

# Seizures & Epilepsy: Neurosurgical Options

*George Jallo, MD*

Division of Pediatric Neurosurgery  
Johns Hopkins University  
Baltimore, Maryland

# Definition of Seizures

- Time-limited paroxysmal events that result from abnormal, involuntary, rhythmic neuronal discharges in the brain
- Seizures are usually unpredictable
- Seizures usually brief ( < 5 minutes) and stop spontaneously
- Convulsion, ictus, event, spell, attack and fit are used to refer to seizures

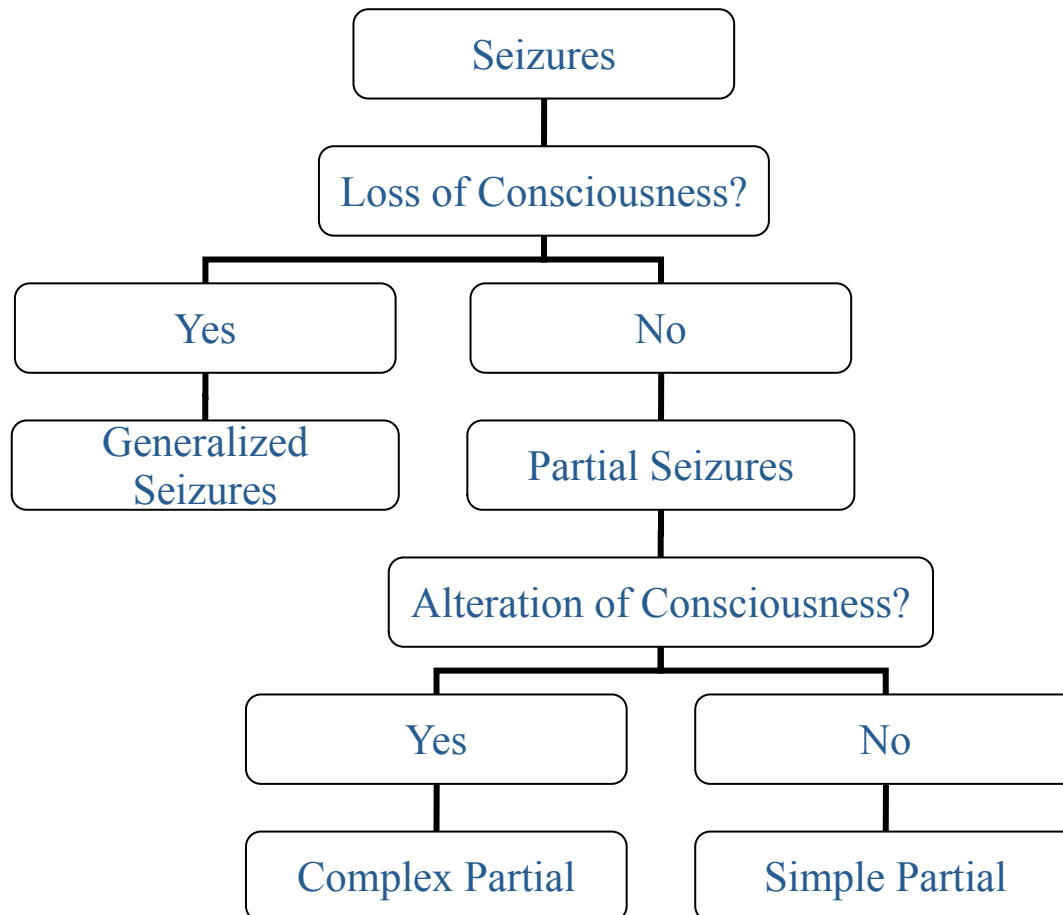
# Etiology of Seizures

- Seizures are either provoked or unprovoked
- Provoked Seizures: Triggered by certain provoking factors in otherwise healthy brain
  - Metabolic abnormalities (hypoglycemia and hyperglycemia, hyponatremia, hypocalcemia)
  - Alcohol withdrawal
  - Acute neurological insult (infection, stroke, trauma)
  - Illicit drug intoxication and withdrawal
  - Prescribed medications that lower seizure threshold (theophylline, TCA)
  - High fever in children
- Unprovoked Seizures: Occur in the setting of persistent brain pathology

# Classification of Seizures

- Traditionally divided into “ grand mal” and “petit mal” seizures
- ILAE classification of epileptic seizures in 1981 based on clinical observation and EEG findings
- Seizures were divided into partial and generalized seizures based on loss of consciousness
- Partial seizures were divided into simple partial and complex partial based on alteration of consciousness

# Classification of Seizures



# Definition of Epilepsy

- A disease characterized by spontaneous recurrence of unprovoked seizures (at least 2)
- Seizures are symptoms, while epilepsy is a disease, so those terms should not be used interchangeably
- Epilepsy = “seizure disorder”
- Epilepsy is a syndromic disease
- Each epilepsy syndrome is determined based on;  
Type of seizures, age at seizure onset, family history, physical exam, EEG findings, and neuroimaging

# Etiology of Epilepsy

- Any process that alters the structure (macroscopic or microscopic) or the function of the brain neurons can cause epilepsy
- Processes that lead to structural alteration include;
  - Congenital malformation
  - Degenerative disease
  - Infectious disease
  - Trauma
  - Tumors
  - Vascular process
- In majority of patients, the etiology is proposed but not found

# Classification of Epilepsy

- ILAE classification of epilepsy and epileptic seizures in 1989
- Depends on 2 distinctions;
  - Location of pathology (Localized or generalized)
  - Know or presumed etiology
    - Idiopathic
    - Symptomatic
    - Cryptogenic



# ILAE Classification of Epilepsy

	<i>Localization-Related (named by location)</i>	<i>Generalized (named by disease)</i>
<b><i>Idiopathic</i></b>	<p>Benign Rolandic epilepsy (Benign childhood epilepsy with centro-temporal spikes)</p> <p>Benign occipital epilepsy of childhood</p> <p>Autosomal dominant nocturnal frontal lobe epilepsy</p> <p>Primary Reading Epilepsy</p>	<p>Benign Neonatal Convulsions (+/- familial)</p> <p>Benign myoclonic epilepsy in infancy</p> <p>Childhood absence epilepsy</p> <p>Juvenile absence epilepsy</p> <p>Juvenile myoclonic epilepsy</p> <p>Epilepsy with GTCs on awakening</p>
<b><i>Symptomatic</i></b>	<p>Temporal lobe</p> <p>Frontal lobe</p> <p>Parietal lobe</p> <p>Occipital lobe</p> <p>(Rasmussen's encephalitis)</p> <p>(Most Reflex epilepsies)</p>	<p>Early myoclonic encephalopathy</p> <p>Early infantile epileptic encephalopathy with suppression-burst (Ohtahara's syndrome)</p> <p>Cortical abnormalities</p> <ul style="list-style-type: none"> <li>-malformations</li> <li>-dysplasias</li> </ul> <p>Metabolic abnormalities</p> <ul style="list-style-type: none"> <li>- amino acidurias</li> <li>- organic acidurias</li> <li>- mitochondrial diseases</li> <li>- progressive encephalopathies of</li> </ul>
<b><i>Cryptogenic</i></b>	<p>(Any occurrence of partial seizures without obvious pathology.)</p>	<p>Epilepsy with myoclonic-astatic seizures</p> <p>Epilepsy with myoclonic absence</p>

