Surgical Treatment of Epilepsy

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Disclosure

* Dr. Norton has nothing to disclose.
Epilepsy

* Two or more seizures that are not provoked by other illnesses or circumstances
Goal of Therapy

∗ “No Seizures, No side effects”
Antiepileptic drugs

* Phenobarbital
* Phenytoin (Dilantin)
* Valproate (Depakote)
* Carbamazepine (Tegretol)
* Lamotrigine (Lamactil)
* Topiramate (Topomax)
* Ethosuximide (Zarontin)
* Levetiracetam (Keppra)
* Oxcarbazine (Trileptol)
Chances of seizure control with third medication, following failure of two appropriate antiepileptic drugs is less than 1%
Consequences of Uncontrolled Seizures

* **Adults**
  * Physical injury
    * Oral Trauma
    * Head Trauma
    * Orthopedic Injury
    * Aspiration Pneumonia
  * Depression
  * Loss of Independence
  * Employment issues
  * Restrictions on Exercise, Travel, Driving
  * Cognitive decline
  * Sudden Unexplained Death in Epilepsy
Consequences of uncontrolled Seizures

* Pediatrics

* Interictal epileptiform discharges may cause an irritable, dysfunctional cortex and possibly, secondary epileptogenesis

* Mental retardation

* Psychosocial and cognitive impairment

* Debilitating behavioral problems, aggression
Concepts of Zones

- Epileptogenic Zone
- Irrigative Zone
- Epileptic lesion
- Symptomatogenic Zone
- Functional Deficit Zone
- Eloquent Cortex
The Epileptogenic Zone

* Area of cortex that is indispensable for the generation of epileptic seizures

* This region needs to be resected or disconnected for successful epilepsy surgery
  * Actual seizure onset zone
  * Potential seizure onset zone
The Irritative Zone

* The region that produces interictal epileptiform discharges
* Does not always necessarily overlap with the epileptogenic zone
* sEEG
* SEEG
* MEG
* fMRI
The Epileptic Lesion

* Lesion on Neuroimaging or Pathology that is considered to cause the seizures

* More than just a simple “Lesionectomy” may be required
  * Tumors and vascular malformations often have a perilesional epileptogenic zone that is responsible for seizure generation
The Symptomatogenic Zone

* The eloquent area that produces the clinical symptoms when activated during an epileptic seizure
* Frequently close to the epileptogenic zone but there may be no direct overlap
The Functional Deficit Zone

* The region that functions abnormally during the interictal period
  * May be related to functional abnormalities without structural abnormalities
    * e.g., interictal epileptiform discharges may influence speech organization
The Eloquent Cortex

* Encompasses regions of cortex that are responsible for particular functions, including motor, sensory, language, memory and other higher cortical functions.

* Pre surgical planning to prevent or predict postoperative deficits.
Classification of Seizures

* Partial (Focal, Local) Seizures
  * Simple Partial Seizures
  * Complex Partial Seizures
    * With impairment of consciousness at onset
    * Simple partial onset, followed by impairment of consciousness
  * Partial Seizures evolving to generalized tonic-clonic convulsions (GTCs)
    * Simple evolving to GTC
    * Complex evolving to GTC (including those with simple partial onset)
**Epilepsy and Seizures**

- **Partial seizure**
  - = focal onset seizure

- **Simple Partial**
  - = remains conscious

- **Complex Partial**
  - = lose consciousness
  - secondarily generalised seizure

- **Generalized seizure**
  - = tonic clonic seizure with unconsciousness
Partial Seizure
Secondary Generalization
Primary Generalized Seizure
Strategies to Identify Seizure Focus

* **Semiology**

* **EEG**
  * sEEG or vEEG
  * Invasive EEG
    * Subdural Grids or Strips
    * Depth Electrodes
  * MEG

* **Anatomic – MRI**

* **Functional**
  * PET
  * SPECT
  * fMRI
Studies

* Electrophysiologic Studies
  * Scalp EEG
  * Invasive EEG
  * Cortical Stimulation
  * Magnetoencephalography (MEG)

* Structural Imaging
  * MRI

* Functional Imaging
  * PET
  * fMRI
  * SPECT

* Neuropsychological Testing
Localization - Semiology (Temporal Lobe)

* Archicortical Auras Mesial
  * Gastric rising sensations
  * Uncinate smells
  * Ictus emeticus
  * Spitting Automatism

* Neo-Cortical Auras
  * déjà vu
  * Formed visual hallucinations
  * Formed auditory hallucinations
  * Macropsia/Micropsia
EEG

* The EEG identifies specific interictal or ictal abnormalities that are associated with an increased epileptogenic potential and correlate with a seizure disorder

* Limitations of Extra Cranial Recordings
  * Epileptiform activity in cortex remote from surface electrodes may not be associated with interictal EEG alterations
  * Attenuation of spike activity by the dura, bone and scalp limits the sensitivity of recordings
  * Muscle artifact
Subdural Grid
Invasive Recordings
Sub Dural Strip Electrode
Stereoelectroencephalography
SEEG
Stereoelectroencephalography
SEEG
How does MEG work?

