Managing Epilepsy III: Surgery for Intractable Epilepsy

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Surgical treatment for intractable seizures is a well accepted, and effective option for patients with focal epilepsy. An identified focus (which can be a lesion, hippocampal sclerosis, or a diseased hemisphere) with acceptable surgical risks can lead to good outcomes when electroencephalography (EEG) and imaging data correspond. Even in the absence of magnetic resonance imaging (MRI) findings, strong EEG localization is associated with good outcome. The various surgically treatable epilepsies are discussed along with a discussion of groups of patients that can be targeted for good outcomes if an epilepsy program is being developed. Temporal lobectomy is described in detail as the mainstay of surgery for epilepsy. Extratemporal surgeries also have good outcomes in appropriate circumstances.

Key Words: EEG, MRI, review, seizures, temporal lobe

Epilepsy is a common neurological disorder, with a prevalence that approaches 1% of the population.[11] Epilepsy is a disorder of repetitive seizures, with recurrence of unprovoked seizures required to make the diagnosis. Seizures can be classified as *partial* seizures, that arise from a focal cortical region, or *generalized* seizures that simultaneously involve both hemispheres. Partial seizures can involve alterations of consciousness, making them *complex partial* seizures, and they can spread, causing *secondarily generalized* seizures. Over 50% of seizure types are partial seizures, and the majority of these are complex partial seizures.[4]

Evaluation of Epilepsy

The evaluation of a patient with epilepsy should include a history of the type of seizure. Witnesses are important as many patients underestimate the frequency and severity of their seizures. Auras, or warnings, at the start of a seizure may suggest a partial seizure. Temporal lobe seizures often begin with epigastric sensations or psychic phenomena (such as déjà vu). If a deficit is seen post-seizure (Todd's paralysis) it may help localize the seizure as well. A history of trauma is often seen. Provoked seizures should be excluded, including drug use or withdrawal, electrolyte abnormalities, hypoglycemia, hypoxia, and fever. Structural imaging, such as computerized tomgraphy (CT) or MRI, can evaluate for tumor or other structural origin of epilepsy. EEG can also be helpful but should be interpreted quite cautiously – a routine EEG is *normal* in up to 50% of those who go on to have epilepsy. Medications are usually tried first in epilepsy. About 40% of those with an unprovoked seizure will go on to develop epilepsy.[5] Medical control can be achieved in about 75%, but the remainder will go on to have intractable seizures. Intractability can be established after only two drugs[10] and consideration can be given to whether the patient is a candidate for surgery or not.

Surgical Treatment

The goal of surgical treatment is the removal of a focal source for intractable seizures. If an isolated origin of seizures, or *focus*, is in an area of 'acceptable' risk, then surgery can be considered. In some cases, a focus may represent a small cavernous malformation, in other patients, the entire hemisphere. In the one, the location and expected benefit need only justify a focal resection, in the latter, surgery may equally be considered if the patient has severe seizures and is already with deficit. Thus, the risk/benefit discussion will always be individualized for a patient's seizures and proposed surgery. In general, patients with lesion-associated epilepsy are the best candidates for surgical treatment, the patient with seizures originating from a tumor or arteriovenous malformation being the most straightforward of this category. Partial seizures with

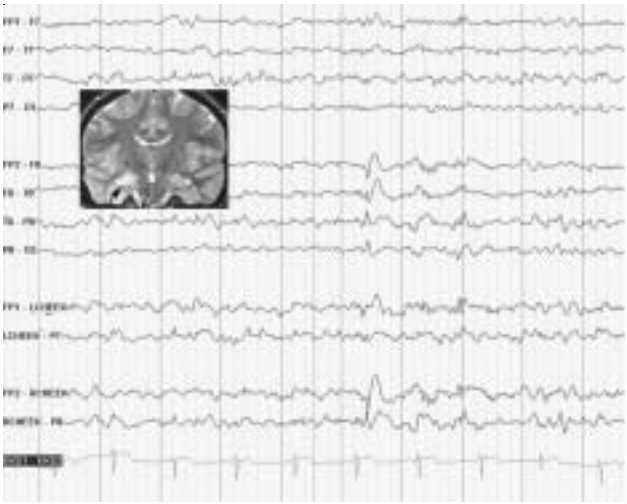

Figure 1. Right temporal lobe seizures. The inset is a coronal MRI showing increased signal in the right hippocampus (arrow), which is also atrophic and lacks the normal architecture of the opposite, normal, side.