# Evaluation - Differential Diagnosis

- When a paroxysmal event occurs, especially if associated with loss of consciousness;
  - Is this event (spell) a seizure ?
  - If it is a seizure, is it provoked or unprovoked?
  - If it is an unprovoked seizure, what is the chance of recurrence? (making decision about treatment)
  - Does this patient have epilepsy? What type?
  - What is the appropriate treatment?
- “Diagnosis of epilepsy is a clinical one”
  - History is the key

# Treatment of Seizures

- Provoked Seizures
  - Treatment directed to the provoking factor
- Unprovoked Seizures
  - First Seizure
    - Usually no treatment
    - Treatment can be initiated if risk of recurrence is high or if a second seizure could be devastating
  - Second Seizure
    - Diagnosis of epilepsy is established and risk of a third Seizure is high
    - Most physician treat at this stage
    - In children, some may wait for a third seizure

# Treatment of Established Epilepsy

- First Line
  - Approved Anti-Epileptic Drugs (AEDs)
- Second Line (intractable epilepsy)
  - Epilepsy Surgery
  - Vagus Nerve Stimulation Therapy
  - Experimental Therapy
    - AEDs
    - Implanted Devices
- Dietary Options

# Antiepileptic Drugs (AED)

<b>First Generation</b>	<b>Second Generation</b>	<b>Unconventional</b>
Carbamazepine (Tegretol) Clonazepam (Klonopin) Clorazepate (Tranxene) Ethosuximide (Zarontin) Phenobarbital Phenytoin (Dilantin) Primidone (Mysoline) Valproic acid (Depakote)	Felbamate (Felbatol) Gabapentin (Neurontin) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal) Pregabalin (Lyrica) Tiagabine (Gabitril) Topiramate (Topamax) Zonisamide (Zonegran)	Adrenocorticotrophic hormone (ACTH ) Acetazolamide (Diamox) Amantadine (Symmetrel) Bromides Clomiphene (Clomid) Ethotoin (Peganone) Mephenytoin (Mesantoin) Mephobarbital (Mebaral) Methsuximide (Celontin)

# Treatment of Medically Intractable Epilepsy

- An epilepsy that is not responding well to medical treatment
- Most expert agree if a patient fails adequate trial of 2 AEDs, his/her epilepsy is intractable
  - 25-35% of all epilepsies are intractable
- Medical treatment should be continued and other options should be explored

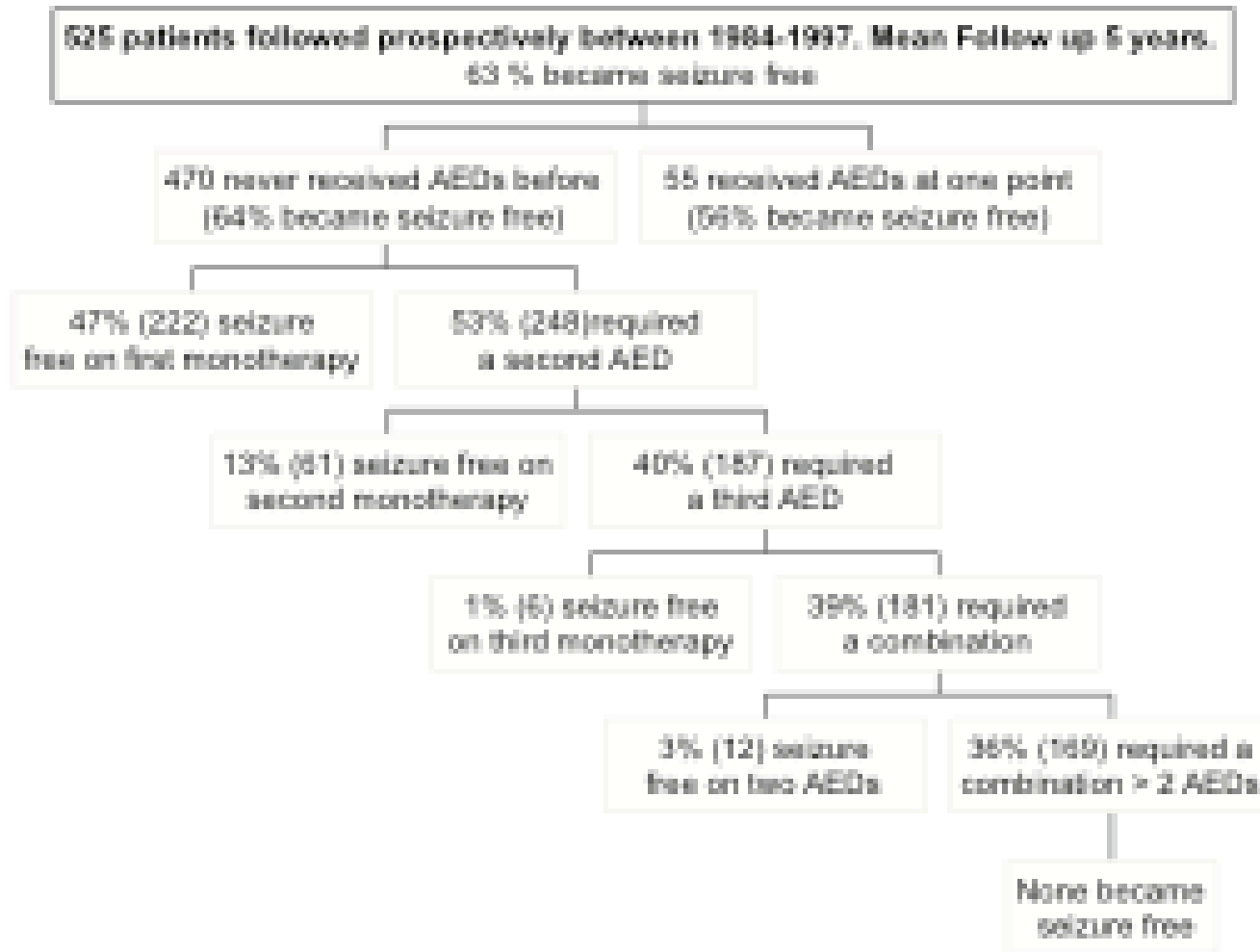
# Growth of Epilepsy Surgery in United States

- 1985: ~ 500 cases/year\*
- 1990: ~1500 cases/year\*\*
- Currently >100 specialized epilepsy centers

Based on data collected at 1st \* and 2nd \*\* Palm Desert Conference  
of Epilepsy Surgery