- MEG is short for Magnetoencephalography
- It starts with recordings of the magnetic fields naturally generated by neuronal sources in the brain
- The magnetic fields are detected by a sophisticated technology based on super-conducting detectors and amplifiers known as SQUIDs
- The magnetic fields are analyzed to find the locations of the neuronal sources within the brain
- The resulting source locations are superimposed on an MRI image for surgical planning
MEG co-registered with MRI
MEG
MRI
Medial Temporal Sclerosis
Positron Emission Tomography
“PET SCAN”
Single Photon Emission Computed Tomography
“SPECT SCAN”
Functional MRI
Establishing Diagnosis

* Semiology
* EEG
* MRI scan
* PET scan
* MEG
* Subdural Strips or Grids
* SEEG
* WADA test
* fMRI
# Lesional Focal Epilepsies

## Causes of Intractable Epilepsy

<table>
<thead>
<tr>
<th>MTS</th>
<th>Developmental</th>
<th>Epileptogenic tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mesial temporal sclerosis</td>
<td>Focal Cortical Dysplasia Heterotopia Polymicrogyria Hemimegalencephaly Schizencephaly</td>
<td>Ganglioglioma DNET Pleom. Xanthoastrocytoma Hypothalamic hamartoma</td>
</tr>
<tr>
<td>Gliosis</td>
<td>Miscellaneous</td>
<td>Neurcutaneous syndr.</td>
</tr>
<tr>
<td>Scars</td>
<td>Rasmussen encephalitis Cavernous hemangioma</td>
<td>Sturge-Weber Tuberous sclerosis</td>
</tr>
</tbody>
</table>
Lesions Which may cause Epilepsy
Diffuse Hemispheric Epilepsies
Epileptogenic Structural Disturbances that are limited to one hemisphere

* Rasmussen Encephalitis
* Sturge-Weber Syndrome
* Hemimegalencephaly
Lesional Focal Epilepsies

* Mesial Temporal Lobe Epilepsy-HS
* Primary Brain Neoplasm
  * Low grade gliomas
  * Ganglioglioma
  * Dysembryoplastic neuroepitheliomas (DNET)
* Vascular anomaly
* Malformation of Cortical Development
  * Focal Cortical Dysplasia
Not All Patients are the Same

* Temporal Lobe Epilepsy secondary to tumor - 90% seizure free
* MTS Patients – 75% seizure free
* Cortical Dysplasia 55-60 % seizure free
* Non Lesional 50-60 % seizure free
A Randomized Controlled Trial of Surgery for Temporal-Lobe Epilepsy
Wiebe S, et al, NEJM 2001 345, 311-318

80 Patients

40 surgical- Anterior Temporal Lobectomy

40 Medical- Best Medical Management

Seizure Free

Surgery – 58%

Medical – 8%
Kaplan–Meier Event-free Survival Curves Comparing the Cumulative Percentages of Patients in the Two Groups Who Were Free of Seizures Impairing Awareness (Complex Partial or Generalized Seizures) (Panel A) and Free of All Seizures (Including Auras) (Panel B).

Monthly Rates of Seizures According to Type among Patients in the Medical and Surgical Groups.

A Typical Surgical Resection for Temporal-Lobe Epilepsy in This Study.

Anterior Temporal Lobectomy
Temporal Lobe Anatomy
Temporal Lobe Anatomy
Hippocampus
“Sea Horse”
Limbic System

- James Papez - 1937
- Described structures in sub-cortex thought to control emotion, memory, sexual drive, perception of reward, pleasure, addiction
Temporal Lobe

* Speech
* Vision
* Memory
Primum Non Nocere
“First, do no harm”
H.M.

* H. M., 27 year old man with intractable post traumatic seizures, underwent bilateral temporal lobectomies by Dr William Scoville in 1953

* After surgery;
  * Better seizure control
  * Short term memory intact, normal speech , normal IQ, normal long term memory for events prior to surgery.
  * Complete loss of ability to transfer short term memory into long term memory
H. M.

