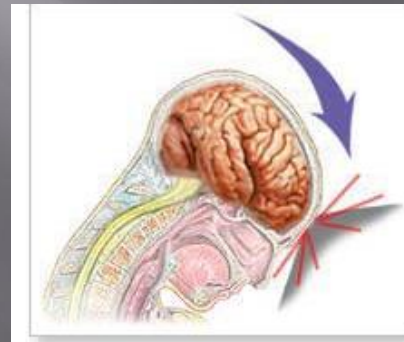
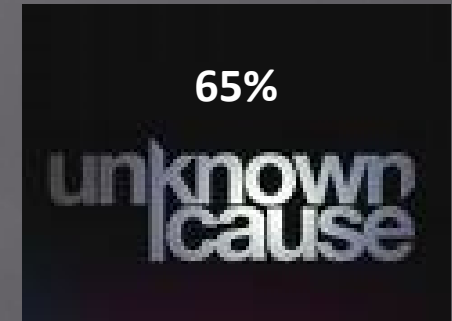
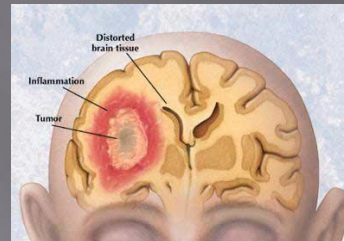
Epidemiology and course

- 5% of the population suffer a single sz at some time
- 0.5-1% of the population have recurrent sz = EPILEPSY
- 70% = well controlled with drugs (prolonged remissions)
- 30% epilepsy at least resistant to drug treatments = INTRACTABLE EPILEPSY.



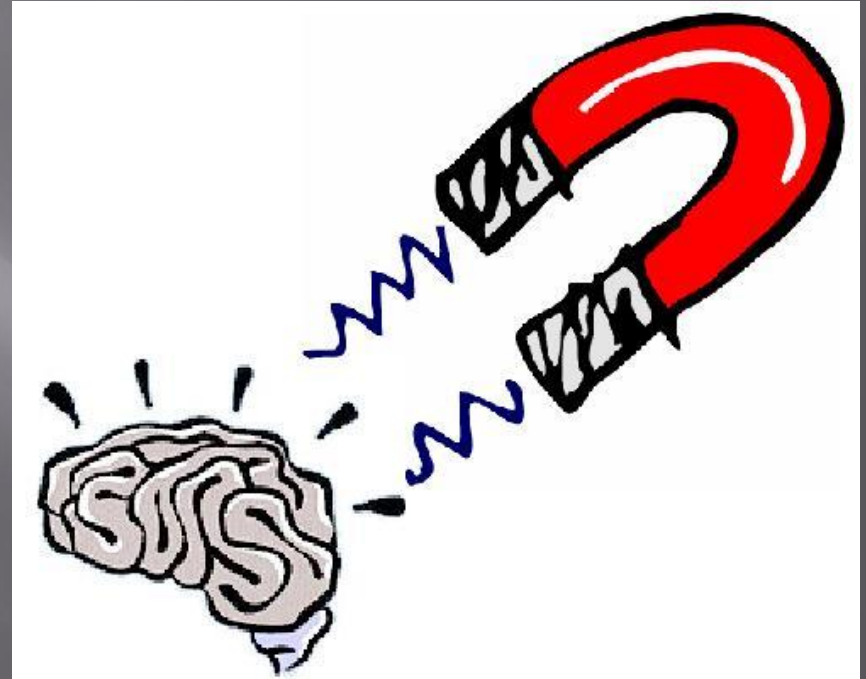
Risk Factors for Epilepsy

- ▣ Febrile convulsion
- ▣ Perinatal insult
- ▣ CNS infection
- ▣ CNS mass lesion
- ▣ Family history of epilepsy
- ▣ Head injury
- ▣ Abnormal gestation or delivery
- ▣ Developmental delay
- ▣ Stroke (ischemic or hemorrhagic)



Triggers for seizure:

- ▣ Poor compliance
- ▣ Sleep deprivation
- ▣ Stress
- ▣ Alcohol
- ▣ Infection
- ▣ Menstrual cycle



DANGER



Status Epilepticus

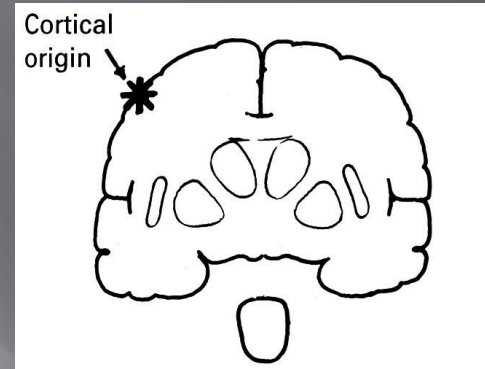
**SUDDEN
SUDDEN
DEATH**

Seizure Classification

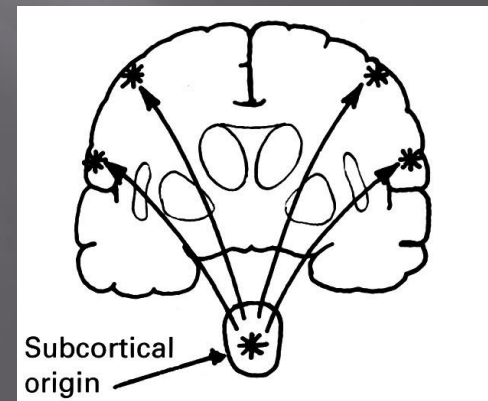


Epilepsy – Classification

- ▣ **Focal seizures** – *account for 80% of adult epilepsies*
 - Simple partial seizures
 - Complex partial seizures
 - Partial seizures secondarily generalised



- ▣ **Generalised seizures**
- ▣ **Unclassified seizures**



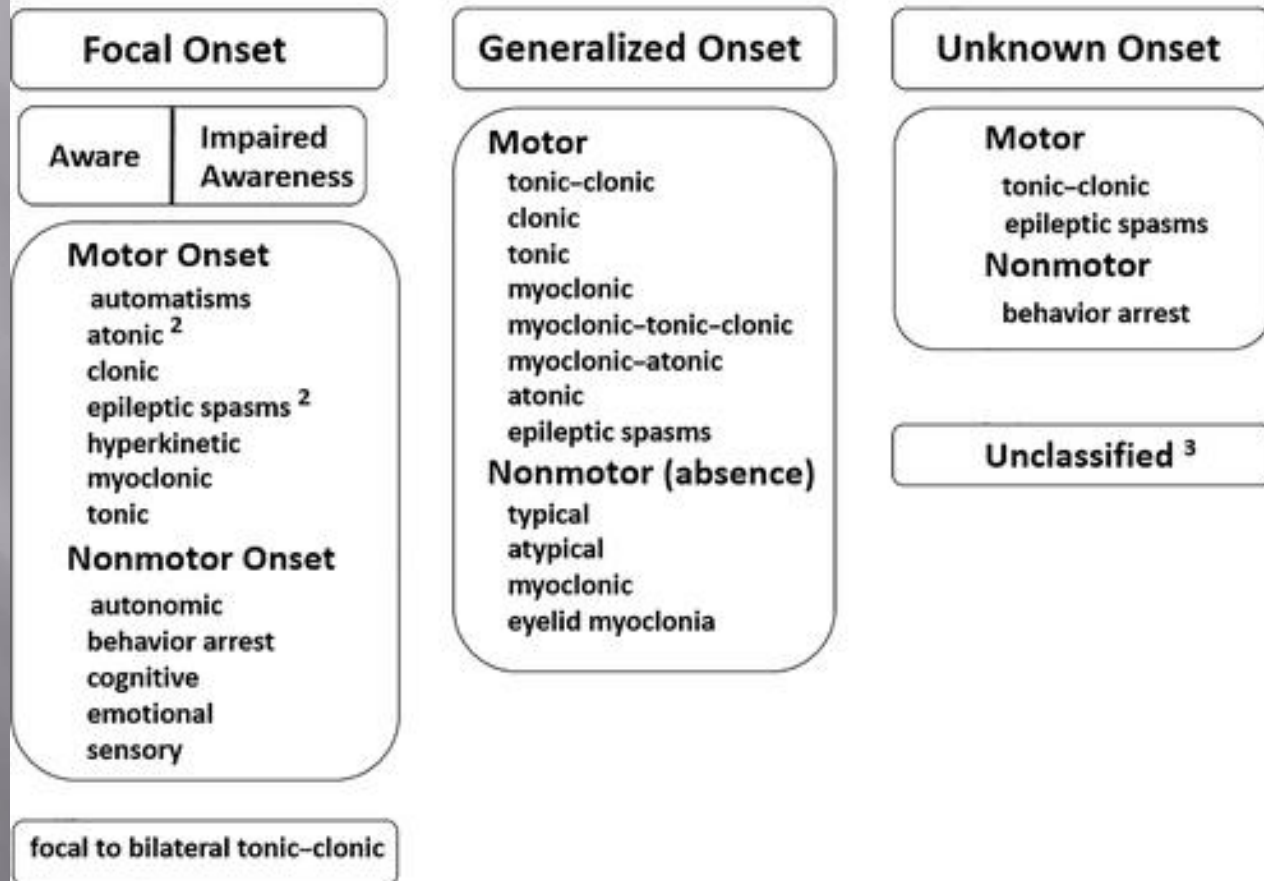
INTERNATIONAL CLASSIFICATION OF SEIZURES 1981