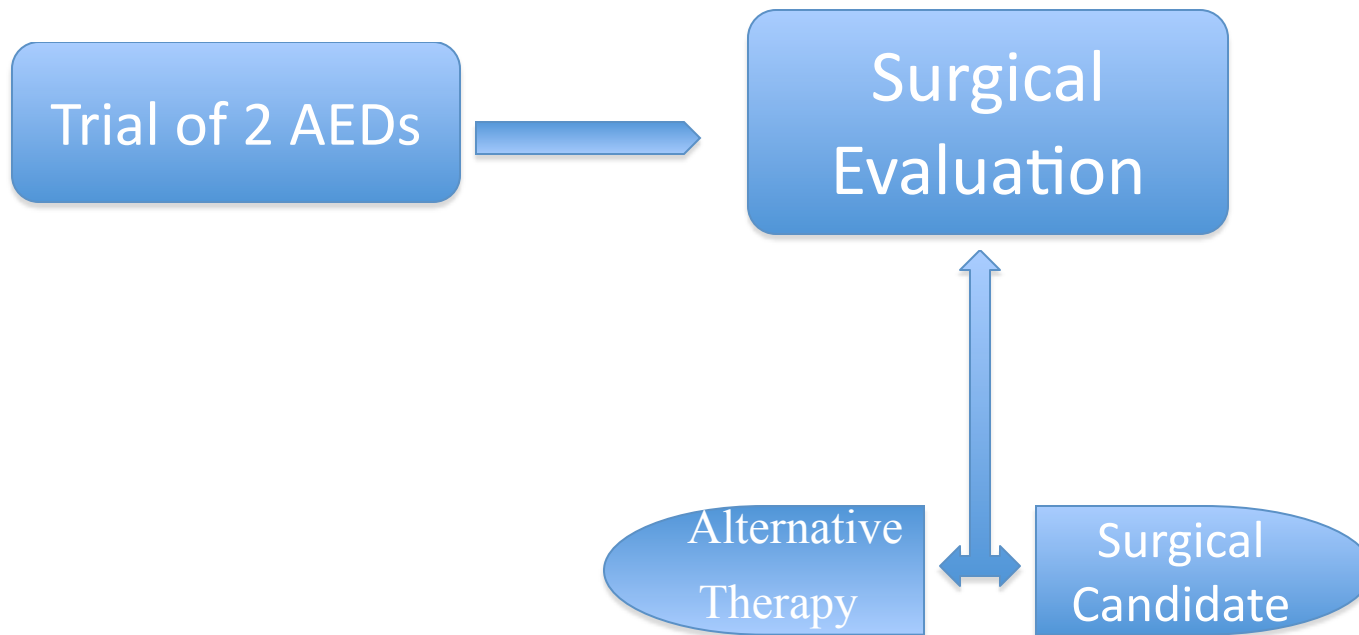
# Early Identification of Refractory Epilepsy

(Kwan & Brodie, NEJM 2000)





# Proposed Treatment Approach



# Treatment of Intractable Epilepsy

## “Other Options”

- Epilepsy Surgery
  - Removal of seizure focus
  - Requires extensive evaluation
  - Results are superior to medical treatment in patients who are good candidate
  - Surgery is associated with a small risk; however, the benefit justifies the risk
- Vagus Nerve Stimulator (VNS)
  - Not superior to medical treatment
  - Advantage: compliance, no side effects
  - Disadvantage: expensive

# Ideal Candidate for Epilepsy Surgery

- Refractory to treatment ( $\geq 2$  AEDs)
- Well-defined focus of seizure onset
- Epileptogenic zone in “functionally silent” region
- Seizures must be debilitating
- There should be no chance for spontaneous resolution

# *Epilepsy Surgery*

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- Temporal lobectomy
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- Functional hemispherectomy
  - considered in extreme circumstances