* Perfectly good long term memory for those events prior to his surgery
* Would not recognize Brenda Milner The neuroscientist who would exam him each month
* Would recognize himself in pictures taken prior to his surgery but not afterward
H.M.
F.C. and P. B.

* Two patients of Wilder Penfield who were amnesic immediately following surgery to remove part of their left temporal lobes to alleviate epileptic seizures

* P.B. died of cardiac event 14 years later and on post mortem was found to have shrinkage of his right hippocampus

* Post operative EEG on F.C. showed abnormalities in right temporal area
Temporal Lobe and Memory

- Medial Temporal Lobe
  - Encodes
  - Stores
  - Retrieves
Implicit Memory
Long Term Memory

* Explicit (declarative)                     Medial Temporal Lobe
  * Facts
  * Events

* Implicit (Non declarative)                Striatum
  * Procedural (skills and habits)
  * Associative learning: classical and operant conditioning
  * Emotional responses
  * Skeletal musculature

Amygdala
Cerebellum
Long Term Memory

Two forms of long term memory

Explicit (declarative)
- Facts
  - Medial temporal lobe

Explicit (declarative)
- Events

Implicit (nondeclarative)
- Priming
- Procedural (skills and habits)
  - Neocortex
  - Striatum
  - Amygdala
  - Cerebellum
- Associative learning: classical and operant conditioning
  - Emotional responses
  - Skeletal musculature
- Nonassociative learning: habituation and sensitization
  - Reflex pathways
Henry Molaison (HM)
1926-2008
Temporal Lobe Vision

Visual Field Defects

1. L anopia
2. Bitemporal hemianopsia
3. L homonymous hemianopsia
4. L upper quadrant anopia
5. L lower quadrant anopia
6. L hemianopsia with macular sparing
7. Central scotoma

Visual Pathway

- Geniculocalcarine fibers for lower field of vision
- Calcarine fissure
- Lateral geniculate nucleus
- Geniculocalcarine fibers for upper field of vision
- Meyer’s loop
- Occipital cortex
- Parahippocampal gyrus
- Fimbria
- Dentate gyrus
- Optic radiation
- Optic tract
- Chiasm
- Optic nerve
- Hippocampus
- Lateral geniculate nucleus
- Lateral ventricle
Visual Deficit ATL
Temporal Lobe - Speech
WADA Test

* Direct infusion of Sodium Amytal into internal carotid artery
  * Will cause suppression of activity of ipsilateral hemisphere allowing for evaluation of:
    * Speech
      * Verbal fluency
    * Memory
      * Verbal memory
      * Visual memory

* Selective Injection of Posterior Cerebral artery
  * Hippocampus without Neo-Cortex
## Temporal Lobectomy

### TABLE 1:

**Predictors of memory outcome after ATR**

<table>
<thead>
<tr>
<th>Predictors of Verbal Memory Decline</th>
<th>Predictors of Visual Memory Decline</th>
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</thead>
<tbody>
<tr>
<td>dominant, lt ATR</td>
<td>nondominant, rt ATR</td>
</tr>
<tr>
<td>greater pre-ATR lt temporal lobe fMRI activation</td>
<td>greater pre-ATR rt temporal lobe fMRI activation</td>
</tr>
<tr>
<td>absence of hippocampal sclerosis</td>
<td>larger rt hippocampus</td>
</tr>
<tr>
<td>good preop verbal memory</td>
<td>good preop visual memory</td>
</tr>
<tr>
<td>good preop Wada verbal memory w/ rt-side injection</td>
<td>good preop Wada visual memory w/ rt-side injection</td>
</tr>
<tr>
<td>no asymmetry in activation on PET scan</td>
<td>later age at seizure onset</td>
</tr>
<tr>
<td>later age at seizure onset</td>
<td>poor postop seizure control</td>
</tr>
<tr>
<td>poor postop seizure control</td>
<td>larger rt-lateral neocortex &amp; mesial temporal excision</td>
</tr>
<tr>
<td>more extensive resection</td>
<td>pathology of resected tissue (atypical sclerosis)</td>
</tr>
<tr>
<td>male sex</td>
<td></td>
</tr>
<tr>
<td>older age at cm</td>
<td></td>
</tr>
<tr>
<td>preop major depression</td>
<td></td>
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</tbody>
</table>

