Epilepsy Surgery - A Short Update

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Abstract

Epilepsy surgery has been rapidly progressing over the last decade or so, with many previously untreatable conditions now satisfactorily managed to allow improved quality of life and seizure control without excessive medication and debilitating neurological deficits. We present a brief recap on accepted axioms of epilepsy surgery with a look at the future with a short summary of seizure disorder itself and the various management options.

Keywords: Drug recalcitrant epilepsy; Intractable epilepsy; Epilepsy surgery; Temporal love epilepsy

Introduction

Epilepsy surgery has been the ugly sister of neurosurgery’s charmed souls vascular and skull base surgery. But in the last decade or so, it has occupied an enviable niche for drug recalcitrant epilepsy especially in children. We explain the basic concepts of Epilepsy surgery along with suitable examples below.

Indications

Patients with refractory epilepsy are generally suitable for one or more procedure. The aim is to either enable seizure free survival or marked decrease in seizure frequency and intensity enabling better quality of life. Epilepsy which is disabling in any way is a candidate for invasive investigations and eventual surgery. All that is expected is an acceptable risk to benefit ratio.

Contraindications

There are a few diseases that are not suitable for surgery. These include disorders such as Idiopathic age-related epilepsies, Progressive underlying neurological diseases, infectious causes, severe mental retardation, and psychopathology. An incapability to comprehend and cooperate with the procedure can also be problematic as some procedures require the patient to stay away during surgery and cooperate in an intimate manner. Bilateral, independent inter ictal and/or ictal EEG involvement also makes surgery difficult. Involvement of eloquent cortex by even benign lesions makes surgery difficult as post op deficits become unavoidable. Unrealistic expectations at the end of the day are the most difficult and painful obstacle to surmount in the charge to improve quality of life.

Intractability

Stringent criteria for medical intractability as defined are:

1. Failure of two appropriate anticonvulsants,
2. The occurrence of an average of one seizure per month for at least 18 months, and
3. No more than 3 months of seizure-free hiatus during those 18 months.

Surgically remediable conditions

Surgery has traditionally been recommended for tumors precipitating epilepsy. The definition has been expanded to include, vascular lesions such as cavernomas, Arteriovenous malformations, aneurysms and hemangioblastomas, developmental malformations such as hemimegalencephaly, cortical dysplasia’s, porencephaly, lissencephaly and others, scar epilepsy, infectious lesions such as abscesses, empyema and encephalitis, strokes and other ischemic insults, and finally traumatic injuries. The lesions are summarized in Diagram 1, where epilepsy has been divided into Temporal, Extra temporal, and generalized epilepsy (also called catastrophic epilepsy).

Surgical options

Surgery can be classified as listed in Diagram 2. There can be resective options such as topectomies, lesionectomies and lobectomies, disconnections such as callosotomies, hemispherotomies, Neuroaugmentative surgery such as anterior thalamic nucleus DBS and vagal stimulation and finally radio surgery.

Patient evaluation

All patient evaluation must be done holistically as a multidisciplinary team approach. Diligent an intensive evaluation is essential to ensure good outcomes and prevent unnecessary surgery. Investigation is divided into 2 phases: I and II as shown in Diagram 3.

Phase I

This phase includes non-invasive investigations to attempt localization of the epileptic focus over the surface of the brain before deciding upon surgery and approach. The phase consists of:

History & examination: An accurate history and examination provide a window into the semiology of the disease. Important points to ask and investigate include Auras, Seizure onset, progression, completion, Aphasia, manual automatism, any and all neurological deficits and lastly neurocutaneous syndromes. 2 or more semiologies would be possible if multifocal epilepsy is present (Table 1). Localization of the seizure focus based on Language (Table 2), Autonomic phenomena (Table 3), Motor symptoms (Table 4) and examination findings (Table 5) are summarized as stated.

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Temporal Lobe seizures can be separated into
1. Limbic seizures arising from the amygdala (80%).
2. Antero infero-mesial seizures arising from the entorhinal cortex & hippocampus area.
3. Neocortical seizures arising from the neocortex.

The auditory illusory auras may originate from either side of temporal neocortex.

Frontal lobe seizures: These are much briefer than their temporal lobe counterparts and are associated with less post-ictal confusion but are more motor in their characteristics. They are more likely to be involved with secondary generalization but are less likely to demonstrate psychic, emotional or other affective phenomena. Frontal epileptics are more likely to exhibit a rapid onset and offset and are more likely to occur nocturnally than other partial seizures. The automatisms of frontal lobe are of a “forced nature” These collectively stand in particular contrast to temporal lobe seizures. Frontal seizures can be classified anatomically into the following types.

Fronto-polar seizures: Origins are often from scars following head injuries. They have the greatest likelihood of simply being characterized by what appear clinically to be primary generalized seizures. They may have some of the general characteristics of FLE, especially contralateral head deviation.

Orbitofrontal seizures: These patients may have a semiology that mimics temporal lobe seizures in which case the origin is usually attributed to the posterior part of the orbital cortex. Once again, however, it may involve, in various combinations, other frontal lobe semiology, especially contralateral head and eye deviation.