temporal lobe origin **(Figure 1)** and both inter-ictal EEG and MRI pointing to unilateral mesial temporal origin are good candidates for temporal lobectomy. In patients selected this strictly, outcomes of up to 75% have been reported.

Temporal lobectomy for mesial temporal sclerosis (MTS) is the most commonly performed epilepsy operation. In practice, temporal lobectomy includes a variety of surgeries including resections for medial temporal lobe pathology (e.g., MTS), lesions within the medial or lateral temporal lobe, or resections of lateral, neocortical temporal lobe. Hippocampal sclerosis can occur in adults or children,[7,16] but in children it often occurs with other pathologies, especially cortical dysplasia.[13] Temporal lobectomy has been shown, in a randomized trial, to give improved seizure control compared to conservative management, for patients with temporal lobe epilepsy.[26]

In areas where cost-efficacy is at a premium, either due to national health-care resources, or attempts to expand the availability of surgery to the greatest number of populations, the highest yield groups are usually targeted.[21] Not only have temporal lobectomy for epilepsy been successful in lower-resource areas, they are actually cost-effective and save money compared to lifelong medication.[20,21] In countries where the financial burden is often on the patient and family entirely, surgery may be much more affordable than lifelong medication.

Typically, the best outcome patients would be patients with structural lesions. However, outcomes were excellent in Europe and the USA before the advent of CT and MRI,[2] in part because strongly focal EEG findings can predict a good response to surgery, even if MRI findings are absent.[9] Anterior temporal lobe seizures with lateralized onset *and* lateralized interictal activity will respond well to temporal lobectomy even in MRI negative cases. Focal, consistent, EEG abnormalities in extratemporal cases are likely to be associated with an underlying focal pathology and may also respond well to surgery,[8] although most of these cases would be evaluated with invasive monitoring prior to resective surgery unless a clear lesion was demonstrated on imaging studies. Certainly, MRI and ictal/interictal EEG findings suggestive of temporal lobe epilepsy could be pursued surgically under a wide variety of economic settings.[28]

Lesions that are particularly close to the motor or language cortex may also require invasive monitoring and/or functional mapping during surgery to avoid unacceptable deficits. Other methods, such as subpial transactions, can be used if functional areas and seizure origin overlap.[17]

Surgical Techniques

Temporal Lobectomy

Several variations of temporal lobectomy are used. Recently, selective procedures that resect the amygdala and hippocampus, sparing as much lateral temporal cortex as possible, have been used, with good outcome in patients with congruent EEG and MRI. In patients with possible dual pathology (both a cortical and hippocampal etiology for seizures), more common in pediatric series, the selective procedures may be less appropriate. Options to get to the hippocampus include resection of the lateral temporal lobe (anterior 4 cm on the dominant side, 6 cm on the non-dominant hemisphere[23]), entry to the ventricle through the middle temporal gyrus,[17] inferior temporal gyrus, subtemporally, or a trans-Sylvian approach.[28]

For all procedures, patients are positioned lateral, or with head turned 30-60 degrees, depending on surgeon's comfort with the anatomy. General anesthesia is used, although lightening the agent, or using propofol, is preferable if cortical recording is planned. Options to relax the brain include administration of mannitol prior to opening the dura, mild hyperventilation and diuretics. Usually CSF drainage is sufficient and none of those previous steps are required - CSF can usually be drained from the convexity, or from gentle exposure of the basal temporal lobe. Once the temporal horn is exposed CSF drainage is sufficient to achieve relaxation.

