

An Overview on Resective Surgery for Drug Resistant Focal Epilepsy

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Abstract:

Epilepsy occurs in 1% of the US population. Approximately 30% to 35% of patients with seizures have drug-resistant epilepsy, defined as failure of 2 antiepileptic medications given at appropriate doses. Of the 750 000 persons in the United States with drug-resistant epilepsy, only 1500 undergo epilepsy surgery per year. Epilepsy surgery is indicated for patients with focal seizures who do not respond to appropriate antiepileptic drug therapy consisting of 2 or more medications.

Keywords: Resective Surgery, Drug Resistant Focal Epilepsy, Brain.

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Introduction:

The goals of epilepsy surgery are seizure control by resection of the epileptogenic tissue on the one hand while sparing essential brain areas to avoid neuropsychological and other neurological deficits on the other hand. [1].

This can be achieved only by a thorough presurgical evaluation clearly delineating epileptogenic and essential brain areas and by defining selective resection strategies in each individual patient. [1].

Drug resistant Focal epilepsy

Patients with drug-resistant focal epilepsy are more suitable for surgical operation, and are more likely to benefit from removal of the culprit tissue. [2].

An extensive preoperative evaluation should then be conducted, including clinical symptoms, underlying brain conditions (such as brain infection, chronic syndrome, neurofibromatosis, tuberous sclerosis, brain tumor, stroke, and blood vessel malformations), medical history, blood tests, cerebrospinal fluid (CSF) analysis, neuropsychology testing, electroencephalography, and imaging scans. [2].

Available neuroimaging scans include CT scan, MRI scan, positron emission tomography, single photon emissions computerized tomography (SPECT), and magnetoencephalography (MEG). [2].

Drug-resistant focal epilepsy surgery should follow the —3M principle: (1) —Maximum removal of structural brain lesions (i.e., malformations of cortical development and low-grade neoplasms) (2) —Minimum injury to neurologic function ; and (3) —Maximum recovery to control seizures without inducing other morbidities. These resections may not only involve of the medial structures of the temporal lobe such as the amygdala, hippocampus, and entorhinal cortex, but also involve the neocortex of the temporal and other lobes. Resections of the cortex are guided by imaging results and intracranial electroencephalography. [3].

In general, a complete resection of the epileptogenic brain region provides higher chances of seizure freedom but the risks of postoperative deficits would increase with the extension of resection. Therefore, the extent of resection should be weighed against such risks and individualized in every case. [4].

Surgery of Temporal Lobe Epilepsy:

Temporal lobe epilepsy (TLE) affects a substantial number of individuals with medically intractable epilepsy. TLE is the most common operated epilepsy, and the majority of patients with localization related epilepsy seen in tertiary epilepsy centers have TLE. [5].

The frequent occurrence of intractable epilepsy in the temporal lobe bears witness to the highly epileptogenic nature of the limbic structures that comprise the mesial portion of the temporal lobe. The mesial part of the temporal lobe is richly connected with surrounding extra-temporal cortical regions especially the orbitomesial frontal lobe via the uncinate fasciculus and the fornix carries fibers from the hippocampus that project to the anteromesial frontal lobe and anterior nucleus of the thalamus. The mesial temporal structures are highly connected as well with the anterolateral neocortical temporal lobe. Therefore, due to the strong connections of the mesial temporal structures with the anterior and lateral temporal lobe in addition to other limbic regions, TLE most commonly manifests the semiology of staring and automatisms regardless of the seizure onset zone in lateral or mesial structures of the temporal lobe [6].

Despite the frequent occurrence and intractable nature of temporal lobe epilepsy, it responds very well to surgery with high rates of resulting seizure freedom and the risks of surgery are quite low. [7].

The decision to consider a patient with medically intractable TLE for surgery has become much clearer nowadays since the International League Against Epilepsy (ILAE) defined medical intractability as the failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drugs. A clear definition of intractable epilepsy combined with the excellent results of surgery for symptomatic epilepsy especially arising in the temporal lobe, has resulted in numerous consensus reports affirming that individuals with drug resistant epilepsy should be evaluated in a comprehensive epilepsy program to identify opportunities for surgical cure. [7].