Premotor seizures: The epileptiform area includes the Supplementary Motor Area (SMA). Prominent leg movements favour involvement of the supplementary motor area. Head and eye deviation with varying bilateral tonic posturing are the commonest seizure. When the deviation occurs at the onset of the seizure when consciousness is intact it has significant localizing value to the contralateral frontal cortex. Those seizures arising in the mid part of the frontal lobe have a prominent bilateral tonic posturing. Bipedal automatisms may take the form of symmetric bicycling or kicking movements.

The so-called “fencing posture” is classically associated with the contralateral FL, particularly the SMA. This complex posture is characterized by abduction, external rotation, and partial flexion of
Table 1: Differences between frontal and temporal seizures.

<table>
<thead>
<tr>
<th>Features</th>
<th>Frontal Lobe</th>
<th>Temporal Lobe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seizure Frequency</td>
<td>Frequent often daily</td>
<td>Less Common</td>
</tr>
<tr>
<td>Seizure Onset</td>
<td>Abrupt, Explosive</td>
<td>Slower</td>
</tr>
<tr>
<td>Progression</td>
<td>Rapid</td>
<td>Slower</td>
</tr>
<tr>
<td>Initial Motor Signs</td>
<td>Less Common</td>
<td>Common</td>
</tr>
<tr>
<td>Automatism</td>
<td>Less Common</td>
<td>More Common and Longer</td>
</tr>
<tr>
<td>Hipedal Automatism</td>
<td>Characteristic</td>
<td>Rare</td>
</tr>
<tr>
<td>Complex Posture</td>
<td>Early, Frequent and Prominent</td>
<td>Late, Less Frequent and Less Prominent</td>
</tr>
<tr>
<td>Hyperkinetic Motor Signs</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Somatosensory Symptoms</td>
<td>Common</td>
<td>Rare</td>
</tr>
<tr>
<td>Speech</td>
<td>Loud Vocalisation, Verbalization Speech</td>
<td>Non Domenint Seizure</td>
</tr>
<tr>
<td>Seizure Duration</td>
<td>Brief</td>
<td>Longer</td>
</tr>
<tr>
<td>Secondary Generalisation</td>
<td>Common</td>
<td>Less Common</td>
</tr>
<tr>
<td>Postictal Confusion</td>
<td>Less Prominent or Short</td>
<td>More Prominent and Longer</td>
</tr>
<tr>
<td>Postictal Dysphasia</td>
<td>Rare unless it spreads to the Common in Dominent Temporal Lobe</td>
<td>Temporal Lobe Seizure</td>
</tr>
</tbody>
</table>

Table 2: Showing speech as a localizing factor in epilepsy.

| Ictal Speech Arrest | Temporal Lobe Seizures, Usually Dominant Hemisphere |
| Ictal Speech Preservation | Temporal Lobe Seizures, Usually Non-Dominant Hemisphere |
| Postictal Dysphasia | Dominant Hemisphere Involvement |

Table 3: Showing autonomic features of specific seizure syndromes.

| Ictus Emeticus  | Right Temporal Seizures |
| Ictal Urinary Urge | Right Temporal Seizures |
| Piloresciton (Goose Bumps) | Left Temporal Seizures |

Table 4: Showing motor system features of seizures to clue in localization.

| Early Nonforced Head Turn | Ipsilateral of Seizure Origin |
| Lateforced Head Turned    | Contrateral of Seizure Origin |
| Eye Deviation             | Contrateral of Seizure Origin |
| Focal Clonic Jerking      | Contrateral of Seizure Origin, Perirolandic |
| Asymmetric Clonic Ending  | Contrateral of Seizure Origin |
| Dysmetric Limb Posturing  | Contrateral of Seizure Origin |
| Fencing Posture           | Contrateral Frontal Lobe (Supplementary Motor) seizures |
| Figure of 4 Sign          | Contrateral to Extended Limb, Usually Temporal Lobe |
| Unilateral Ictal Paresis  | Contrateral of Seizure Origin |
| Post Ictal Todds Paresis  | Contrateral of Seizure Origin |

Table 5: Examination findings in epilepsy syndromes.

<table>
<thead>
<tr>
<th>Examination</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response to Communication</td>
<td>Level of Awareness</td>
</tr>
<tr>
<td>Speech (Naming, Reading)</td>
<td>Dominant Hemispheric Involvement</td>
</tr>
<tr>
<td>Memory (Presenting words or Phrases for later Recall)</td>
<td>Temporal Lobe Involvement</td>
</tr>
<tr>
<td>Distractibility</td>
<td>Frontal Lobe Involvement</td>
</tr>
<tr>
<td>Response to Passive Eye opening</td>
<td>To Exclude Pseudoseizure (Tight Closure)</td>
</tr>
<tr>
<td>Response to physical Stimulation</td>
<td>Attention, Motor Dysfunction</td>
</tr>
<tr>
<td>Weakness or Lack of Motor Control</td>
<td>Contralateral Seizure Origin</td>
</tr>
<tr>
<td>Planter Extensor Response</td>
<td>Post Ictal Paresis</td>
</tr>
</tbody>
</table>

Table 6: Differences between frontal and temporal seizures.

