

CHAPTER

77

Refractory Epilepsy- How Much to Investigate ?

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Historical Aspects

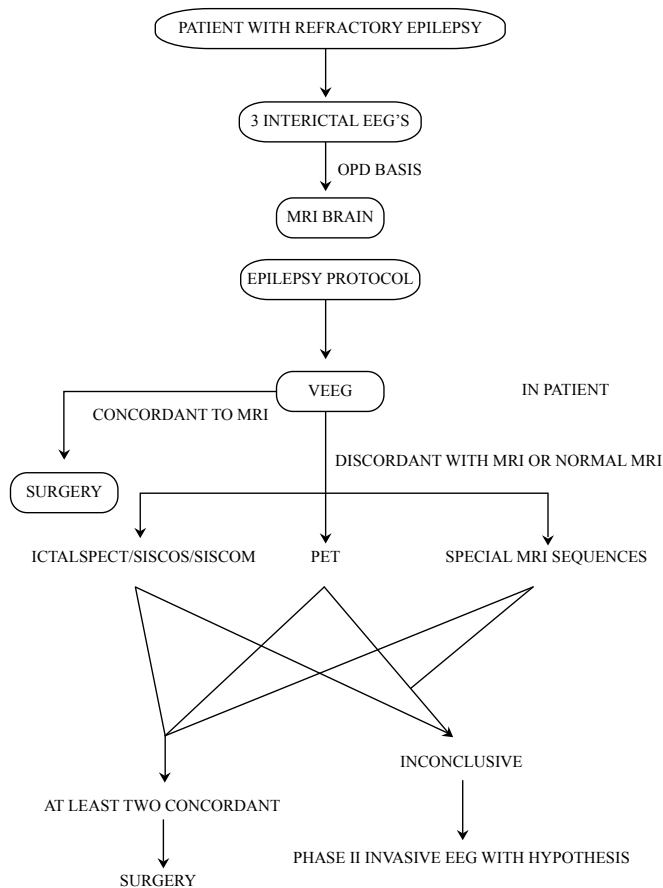
Systematic localization of the epileptic zone and procedures for surgical resection are not recent developments in the treatment of epilepsy. based on the work of Hughlings Jackson. Between 1890 and 1910, Horsley¹ reported series of patients who received craniotomy for the treatment of symptomatic epilepsy from a known cause, often traumatic. Wilder Penfield and Herbert Jasper,^{2,3} and many others followed with important advances in the development of evaluative and surgical techniques for refractory epilepsy. Percival Bailey and Frederick Gibbs were among the first teams to resect the epileptogenic region based on EEG localization and semiology without identified structural brain abnormalities.⁴

Which patients to investigate and when ?

Defining Surgical Candidacy and Medical Intractability

Anyone with recurrent seizures who is interested in surgery as a possible treatment is a good candidate for a detailed discussion of the potential risks and benefits of surgical intervention. For most patients this discussion can only take place after video/EEG confirmation of the classification of the epilepsy and localization of the epileptogenic region. Another

reasonable criteria is anyone who is disabled due to their epilepsy, regardless of seizure rate, should be offered the option of presurgical evaluation. Patients considered for epilepsy surgery should meet two criteria: 1) disabling seizures that have not been controlled by adequate trials of antiepileptic drugs without adverse side effects, 2) clinical, neuroimaging, or EEG evidence of an epileptogenic brain region that may be safely resected.^{5,6} The specific aspects of these criteria, however, are not simple and are subject to numerous variations. Some patients without a specific localizable epileptogenic region should be evaluated for palliative procedures. There is no clear consensus on what the definition of intractable epilepsy is.^{7,8} Most conventional definitions include the failure of two first-line antiepileptic drugs over a period of at least two years. Recent large cohort studies,⁹ however, indicate that most patients who will remain refractory to medications can be accurately identified within one year after diagnosis, based on response to the initial medication, classification of the epilepsy, and the presence of a structural cerebral abnormality. Other important factors to weigh in the decision for surgical candidacy include the risk of increased morbidity and mortality from continued seizures. An important consideration is the increased mortality in patients with recurrent seizures, if surgery is not offered as a treatment.