When the approach is taken through the lateral temporal lobe, the ventricle is typically found directly medial to the middle temporal gyrus. The lateral corticectomy is performed under direct vision and the white matter resected medially. By extending the resection inferiorly as it progresses medially, the ventricle will be entered without inadvertently entering the temporal stem superiorly to the ventricle. In this superior direction, there are no boundaries between the temporal white matter and the midbrain. Therefore, care must always be taken to err in the inferior and anterior direction when finding the ventricle. The collateral sulcus projects superiorly from the fusiform gyrus running along the inferior aspect of the temporal lobe. This structure usually points to the lateral ventricle, just posterior to the tip of the temporal horn of the ventricle, and can be useful in finding the temporal horn. In a selective procedure, the collateral sulcus may not be exposed routinely.

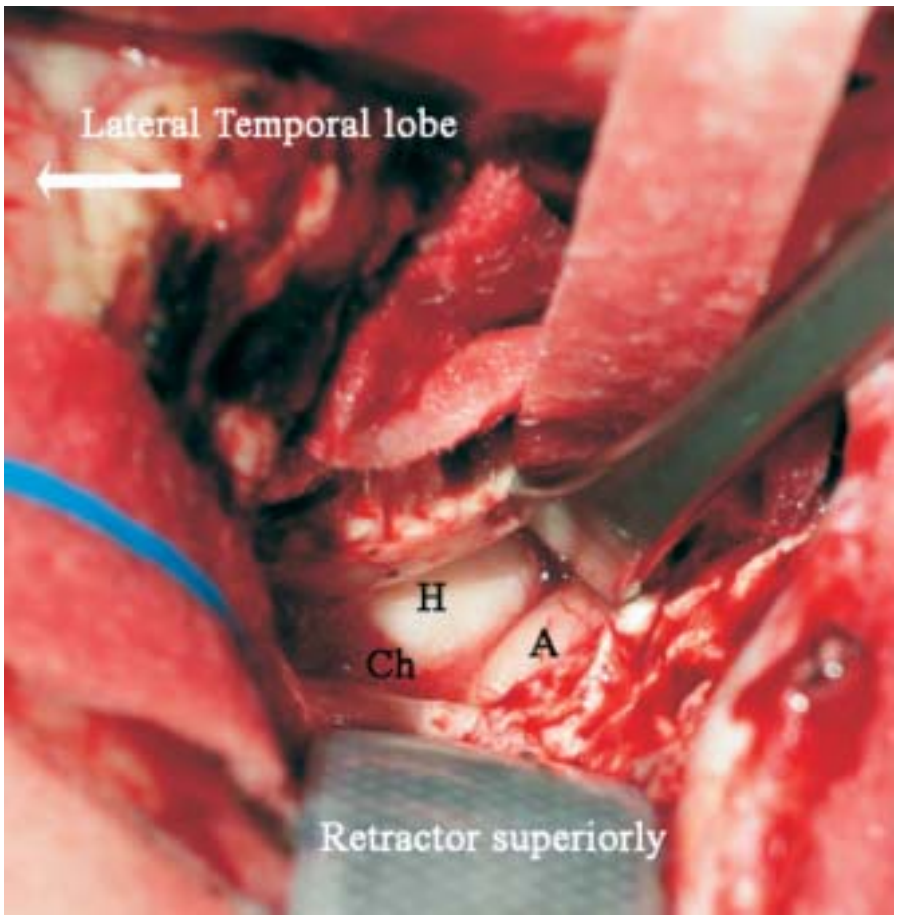

Figure 2. Intraoperative photograph of a left temporal lobectomy after the lateral resection. Anterior is to the right and inferior to the top of the photograph. The temporal horn and contents are visible. Residual lateral cortex is labeled on the upper left. The middle temporal gyrus was resected and the remainder of the lateral temporal lobe is retracted superiorly. The head of the hippocampus (H), the lateral amygdala (A) and the choroids plexus (Ch) are all evident and orient the surgeon to the hippocampal resection.