- **Partial Seizures (start in one place)**
- **Simple (no loss of consciousness or memory)**
 - Sensory
 - Motor
 - Sensory-Motor
 - Psychic (abnormal thoughts or perceptions)
 - Autonomic (heat, nausea, flushing, etc.)
- **Complex (consciousness or memory impaired)**
 - With or without aura (warning)
 - With or without automatisms
- **Secondarily generalized**
- **Generalized Seizures (apparent start over wide areas of brain)**
 - Absence (petit mal)
 - Tonic-clonic (grand mal)
 - Atonic (drop seizures)
 - Myoclonic
 - Other Unclassifiable seizures



Updated INTERNATIONAL CLASSIFICATION OF SEIZURES

ILAE 2017 Classification of Seizure Types Expanded Version ¹



Seizure Semiology

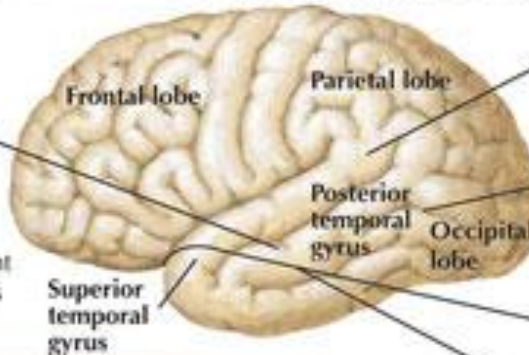


Impairment of consciousness:
cognitive, affective symptoms



Dreamy state; blank, vacant expression; déjà vu; jamais vu; or fear

Complex Partial Seizures



Formed auditory hallucinations. Hears music etc



Formed visual hallucinations. Sees house, trees that are not there



Bad or unusual smell

Olfactory hallucinations

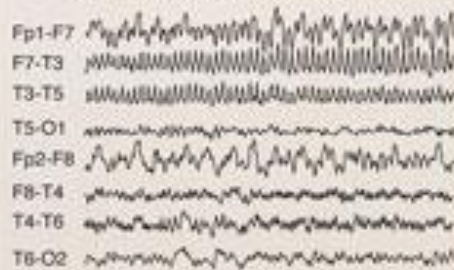
Psychomotor phenomena. Chewing movements, wetting lips, automatisms (picking at clothing)



Dysphasia



EEG: left temporal lobe seizure

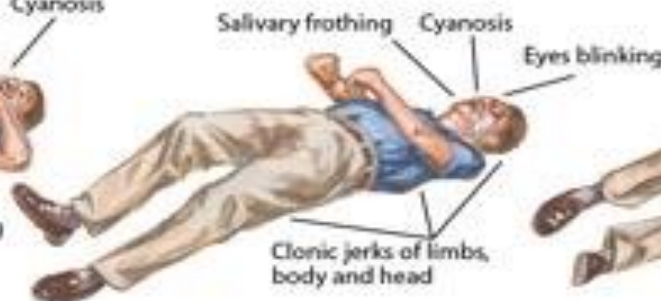


Repetitive sharp waves over left temporal region

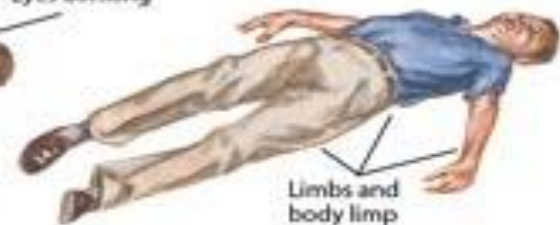
A. Tonic phase



B. Clonic phase



C. Post-ictal confusional fatigue



VEDIO











Summary of typical signs on video EEG

Typical EEG sign	Localizes to
Oral automatisms	Temporal lobe
Hypermotor automatisms	Frontal lobe
Manual picking automatisms	Temporal lobe
Visual hallucinations	Occipital lobe
Auditory hallucinations	Temporal neocortex (Heschl's Gyrus)
Olfactory hallucinations	Mesial temporal lobe
Nystagmus, eye blinking, eye pulling sensation	Occipital lobe
Ictal amaurosis	Occipital lobe
Tonic arm elevation	Supplementary motor area
Epigastric aura	Temporal lobe
Throat tightening sensation	Insula
Ictal pain	Parietal lobe
Somatosensory sensations	Postcentral gyrus or supplementary motor area
Clonic activity	Precentral gyrus
De-ja vu or jamais vu aura	Mesial temporal lobe
Fear	Most often temporal, but also frontal



DDx for seizure attacks

- ▣ TIA
- ▣ Syncope
- ▣ Migraine
- ▣ Movement disorders
- ▣ Panic attack
- ▣ Psychogenic seizure



Seizure vs syncopy

Comparison of clinical features in cardiogenic syncope versus seizure disorders

Clinical features	Cardiogenic syncope	Seizure disorders
Loss of consciousness	Typical	Common
Episode duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Arrhythmia	Common	Rare*
Electroencephalogram	Slow waves Flattening	Focal or general spike activity
Responsive to AEDs	No	Often
Short term mortality†	High	Low



Seizure approach

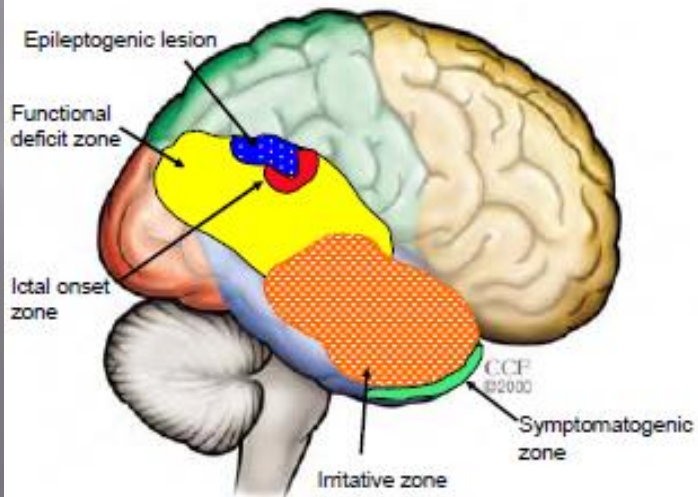
- ▣ **Non invasive tests**
 - Clinical history
 - MRI
 - video EEG
 - neuropsychological evaluation
 - nuclear medicine
- ▣ **Invasive monitoring**