Figure 1 : Evaluation of Potential Epilepsy Surgery Candidates

recent investigations of medically resistant epilepsy suggest that the overall mortality rate in this population is between 0.5 and 1.5% per year. Sperling et al¹⁰ reported that none of the 199 patients who were seizure-free after surgery died, whereas 11 of the 194 with seizure recurrence after surgery died. The only death in the recent randomized trial of surgery for temporal lobe epilepsy occurred in the medical treatment arm.¹¹ Multiple subsequent studies have replicated similar findings,¹²⁻¹⁴ but not all studies have concurred.^{15,16} Head trauma was reported by 24% and burns by 16% of patients with active epilepsy in a recent survey.¹⁷ The risk of major injuries or death must be seriously considered before delaying the presurgical evaluation or committing to additional trials of antiepileptic drugs in patients at increased risk for pharmacoresistant epilepsy.¹⁸

The patient's perspective, especially regarding the importance of controlling the seizures compared to the surgical risk of injury to a functionally eloquent brain region, must be emphasized in the decision regarding surgical options.^{19,20} Like patients undergoing evaluation for surgical treatment of other disorders, patients with medically resistant epilepsy also experience anxiety over the option of an invasive surgical procedure. Many epilepsy patients may not be receiving appropriate education regarding their surgical options and risk of continued seizures.²¹ Treatment with the vagal nerve stimulator does not appear to improve mortality rates in refractory epilepsy.²² Mortality for epilepsy surgery procedures in published series is less than 0.2%.³⁹

Hence patients should be assured and preferably be referred to centers having an epilepsy surgery team with adequate experience with availability of all possible non invasive methods of investigation as mentioned below if these seizures are not controlled with two or more drugs in appropriate choice and dosage as early as possible this will ensure the right for equal life opportunities in persons with refractory epilepsy.

What Lesions can be operated upon?

As a prerequisite to this it is mandatory that a systematic approach to the identification of the lesion or cause is carried out.

Identifying the epileptogenic region

The clinical history and physical examination

As with most neurological disorders, the history and physical examination can contribute critically important information for localization of the relevant pathology. For example, an initial simple partial seizure, or aura, of an unusual epigastric sensation is reported by nearly one half of patients with temporal lobe epilepsy, but is uncommon in seizures arising from other regions. Similarly, déjà vu or an olfactory sensation at seizure onset usually indicates a temporal lobe seizure.²⁴ These symptoms, however, are not highly accurate for

Table 1 : Techniques used to localize the primary epileptogenic zone.

- Neurological History and Examination
- Routine EEG
- Video/EEG Monitoring
- High Resolution MRI
- Interictal PET
- Ictal SPECT
- Neuropsychological Testing
- Sodium Amobarbital Test (WADA)
- MR Spectroscopy
- EEG Spike Triggered MRI
- Magnetoencephalography
- Intracranial EEG and Cortical Stimulation

lateralization of the temporal lobe of seizure onset. Ictal behavior, such as unilateral automatisms, often occurs ipsilateral to the temporal lobe of onset, while dystonic posturing of the hand may occur contralateral to side of onset.²⁵⁻²⁶ Prolonged postictal dysphasia suggests a dominant temporal lobe seizure.²⁷ Postictal nose wiping also strongly lateralizes in temporal lobe epilepsy to the side of the involved upper extremity.²⁸ Brief, hypermotor, frantic, bizarre behavior with minimal postictal confusion is associated with inferior or anterior frontal seizures, while posturing and abduction of the upper extremities is often present with mesial frontal (Supplementary Sensory Motor Area-SSMA) onset.²⁹⁻³³ Primary somatosensory symptoms are less reliably localizing, and may indicate an epileptogenic region in the SSMA or extrasensory area (i.e., not necessarily parietal primary sensory area onset). Asymmetric facial movement during spontaneous smiling on examination is highly specific and moderately sensitive for contralateral mesial temporal sclerosis in temporal lobe epilepsy.³⁴

Neuroimaging (Fig. 2-12)

Advances in MRI technology have improved the sensitivity and specificity of the clinical evaluation for identification of potentially epileptogenic cerebral pathology. Mesial temporal or hippocampal

sclerosis is the best characterized indicator of the epileptogenic region identifiable by MRI.³⁵⁻³⁷ The predictive value of MRI identified unilateral mesial temporal sclerosis, however, ranges from 61% to 96% in published series.³⁸⁻⁴²

Focal MRI abnormalities in extratemporal lobe epilepsy also provide targets to guide intracranial EEG monitoring and allow better surgical outcomes compared to patients with nonlesional extratemporal epilepsy.⁴³ Specific MRI protocols including FLAIR and inversion recovery highlight detailed anatomy and signal abnormalities that provide increased sensitivity for localization of potentially epileptogenic pathology.⁴⁴ MR spectroscopy may improve localization and advance our understanding of epileptogenesis by identification of metabolic and neurotransmitter changes in specific brain regions.⁴⁵⁻⁴⁷ Limitations include, however, the labor-intensive requirements of a well-trained team in the setting of an inpatient video/EEG monitoring unit. PET imaging, on the other hand, can provide data on metabolic dysfunction,⁴⁸ but its predictive value in extratemporal epilepsy is not clearly defined.