In all of the approaches through the ventricle, the hippocampus is observed at the medial aspect, once the ventricle is opened **(Figure 2)**. The lateral amygdala overhangs the anterior hippocampus and can be removed. Procedures that spare the amygdala have had good outcome.[3] But amygdala, and basal temporal lobe, have been said to be epileptogenic along with the hippocampus.[25] In my preferred procedure, as a minimum, the basal temporal lobe (inferior temporal, fusiform, parahippocampal gyri) are removed along with the hippocampus and amygdala **(Figure 3)**.

Once the ventricle is exposed, a cottonoid is placed in the temporal horn to keep excessive blood from entering the ventricle. The ventricle wall often has small veins which should be coagulated. Care is taken to avoid excessive coagulation or manipulation of the posterior-superior-medial wall of the ventricle, which includes the optic radiations and lateral geniculate body. The ventricle is opened more widely and retractors are then advanced into the ventricle. Posteriorly, the choroid plexus is seen overlying the posterior hippocampus. The choroidal fissure, carrying the anterior choroidal artery, marks the medial border of the posterior aspect of the hippocampus. Anteriorly, the hippocampus courses medially, anterior to the cerebral peduncle, following the contour of the uncus of the temporal lobe. The important anatomical landmarks for hippocampal removal are its borders, namely the temporal horn of the lateral ventricle, the choroidal fissure, and the medially placed structures, including the internal carotid artery, brainstem, and oculomotor (III) nerve. Although the order of resection is not uniform, the hippocampus must be disconnected from surrounding structures, with special care medially to avoid the brainstem, vessels, and cranial nerves. Resection of the parahippocampus is performed in a subpial fashion with either suction and/or the ultrasonic aspirator. This is usually done under microscopic dissection providing superior illumination and magnification when working near the brainstem. The mesial pia will protect the carotid and third nerve, which are visible medial to the edge of the tentorium. The fourth nerve is sometimes visible as it deviates slightly from its usual course inferior to the tentorial edge. The resection is carried anterior to posterior and the hippocampus is thereby disconnected inferiorly as the basal temporal lobe is removed.

Removal of the lateral amygdala provides a more extensive view of the hippocampal complex anteriorly. The amygdala is somewhat vascular and care is taken to only

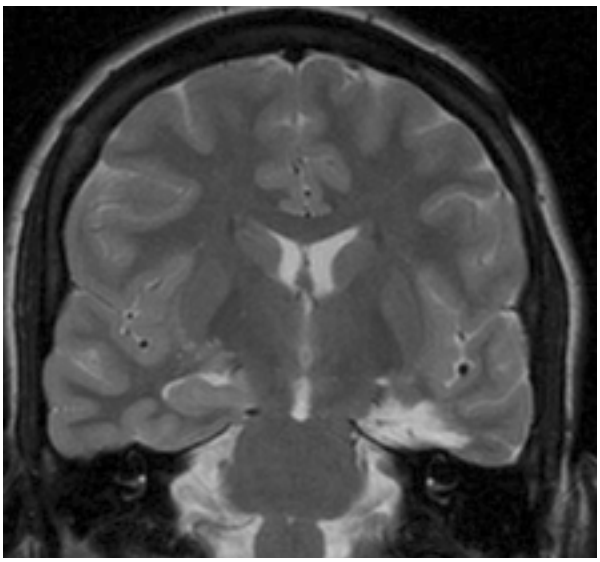

Figure 3. Coronal T2-weighted MRI showing resection of a left hippocampal lesion. The superior and middle temporal gyri are spared and the hippocampus and ventricle were accessed through resection of basal temporal lobe, including inferior temporal gyrus.

remove the lateral component. As there is no boundary between amygdala and midbrain/basal ganglia, the roof of the ventricle is typically used as the limit of amygdala resection – thus the amygdala is resected until flush with the remainder of the ventricular wall, and a complete amygdalar resection is not attempted.

At this point, the amygdalo-hippocampal connections are evident and can be resected down to the medial pia. The pia should be left intact and the carotid and third nerve are typically visualized at this point. Removal of the amygdala also exposes the uncus medially which can be resected if desired.