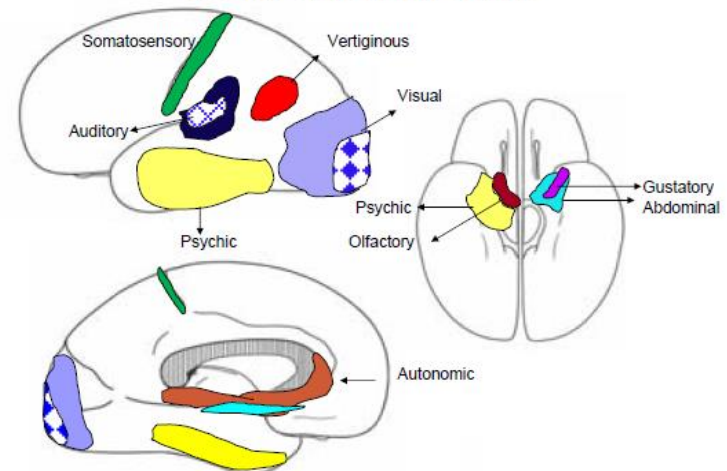
Clinical history



Defining the Epileptogenic Zone



Localization of Auras



Questions that help clarify the type of seizure include the following:

- ▣ Was any warning noted before the spell?
- ▣ What did the patient do during the spell?
- ▣ Was the patient able to relate to the environment during the spell ?
- ▣ How did the patient feel after the spell? How long did it take for the patient to get back to baseline condition?
- ▣ How long did the spell last?
- ▣ How frequent do the spells occur?
- ▣ Are any precipitants associated with the spells?



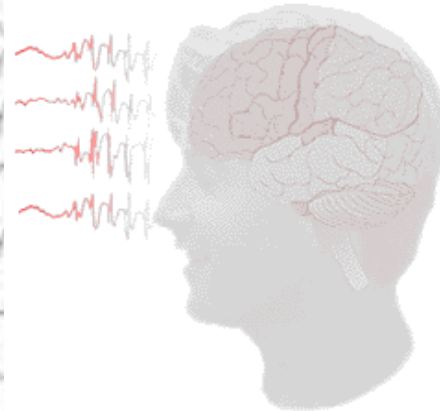
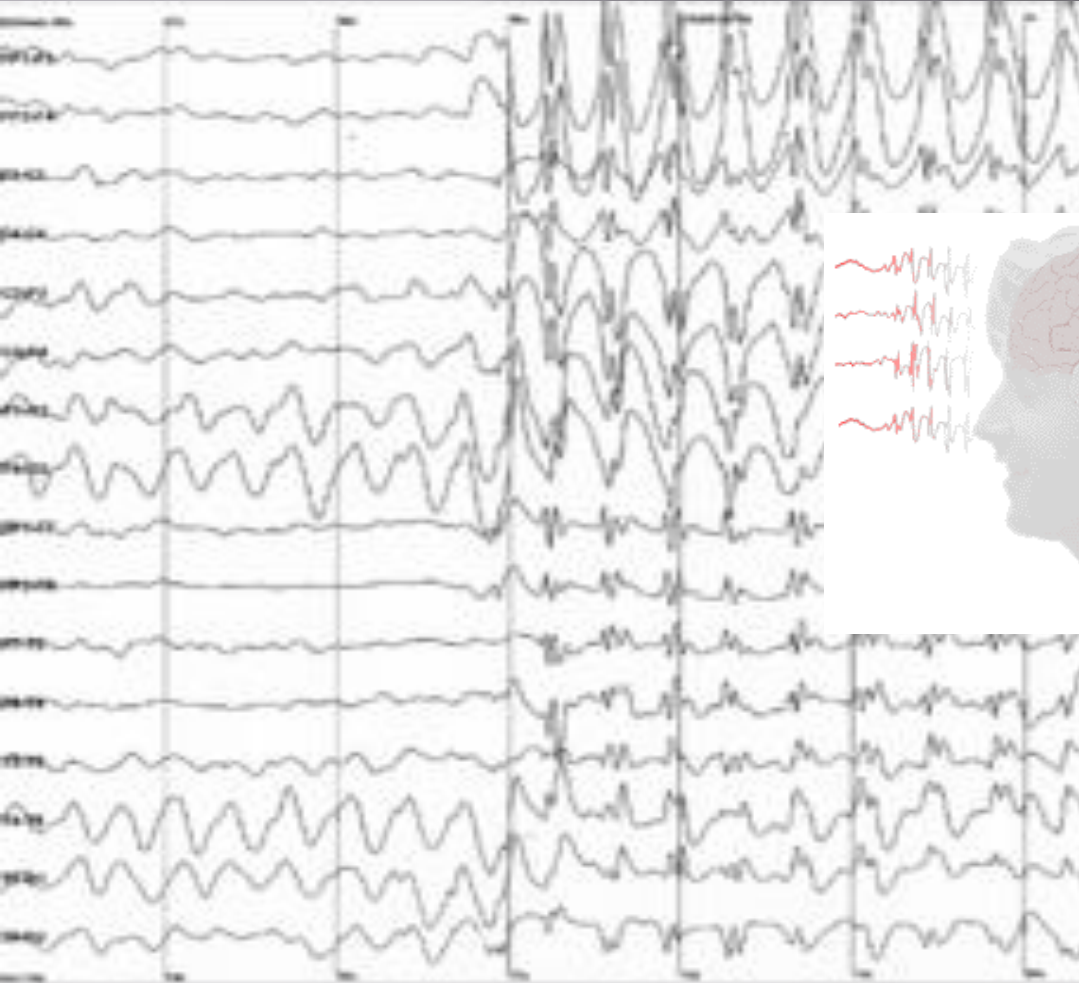
Investigations

MRI

- Lesional
 - Tumor
 - Vascular
 - Trauma
 - Developmental
 - Mesial Temporal Sclerosis
- Non lesional



