EPILEPSY

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Objectivs

- 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.
  - Trigers 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

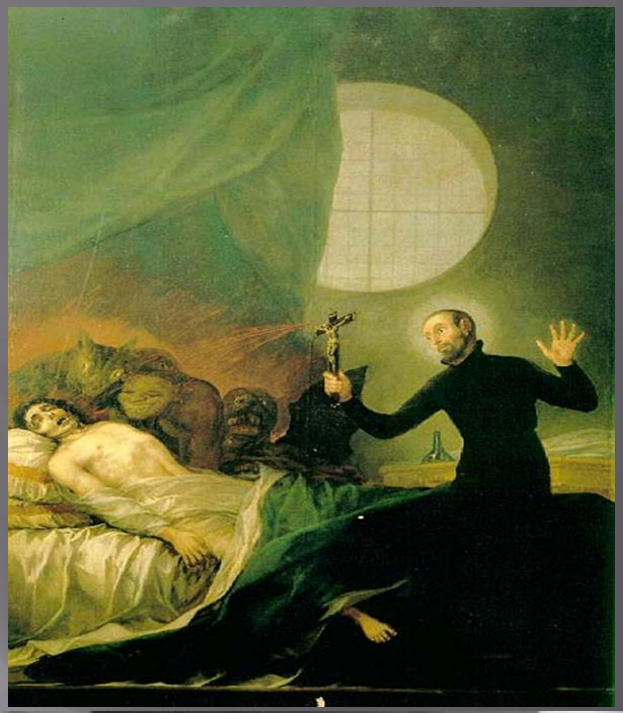
- One of the earliest descriptions of a secondarily generalized tonic-clonic seizure was recorded over 3000 years ago in Mesopotamia.
- The seizure was attributed to the god of the moon.
- Epileptic seizures were described in ancient cultures, including those of China, Egypt, and India.

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.

Epidemiology

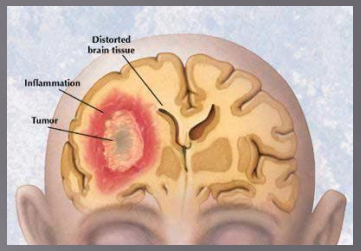
Epidemiology and course

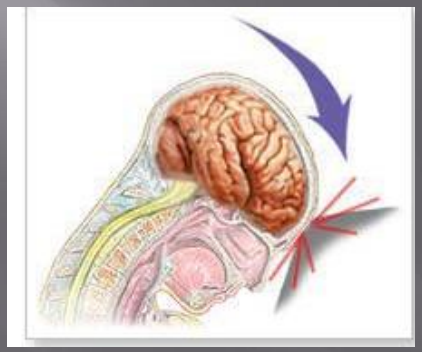
- 5% of the population suffer a single sz at some time
- 0.5-1% of the population have recurrent sz = EPILEPSY

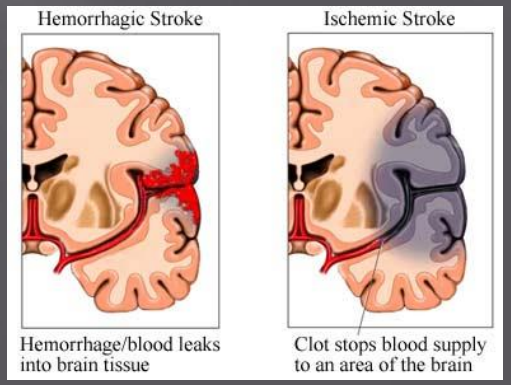
- 70% = well controlled with drugs (prolonged remissions)
- 30% epilepsy at least resistant to drug treatments = INTRACTABL EPILEPSY.

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)

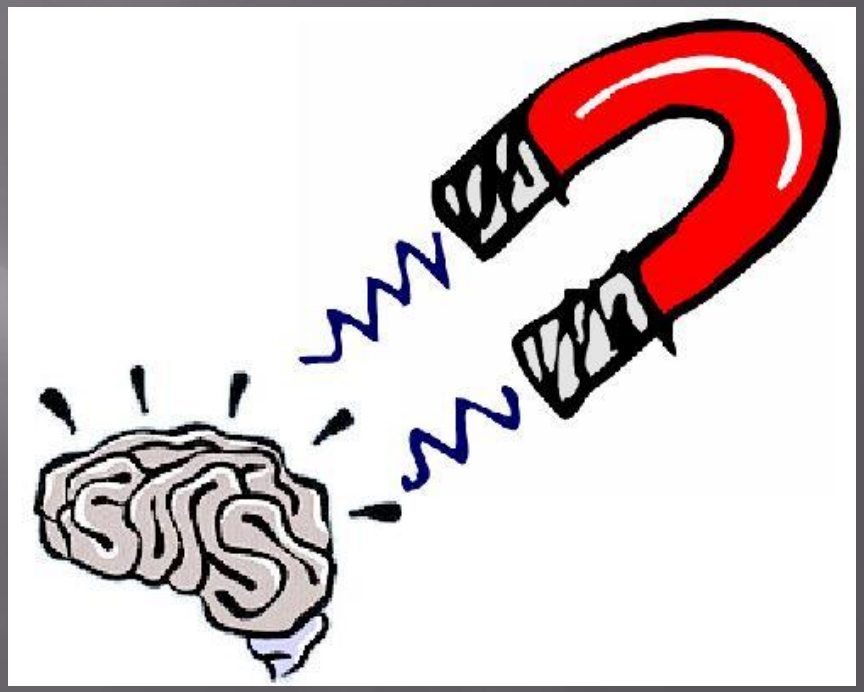






Triggers for seizure:

- Poor compliance
- Sleep deprevation
- Stress
- Alcohol
- Infection
- Menstrual cycle