Video/EEG Monitoring

In addition to video confirmation of features of seizure semiology discussed above, video/EEG monitoring provides ictal EEG⁴⁹ and extended sampling of interictal EEG abnormalities that have high predictive value for localization of the epileptogenic region. Interictal sharp waves or spikes appear to be the strongest indicator of regional cerebral hyperexcitability, but temporal intermittent rhythmic delta activity (TIRDA) may also be highly accurate for unilateral temporal lobe epilepsy. Temporal lobe polymorphic delta activity is less specific for temporal lobe epilepsy. In one study of 90 consecutive patients with medically refractory epilepsy considered for surgery, 61% had unilateral temporal interictal abnormalities that were concordant with mesial temporal sclerosis identified by MRI. However, bitemporal interictal EEG abnormalities are not a contraindication for surgery, as up to 50% of such patients may become

Table 2 : Surgical procedures used to treat medically refractory epilepsy

- Anterior Temporal Lobectomy
- Amygdalohippocampectomy
- Focal or Regional Cortical Resection
- Corpus Callosotomy
- Hemispherectomy
- Subpial Transection
- Vagal Nerve Stimulation
- Cortical Stimulation
- Vagus Nerve Stimulation

seizure free after temporal lobe resection.⁵¹ Mapping of the maximal fields of interictal and initial ictal epileptogenic abnormalities is a critical component of the presurgical localization process.

Surgical Procedures

Although many nonpharmacologic therapies have been reported for seizure control, including yoga and herbal treatments, only vagus nerve stimulation (VNS)⁵² has undergone controlled clinical trials adequate to support a Food and Drug Administration approval. Randomized, double-blind clinical trials comparing two intensities of intermittent stimulation of the left vagus nerve demonstrated a significant reduction in seizures in the high intensity stimulation group.⁵³ Although no patients remained seizure-free during these studies, the 25% to 30% reduction in seizure rate compared to baseline was adequate to allow an American Academy of Neurology Subcommittee to conclude that “VNS is indicated for adults and adolescents over 12 years of age with medically intractable partial seizures who are not candidates for potentially curative surgical resection. The committee believes that patients should undergo a thorough evaluation of the epilepsy to rule out nonepileptic conditions or treatable symptomatic epilepsies before implantation of a vagus nerve stimulator.”⁵⁴ Long term outcomes based on open-label studies suggest that seizure control may gradually improve during the first one to two years of treatment.⁵⁵ Adverse effects of VNS reported

by more than 5% of patients include hoarseness/voice change, throat pain, and coughing. Cardiac asystole has been reported in five cases of initial VNS testing at time of implantation. In a study of 24 children, 12 had unexpected adverse events; the severity of the adverse events led to surgical removal of the device in two of the patients.⁵⁶

After implantation during surgery under general anesthesia, the VNS device requires gradual increase in stimulation intensity until optimal seizure control with tolerable adverse effects is achieved. The stimulation period is usually one minute, occurring every five minutes, although these parameters may be altered. A magnet controlled by the patient or assistant may also be used to initiate stimulation. The increase in stimulation intensity is performed through a simple computer-assisted procedure using a “wand” placed over the patient’s skin at site of the device. The interval between stimulation setting changes is dependent on seizure frequency (i.e., enough time to determine change in seizure frequency), patient tolerance of the initial discomfort after stimulation increase, and convenience for the patient. The typical higher end of the stimulation range is 3 mA, achieved by incremental increase of 0.5 mA. The expected battery life prior to surgical replacement is estimated to be five years.

Why Consider Surgery?

The most compelling reason to consider epilepsy surgery from the patients’ perspective is the possibility to live an independent and autonomous, and lead a normal social and vocational life. As alluded to above however, minimizing mortality and morbidity risk is a major consideration as well. Other potential benefits for many individuals include the reduction of mood dysfunction, arresting cognitive decline, and reducing medication burden and toxicity.