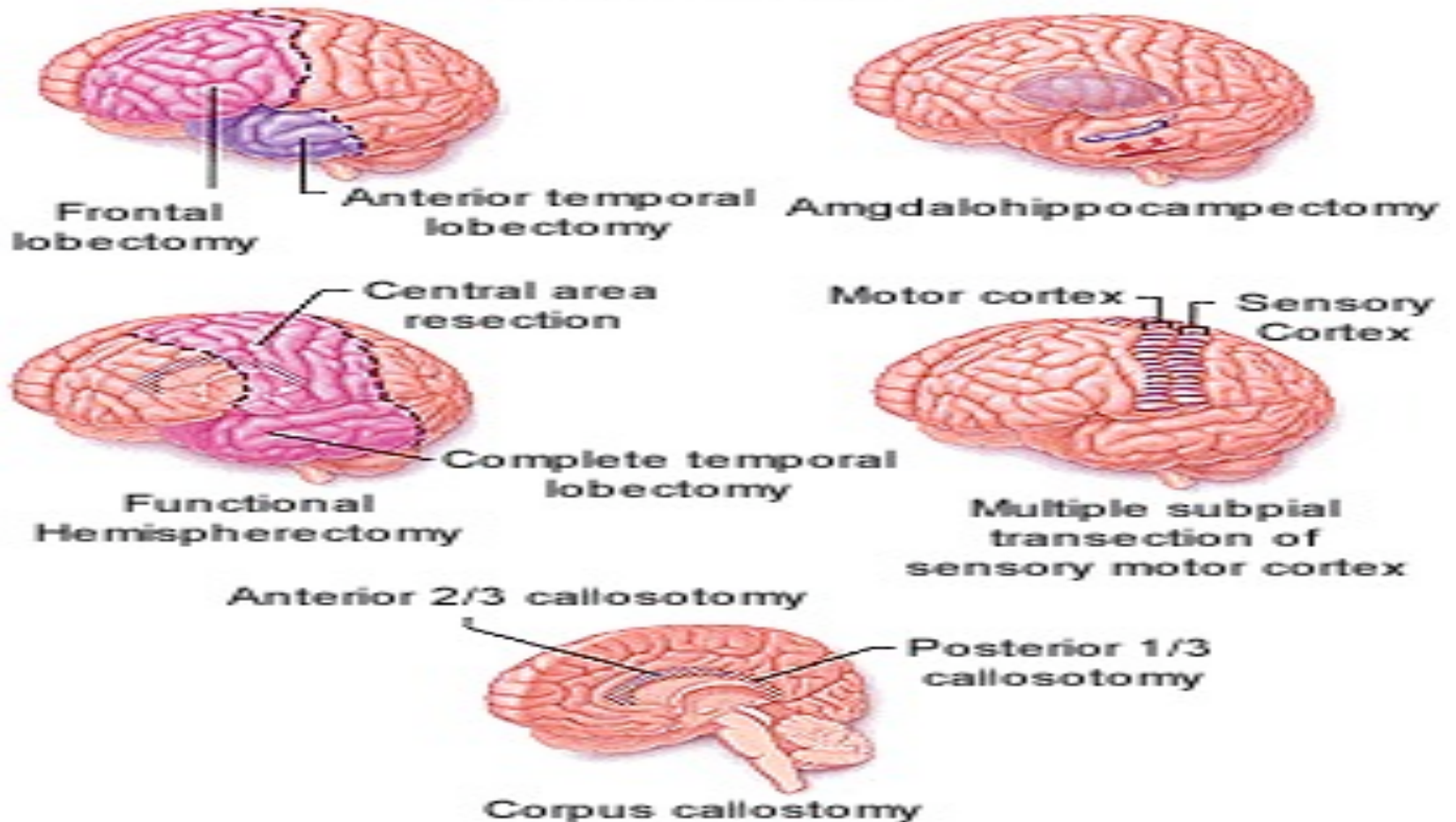


# *Epilepsy Surgery*

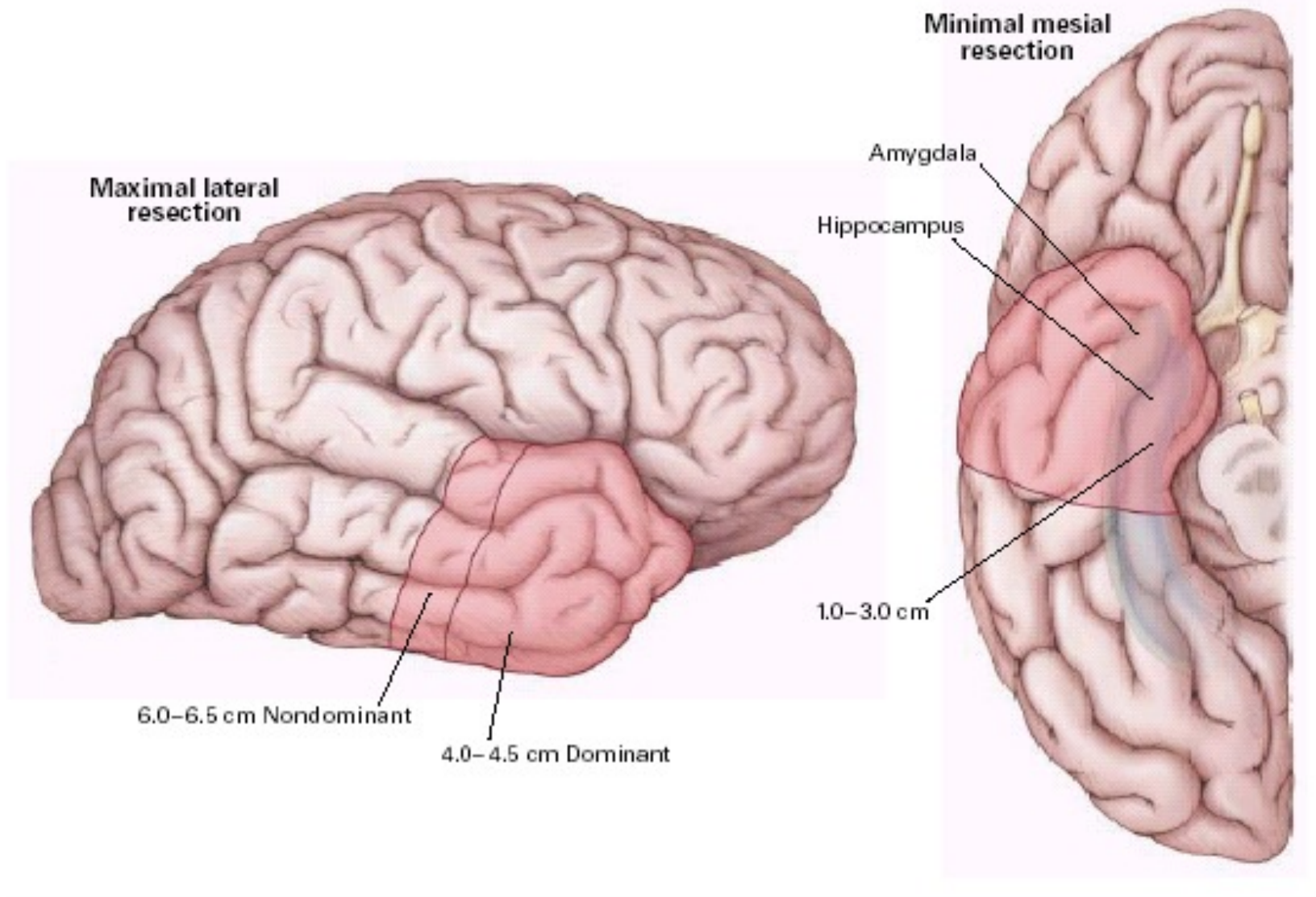
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- Functional hemispherectomy
  - considered in extreme circumstances
- Corpus callosotomy
  - good for atonic and brief tonic seizures

# Surgical Options for Epilepsy Surgery

## Types of Surgical Procedures



# Temporal Lobectomy with Mesial Resection



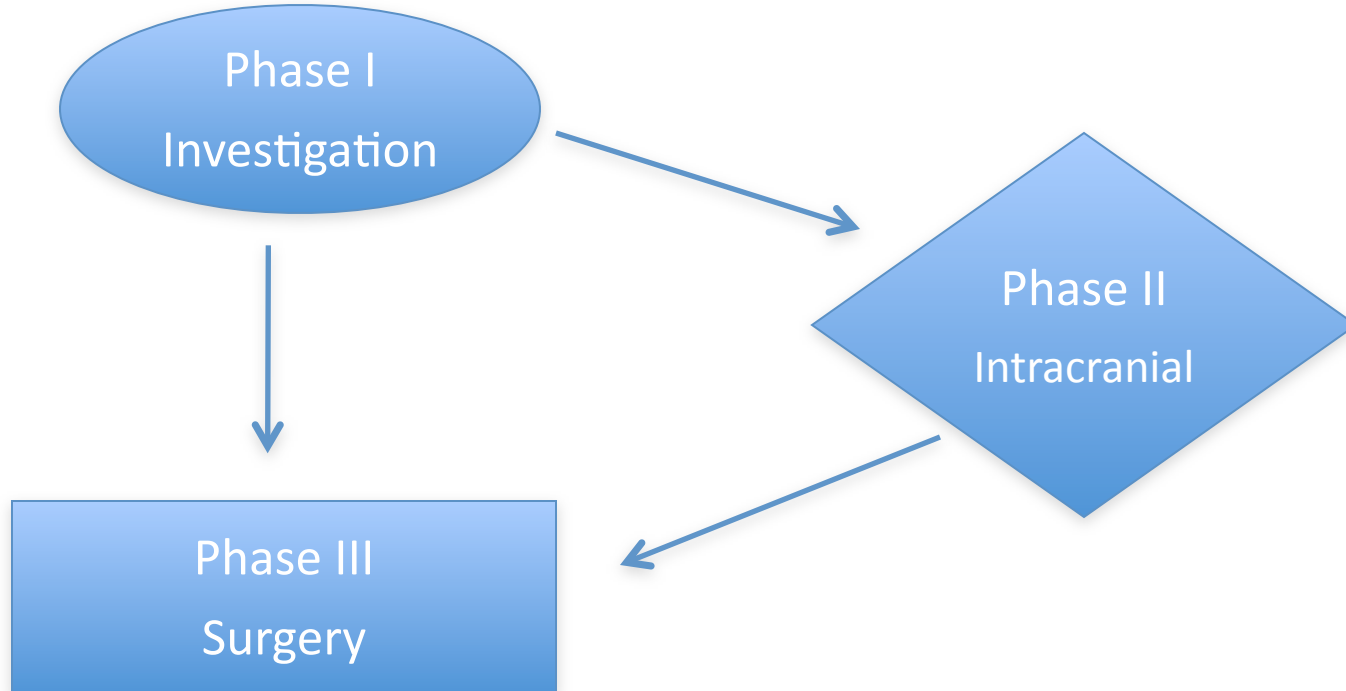
# A Randomized Controlled Trial of Surgery in TLE (Wiebe et al, NEJM 2001)