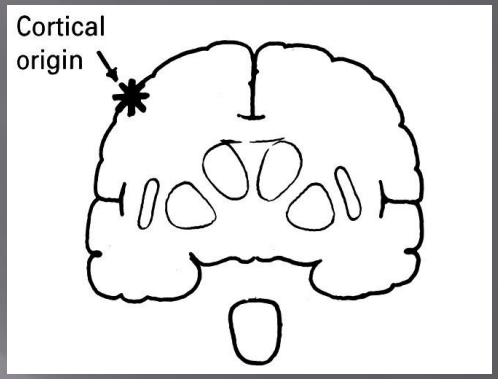



Status Epilepticus

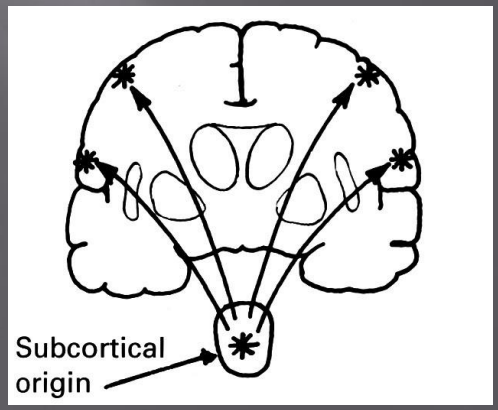
Seizure Classification

Epilepsy - Classification

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



- Generalised seizures

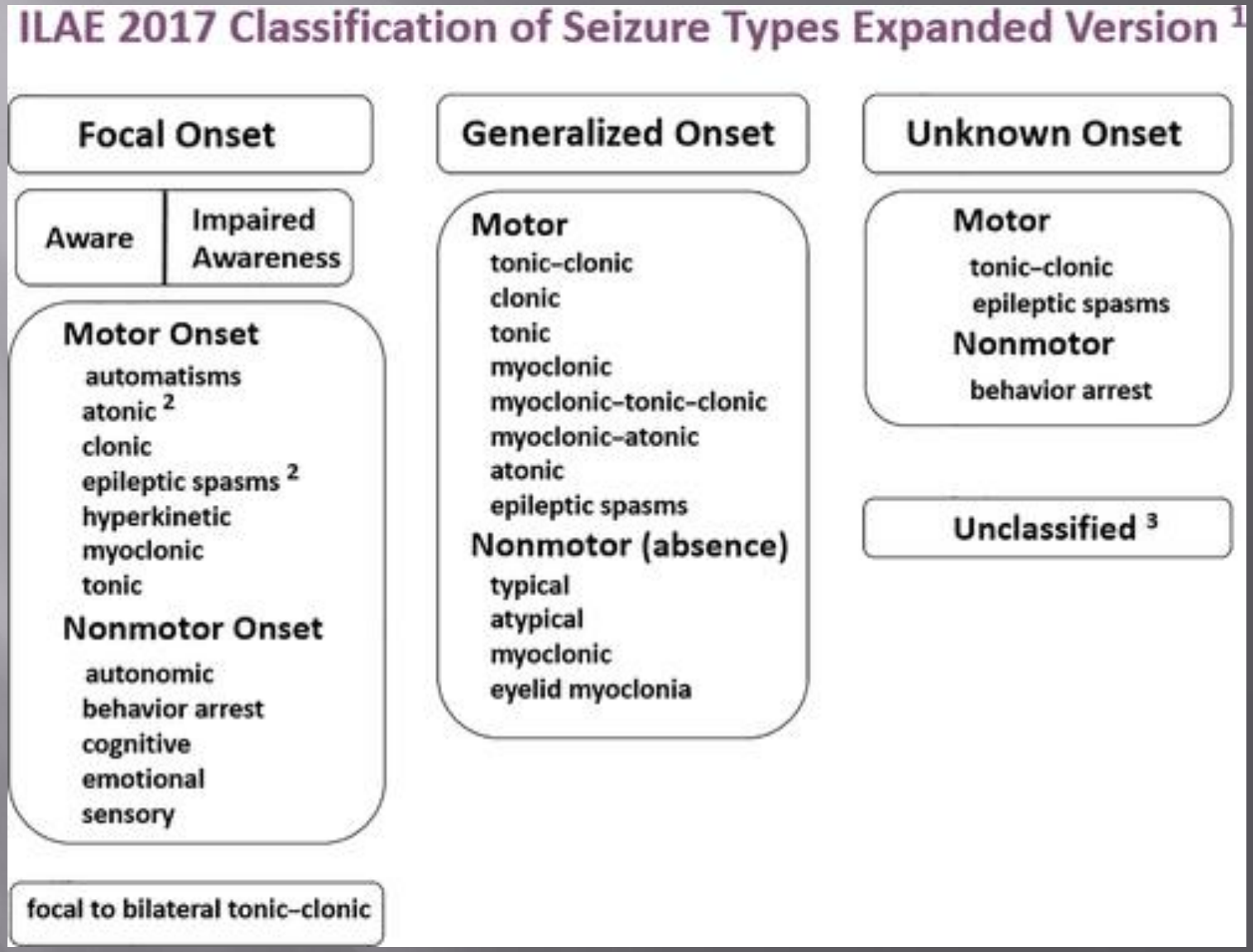


- Unclassified seizures

INTERNATIONAL CLASSIFICATION OF SEIZURES 1981

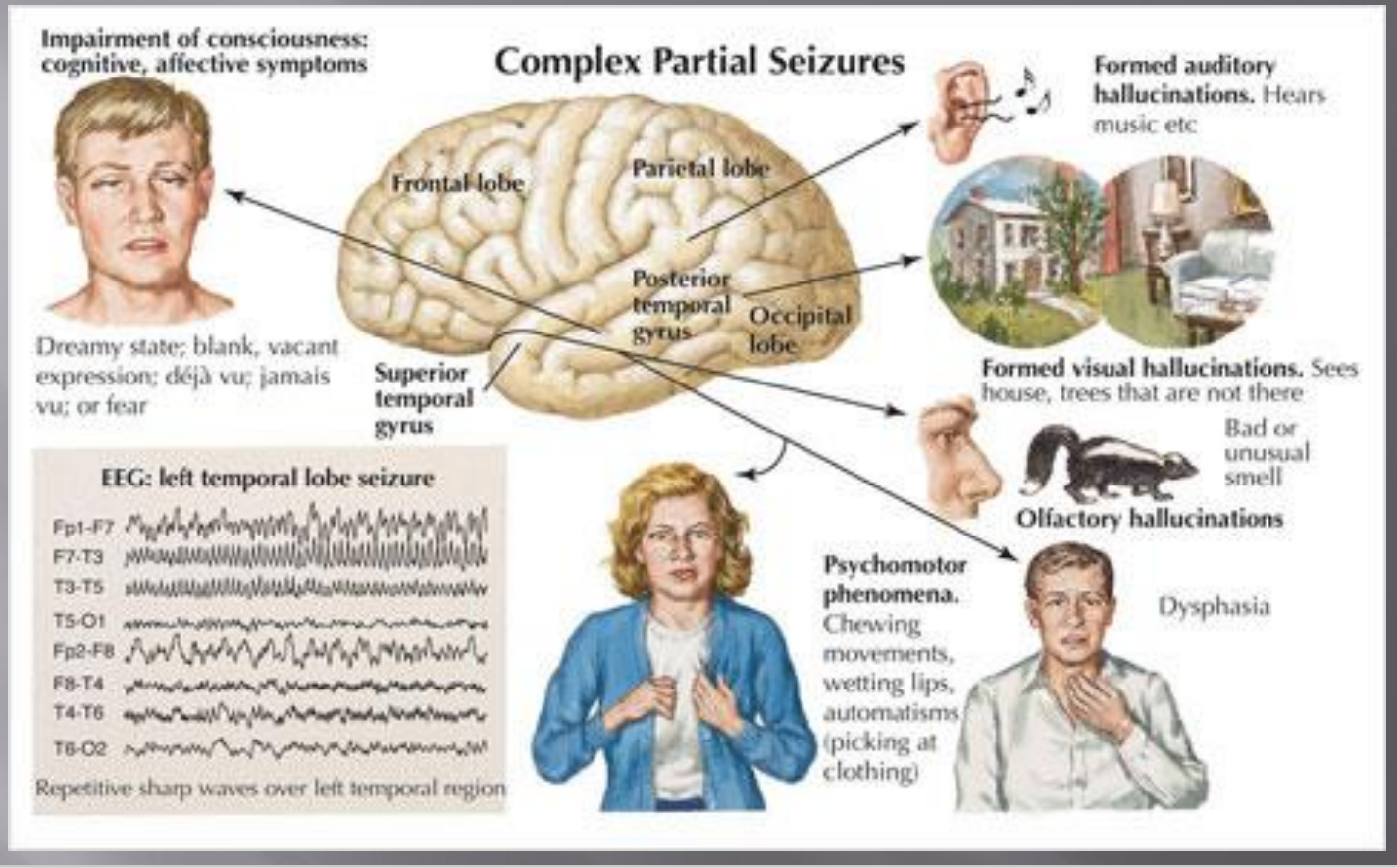
- **Partial Seizures (start in one place)**
- **Simple (no loss of consciousness of memory)**
  - Sensory
  - Motor
  - Sensory-Motor
  - Psychic (abnormal thoughts or perceptions)
  - Autonomic (heat, nausea, flushing, etc.)
- **Complex (consciousness or memory impaired)**
  - With or without aura (warning)
  - 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

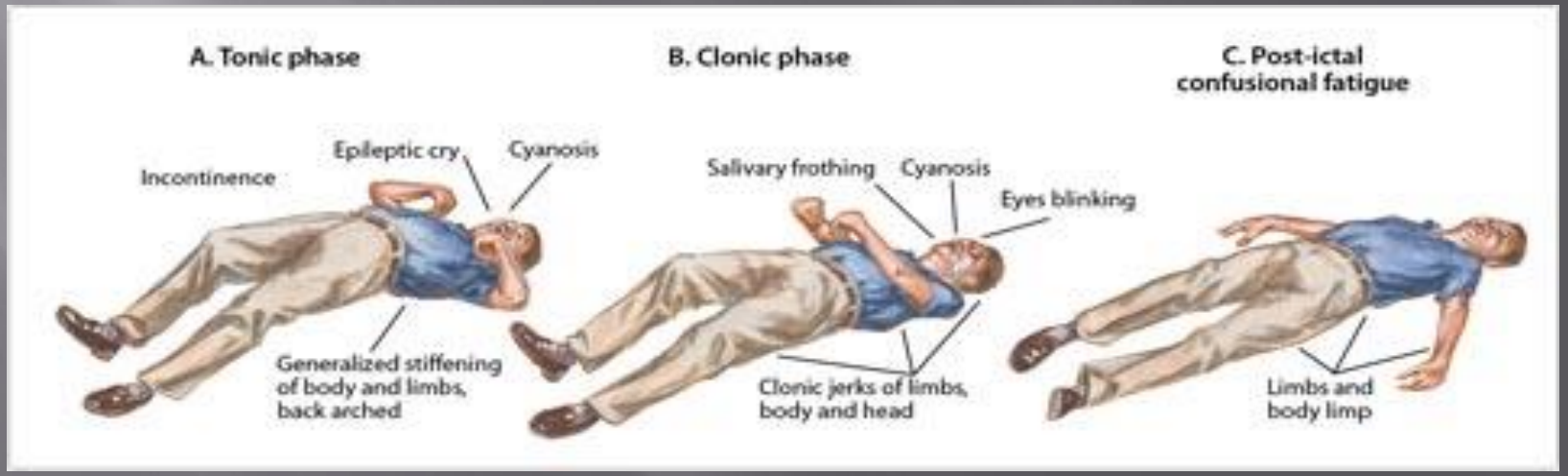
Dreifuss et al. From the Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia. 1981;22:489-501.