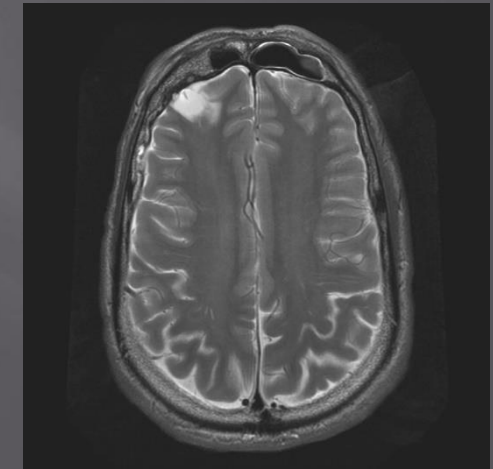
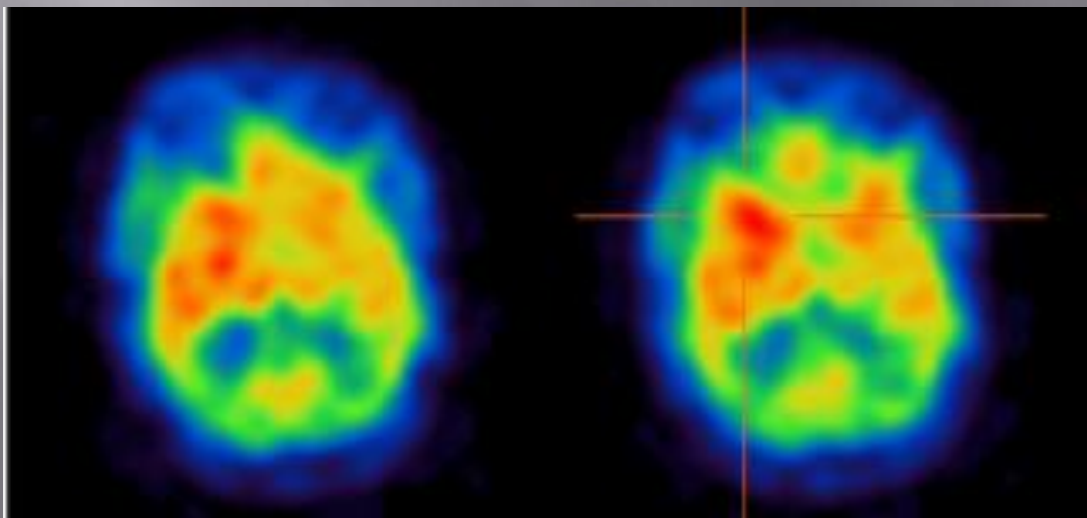
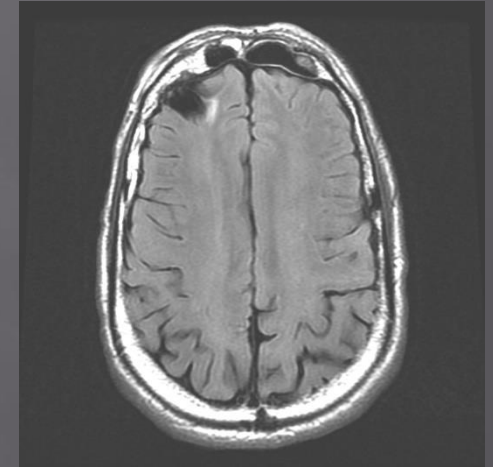
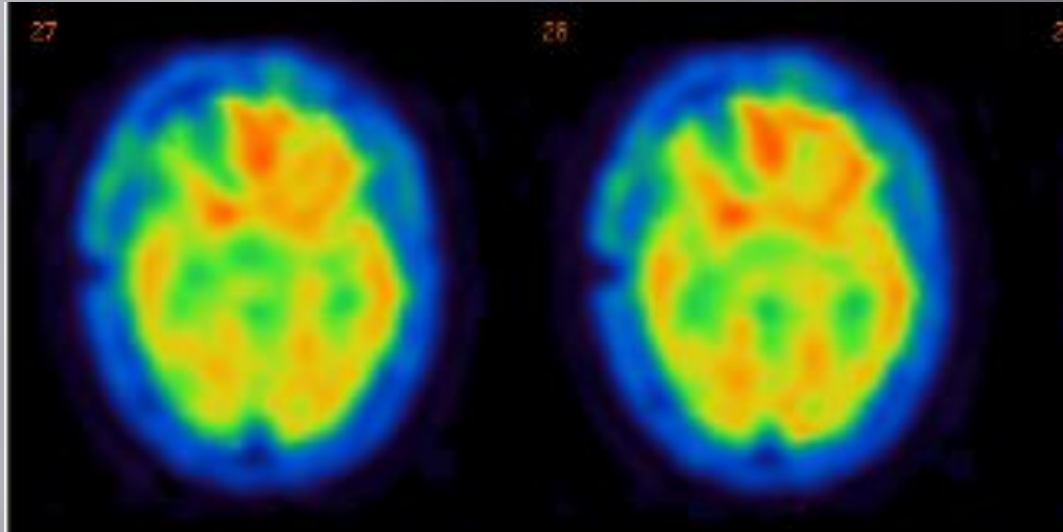
EEG