Temporal lobe epilepsy can be categorized into one of two types based on the anatomical region of seizure onset. Seizures that originate from the temporal cortex lateral to the collateral sulcus are defined as lateral or neocortical epilepsy, and seizures that have a focus of onset medial to the collateral sulcus are named mesial temporal lobe epilepsy (MTLE). The imaging finding that defines MTLE is atrophy and sclerosis of the hippocampus, so-called mesial temporal sclerosis (MTS). The childhood history of patients with MTLE commonly includes the presence of childhood febrile convulsions, especially of a prolonged and complicated nature. [8].

Individuals with neocortical epilepsy are more likely to manifest signs related to peri-Sylvian structures such as simple auditory hallucinations or, in the dominant hemisphere, postictal aphasia. Although neocortical epilepsy often spreads along fibers richly connected with the mesial temporal structures manifesting the signs and symptoms of limbic involvement, which are the semiological features of MTLE as well. Due to the considerable overlap in semiology between the two categories of temporal lobe epilepsy, multiple non-invasive data elements must converge to localize the TLE focus to the mesial or lateral structures of the temporal lobe. [9].

However, when patient history, seizure semiology, EEG localization, and imaging findings point to MTLE, there is a high degree of confidence in the diagnosis. In a minority of patients, intracranial electrode monitoring may be required to investigate lateralization of the seizure onset to a temporal lobe [or to confirm temporal lobar localization in one hemisphere]. [10].

Standard Anterior Temporal Lobectomy

Performing a standard anterior temporal lobectomy (ATL) consists of resecting the lateral temporal and mesial temporal structures, either en bloc or separately. Removal of the lateral temporal structures allows better visualization of the mesial structures, allowing en bloc removal of the hippocampus. The procedure is usually performed with the patient in the supine position, elevating the ipsilateral shoulder with a roll and rotating the head to the contralateral side. The head is tilted slightly laterally to place the zygoma at an approximately 10-degree angle from the horizontal plane of the surgical floor. There are several techniques for opening the skin and temporalis muscle. Some surgeons perform a question-mark skin incision followed by reflection of the myocutaneous flap. Others use curvilinear or straight skin incisions. To avoid injury to the frontalis branch of the facial nerve, the incision is begun 1 cm above the zygoma and 1 cm anterior to the tragus. The superficial temporal artery is dissected and preserved if possible. A subperiosteal dissection is used to remove the muscle from the bone. Extensive cauterization is avoided to minimize the subsequent atrophy of the temporalis muscle. A craniotomy is performed on small portion of the frontal bone posterior to the pterion. [11].

Some surgeons tend to expose the pterion at the frontal bone. Venous oozing from the sphenoid ridge can usually be controlled using bone wax or gelfoam. Bleeding from the middle meningeal artery branches is controlled by bipolar coagulation. [12].

A U-shaped durotomy is often preformed with the base reflected anteriorly. A cruciate durotomy can also be used. A posterior cortical incision at the lateral temporal gyri begins approximately 5.5 cm from the temporal tip on the nondominant hemisphere and 4.5 cm from the temporal tip on the dominant side at the level of T2. A number 1 Penfield dissector is used to measure the

length from the temporal tip. The posterior resection is slanted anteriorly across T1 to avoid the primary auditory cortex. The pia mater at the upper border of T1 is coagulated and divided. A subpial dissection is performed to elevate T1 from the sylvian fissure using bipolar cauterization and controlled suction, an ultrasonic aspirator, or a dissector technique. The pia and middle cerebral artery (MCA) branches are protected. Oozing from the pia can be controlled using cottonoid packing or Surgicel. The insula is exposed, and dissection extending to the lateral uncus is performed. The temporal pole is reflected laterally after the coagulation and division of the anterior leptomeninges. [12].