Fisher et al. Instruction manual for the ILAE 2017 operational classification of seizure types. Epilepsia doi: 10.1111/epi.13671

Seizure Semiology


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


A. Tonic phase
Incontinence
Epileptic cry
Cyanosis
Generalized stiffening of body and limbs, back arched
B. Clonic phase
Salivary frothing
Cyanosis
Eyes blinking
Clonic jerks of limbs, body and head
C. Post-ictal confusional fatigue
Limbs and body limp

VEDIO


10-08-99 TUE
10:54:53:0

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

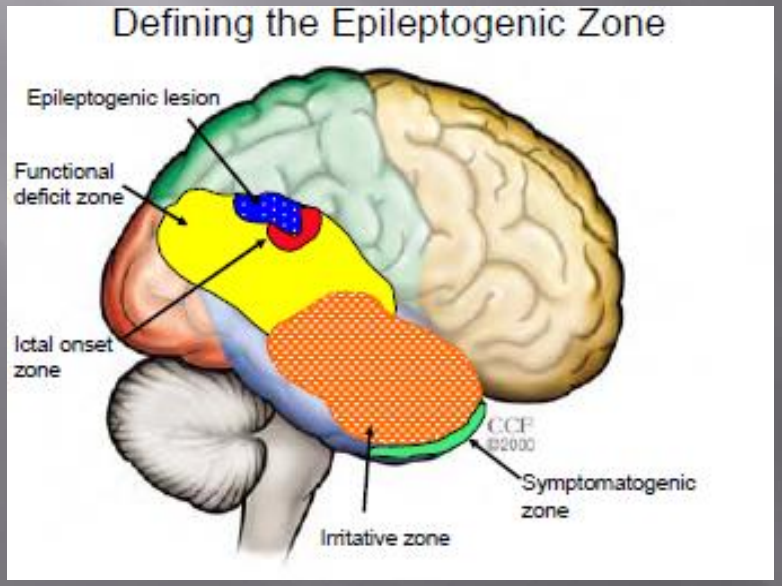
Clinical features	Cardiogenic syncope	Seizure disorders
Loss of consciousness	Typical	Common
Episode duration	Seconds	Minutes
Involuntary movements	Common	Typical
Amnesia	Yes	Yes
Arrhythmia	Common	Rare*
Electroencephalogram	Slow waves Flattening	Focal or general spike activity
Responsive to AEDs	No	Often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

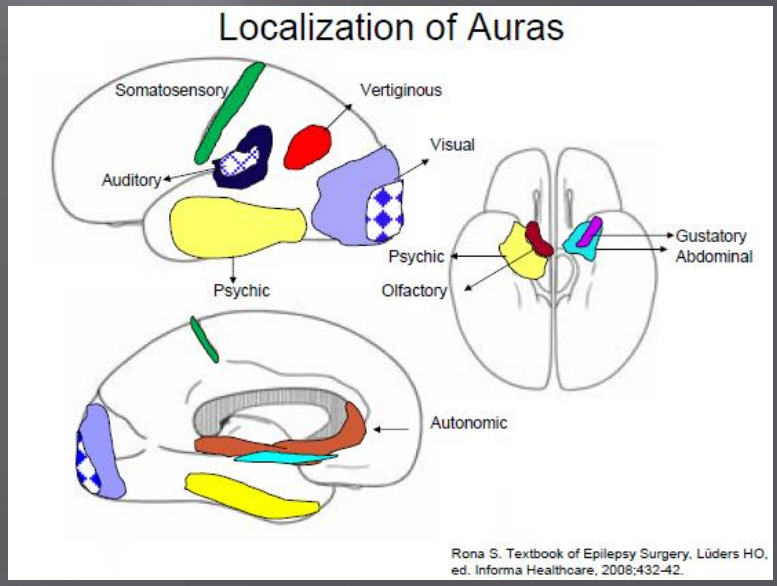
Bergfeldt L., Heart 2003

Seizure approch

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

Clinical history





Rona S. Textbook of Epilepsy Surgery, Lüders HO, ed. Informa Healthcare, 2008;432-42.

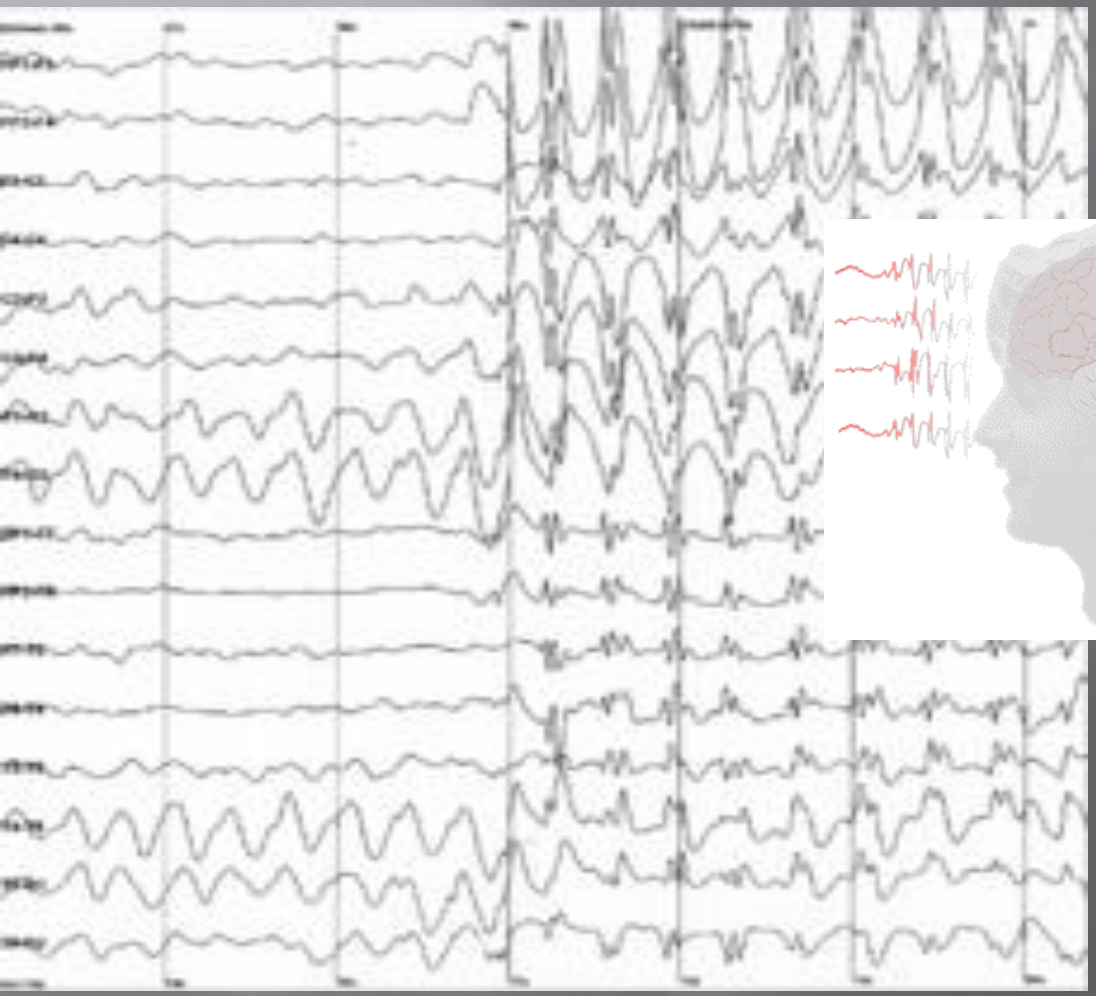
Questions that help clarify the type of seizure include the following:

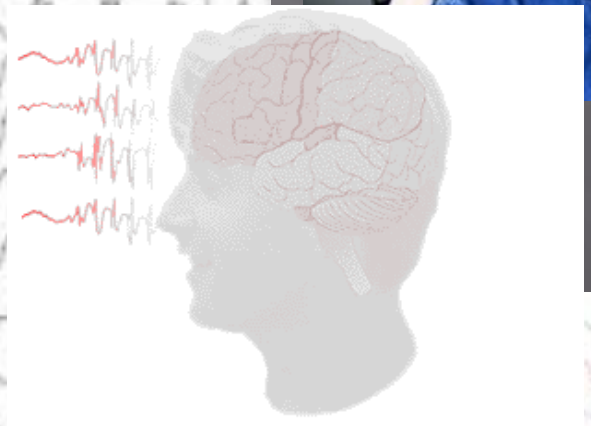
- Was any warning noted before the spell?
- What did the patient do during the spell?
- Was the patient able to relate to the environment during the spell ?
- How did the patient feel after the spell? How long did it take for the patient to get back to baseline condition?
- How long did the spell last?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