Table 1 of 1
Temporal Lobectomy

* Classic Resection (Neocortex + Amygdalo-Hippocampotomy)
  * Standard (4.5 - 6 cm)
  * Tailored (3.5 cm, Electrocorticography)

* Selective Amygdalo-Hippocampotomy
  * Trans-cortical
  * Trans-sylvian
  * Subtemporal

* Ablative Stereotatic Surgery
  * Laser
  * SRS
Surgical Strategies to avoid adverse sequelae in temporal lobe surgery

* Selective Amygdalo-hippocampectomy
  * Trans-sylvian
  * Trans-cortical
  * Sub-temporal

* Stereotatic
  * Laser
  * Ultrasound
  * Radiosurgery
Selective Amygdalo-hippocampectomy
Selective Amygdalo-hippocampectomy
Selective Amygdalo-Hippocampectomy
Selective Amygdalo-hippocampectomy
Selective amygdalohippocampectomy versus anterior temporal lobectomy in the management of mesial temporal lobe epilepsy: a meta-analysis of comparative studies

A systematic review

Wen-Han Hu, M.D., Ph.D.,¹ Chao Zhang, M.D.,² Kai Zhang, M.D., Ph.D.,² Fan-Gang Meng, M.D., Ph.D.,¹ Ning Chen, M.D.,² and Jian-Guo Zhang, M.D., Ph.D.,¹,²
SAH vs ATL in the management of mesial temporal lobe epilepsy: a meta-analysis of comparative studies
HU, ZHANG ET AL, J NEUROSURG 119:1089-97, 2013

* LITERATURE REVIEW, 1990-2012
* ATL HAD A HIGHER ODDS OF CONTROLLING SEIZURES THAN SELAH FOR PATIENTS WITH MTLE
* THE 2 TYPES OF SURGERY SHOWED COMPARABLE EFFECTS ON INTELLIGENCE
* SELAH STATISTICALLY REDUCE THE ODDS OF BEING SEIZURE FREE COMPARED WITH ATL
Take Away

ATL vs SAH

* Patient Selection

* Surgeons Experience
The Ideal Temporal Lobe Epilepsy Patient

* History of febrile Convulsion
* Normal Cognition
* Hippocampal Volume Loss
* Non Dominant Hemisphere
* EEG/Neuropsychological testing are all concordant with MRI findings
Visualase

* A stereotatic, MRI-guided, minimally invasive, laser ablation system which allows monitoring of the ablation in real time
The Visualase Thermal Therapy System is an MRI-guided, minimally invasive laser ablation system which allows monitoring of the ablation in real time. The system is FDA-cleared for the ablation of soft tissue including use in neurosurgical procedures (see www.visualaseinc.com for complete indication).
Laser Ablation
Minimally Invasive
“One Stitch Closure”
Visualase

* Pros
  * Minimally invasive
  * Can be used for varied epileptogenic lesions
    * MTS
    * Tuberose Sclerosis
    * Hypothalamic Hamartoma
    * Cortical Dysplasia

* Cons
  * Concern about volume of tissue treated
  * Treatment of “dual” pathology
  * Expense
Hemispheric Disconnection

* Corpus Callosotomy
* Hemispherotomy
Corpus Callosotomy

Indications

* Medical intractability
* No surgically resectable seizure focus
* Drop attacks or atonic (akinetiс) seizures
Corpus Callosotomy
Callosotomy
“ No Seizures, No side effects”

* No Seizures
  35% Atonic Seizures
  57% of Tonic-Clonic seizures had > 50% reduction in Seizures

No Side Effects
  Split Brain Syndrome
    Language impairment
    Hemispheric competition (alien hand)
  Mortality 1-2%
Hemispherectomy

* Pathological Process affects one entire cerebral hemisphere
  * Sturge-Weber Syndrome
  * Rasmussen’s Encephalitis
  * Cortical Dysplasia
  * Hemimegalencephaly
  * Porencephaly
  * Schizencephaly
Hemispherectomy
Hemispherectomy
Neurological Status

* Maximum hemiplegia
  * Inability to perform finger movements or toe tapping
  * Increased Tone and Hyperreflexia

* Hemianopsia

* Altered Sensory modalities

* Some degree of psycho-motor retardation
Anatomical Hemispherectomy
Complications
Anatomic Hemispherectomy
Complications

Anatomic Hemispherectomy

* Brain Shift
* Hydrocephalus
* Superficial Cerebral Hemosiderosis (SCH)
  * Median Interval of 8 years following anatomic hemispherectomy in 25% of cases
Functional Hemispherectomy
Hemispherectomy