The posterior resection of the hippocampus is then determined. In a standard resection, this is usually selected just where the tail of the hippocampus begins to curve medially behind the collicular plate. This usually will allow for resection of approximately 2.5 cm behind the hippocampal head. Some authors advocate intraoperative corticography to determine the posterior extent of resection[12] and this may be especially helpful on the dominant hemisphere to limit cognitive side effects. At the posterior margin of the resection, the hippocampus is resected from the exposed hippocampal surface down to the choroidal fissure. The hippocampal fissure will arise from medially. The hippocampus can be resected or peeled off of the medial pia, which protects the brainstem. If the pia is violated, great care must be taken to be oriented to the location of the brainstem. Conversely, the hippocampal sulcus should not be mistaken for the pia around the brainstem, or the hippocampus will be left behind.

Vessels in the hippocampal fissure can be coagulated, but coagulation of more medial pia can endanger perforating vessels off of the internal carotid artery, posterior communicating artery, and/or choroidal arteries and should be avoided. Gentle application of oxidized cellulose usually can control medial oozing.

In the subgroup of patients with mesial sclerosis and concordant EEG, resection leads to good outcome (seizure freedom) in a large majority.[13] In a given patient, the outcome from temporal lobectomy cannot be established until at least 1 year post-operatively, as seizure control will change over time,[2] even over several years post-operatively. Additionally, seizures in the immediate post-operative period do not predict long-term seizure control,[14] although recurrence of seizures within the first year post-operatively carries a worse prognosis.[2]

Some degree of visual field loss, usually a superotemporal quadrantanopia,[1] is common following temporal lobe resection, as Meyer's loops fibers pass from the lateral geniculate body to the occipital lobe via the temporal lobe white matter.[18,24] This is rarely of any problem for the patient.[30] In dominant temporal lobe resections, transient speech difficulties may result from post-operative edema, especially when resections are taken close to language areas.[19,30] Some series have reported a small incidence of significant verbal performance loss after dominant temporal lobectomy especially in patients with normal pre-operative MRI and patients with higher pre-operative verbal memory scores.[6,18] Since the extent of lateral temporal resection has been correlated with verbal memory deficits,[15] selective procedures that minimize lateral resection may be less prone to give memory problems post-operatively,[22] but this is not established.

The mortality of anterior temporal lobectomy is low[18,19] with general neurosurgical risks including infection (less than 0.5% risk[19]), CSF leak, and hemorrhage. The incidence of damage to brainstem and vascular structures appears to be below 1%.[18]

Other Surgeries for Epilepsy

In patients with tumors or other structural lesions, resection of the lesion often results in seizure freedom. However, the rate of seizure freedom seems to improve if recordings directly from the brain surface (electrocorticography) are obtained, either through intraoperative measurements or invasive monitoring with implanted electrodes. Sometimes brain adjacent to pathology is also involved **(Figure 4).**

If seizures can be lateralized, but not localized within a given hemisphere, consideration is given to a hemispherectomy.[16] Ideally, this is in a patient with evidence of significant dysfunction of the one side, as in a patient with a large perinatal infarction. In this setting, resection and/or disconnection of one hemisphere offers as much as a two-thirds chance of seizure freedom with little new deficit. Patients who are ambulatory prior to hemispherectomy generally remain so postoperatively. The major considerations are establishing that structural and electrical abnormalities are strictly unilateral and that the hemisphere is not responsible for critical functions such as language. Spastic hemiparesis and visual field deficits should be expected postoperatively, if not already present in the candidate for hemispherectomy.