MRI

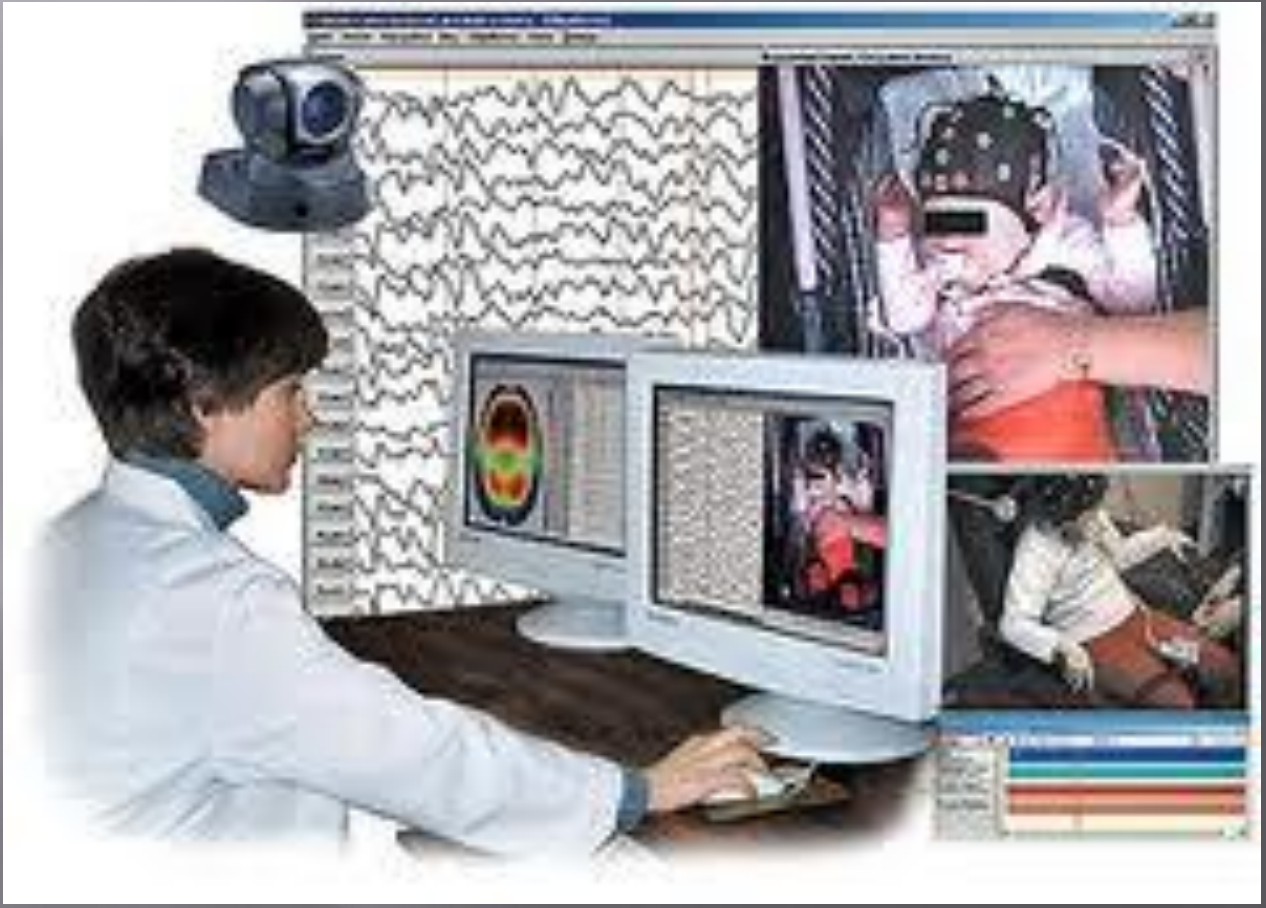
- Lesional
  - Tumor
  - Vascular
  - Trauma
  - Developmental
  - Mesial Temporal Sclerosis
- Non lesional