- The contralateral arm at the shoulder, contralateral deviation of the head and eyes such that they "look at" the contralateral arm, extended ipsilateral arm downwards and backwards, and with the feet apart so as to support the partially contralaterally rotated trunk. Occasionally, the upper limb is also flexed at the elbow with the hand raised to the face that has turned forcefully towards it. There is occasionally guttural, ill-understood speech.

- **Dominant opercular seizures:** These usually begin with an alteration in speech. The alteration may be typical dysphasic speech, a form of non-specific guttural speech, or an arrest of speech. Post-ictal dysphasia is commonly seen.

- **Rolandic Seizures:** Rolandic seizures combine both motor and sensory components. The sensory features can be positive (e.g. pins and needles, pain, pricking, tingling) or negative (numbness). Elementary paraesthesiae are reported to be the most characteristic of seizures arising in the post-central gyrus. In pure sensory seizures there is nearly always dysfunction of the part involved, which may be awkwardness, typical sensory ataxia, or paralysis. The spread (intracortically) within the Rolandic cortex, e.g., sensory and/or motor, over contiguous parts of the associated homunculus, clinically is reflected in a "march" from one place on the body to another.

Unlike the tonic activity associated with seizures arising outside of the Rolandic cortex, which often has unreliable localizing and lateralizing value, Rolandic motor activity is clonic and is unambiguously localizing to the contralateral motor cortex in the area of the homunculus from which it arises, and usually is associated with transient post-ictal weakness in the involved part.

The differences between temporal and frontal seizures are summarized in Table 1. Apart from history & clinical examination, investigations form an important part of the phase 1 test battery. These include:

**EEG (Electro Encephalogram)**

This is probably the most important investigation that separates pseudo seizures from true epilepsy. It is Positive in 50% to 60% of patients with epilepsy. The importance of EEG lies in its ability to:

1. Diagnose epilepsy.
2. To localize the site (using Ictal EEG recordings).
3. To delineate the epileptogenic zone (using Inter ictal EEG).

An Ideal candidate would have a well localized IED's supporting presence of one EZ. Continuous video EEG allows visuo-electrophysiological analysis and convergence. Video EEG is therefore considered the mainstay of localization. The usage of EEG offers the investigator a threefold advantage. It allows a too further characterize the inter ictal EEG, to detect, characterize and quantify the patient's habitual seizures and to acquire physiologic data regarding seizure localization that can be correlated and compared with anatomic data obtained from Neuroimaging.

**Continuous video EEG**

This is typically done over 5-7 days. The procedure requires inpatient care and close observation. The first stage involves activating procedures such as sleep deprivation and cessation of Anti-Epileptic Drugs. The patient is in a room with continuous video and electrophysiological recordings simultaneously progressing. This
allows characterizing the seizure behavior which allows correlation of ictal behavior with EEG discharge, establishment of whether a patient has more than one seizure type, and finally lateralization and localization patterns of the seizure critical for further decision making.

**Imaging studies**

The most important subset of investigations regarding surgical planning involves imaging. MRI is the modality of choice. MRI epilepsy protocol which includes T1, T2 FLAIR, and susceptibility weighted sequences are used commonly to detect lesions and regions of abnormal development, such as DNETs, cavernomas and gliomas. Hippocampal sclerosis is the most common pathology detected. fMRI, MRS, DTI, tractography are also important in surgical planning. Other imaging modalities of import include PET scan and SPECT.

Quantitative MR imaging: In some patients with intractable focal epilepsy, structural MRI does not demonstrate a lesion. Usually a 3D T1 weighted image offers an objective means of analyzing MR images and presents an improved likelihood of detecting subtle lesions. Volumetric neocortical measurements may provide an objective way to evaluate the extent of resection and its relation to surgical results. This is especially true in early Mesial Temporal Sclerosis and subtle dysplasia of the cortex (Figure 1).

**DTI (Diffusion Tensor Imaging):** Diffusion of substances soluble in water presents an analysis of membrane integrity which differs from normal to abnormal. Diffusion is greatest parallel to the white matter tracts but minimal perpendicular to them. Hence Tractography enables the visualization of tracts with respect to the lesion and allows accurate planning and deficit free outcomes for surgery. DTI is useful in MCD and acquired lesions where there is increased mean diffusivity, increased perpendicular diffusivity. Intraoperative DTI is also available in on table MRIs where real time analysis of tract position is available.

**MRS (Magnetic Resonance Spectroscopy):** This is a newer adjunct to MRI. Here the altered concentration of NAA and Choline shows the nature of Lesional metabolism characteristic of certain lesions. The MR spectroscopy findings are consistent with the Histopathological characteristics of reduced neuron cell counts or neuronal dysfunction with increased glial cell numbers. This is of relevance in extra temporal lobe epilepsy, where the ability of MR spectroscopy to lateralize the epilepsy is less than 50%.