VEM



Nuclear Medicine



Cognitive Testing Neuropsychology

▣ Intelligence

▣ Memory

■ Verbal

■ Visual

▣ Language



Treatment

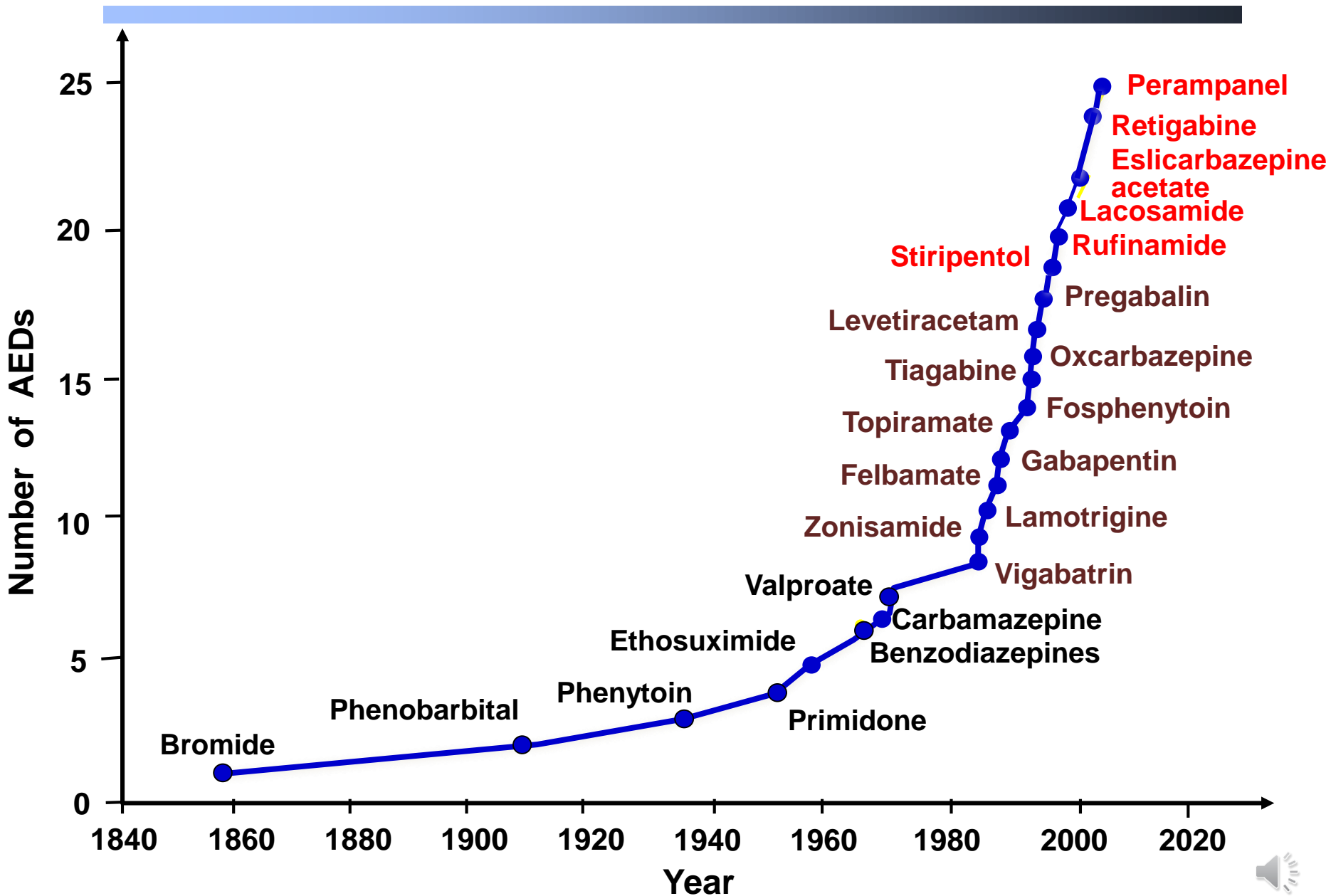
Medical



Surgical

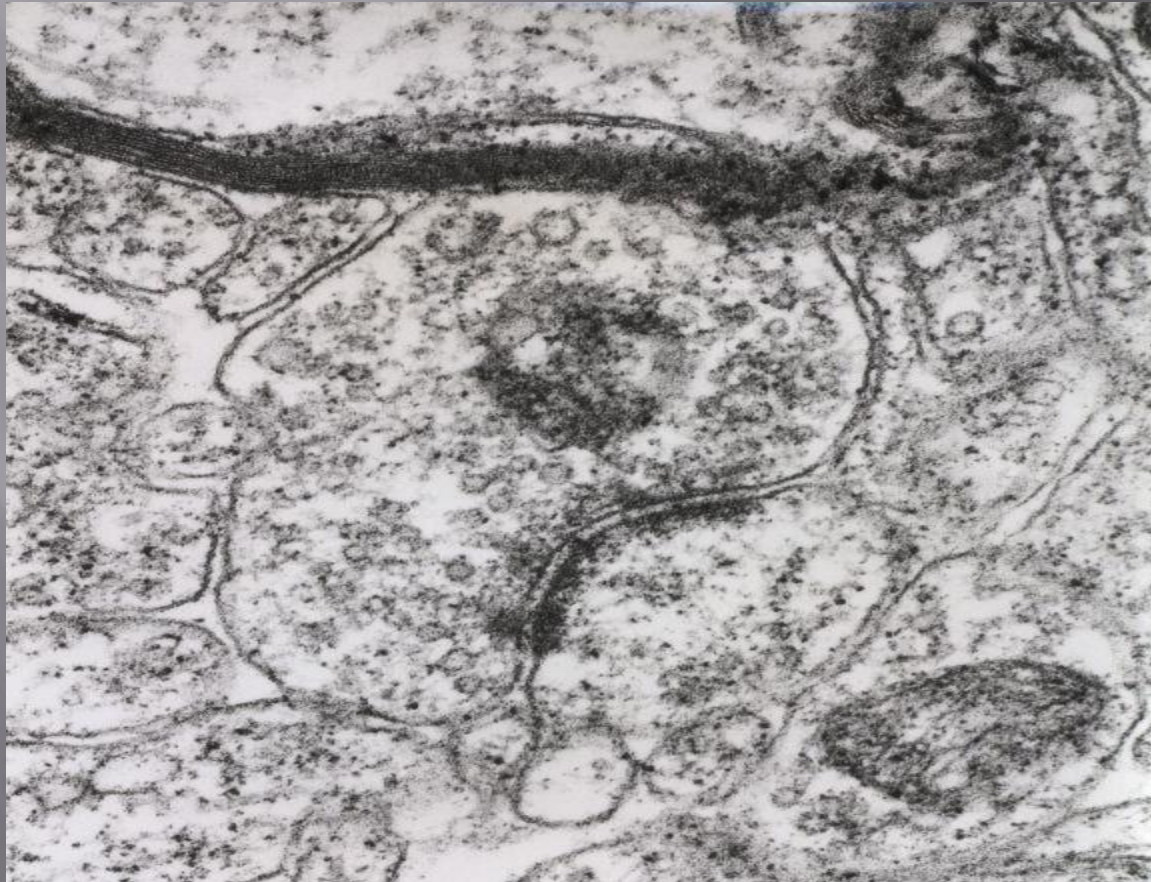


AEDs over the Years



Mechanism of Action

- *Current antiepileptic drugs are thought to act mainly by two main mechanisms:*

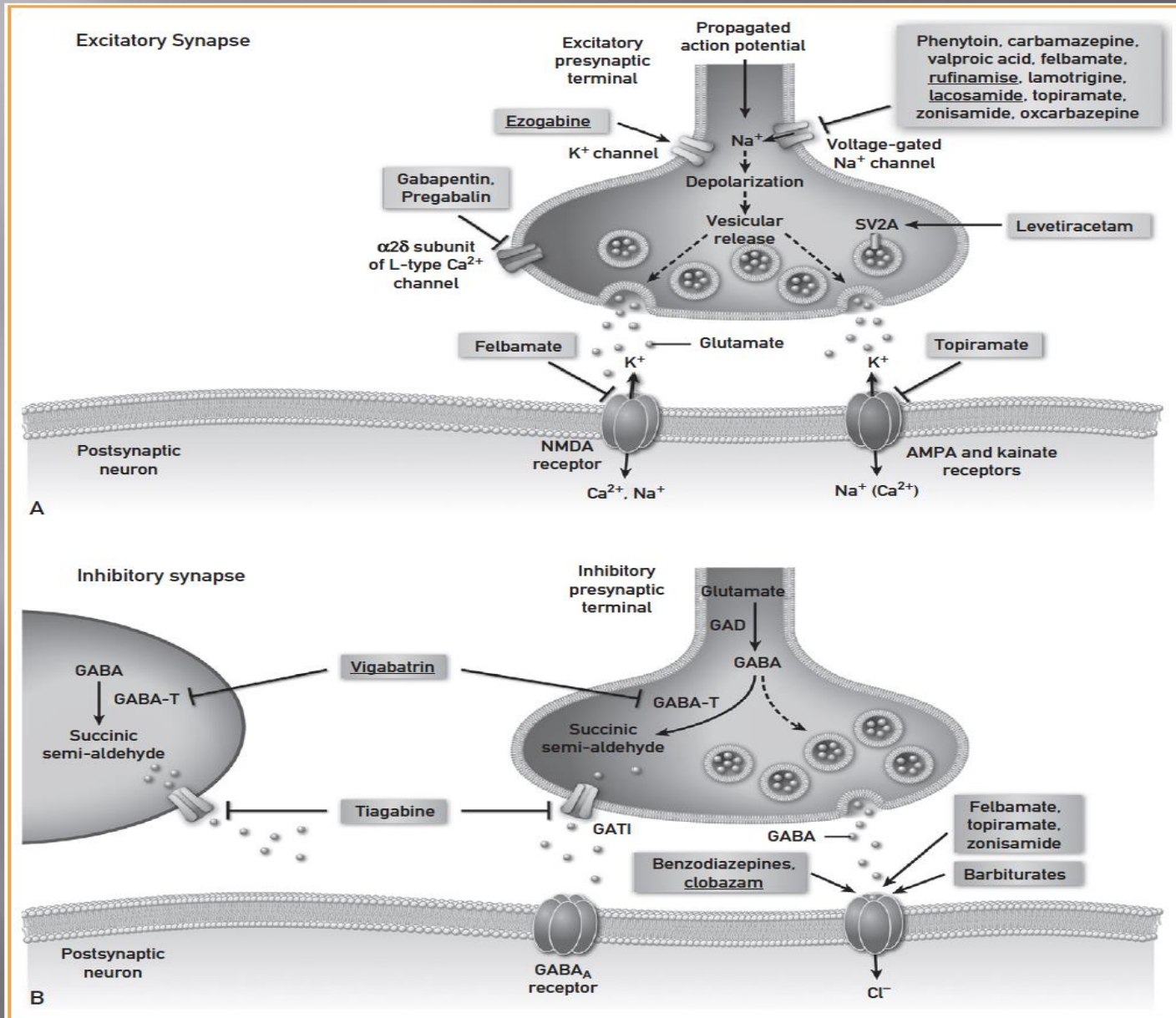


Mechanism of Action

- Reducing electrical excitability of cell membranes, possibly through inhibition of **sodium channel**.
- **Enhancing GABA**. This may be achieved by
 - inhibiting GABA-transaminase
 - Or
 - by drugs with direct GABA-agonist properties.



Mechanism of action of different AED



Clinical Uses of Antiepileptic Drugs

- ▣ *Tonic-clonic (grand mal) seizures*: **phenytoin, valproate**. Use of single drug is preferred when possible, because of risk of pharmacokinetic interactions.
- ▣ *Partial (focal) seizures*: **carbamazepine, valproate**; **clonazepam** or **phenytoin** are alternatives.
- ▣ *Absence seizures (petit mal)*: **ethosuximide** or **valproate**.
- ▣ *Myoclonic seizures*: **valproate** or **clonazepam**.



GENERALIZED-ONSET TONIC-CLONIC	FOCAL	TYPICAL ABSENCE	ATYPICAL ABSENCE, MYOCLONIC, ATONIC
First-Line			
Valproic acid Lamotrigine Topiramate	Lamotrigine Carbamazepine Oxcarbazepine Phenytoin Levetiracetam	Valproic acid Ethosuximide	Valproic acid Lamotrigine Topiramate
Alternatives			
Zonisamide ^a Phenytoin Carbamazepine Oxcarbazepine Phenobarbital Primidone Felbamate	Topiramate Zonisamide ^a Valproic acid Tiagabine ^a Gabapentin ^a Lacosamide ^a Phenobarbital Primidone Felbamate	Lamotrigine Clonazepam	Clonazepam Felbamate

^aAs adjunctive therapy.