Epilepsy Surgery Outcomes

Although only one randomized trial comparing epilepsy surgery to optimal medical management has been completed, consistent findings in numerous observational studies in patients with

Figure 2 : MRI-T1-Right Mesial temporal sclerosis

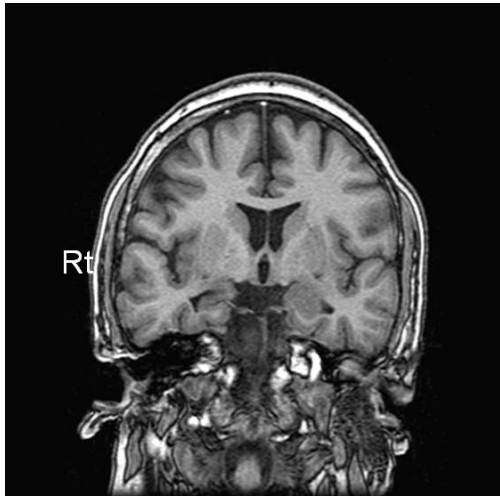


Figure 5 : MRI-FLAIR-Rt parietal cavernous angioma

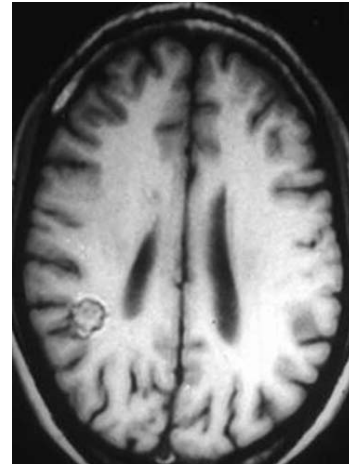


Figure 3 : MRI-Flair-Hemispheric cortical dysplasia-Rt

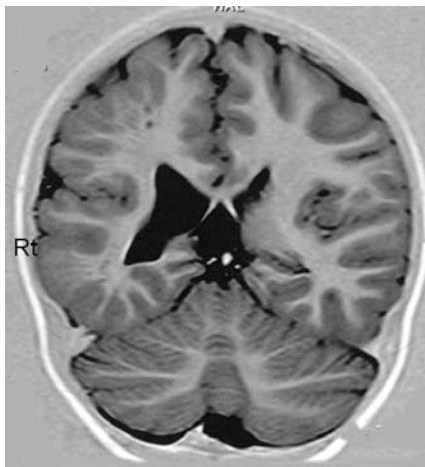


Figure 6 : MRI-DNET Rt temporal

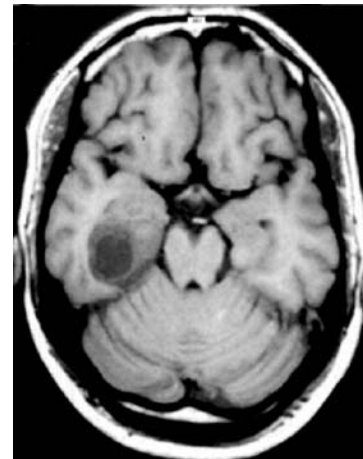


Figure 4 : MRI-FLAIR-Bilateral MTS

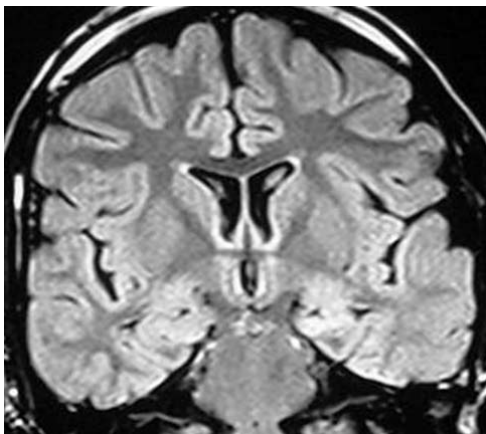


Figure 7 : CT-Brain- Sturge Weber syndrome presenting with refractory epilepsy

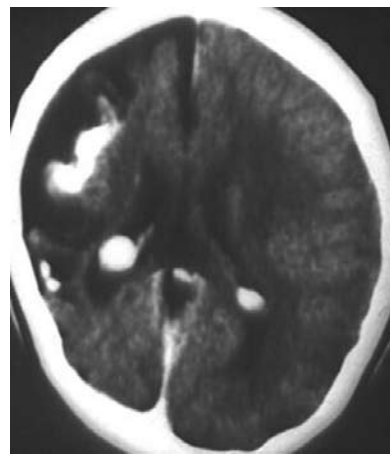


Figure 8 : MRI-FLAIR -Rasmussens encephalitis Lt Hemispheric atrophy and hyperintensity posterior left parieto-occipital