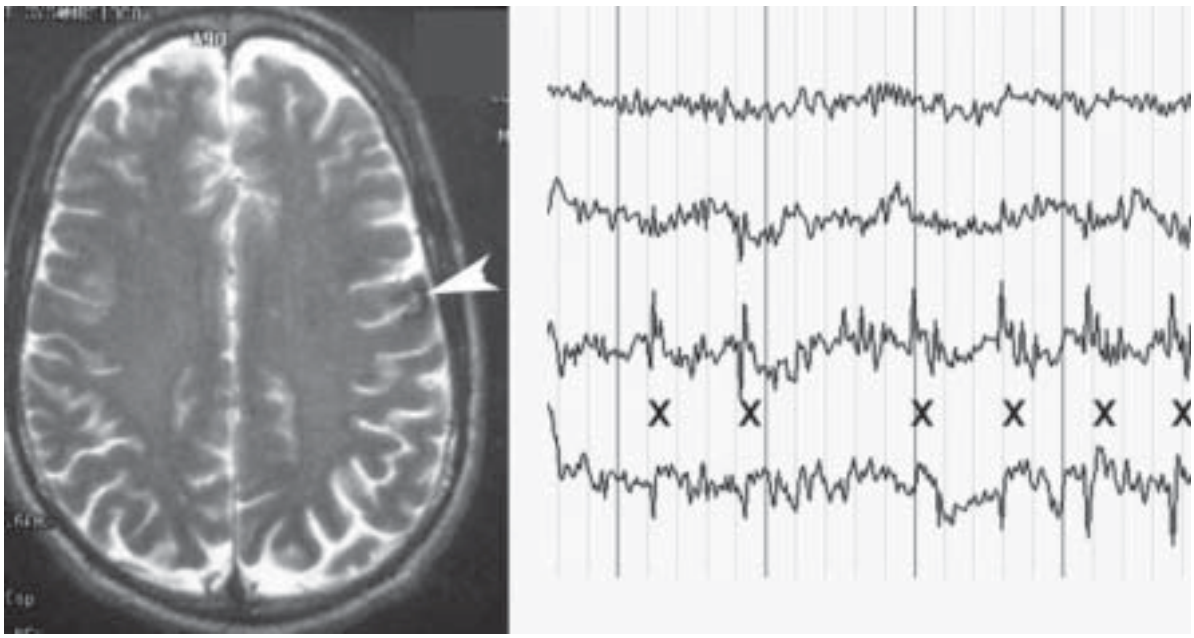

Figure 4. Axial T2-weighted MRI showing cavernous malformation (arrowhead) that was the source of intractable seizures. The focality of the patient's epilepsy is evident on intraoperative corticography that shows focal spikes (asterisks) that were only over the lesion. He is seizure free with resection of the lesion and surrounding hemosiderin, which was adjacent to, but distinct from, Broca's area.

In patients with severe generalized seizures, especially drop attacks, division of the corpus callosum may offer benefit. Generally the anterior two-thirds of the corpus callosum are divided through an interhemispheric approach. This can convert sudden drop attacks into seizures in which the patient has warning and can avoid severe injury. Although seizure freedom is not expected after such a procedure, a considerable reduction in the severity of seizures is common, with approximately 60 – 65% improvement.[2] Vagus nerve stimulation (VNS) has emerged as a surgical treatment approved for treatment of partial seizures, but sometimes used for generalized seizures if medications fail.[16] VNS is unlikely to provide seizure freedom but often gives a 50–75% reduction in seizure frequency, making it particularly attractive to those with intractable epilepsy who are not candidates for resective surgery. The electrodes are implanted around approximately 3 cm of exposed vagus nerve. Implantation is always performed on the left vagus nerve to avoid cardiac effects. Difficulties with chronic cough and hoarseness are common in the initial use of the stimulator, but typically subside with time. The risks of vocal cord paralysis and damage to surrounding structures are similar to other surgeries of the cervical region. Another disadvantage especially in country like Nepal is the cost of the implant.

Summary

Although the majority of seizures can be controlled with medications, a large percentage of patients will be refractory. If a focal source of seizure activity is found, seizure freedom is possible with surgery. Temporal lobectomy in particular is cost-effective and has a high chance of seizure remission with low morbidity and very low mortality. With MRI and long-term EEG, many surgical candidates can be identified, both for temporal and extratemporal lobe epilepsy.

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