Basic rules for drug treatment

- ▣ Drug treatment should be simple, preferably using one anticonvulsant (monotherapy). “Start low, increase slow”.
- ▣ Add-on therapy is necessary in some patients...
- ▣ If patient is seizure-free for three years, withdrawal of pharmacotherapy should be considered.
- ▣ It should be performed very carefully and slowly! 20% of pts will suffer a further sz within 2 yrs.



Seizure Freedom with AED use

- ▣ 1st drug ----- seizure free (47%)
- ▣ 2nd drug----- seizure free (14%)
- ▣ 3rd drug----- seizure free (3%)

- ▣ Medication resistant 36%



Drug resistant epilepsy

- Failure of at least TWO antiepileptic medications to completely control seizures
 - Appropriately chosen for seizure type
 - Taken as prescribed
 - Well tolerated (not failed due to side effects)



Epilepsy treatment and pregnancy

- The risk of teratogenicity is well known (~5%), especially with valproates, but withdrawing drug therapy in pregnancy is more risky than continuation.
- **All** antiepileptic medications are not safe, however lamotrigine is the safest.
- Epileptic females must be aware of this problem and thorough family planning should be recommended.
- Over 90% of pregnant women with epilepsy will deliver a normal child.



Antiepileptic medication adverse effect

Risk of in utero AED exposure

- Major Congenital Malformations (MCM)
 - 1.6 – 2.1% in general population
 - Studies comparing to WWE on no AEDs
 - Increased w/ AEDs in 2 Class II studies (OR 3.9 (1.29-11.9))
 - No increased risk w/ AEDs in 1 Class I study
- Minor anomalies
- Small for Gestational Age (SGA)
- Developmental Disability
- Microcephaly



Spina bifida is a neural tube defect (NTD) involving incomplete formation of the spine





Stevens-Johnson syndrome







Tegretol® 200
Carbamazepin.
50 Tabletten 200 mg

EPANUTIN™
100 mg HARD CAPSULES
Phenytoin sodium
Each capsule contains
100 mg Phenytoin sodium.
30 HARD CAPSULES



Gingival Hyperplasia Induced by Phenytoin



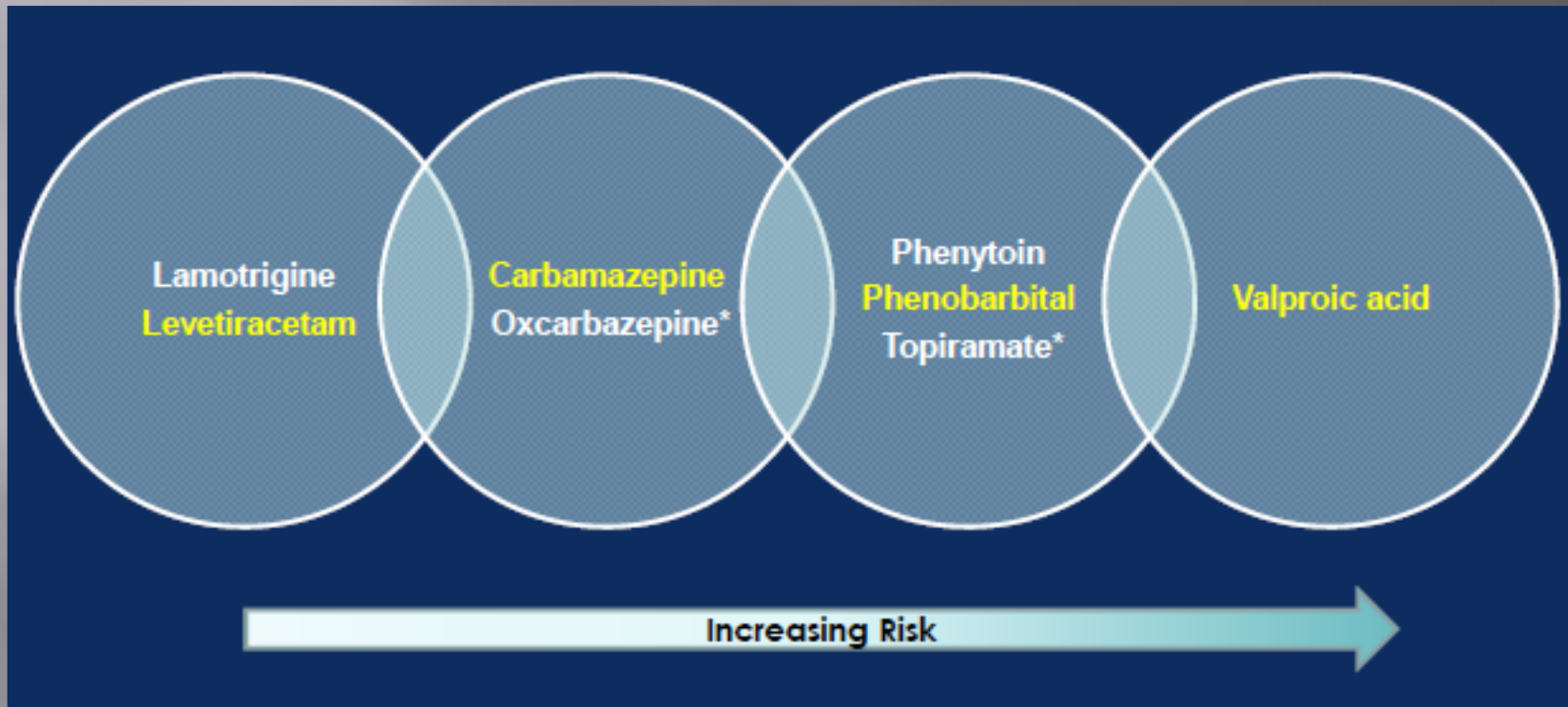
New Eng J Med. 2000;342:325.

After Withdrawal of Phenytoin



AED	Major or Potentially Life Threatening	Minor Side Effects
Phenobarbital	Hepatotoxicity, Steven's-Johnson Syndrome, connective tissue disorders	Sedation, depression, behavioral effects, osteopenia
Phenytoin (Dilantin)	Pancytopenia, hepatotoxicity, Steven's Johnson Syndrome	Dizziness, ataxia, gum hyperplasia, hirsutism, neuropathy, osteopenia
Carbamazepine (Tegretol)	Agranulocytosis*, aplastic anemia*, hepatotoxicity, Steven's-Johnson Syndrome	Dizziness, ataxia, hyponatremia, osteopenia
Valproate (Depakote)	Hepatotoxicity*, thrombocytopenia, pancreatitis*	Weight gain, alopecia, tremor, GI upset, osteopenia
Felbamate (Felbatol)	Aplastic anemia*, hepatotoxicity*	Anorexia, insomnia
Gabapentin (Neurontin)	None	Sedation, weight gain
Lamotrigine (Lamictal)	Stevens-Johnson Syndrome*	Dizziness, ataxia, insomnia
Topiramate (Topamax)	Kidney stones, oligohidrosis, glaucoma	Parasthesias, cognitive impairment, weight loss
Tiagabine (Gabatril)	Spike-wave stupor	Tremor, sedation, impaired concentration
Levetiracetam (Keppra)	None	Sedation, behavioral changes
Oxcarbazepine (Trileptal)	Steven's-Johnson Syndrome	Ataxia, diplopia, hyponatremia
Zonisamide (Zonegran)	Kidney stones, oligohidrosis, rash	Parasthesias, weight loss
Pregabalin (Lyrica)	None	Sedation, weight gain
Lacosamide (Vimpat)	None	Dizziness, nausea, fatigue
Rufinamide (Banzel)	None	Somnolence, dizziness, nausea
Vigabatrin (Sabril)	Peripheral visual field defect	Anemia, neuropathy, weight gain