The posterior resection line is extended from the T1 through T2 and into T3. This line is then extended medially through the fusiform gyrus to the collateral sulcus. The temporal horn is entered through the white matter above the fusiform gyrus. The wall of the temporal horn can be identified by the bluish ependyma. Subsequently, opening of the ventricle anteriorly exposes the hippocampal head. The temporal stem is resected at the inferior circular sulcus. The temporal neocortex is removed by dividing the basal leptomeninges lateral to the temporal horn exposure. If en bloc temporal resection is intended, further resection of the mesial structures is performed. During the resection of the mesial structures, an ultrasonic aspirator is used at a low setting to avoid injury to the arachnoid that overlay the posterior cerebral artery (PCA), the basal vein of Rosenthal, the third cranial nerve, and the midbrain. [13].

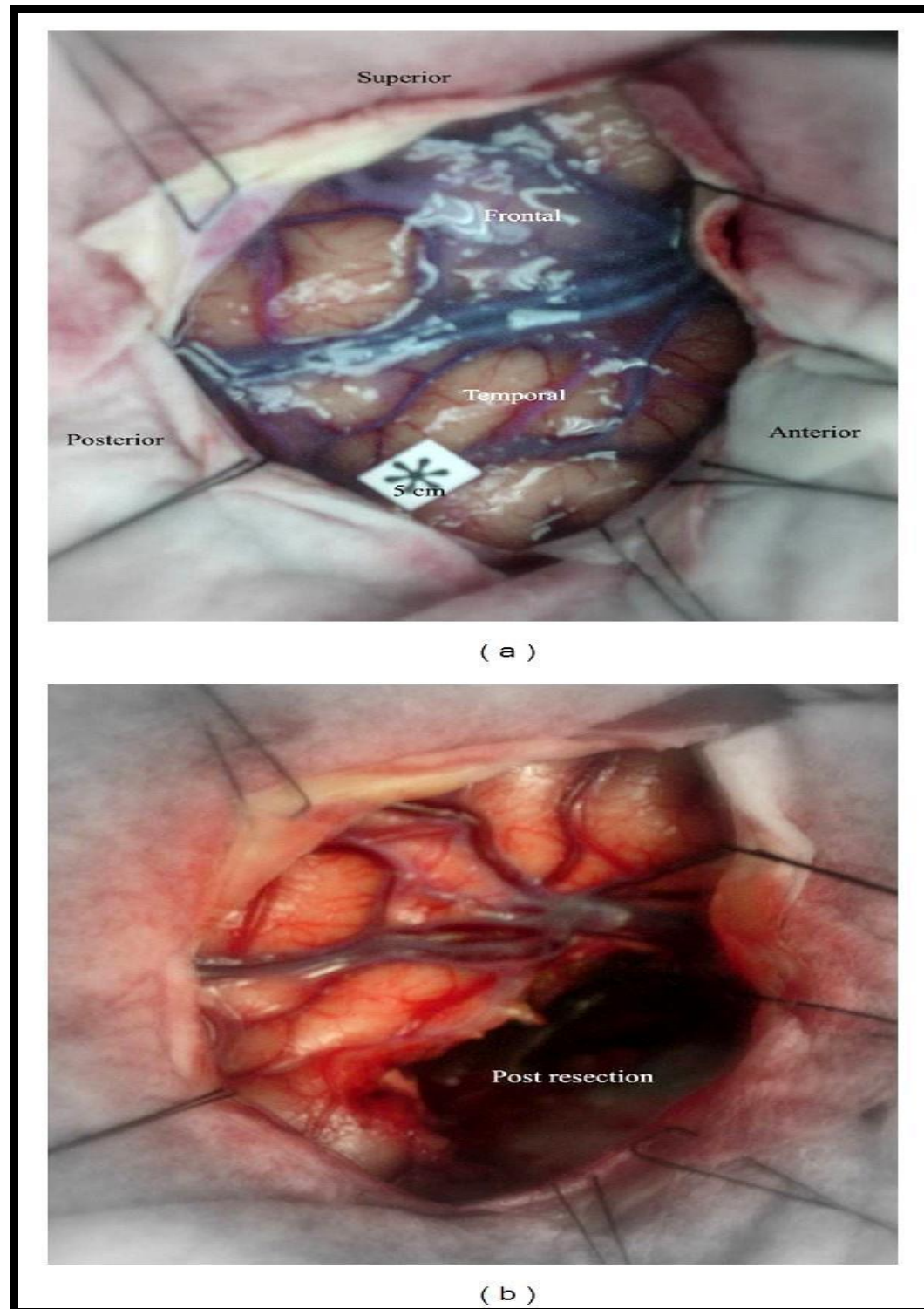


Fig. (1): Intraoperative photographs demonstrating pre and post resection for rightanterior temporal lobectomy. [13].

Different surgical techniques have been used to resect the mesial temporal structures. In general, the areas of the uncus that extends to the level of the limen insulae and the parallel M1 segment

of the MCA are removed with an ultrasonic aspirator. The amygdala is resected at the line that connects the choroidal point and the limen insulae. The choroidal point is located at the anterior portion of choroid plexus. Care should be taken to not extend the resection superior and medial into the globus pallidus. Due to the absence of clear demarcation between the amygdala and globus pallidus, the anatomic landmarks for amygdala resection are variable among different surgeons. Wieser and Yazargil advocate using the insular circular sulcus and uncus to avoid entry into globus pallidus. Based on anatomical dissection study, Wen et al. found that a line interconnecting the inferior choroidal point and the proximal MCA can define the superior limit of amygdalar resection. [14].

Tubbs et al. examined the line connecting the anterior choroidal artery and the MCA bifurcation in 20 sides cadavers. In this study, no damage to the striatum was found using this line for upper amygdala removal. [14].