EEG

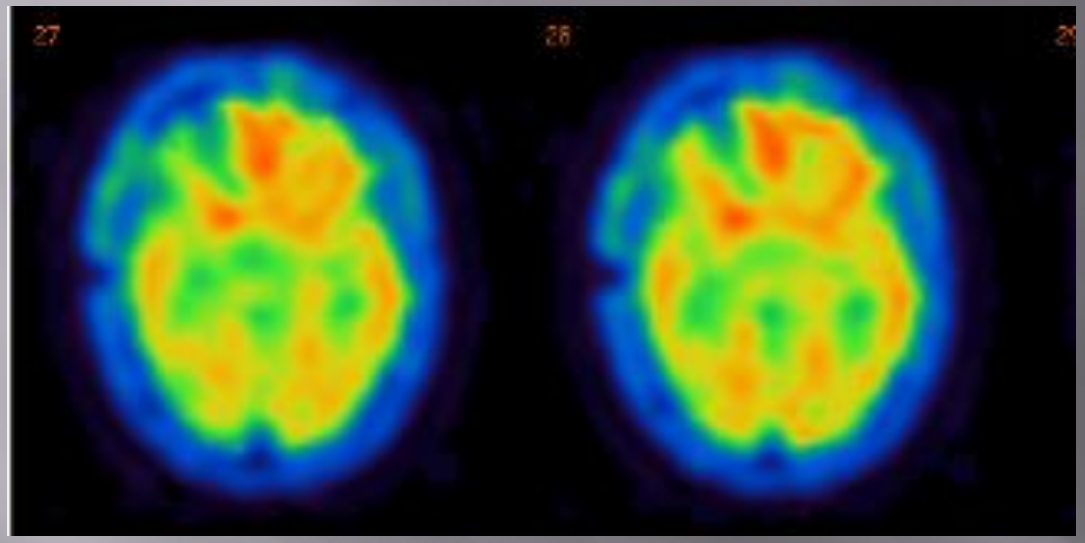


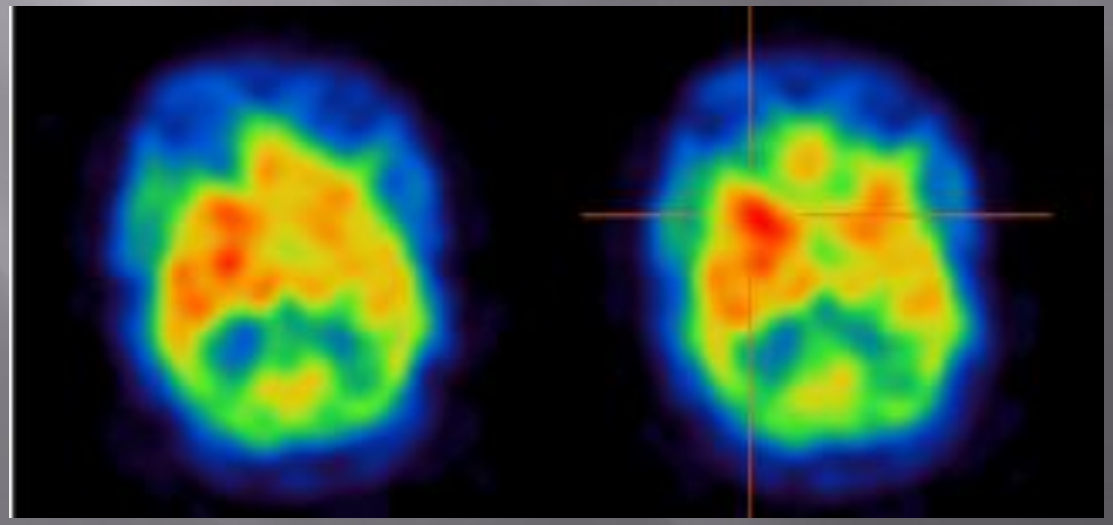


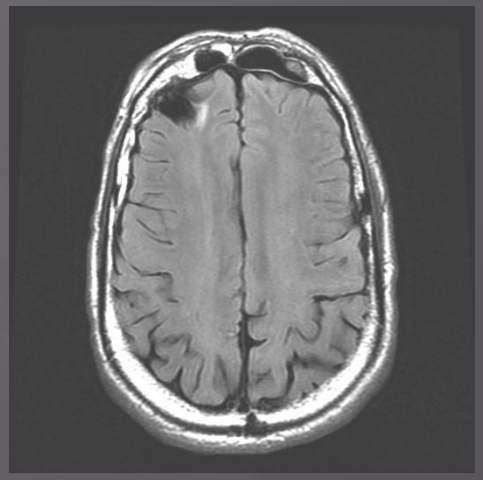
VEM

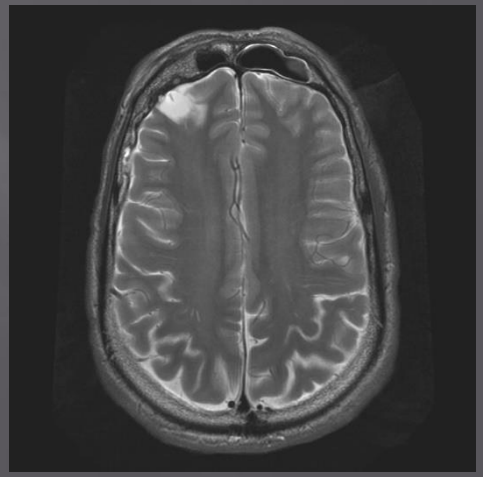


Nuclear Medicine









Cognitive Testing
Neuropsychology

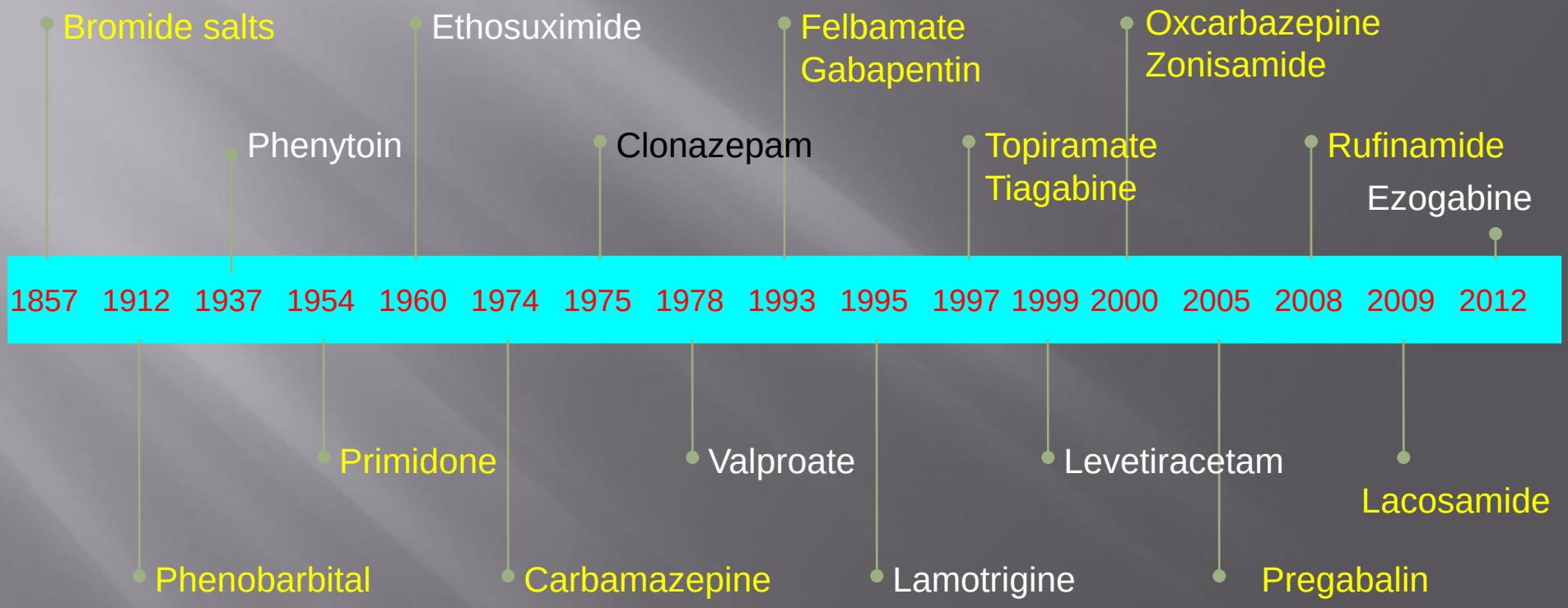
- Intelligence
- Memory
  - Verbal
  - Visual
- Language