- 80 patients with TLE were randomized equally to medical treatment or anterior temporal lobectomy (36/40 underwent surgery) and followed for 1 year
- **After one year; 58% (64%) of the surgical group patients were free of seizures that alter awareness vs. 8% in the medical group**
- Complications related to surgery occur in 4 patients; 1 thalamic infarct caused LT thigh sensory loss , 1 wound infection, 2 verbal memory decline
- One patient in the medical group died (unexplained), none in the surgical group
- Complications not related to surgery (depression, psychosis) were similar in both groups

# Illustrative Case

- 9 year old boy with nocturnal seizures since age 4. Multiple medications without success. Currently on 2 AEDs but continues with 5-7 seizures/week
- EMU evaluation: Frontal lobe seizures  
Discharges left/right.
- MRI normal

# Surgical Evaluation for Seizures

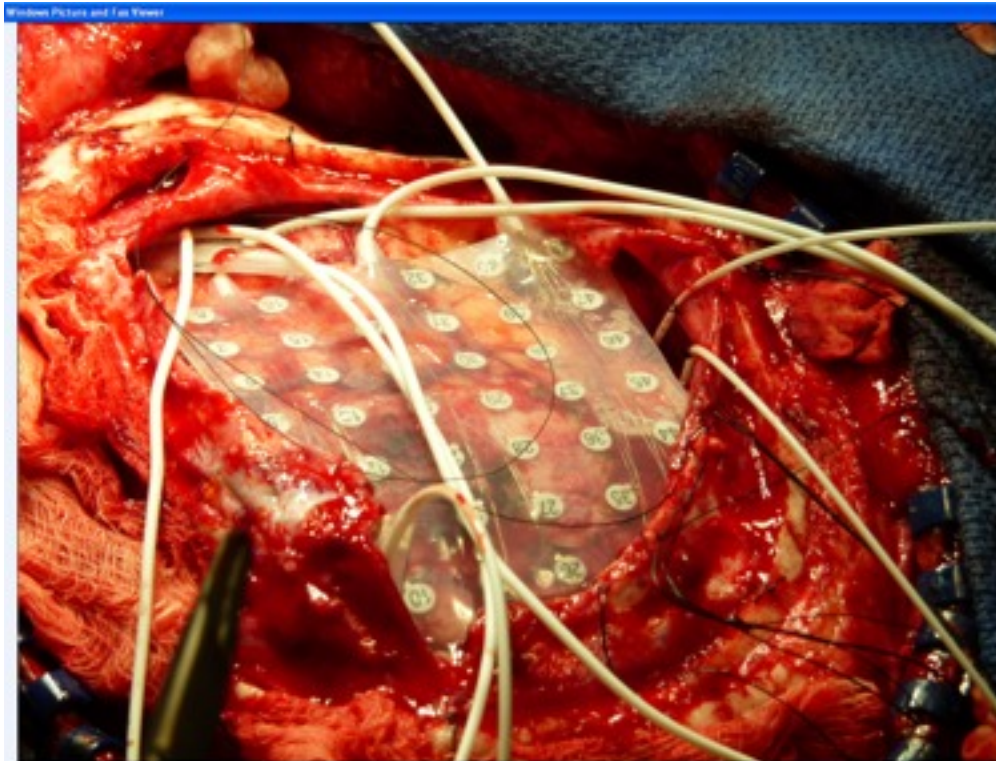


# Phase II evaluation

- Craniotomy for subdural electrode placement
- Monitoring for 6 days in the EMU
- Cortical mapping with seizure zone identified and away from eloquent cortex

# Phase III

- Surgery for removal of EEG defined seizure focus





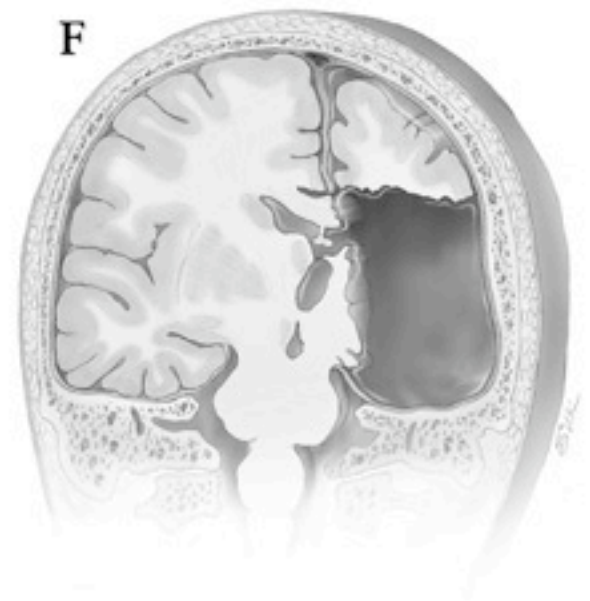
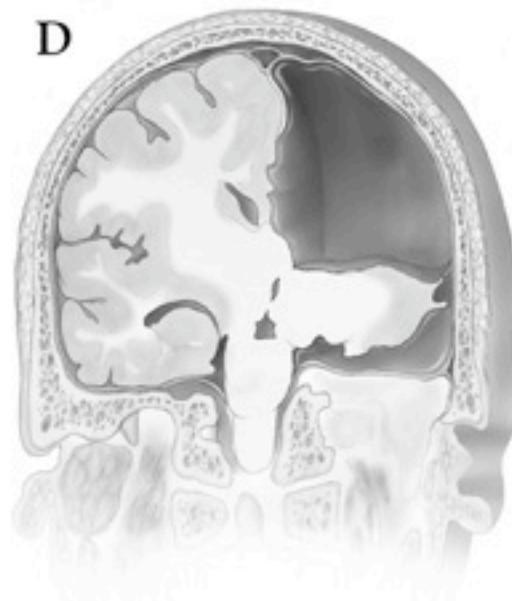
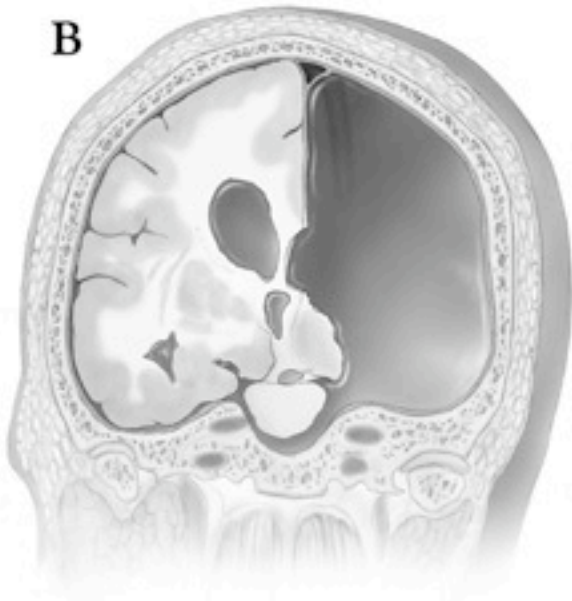
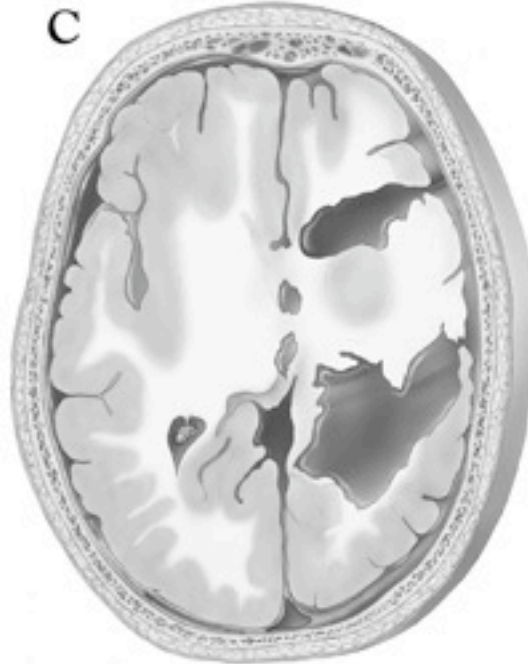
# Hemispherectomy Surgery