**fMRI (functional MRI):** This is used for mapping language, memory and sensorimotor location for presurgical planning. This imaging is based on the observation that increased neuronal activity is associated with increase in Cerebral Blood Flow and therefore an increase in the oxyhaemoglobin/deoxyhaemoglobin ratio, thus predicting active functioning areas of the brain over gliosis or an increase in the oxyhaemoglobin/deoxyhaemoglobin ratio, thus allowing characterizing the seizure behavior which allows correlation of ictal behavior with EEG discharge, establishment of whether a patient has more than one seizure type, and finally lateralization and localization patterns of the seizure critical for further decision making.

**SPECT (Single Photon emission CT):** Ictal SPECT is the ideal method for localization and lateralization of seizure onset. It shows hypermetabolism (99mTc HMPAO) with 89% sensitivity for localization (vs. PET 63%) SPECT also performed better in the setting of negative MRI, and false lateralization is rare. Post Ictal SPECT is comparable to Interictal PET (70%). Inter ictal scan shows hypoperfusion in a large area in the hemisphere of onset. Interictal scan though has less sensitivity for seizure, 50%. Ictal/Interictal quantitative difference analysis provides for the best and most reliable information for seizure focus localization.

**Magnetoencephalography (MEG):** This is a rare non-invasive technique, which measures the magnetic field produced by the electric currents in the brain (epileptiform discharges). The subtle flux created between the magnetic field of the seizure discharge is crossed with an intense magnetic field produced in a confined specially prepared space to effect superb electrophysiological localization. The electric points are superimposed onto an MRI (usually T1 weighted image) to allow structural and spatial localization as well. The advantages are that it is a sensitive tool for localization, where signals generated are not distorted by skull and scalp as in EEGs. The disadvantages are that it is a very expensive investigation and as mentioned earlier, the setup needs to be kept in as hield room. To eliminate outside magnetic signals, this will interfere with the results (Figure 4).

**Neuropsychological testing:** These include Epilepsy related cognitive impairment, Memory status for baseline and Prediction of potential post op deficits, IQ testing-disparity in different components lateralizes the EZ, along with Verbal IQ and performance IQ.

- Post investigation evaluation
  - The analysis of the phase 1 investigations should lead to 1 of the 4 results.
  1. Localization of seizures to one temporal lobe.
  2. Bilateral localization.
  3. Posterior temporal or extra temporal.
  4. Inability to localize the site of seizure onset.

The patients in group 1 to 3 undergo further phase 2 investigations for optimal results during surgery.

**Phase II**

These investigations are invasive and done usually on the cortex after surgical dissection. The investigations allow complete or maximum safe resection of the causative Epileptic Zone (EZ).

The Goals are to confirm the primary EZ is the only focus, and to determine the risk involved post resection causing cognitive and neuropsychological deficits. Indications include situations where the seizure onsets are lateralized but not localized, the seizure onsets are localized but not lateralized, neither lateralized nor localized (Diffuse), dual pathologies, and finally to allow identification of the eloquent cortex. Advantages include allowing recording of seizure activity to be done from close proximity to the brain which is not possible with EEG bypassing the scalp and skull. The exact EZs are identified thus. Disadvantages include the fact that implantation involves a surgical risk. The different implements in phase 2 testing include:

**Electrocorticography (ECoG)**

This novel technique allows for measurement of electrophysiological activity on the brain surface. The electrodes used...
vary as stated below.

**Epidural electrodes:** Electrodes are placed on the dura only. Advantages include a high amplitude EEG without muscle or movement artifact along with Good lateralization. The risk of infection is minor compared to more invasive methods. The disadvantages include the fact that it can record EEG changes only over the lateral convexitities and gives only an approximate localization.

**Subdural electrodes:** These electrodes measure seizure activity on the surface of the cortex. These are of 3 types- Grid, Strip, and Foramen. Grid electrodes allow for more intensive with the placement of a grid of electrodes onto the surface. The advantages are that no motion artifacts occur as it is fixed to dura, and that it does not penetrate the cerebral tissue. A wide area of cortical surface is covered hence making detection of the EZ easy. It can be used for brain mapping as well minimizing post procedure deficits. The disadvantages are all surgical effects such as haemorrhage, oedema and infection. No specific effects have been noted as yet (Figure 5).

**Foramen ovale electrodes:** These are Intra cranial electrodes introduced percutaneously into the foramen ovale using fluoroscopic guidance to measure electric spikes in the mesial temporal structures. It may be used for Mesial Temporal Lobe Epilepsy (MTLE) detection alone. The advantages are that the procedure involved is minimally invasive. However, as it measures only MTLE biased information remote signals are not well recorded. Rarely complications of improper placement of the electrode under fluoroscopic techniques may lead to Facial pain, Temporo-Mandibular joint dysfunction, and mandibular hematomas.

**Intra cerebral depth electrodes:** Flexible electrodes with multiple contact points are placed stereotactically at depths into the brain substance. The readings help to determine the depth of tissue needed for resection allowing no normal white matter to be damaged during resection. Common sites include the hippocampus, amygdala, Orbitofrontal, cingulated gyr. Depth electrodes are indicated in extra temporal EZ as well as with subdural electrodes in dual pathology.