No Seizures, No Side Effects

* Seizure Free
  * 70%

* No Side Effects
  * Mortality 1-5%
  * Hydrocephalus 7-50%
Deep Brain Targets for Epilepsy

* Anterior Nucleus of Thalamus
* Centromedian Nucleus of Thalamus
* Caudate Nucleus
* Cerebellar Nuclei
* Hippocampus and Amygdala
* Subthalamic Nucleus
* Locus Coeruleus
Deep Brain Stimulation in Epilepsy

* Location of stimulating electrode within or near the confirmed or suspected focus or foci that are generating seizure

* Location of stimulating electrode at sites implicated in the genesis or propagation of seizure but remote from the actual seizure focus or foci
Vagal Nerve Stimulation

* Mechanism of Action
  * Over 80% of vagal nerve fibers are afferents that return signals to the nucleus of the solitary tract which projects to limbic system
  * PET scans illustrate changes in regional cerebral blood flow in thalamus with VNS
  * Hippocampal depth electrodes demonstrate reduction in epileptiform sharp waves with VNS
VNS

- Thalamus
- Locus Coeruleus
- Amygdala
- Insula, Anterior Cingulate Gyrus, Orbitofrontal Cortex
- Hippocampus
- Dorsal Raphe
- Nodose Ganglion
- Nucleus Cuneatus
- Medial Reticular Formation
- Parabrachial Nucleus
- Hypothalamus
- Area Postrema
- DMN
- Solitary Tract
- Spinal Cord
- Vagus
Vagal Nerve Stimulation
Vagal Nerve Stimulation

Slides for Epilepsy
Vagal Nerve Stimulator
Deep Brain Stimulation in Epilepsy

* Stimulation paradigms
  * Continuous
  * Cyclical
  * Seizure initiated
Vagal Nerve Stimulation

* Approved by FDA 1997
  * Patients over the age of 12 with partial onset seizures
  * Unilateral left side placement – intermittent stimulation

* Seizure frequency reduced by 35% at one year, a three years 44%. Fewer than 10% achieved seizure freedom

* Side effects/Complications
  * Intermittent hoarseness (28%), cough (14%), voice alteration(13%)
  * Infection 3-5%
DBS of ANT
Mechanism of Action

- Lesions of ANT resulted in improved seizure control
- High Frequency stimulation of the ANT has been shown to increase seizure threshold
Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy “SANTE”

* 110 patients 18-65 years of age who had failed at least 3 AED. Partial seizures occurring > 6/ M, but < 10/D

* Stimulation “on” one minute and “Off” five minutes
Stereotatic Lead Placement
DBS Anterior Thalamus
Stimulation ANT

* Reduced Seizure frequency 42% at one year, 56% at two years and 68% at five years

* Side effects/complications
  * Hemorrhage 4.5% (asymptomatic)
  * Infection 14%
  * Depression 14.8%
Responsive Neurostimulation
Closed Loop/Responsive Neurostimulation

* Mechanism of action similar to DBS

* Instead of targeting a predetermined target in all patients, stimulation only occurs if triggered by early seizure activity
Responsive Neurostimulation
Responsive Neuro Stimulation
Responsive Neurostimulation

* Seizure reduction 41.5% after one year, 53% after three years

* Side effects/Complication
  * Hemorrhage 4.7%
  * Infection 5.2%
Sante vs NRS
Neurostimulation Summary

* Decrease in seizure frequency at three years
  * ANT DBS 51-58%
  * RNS 48%
  * VNS 40-44%

* Seizure free patients < 10%
Epilepsy Test Questions

Patient’s aura (visual, auditory, GI) in Epilepsy may localize the location or source of Generalized Seizure

- True
- False Generalized Seizures do not have Auras

Surgical intervention should not be considered unless the patient has failed at least 3-4 AEDs

- True
- False If a patient has failed 2 AEDs, there is less than 1% chance a third AED would be successful.

Surgery for Medial Temporal Sclerosis is more effective than AEDs

- True In the NEJM study 58% of surgical patient were free if seizures, vs 8% in medical treatment
- False
Epilepsy Test Questions

* Patient’s aura (visual, auditory, GI) in Epilepsy may localize the location or source of Generalized Seizure
  * True
  * False

* Surgical intervention should not be considered unless the patient has failed at least 3-4 AEDs
  * True
  * False

* Surgery for Medial Temporal Sclerosis is more effective than AEDs
  * True
  * False