Treatment

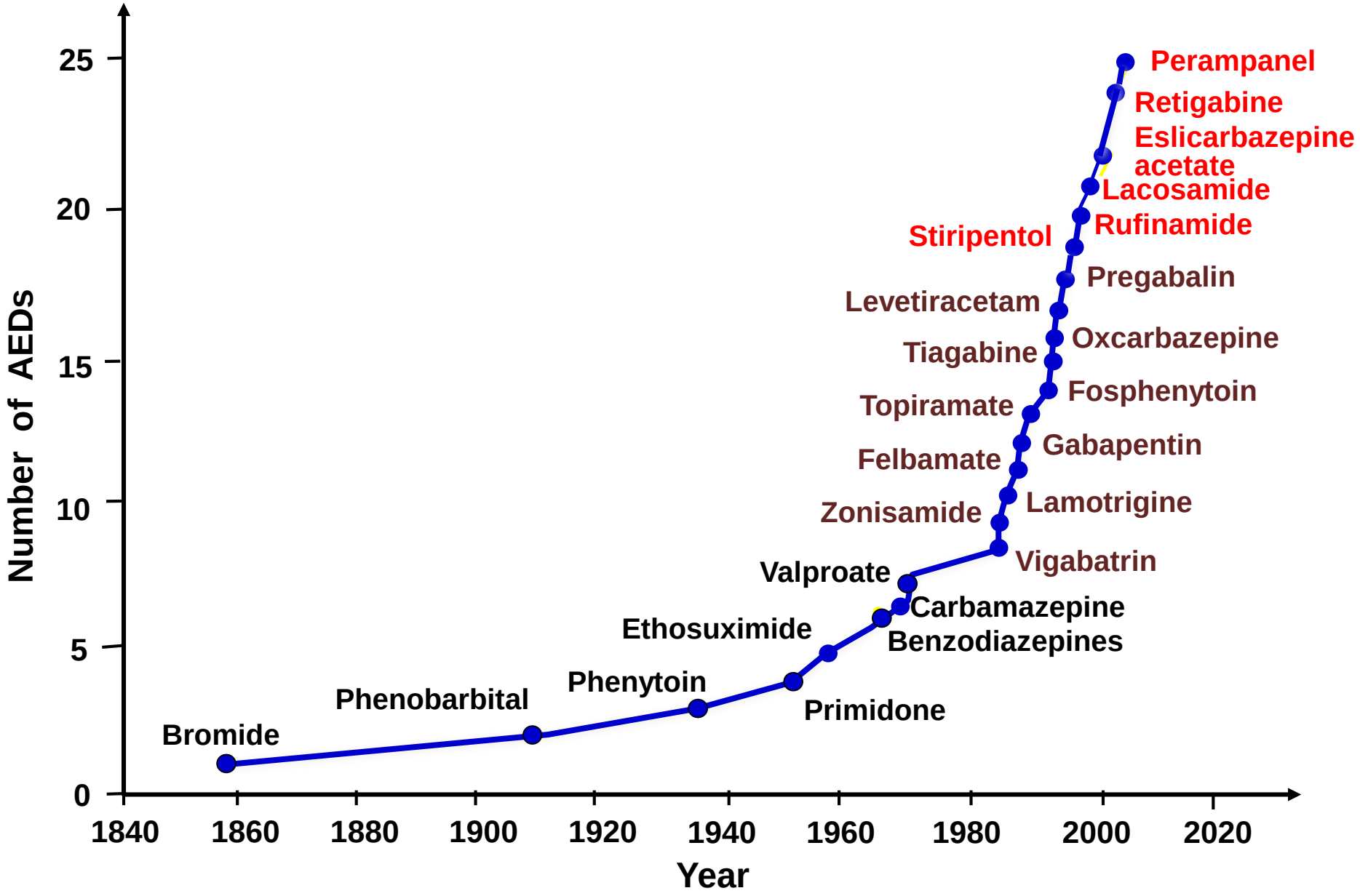
Medical

Surgical

Epilepsy Drug Development



AEDs over the Years



Mechanism of Action

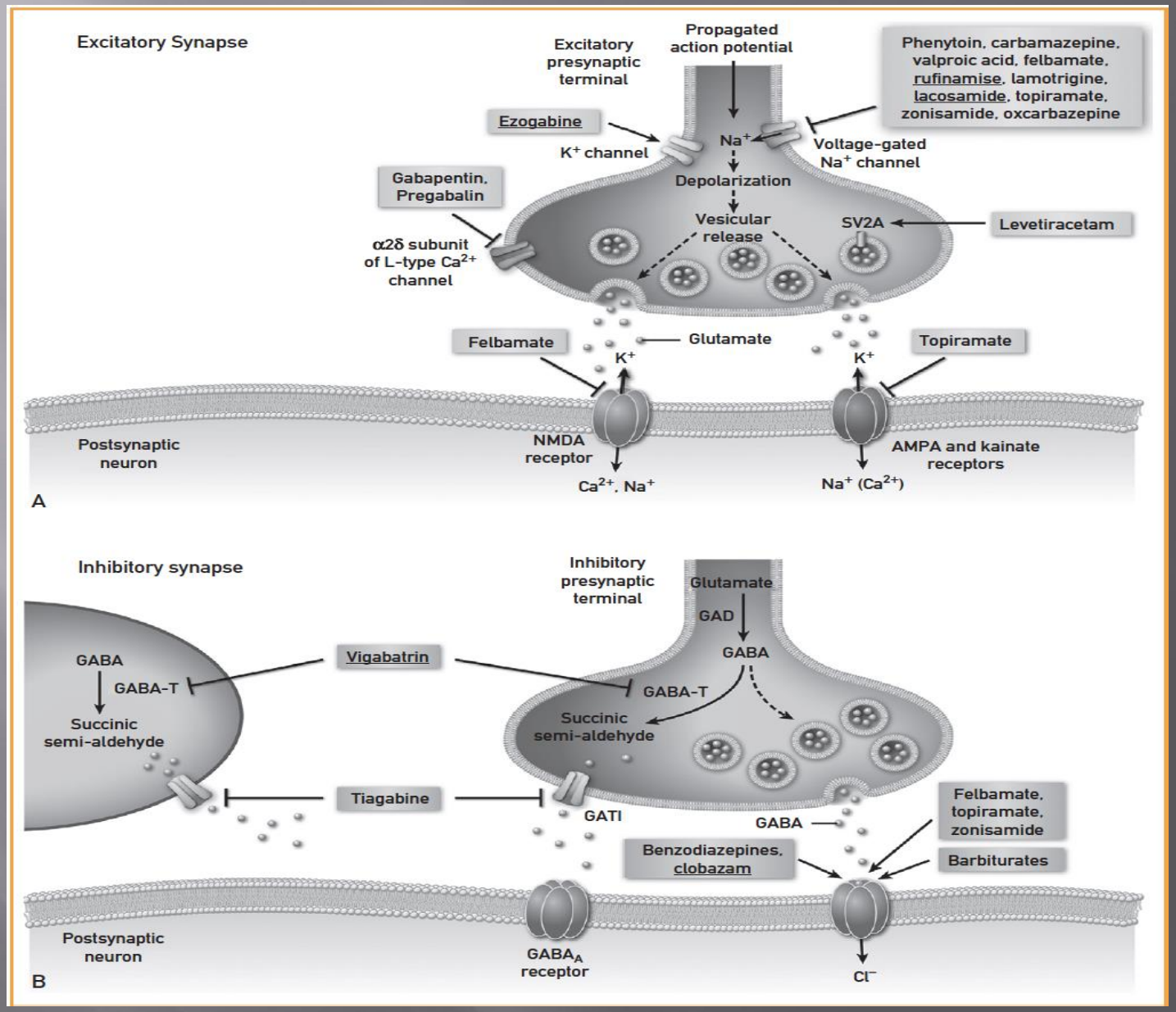
- *Current antiepileptic drugs are thought to act mainly by two main mechanisms:*

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**.

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.

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.

Seizure Freedom with AED use

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

- Medication resistant 36%

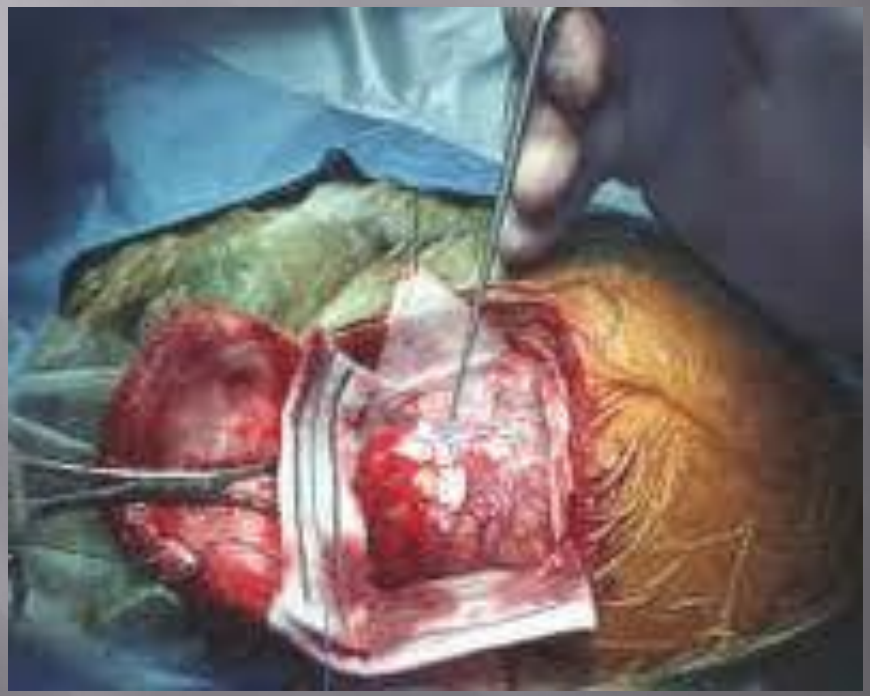
Kwan P, Brodie NEJM. 2000

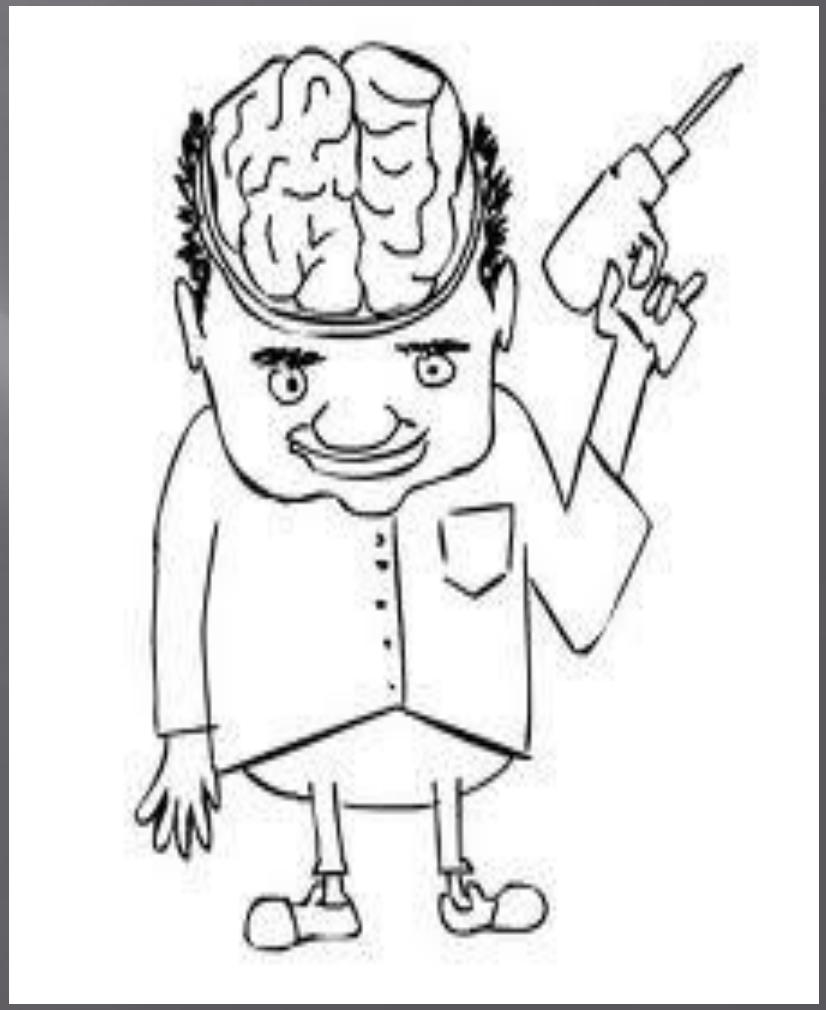
Drug resistant epilepsy

- 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)

When to stop antiepileptic medications?