**WADA test**

Juhn Wada in 1960, at the Montreal Neurological Institute created a unique invasive test to detect dominance. The test is on historic importance now, yet is important to understand the evolution of investigations to decipher dominance and speech control. The procedure involved injecting 150 mg to 200 mg of Amobarbital (Amytal) into the common carotid artery (Prior to this and angiogram must be done to rule out persistent trigeminal, otic, hypoglossal or proatlantic arteries to avoid respiratory and circulatory problems as a result of shunting to the brainstem) The injection is made with the patient counting, the forearms up in the air and the fingers either moving constantly or gripping an examiners hand. As the injection is completed, contralateral hemiplegia and flaccid limbs occur with one hand falling off or loosening its grip on the examiners hand. The hemiplegia lasts for 1.5-5 minutes. At this time speech is tested. If speech is normal, then the side injected is NON dominant. This is followed by dysphasia and lasts for 1-3 minutes following which normal speech. Functional MRI has now replaced the WADA test. Dangers include a 3% possibility of permanent paralysis along with speech loss.

Once investigations are complete and the plan for surgery has been agreed upon, the plan is discussed with the patient and relatives by the multidisciplinary team to apprise them of all features including deficits which may occur post operatively and long-term consequences of surgery and the disease. Five factors which are predictive for good seizure control are

2. Absence of status epilepticus.
3. MR imaging-confirmed ganglioglioma or DNET.
4. Concordant lateralizing memory deficit; and
5. Absence of dysplasia on MR images

No significant differences exist regarding different resection types performed for comparable lesions. Neuropsychological testing done before surgery ensures better postoperative results after limited resections especially in attention level, verbal memory, and calculated total neuropsychological performance.

**Surgical procedures:** Surgical techniques range from curative to palliative procedures which minimize the morbidity of the disease making a significant improvement in the quality of life in a specific subset of patients. As shown in Diagram 4, a variety of factors ranging from pathology, location, age and presence of eloquent cortex around the EZ serve as predictors of surgical outcome.

The utility of temporal lobe surgery for intractable epilepsy vs. continued treatment with antiepileptic drugs was analyzed by Wiebe et al. [1]. The study was a prospective, randomized, controlled trial involving eighty patients randomized to surgery or medical treatment for one year. After a year, those undergoing surgery had a much higher rate of seizure freedom (58% vs. 8%), significantly better quality of life than the observation or medical category making epilepsy surgery highly recommended. These results have been replicated across many centers in different countries showing the increased utility and acceptance of epilepsy surgery over the years in treating medically intractable seizures in patients of all ages. We now present a few important aspects to select surgical techniques and their uses and concerns below.

**Resective procedures**

These include lobectomies, Lesionectomies, topectomies and other similar procedures. Surgery for temporal and extratemporal epilepsy is dealt with in brief below. Due to its extensive use, the temporal lobectomy along with its derivatives will be discussed in some detail.

**Temporal lobe surgery**

The techniques of Temporal Resection include:

1. **Temporal lobectomy**
   a. Anterior Temporal Lobectomy (ATL)
   b. Antero Medial Temporal Resection (AMTR)
   c. Tailored (ECoG with or without speech mapping)

2. **Selective medial resection**
   a. Selective Amygdalohippocampectomy
   b. Transcortical approach
   c. Trans-sylvian approach
Figure 1: Quantitative MRI Studies showing a coronal view of the brain in T2 and FLAIR demonstrating volume loss and gliosis in the right hippocampus as shown by the arrows.

Figure 2: Showing functional MRI images in the brain describing hypermetabolic areas during an activity.

Figure 3: Showing PET images of the brain with areas of hypoperfusion shown are blue and areas of hyper perfusion shown in red.

Figure 4: Showing the output of a MEG scan where the images show a clear localization of the epileptic zone which in the second image is superimposed on a T1 weighted MRI image of the brain to aid in surgical planning.

Figure 5: Showing strip and guide electrodes used for Electroecorticography.

Figure 6: Showing the incision, and extent of resection for an anteromedial temporal lobectomy.

Figure 7: Showing the incision, and extent of resection for a selective amygdalohippocampectomy.
3. Subtemporal approach

**Extratemporal epilepsy surgery**

The techniques described here include:

1. **Topectomy**
2. **Lesionectomy**
3. **Anatomical Hemispherectomy**

**Anterior temporal lobectomy (ATL)**

Here the anterolateral temporal lobe (4 cm to 4.5 cm from temporal tip along middle temporal gyrus), amygdala, uncus, hippocampus and Parahippocampal gyrus to level of collicular plate are removed. Complications include hemiparesis which occurs up to 1.25% of cases due to damage of the perforators to the anterior choroidal artery, contra lateral superior quadrantanopia from damage to the Meyer loop, infection, cranial nerve III or IV palsies seen in up to 20% of cases, and verbal memory problems particularly in speech-dominant temporal lobe resection.