- Hemispherectomy for the treatment of intractable, unilateral hemispheric seizures is a well described, effective surgical intervention that has the potential to significantly improve the quality of life for patients suffering from this disorder.
- First performed by Dandy in 1928<sup>1</sup>, the procedure has evolved from anatomical hemispherectomy, whereby the entire abnormal hemisphere is removed, to variations including functional hemispherectomy and hemispherotomy.

•Anatomical

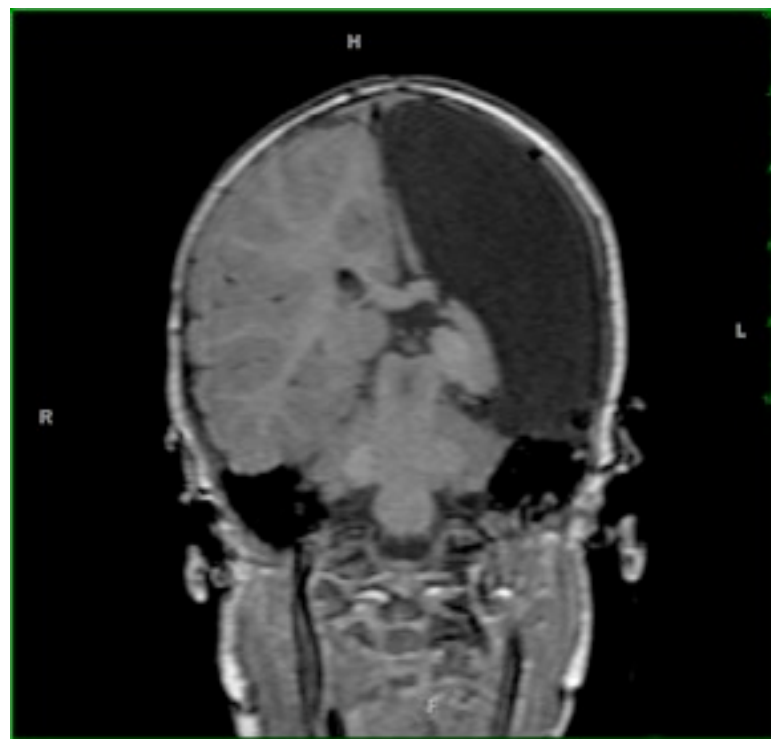
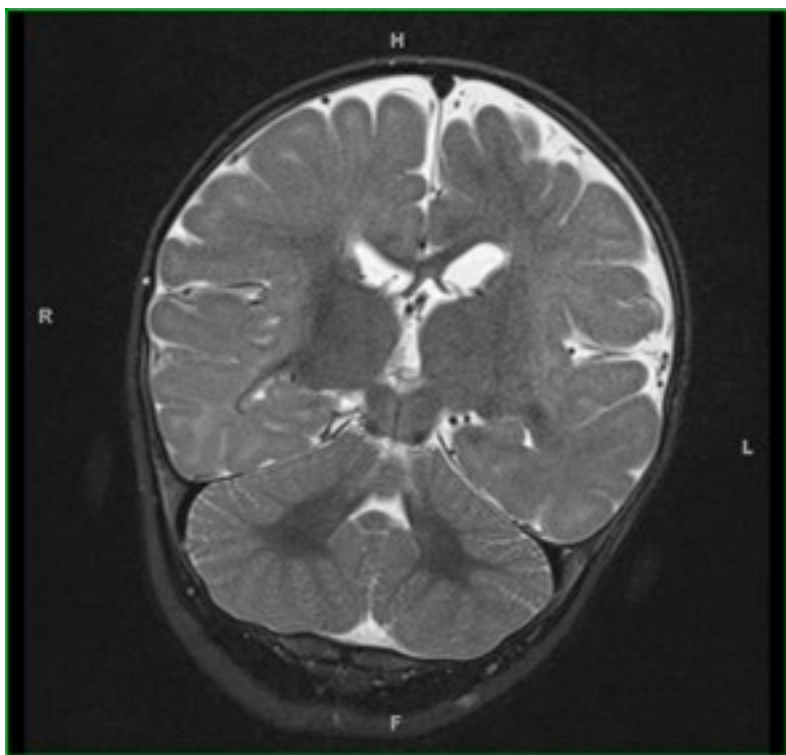
•Functional