Surgery



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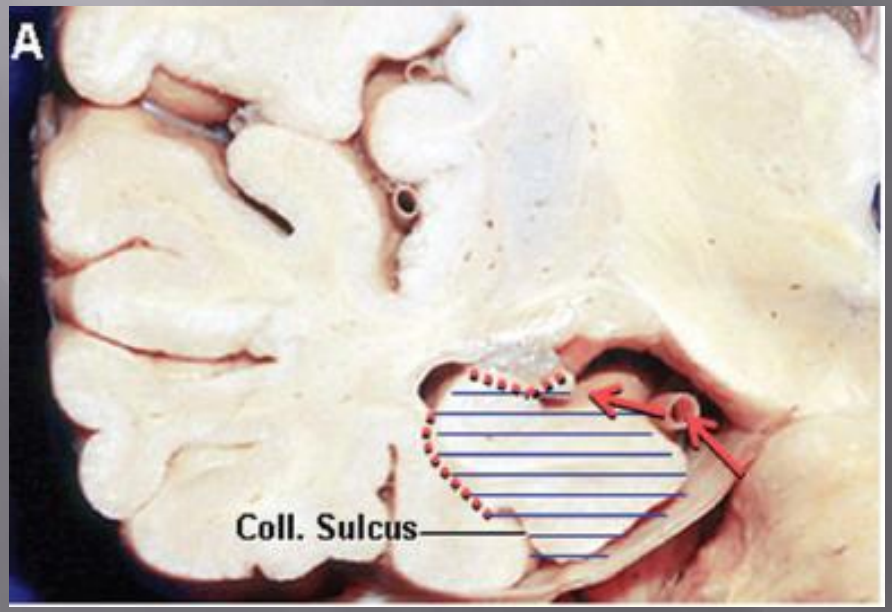
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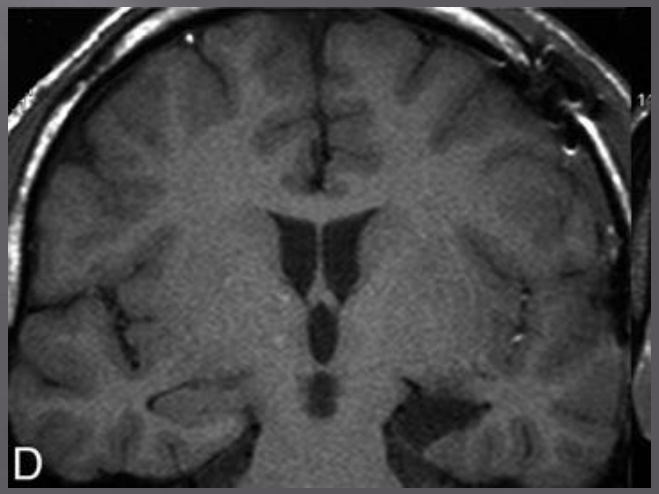
Coll. Sulcus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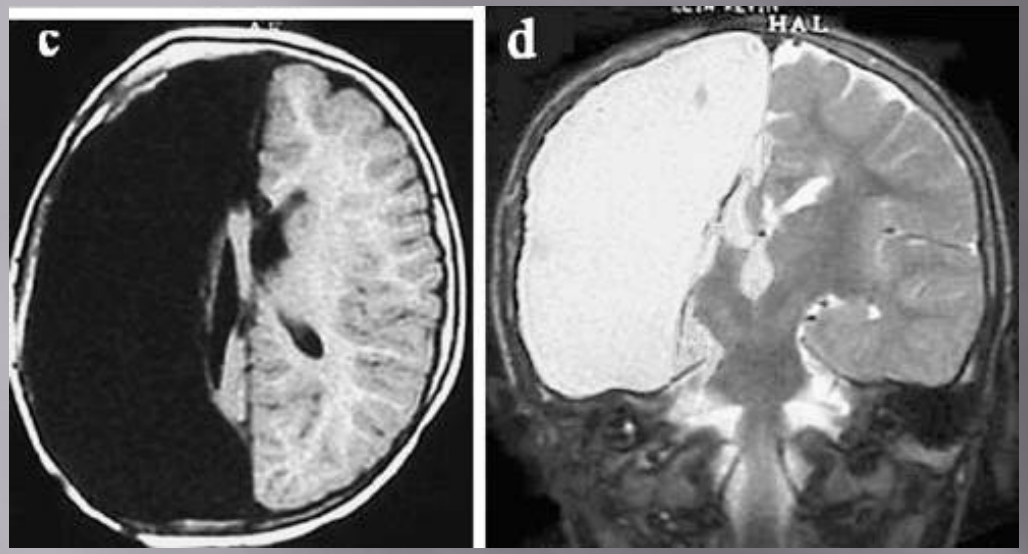
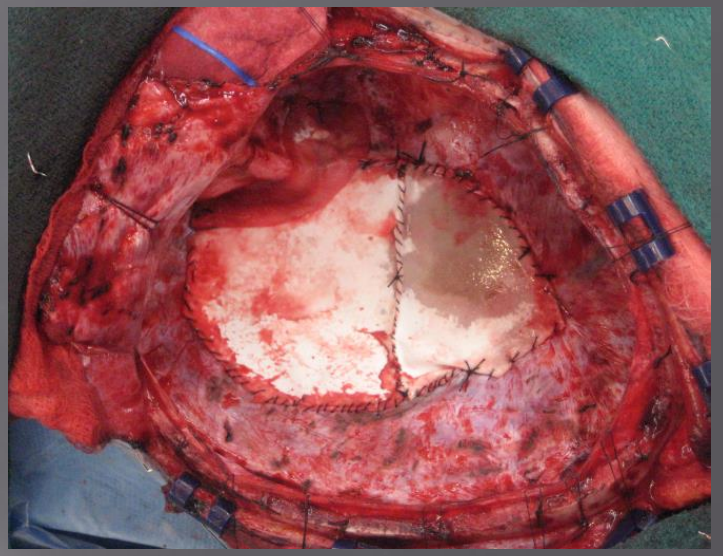
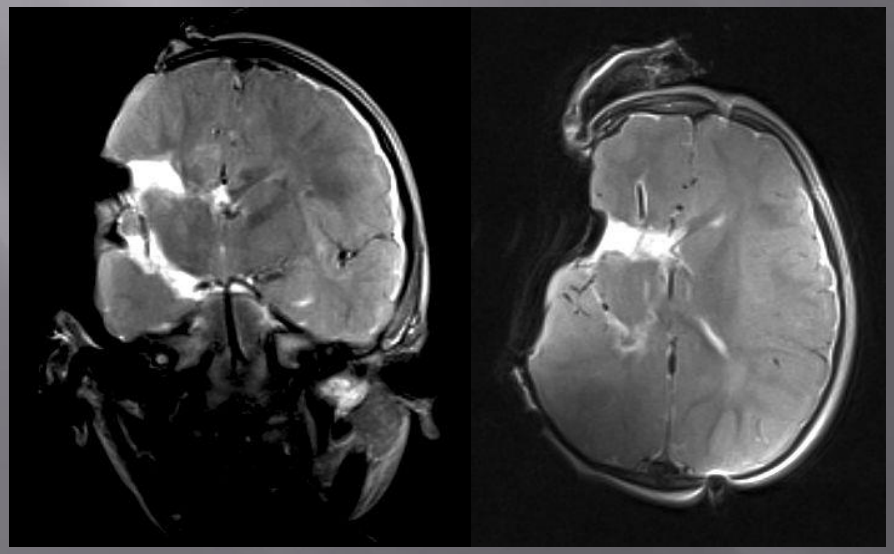
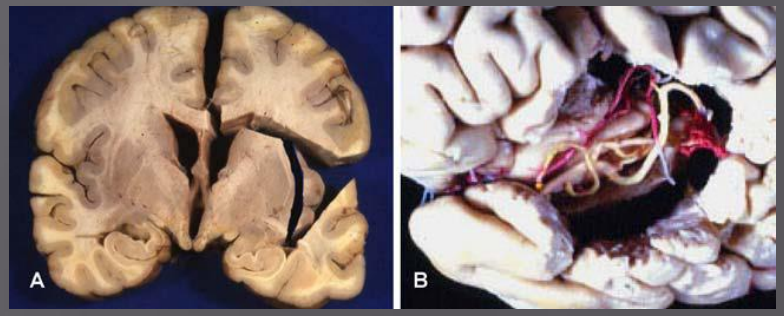
- Hemispherectomy