**Anteromedial temporal resection (AMTR)**

Spencer et al. [2] published the first description of this procedure. Here the anterior 3 cm to 3.5 cm of middle and inferior temporal gyrus, amygdala, 3 cm to 4 cm of hippocampus and the Parahippocampal gyrus are resected. Candidates for AMTR have complex partial seizures with semiology typical of mesial temporal lobe epilepsy. MRI evidence of unilateral hippocampal atrophy and an increased T2-weighted signal from the hippocampus area indicating neuronal loss, unilateral temporal lobe hypometabolism on PET scans and EEG confirmation that seizures begin over the temporal area ipsilateral to the hippocampal atrophy or PET scan evidence of hypometabolism in anteromedial temporal region (Figure 6).

The procedure is a 2-stage surgery. The 1st stage involves removing an anterior temporal lobectomy removing a major part of the temporal neocortex, and the 2nd stage involving the removal of Parahippocampal gyrus, hippocampus and amygdala. Long term seizure outcome is excellent with initial seizure free rate at 80%; 5 year seizure free rate at 50% another reassuring feature of the procedure is the running down phenomenon, where incompletely resected EZs cause seizures initially but gradually loose the power to generate seizures, leading to better results over time. Cognitive outcomes are minimal in non dominant resections. The most common result involves neuropsychological deficits due to excision of the mesial temporal structures resulting in some memory loss. Health related quality of life is better after surgery [3-5].

Specific complications include visual field loss due to injury to the geniculocalcarine fibres, contralateral superior quadrantanopia, contralateral homonymous hemianopia and horizontal & vertical diplopia due to injury to the 3rd & 4th Cranial Nerves during resection. Hemiparesis may also occur due to anterior choroidal artery injury, basal ganglia injury during amygdala resection, injury to arteries in the hippocampal sulcus, and retraction injury of ipsilateral cerebral peduncle. Lastly aphasia may occur during dominant lobe resections due to damage to the superior temporal gyrus and the Wernicke's area.

**Selective amygdalohippocampectomy**

This is a tissue sparing operation with removal of mesial temporal structures, the uncus portion of amygdala, anterior portion of hippocampus, and a portion of Parahippocampal gyrus. The approach may vary from Transcortical (via middle temporal gyrus as proposed by Niemeyer 1958) vs. Transsylvian as proposed by Yasargil in 1982 with a new Subtemporal approach proposed by Hori in 1991. The Trans temporal approach through the middle temporal gyrus proposed by Niemeyer is a more direct approach but causes neocortical breach and injury. The Transsylvian approach has a complete avoidance of neocortical injury but is more demanding and has a danger of causing injury to vascular structures in the sylvian fissure. The sub temporal approach is associated with fewer neuropsychological deficits but has a higher incidence of retraction injury deficits (Figure 7).

**Topectomy**

This is the resection of focal segment of the cerebral cortex. It is primarily used in Extra-Temporal epilepsy. The indications include medically intractable seizures interfering with development and mature EZs with no possibility of spontaneous regression. The procedure involves preservation of the essential motor and language areas followed by a subpial dissection and gyral resection done up to the bottom of sulcus, removing only grey matter. Outcomes are encouraging with seizure free rates approaching 45% [6].

**Lesionectomy**

These are surgical resections aimed at curbing epilepsy by removing structural brain lesions such as malformations of cortical development, low-grade neoplasms, vascular malformations, etc.

Surgical approach depends on lesion location. Intraoperative ECoG is generally used to delineate margins of epileptogenic zone and guide resection as well as evaluate completeness of resection. ECoG correlated significantly with clinical improvement. Its Sensitivity is approximately 100% (95% CI; 96%-100%) and specificity is 68.3% (95% CI; 51.8%-81.4%) with a positive predictive value of 89.9%. The suspected regions of epileptogenesis may involve eloquent cortex, hence mapping of cortical function during diagnostic work-up using fMRI, MEG Coupled with mapping by intraoperative cortical stimulation assists in optimal seizure control as well as in minimizing deficits. In the absence of pathological abnormalities, extratemporal resections represent the poorest outcome of all seizure surgery.

**Hemispherectomy**

Dandy performed the first hemispherectomy in 1923 for a diffuse malignant glioma. Today’s indications are for seizures arising over most of one hemisphere, severe hemispheric damage during development processes, Sturge-Weber syndrome, extensive perinatal Infarcts, Hemimegalencephaly, Rasmussen's Encephalitis and (increasingly rare nowadays but of historical value), failed functional hemispherectomy patients. The goal is to remove or disconnect all of cortex of one hemisphere from the rest of the brain. The steps involve a Tran's sylvian approach to expose the circular sulcus. Temporo-mesial resection is followed by a complete opening of the lateral ventricle and Frontobasal and Posteromedialbasal disconnection. In a resective procedure, all the disconnected hemisphere is removed piecemeal (Anatomical Hemispherotomy) [7,8].

An ideal candidate is one who already has contralateral hemiparesis, hemianopsia along with intractable seizures. In the short-term seizure cure occurs in most patients. However, progressive worsening of the neurological status of the patients a few years after surgery (an average of 8 years after surgery), leading to death in up to 30% to 40% of the patients occurs due to extensive iron deposits on the brain surface, with a membrane lying over the hemispherectomy cavity called “superficial cerebral hemosiderosis” This has led to a
Disconnection procedures

Disconnection procedures are gaining importance in the treatment of wide areas of EZs effecting optimal seizure control with minimal resective surgery. It however does not entail, that the corresponding deficits will also be mild or minor. Depending upon the area disconnected, significant disability can be created, which needs to be discussed and explained before surgery to the relatives and patient in order to allow better post op recovery and acceptance. The various procedures include:

1. Corpus Callosotomy
2. Multiple Subpial transections
3. Posterior Quadrant disconnection, and

We will go through a few prominent procedures here in this section.