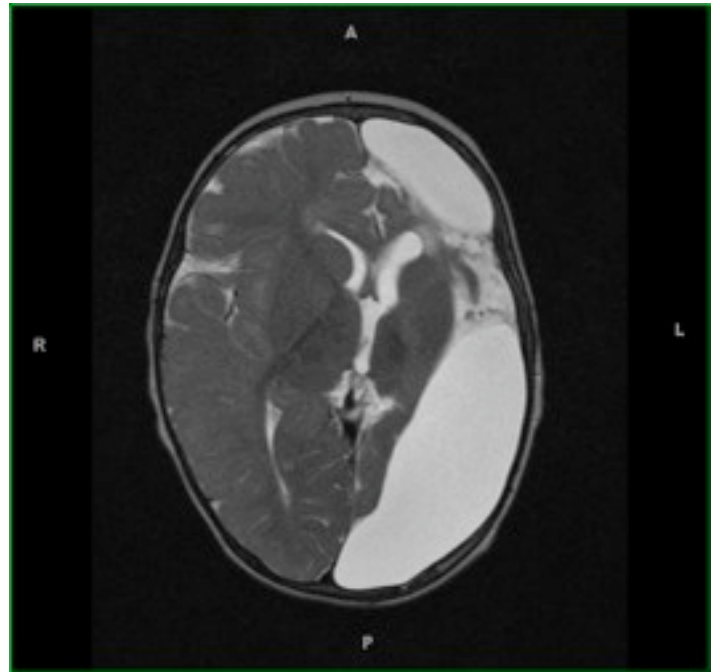
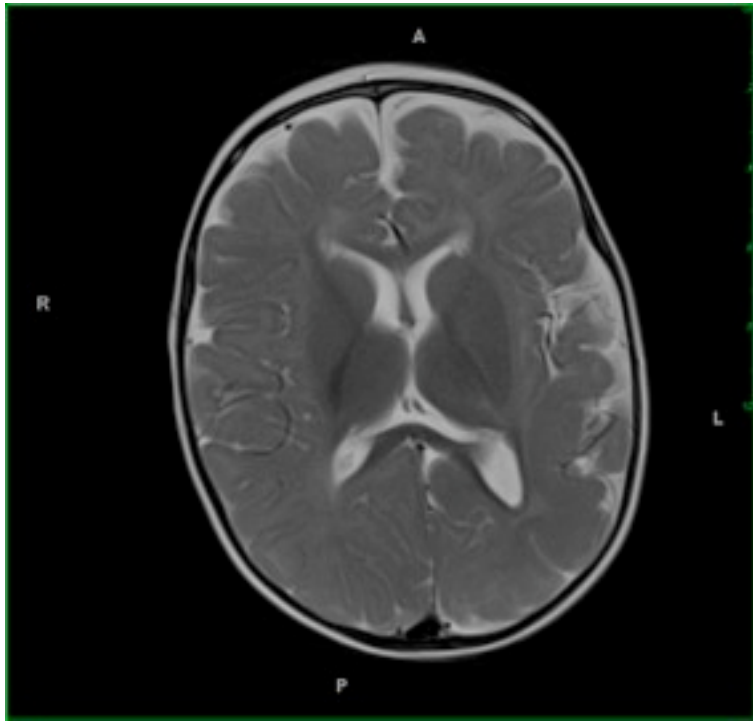
•Hemispherotomy



# Hemispherectomy Surgery

- Symptomatic drug resistant seizures in patients with hemiplegia secondary to unilateral damaged hemisphere
  - HHE hemiconvulsion-hemiplegia epilepsy
  - Sturge Weber Syndrome
  - Hemimegalencephaly
  - Cortical dysplasia
  - Migrational disorders
  - Stroke

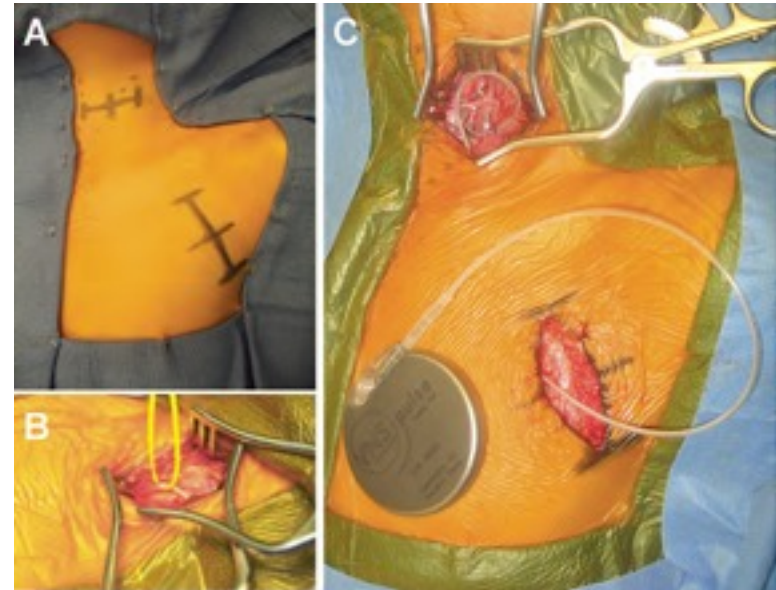
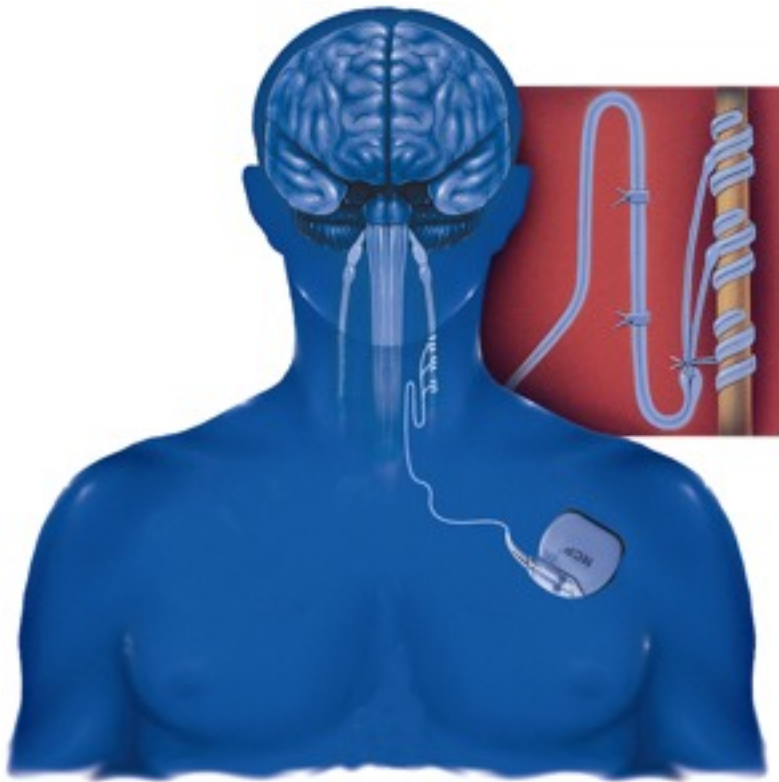




# Hemispherectomy Outcome

- The outcome depends upon the etiology and the type of surgery
- Seizure-free outcome
  - 85% for hemispherotomy
  - 66% for functional and anatomical
  - 61% for hemidecortication

# Vagus Nerve Stimulator (VNS)



# *Vagus Nerve Stimulator: Rule of Thirds*



# *Vagus Nerve Stimulator:*

## *Rule of Thirds*

- 1/3 have prominent improvement

# *Vagus Nerve Stimulator:*

## *Rule of Thirds*

- 1/3 have prominent improvement
- 1/3 have moderate improvement

# *Vagus Nerve Stimulator:*

## *Rule of Thirds*

- 1/3 have prominent improvement
- 1/3 have moderate improvement
- 1/3 have little or no improvement