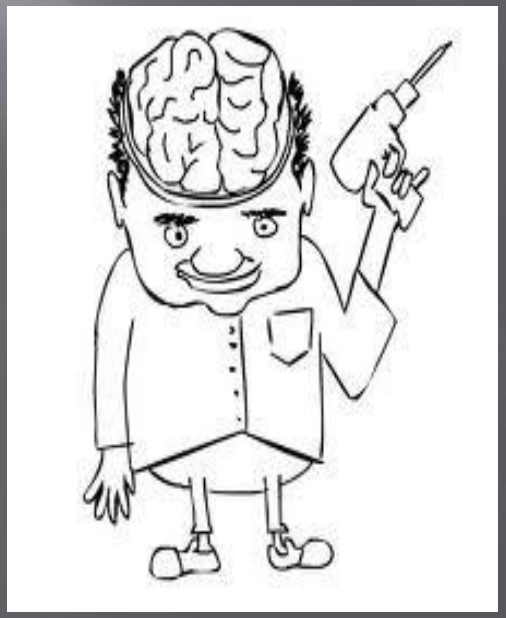


- Hemispherotomy

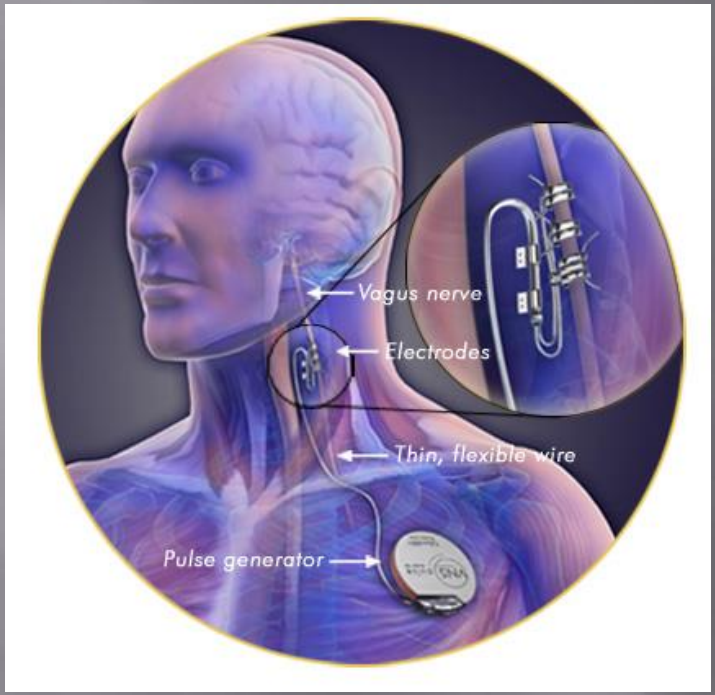


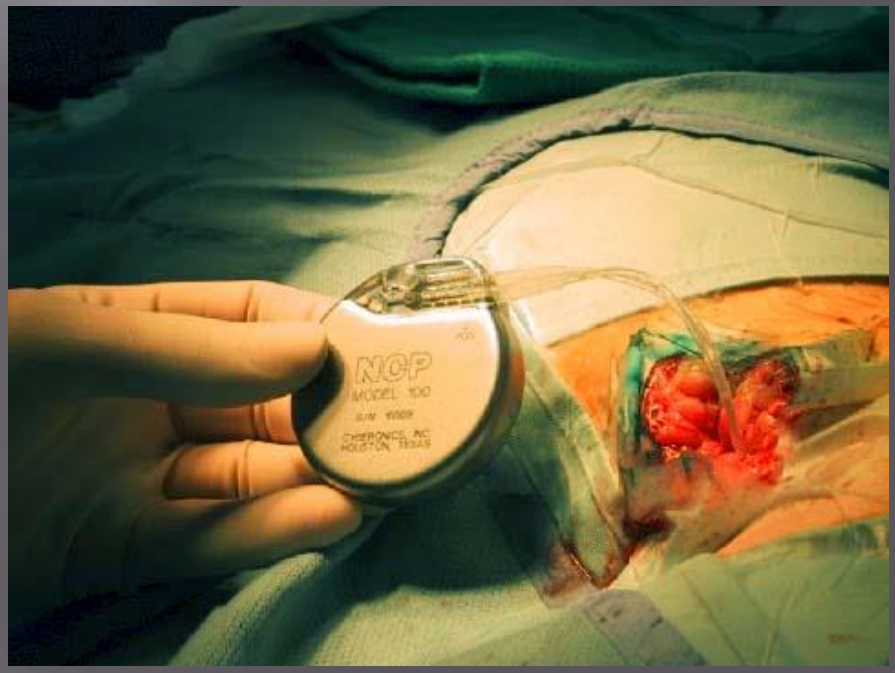


If my patient is not a good candidate for surgery?

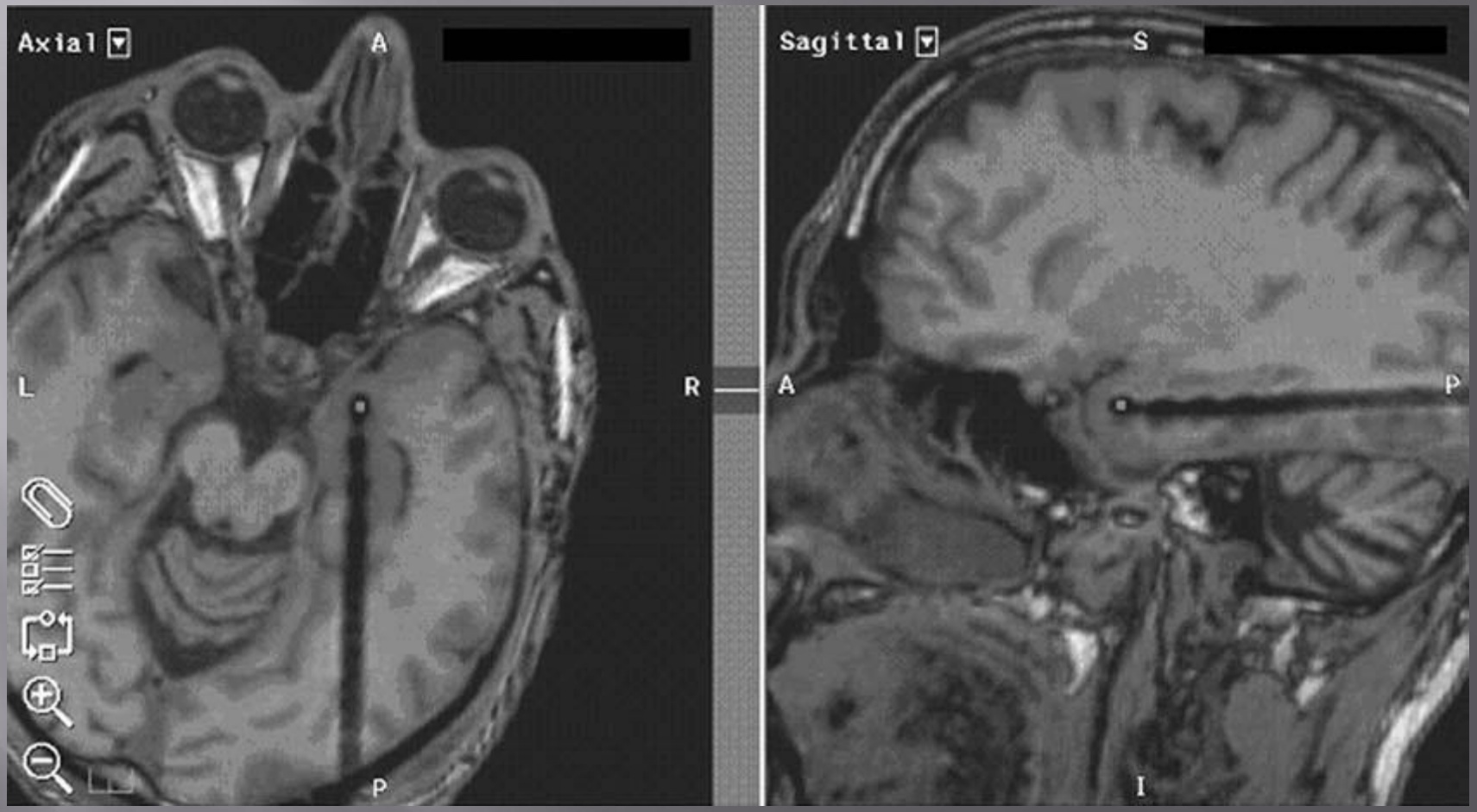


VNS


Vagus nerve
Electrodes
Thin, flexible wire
Pulse generator


NCP
MODEL 100

DBS




Thank you


Epilepsy Awareness