Callosotomy

Introduced in 1940 by van Wagenen and Herren, it involves the transections of anterior third of the corpus callosum. The rationale is that disruption of rapid spread of certain seizures from one hemisphere to the other gives better seizure control and changes a generalized seizure into a partial seizure thereby improving morbidity. Seizures that respond well include Drop attacks, atypical absence, and GTC seizures with diffuse EZs. The most important complication apart from those of surgery is disconnection syndrome. (Alien hand syndrome) which may be problematic post surgery especially for extensive disconnections [9,10].

Multiple subpial transections: Developed to treat epilepsy arising from cortex that cannot be resected (either an eloquent area or a very wide region). The rationale implies that a cortical island wider than 5 mm or with horizontal connections larger than 5 mm is required to support paroxysmal discharge. Thus, disruption of horizontal connections within cortex that are vital for synchronizing neural activity, help in seizure control without affecting ascending and descending fibres. Thus, the procedure involves disconnecting the grey mater columns in the eloquent cortex. Indications include EZ in eloquent cortex (sensory, somatosensory, and visual), associated focus on perioperative intra cranial investigations such as Electro corticalography (ECoG) or MRI, Landau Kleffner syndrome, and patches of EZs caused by Rasmussen's encephalitis. The procedure involves a wide craniotomy and isolating the EZ with ECoG using grid & strip electrodes, followed by transections in the pia and grey matter done for 5 mm to 6 mm a piece all around separating the EZ from the rest of the grey matter. Care is taken to avoid vascular injury.

Post Surgery, ECoG is repeated to ensure all the EZs are within the resected region and to confirm reduced IED's. Complications include transient deficits restricted to the eloquent cortex transected, some Sub Arachnoid Haemorrhage. The Outcomes are usually good with seizure free rates as high as 90%.

Functional hemispherectomy & posterior quadrant disconnection: Described initially in the 1970s by Rasmussen, the procedure attained popularity over the years owing to the efforts of 2 French neurosurgeons in the 1990s. 2 different approaches were described; a vertical approach was described by Delalande and colleagues while a lateral approach was described by Villemure et al. The common goal of all of the Hemispherotomy is the interruption of the corpus callosum, the internal capsule and corona radiata, the mesial temporal structures and partly the frontal horizontal fibres. The standard functional hemispherectomy involves 4 steps, temporal lobectomy including amygdalohippocampectomy, Suprasylvian central block disconnection, and Transventricular Callosotomy (including the splenium) along with Frontal and parieto-occipital disconnections. A smaller version involving only the posterior quadrant and sparing the frontal connections has been popularized as the Posterior Quadrant Disconnection. This is popular in EZs isolated to the posterior quadrant and is less morbid than the complete Hemispherotomy (Figure 8).

Rasmussen's study in 2007 involved a total of 19 patients between 2001 and 2007 which were followed up for 198 weeks after surgery. He reported Engel's class I outcomes in 18 patients and class II in 1 patient. There were deficits which improved well. Postoperative limb power improved in 3 patients while the rest had the same power and movement as preop. Cognitive functions improved in all patients as well.

Neuroaugmentive Procedures

These include Deep brain stimulation of various subcortical nuclei and vagal nerve stimulation techniques. These are described below.

Vagal nerve stimulation (VNS)

FDA approval of VNS was received in 1997 as an adjunctive therapy in patients 12 years of age and older for intractable epilepsy of all kinds. The mechanism of action of VNS not clear. It is thought that desynchronizing electroencephalography activity leads to relief from the physical activity of the seizure thereby effecting remission. Indications for VNS include a failure of medical therapy & the patient being unsuitable for resection. In the procedure, a standard pacemaker generator which houses a lithium battery along with electronics is implanted in a subclavicular pocket. The lead wire is tunnelled into the left carotid sheath via a transverse or longitudinal neck incision. The spiral endings of the leads attached to left vagus nerve. The left vagus is used due to a lower percentage of efferent fibres to the atrioventricular node, thereby sparing the heart from arrhythmias that may occur during stimulation. Seizure Control is well documented. Here 35% to 45% of patients have decreased frequency of seizures exceeding 50%.

Figure 8: Showing the post of a posterior quadrant disconnection demonstrating the region disconnected from the rest of the functioning brain.
And around 2% become seizure free. The complications include infection (5% to 7%), vocal cord paralysis (~ 1% of patients), hoarseness, cough, dyspnoea, nausea, and rarely obstructive sleep apnoea.