Teratogenic Risk Profiles of Antiepileptic Drugs

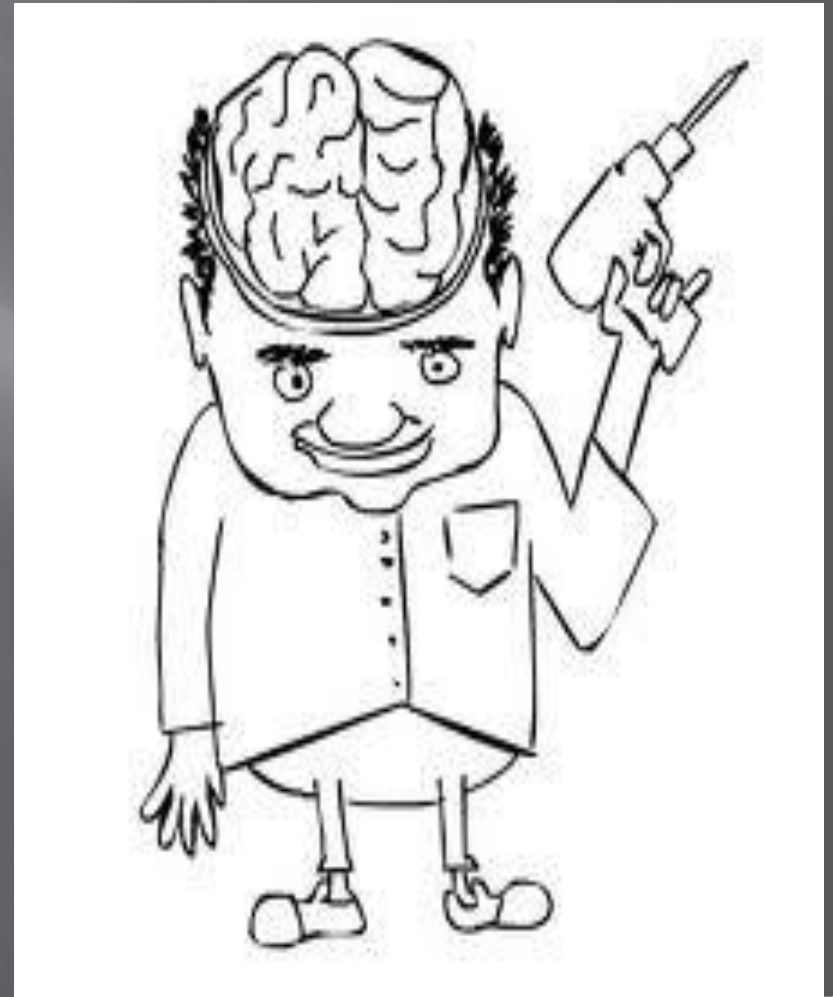


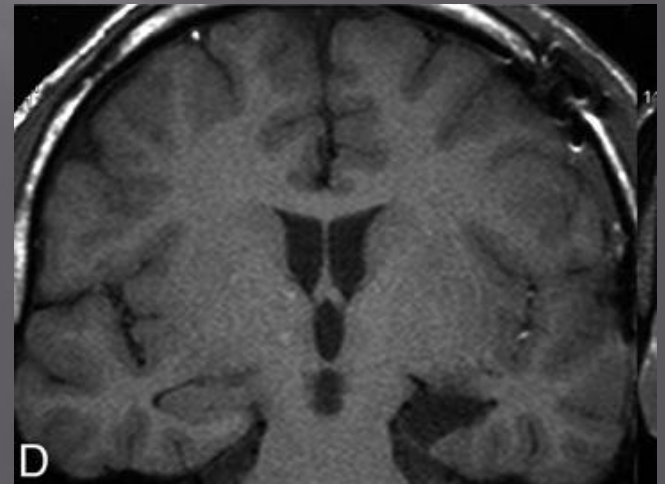
* = neurodevelopmental outcomes are not yet known

When to stop antiepileptic medications?

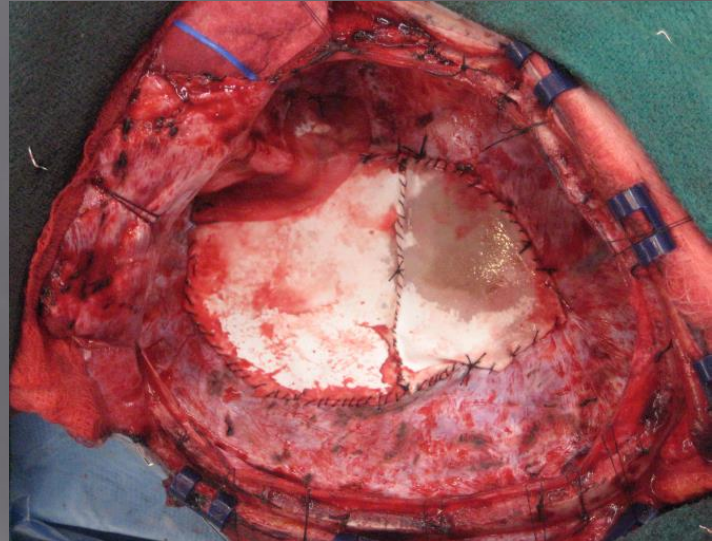
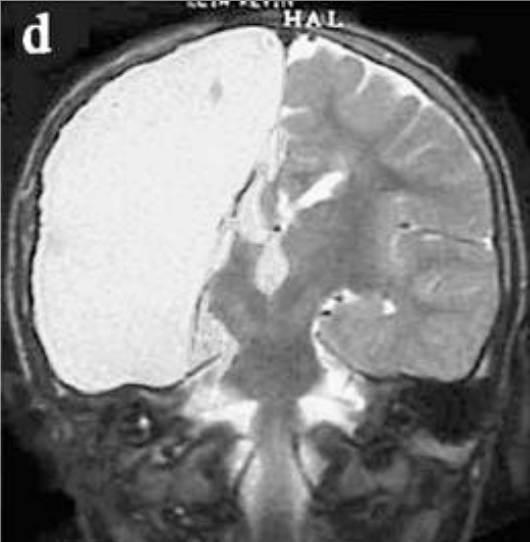
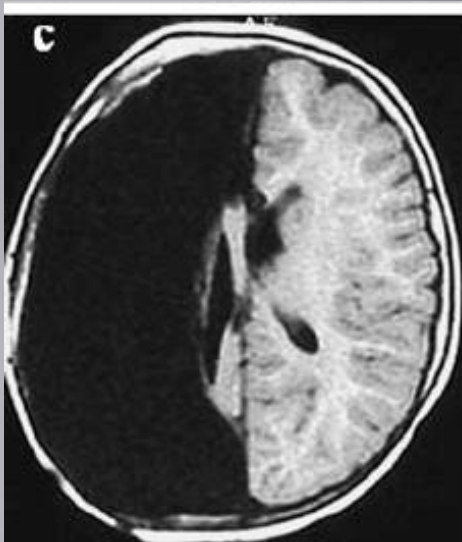