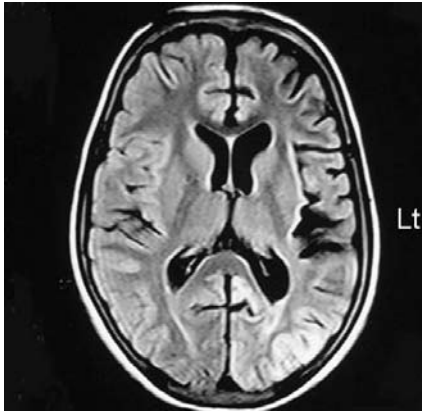


Figure 9 : FMRI- for evaluating limb motor function prior to surgery the lesion is away from motor area

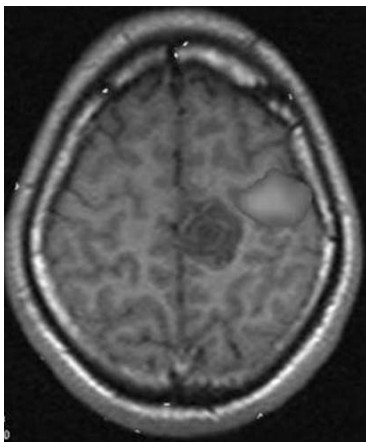


Figure 10 : MRI-Post op Hemispherotomy

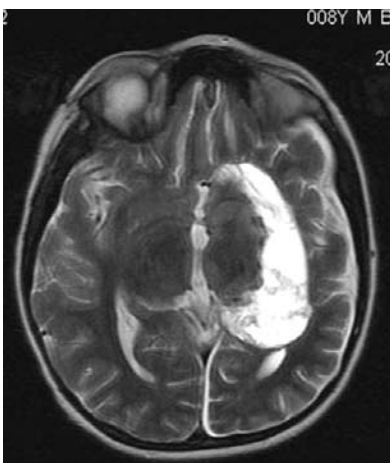


Figure 11: Magnetic source imaging MSI-Shows origin from posterior superior border of lesion which is a postoperative scar. Photo courtesy Dr Gary Mathern Head pediatric epilepsy surgery UCLA.

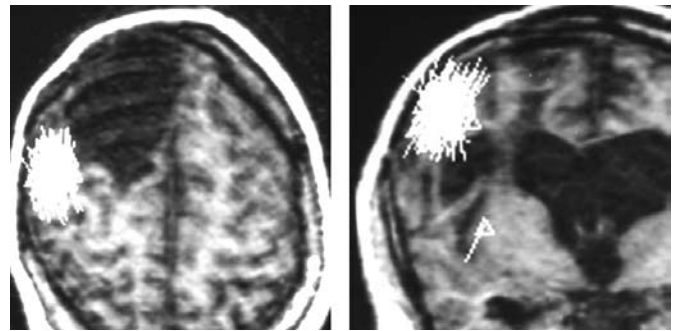


Figure 12: Simultaneous FMRI and EEG showing focus in right temporal

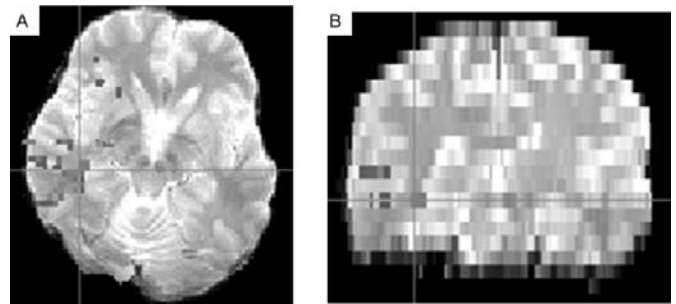


Photo courtesy Dr John Stern , UCLA

medically refractory epilepsy indicate that anterior temporal lobectomy or amygdalohypocampectomy, and extratemporal lesional epilepsy surgery, are highly effective for controlling seizures. Reported success rates range from 60% to 95% depending on selection criteria, procedure, and definition of good outcome. Overall, 60-78% of patients eventually achieve seizure remission after temporal lobectomy or lesional extratemporal resection.

Nonlesional extratemporal epilepsy surgery has less favorable outcome, but may be warranted depending on the clinical situation.⁵⁷

Conclusion

Although epilepsy surgery carries a modest risk of morbidity, the consistently observed improvements in health outcomes, mood status, medication dependence and toxicity, and probable

reduction in overall mortality support its utility in pharmaco-resistant epilepsy. It is a clinician's responsibility to identify patients with recurrent seizures despite adequate medical therapy and offer them a referral to an epilepsy surgical center for evaluation. Few of such centers with established epilepsy surgery programs in India are All India Institute of Medical Sciences, Sri Chitra Institute of Medical Sciences, NIMHANS, PGI Chandigarh etc. There exists not only a wide medical treatment gap of epilepsy in our country but also a wide surgical treatment gap.

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