**Deep brain stimulation (DBS) for epilepsy**

General concept here is to disrupt the seizure generating network in order to prevent initiation of seizures or terminate seizures underway. The target of stimulation has undergone discussion and revision over the years. These include the cerebellar nuclei which cause inhibition of thalamic nuclei by modulating the activity of efferent cerebellar nuclei and more importantly, the anterior nucleus of the Thalamus, which is the central relay station of the limbic system and is closely connected both to the hippocampi as well as to extensive areas of the neocortex, Subthalamic nucleus and Caudate nucleus. Anticonvulsive mechanisms range from inactivation of the neurons by blocking depolarization, reduction of the recruitability of neurons on the basis of the rhythmic activity they induce, activation of inhibiting neurons and their projections, and finally effecting changes in the properties of networks (desynchronization, antikindling effects).

Stimulation Paradigms can either by open loop or closed loop in their activity. Open loop stimulation involves continuous or cyclical stimulation, while in closed loop stimulation, electrical stimulus is delivered in response to the onset of a seizure thereby initiating by the patient or caregiver when they feel or see a seizure. Complications include infection rates of 6.1%, misplacement of electrodes (up to 4.4%), 0.5% to 1% incidence for symptomatic bleeding, electrode breakage in at 1.8% of cases and Skin ulcerations in 1.3% of patients.

**Radio surgery for epilepsy**

Why radio surgery? While selective temporal resections are effective, morbidity is low, but not zero. Infection, neuropsychological changes, blood loss (intra-operative, post-operative) and other focal neurological deficits which maybe are possible during and after surgery make the post-operative recovery difficult. Medical contraindications of open surgery which are a major obstacle in certain disease coupled with some patient's fear of surgery make the prospect of radio surgery appealing. There is however only an indirect evidence for efficacy is seizure control as demonstrated in Tumors, Hypothalamic hamartomas and in AVMs. Neurons themselves are resistant to radio necrosis. However, vasculature and glia are sensitive.

Endothelial damage due to radiation especially to small blood vessels leads to astrocytic reactions. Eventual neuronal damage results from ischemia caused by vascular inflammation. Other hypotheses suggest that irradiated neuronal circuits undergo Neurmodulation that renders an anticonvulsant (or, sometimes, a paradoxically proconvulsant) reaction.

Radiation directed at specific sites to maximize efficacy. The regions include the temporal portion of the amygdala, the anterior 2 cm of hippocampus and adjacent Para hippocampus gyri.

The total volume within the 50% isodose line is between 5.5 and 7.5 cc. A dose of 20-24 Gy to the 50% isodose line is given either directly or fractions. Complications of radio surgery include initial increase in auras, headaches, visual field deficits (52% of patients - mostly quadrantanopia), and lastly a long waiting period for the effects of radiation to occur.

**Surgical outcome**

The outcome of seizure control post surgery is measured by the Engels score shown below.

**Engel's classification of postoperative outcome**

- **Class I**: Free of disabling seizures
  - A: Completely seizure free since surgery
  - B: Nondisabling simple partial seizures only since surgery
  - C: Some disabling seizures after surgery, but free of disabling seizures for at least 2 years
  - D: Generalized convulsions with AED discontinuation only surgical outcome
- **Class II**: Rare disabling seizures (‘almost seizure free’)
  - A: Initially free of disabling seizures but has rare seizures now
  - B: Rare disabling seizures since surgery
  - C: More than rare disabling seizures since surgery, but rare seizures for the last 2 years
  - D: Nocturnal seizures only
- **Class III**: Worthwhile improvement
  - A: Worthwhile seizure reduction

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**Diagram 1**: Showing the various pathologies in yellow and various surgical interventions in green that can affect either cure, or palliation, with some procedures managing to achieve a mix result in between complete cure and palliation.
B: Prolonged seizure-free intervals amounting to greater than half
the followed-up period, but not <2 years
Class IV: No worthwhile improvement
A: No Significant seizure reduction
B: No appreciable change
C: Seizures worse

Predictors of Recurrence
These include:
1. Age at onset of epilepsy: earlier age (usually<5 years), have a
favorable postoperative outcome.
2. Duration of epilepsy: long history correlates with worse
outcome.
3. Age at surgery: Hippocampus Sclerosis patients aged ≤ 24
years were about four times more likely to be seizure free at
5 postoperative years when compared with the older surgical
group (36 years or older).
4. Type of disease involved: Lesional epilepsy has a better
outcome than idiopathic epilepsy.
5. Absence of secondarily generalized tonic-clonic seizures
(GTCs): 57% of MTLE-HS patients with SGTCS have a 1-year
remission compared to 80% remission rate in those who had
only partial seizures. Patients who had no GTCs were 2.2
times more likely to be seizure free 5 years after surgery.
6. Preoperative seizure frequency: Seizures (>20/month) were
associated with lower rates of seizure freedom.
7. History of febrile seizures: Simple febrile convulsions have a
favorable prognostic value for surgery.

Conclusion
Appropriate patient selection with a judicious use of technology
as well as sound clinical acumen coupled with a multidisciplinary
approach can lead to excellent results in drug recalcitrant epilepsy.
Further advances have improved outcomes and reduced risks and
complications. A case by case basis using the axioms discovered
and postulated can lead to even better outcomes for patients and
researcher alike.

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