Surgery

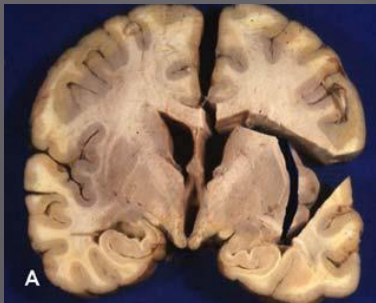
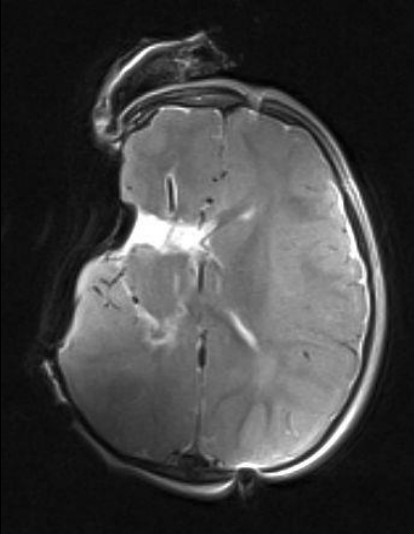
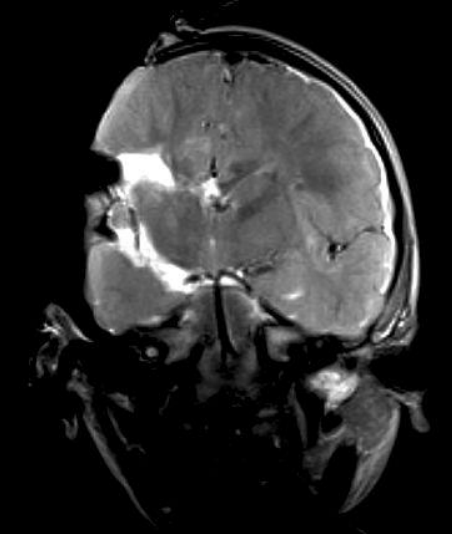




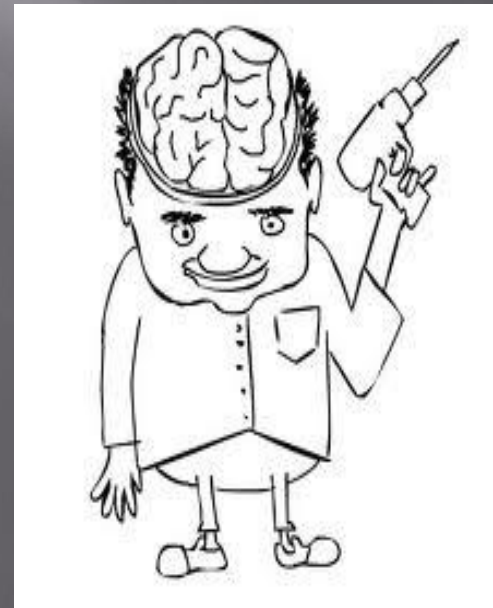
▣ Hemispherectomy



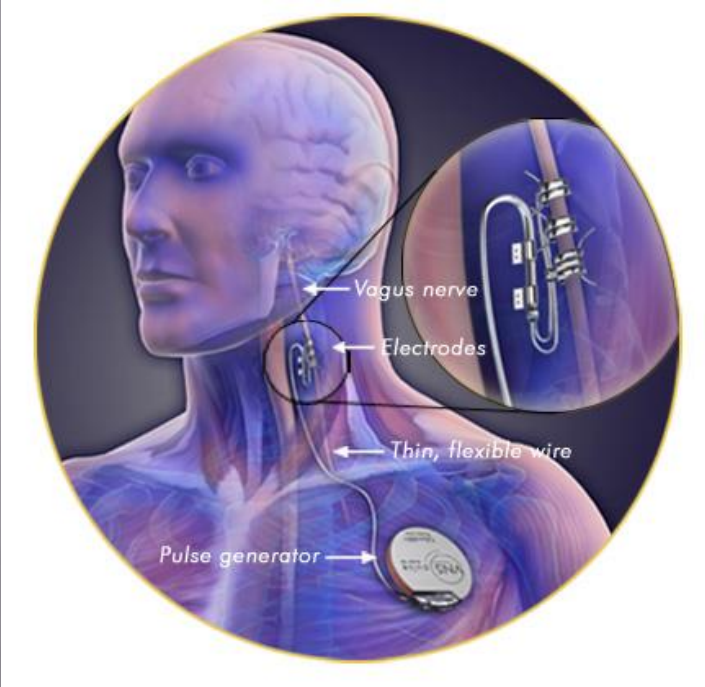
• Hemispherotomy



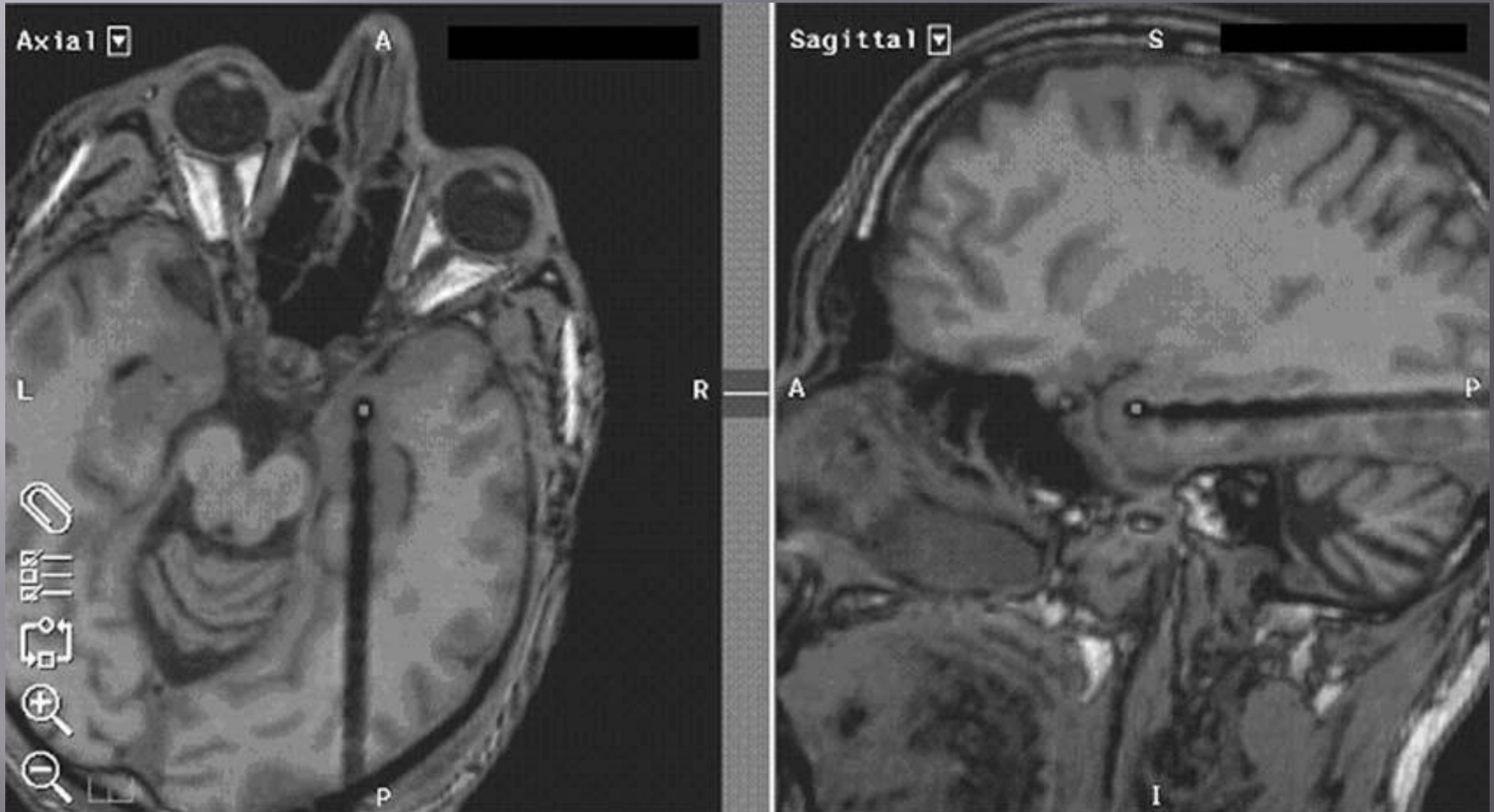
If my patient is not a good candidate for surgery?



VNS



DBS





Thank
You