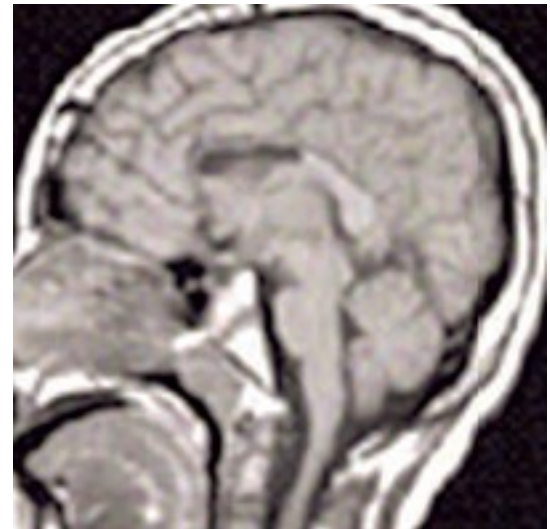
# *Vagus Nerve Stimulator:*

## *Rule of Thirds*

- 1/3 have prominent improvement
- 1/3 have moderate improvement
- 1/3 have little or no improvement
- Benefits
  - fewer seizures, less severe seizures, shorter recovery period, decreased medications and side effects, less fear and anxiety, more control

# Corpus Callosotomy

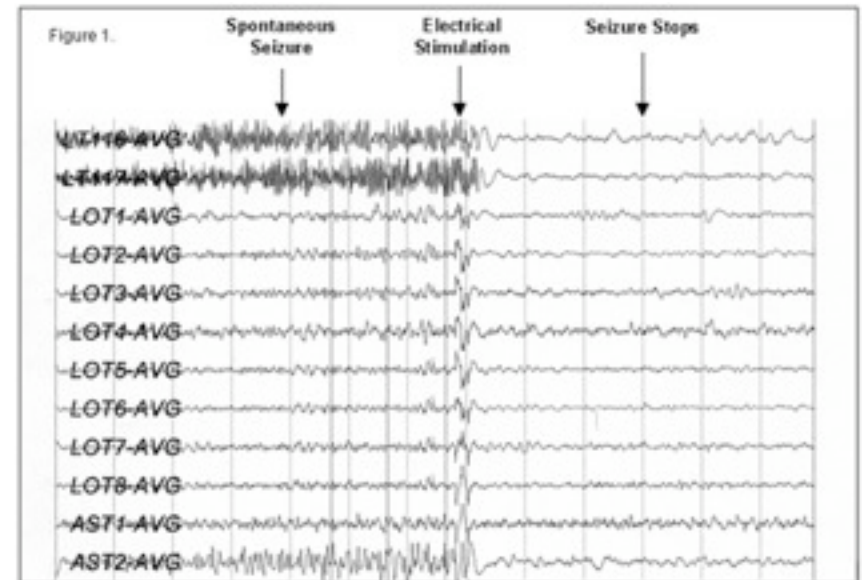
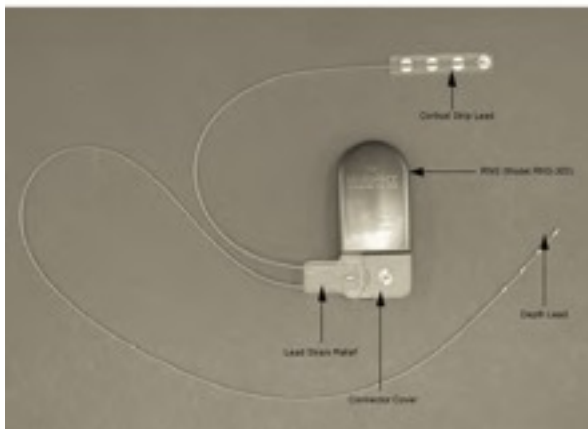
- Indications
  - Drop attacks, refractory seizures with high risk of injury, seizures without a focus



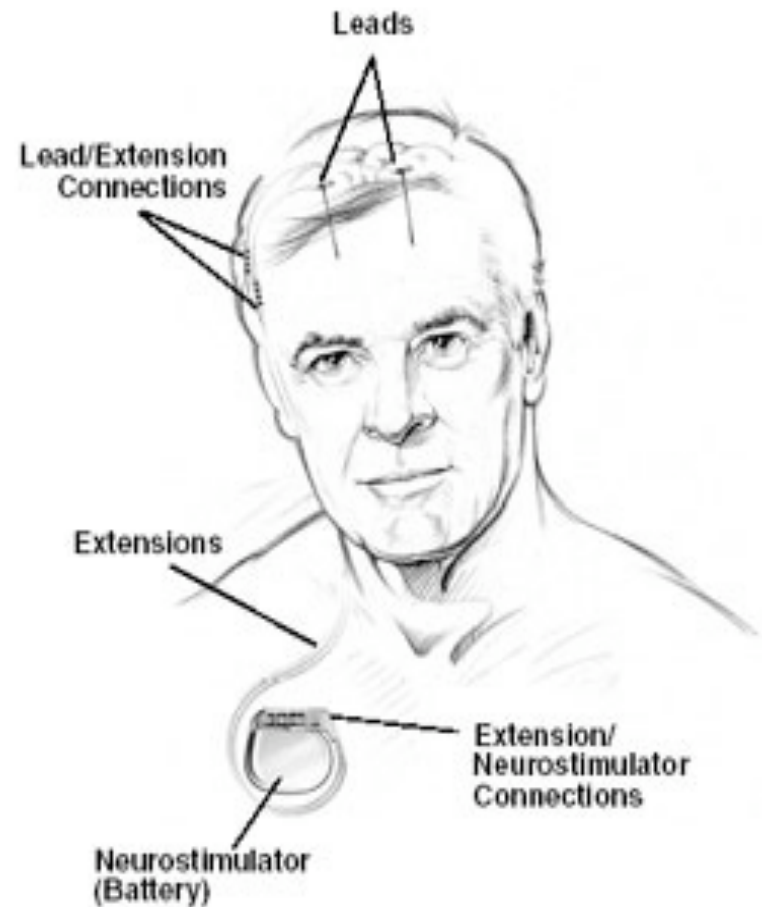
# Outcome following Callosotomy Surgery

- Seizure control >50%: 66-80%
- Seizure-free : 13%
- Improved attention, behavior and performance in daily activities.

# Experimental Treatment- Responsive Neurostimulator (RNS)



# Experimental Treatment – Deep Brain Stimulator (DBS)





# Role of Comprehensive Epilepsy Center

- Comprehensive care of epilepsy patient
  - Broad range of AED options
  - Neurostimulation (vagal nerve stimulator)
  - Dietary options
  - Full diagnostic services
  - Surgical treatment of epilepsy

# Pediatric Epilepsy: 2010

- New treatments: medications, diet, surgery, ? genetic
- New understanding: pathophysiology, pharmacogenomics
- New concerns: susceptibility, neonatal seizures
- New systems of care, emergent and chronic
- Shaping the future of care: sophisticated, rational, evidence-based approach to management