The entorhinal cortex is resected to the anterior portion of the parahippocampal gyrus. At this stage, the fimbria can be dissected laterally from the arachnoid attachment, exposing the hippocampal sulcus that carries the Ammon's horn arteries. Next, the subpial dissection of the parahippocampal gyrus exposes the hippocampal sulcus. This step will allow the lateral reflection of the hippocampal body. The hippocampal feeders are coagulated and divided at the hippocampus edge, and the tissues of the hippocampus and parahippocampus are removed en bloc. The posterior portion of the hippocampus is removed using an ultrasonic aspirator to the level of the midbrain tectum, as identified by image guidance. Next, hemostasis is secured, and wound closure is performed in a standard manner. [14].

Anteromedial Temporal Resection

The anteromedial temporal resection technique was developed by Spencer to preserve the function of lateral temporal cortex and to access the mesial temporal structures through the temporal pole corridor. Approximately 5 to 6 cm of the temporal lobe is exposed in this technique. The cortical incision begins in the T2, 3 to 3.5 cm from the temporal tip, and curves toward T3 and temporal base. The T1 is usually spared. The temporal tip is removed lateral to the temporal horn. [15].

At this stage, the mesial temporal structures are removed using an ultrasonic aspirator. The temporal horn is entered, followed by resection of the uncus and amygdala. Resection of the hippocampus and parahippocampal gyrus is performed from anterior to posterior. The parahippocampal gyrus is removed as it curves medially posterior to the brainstem. The hippocampus is removed posterior to the tail region. After mesial temporal resection, hemostasis is achieved, and the wound is closed in a standard manner. [15].

Transcortical Selective Amygdalohippocampectomy

Transcortical SAH was introduced in 1958 by Niemeyer and was originally referred to as —transventricular amygdalohippocampectomy. Niemeyer used a cortical incision through the T2 to reach the mesial temporal structures. Subsequently, Olivier modified this technique to include resection of the anterior portion of T1. [16]

The head position in this procedure is similar to that used for ATL. A linear or slightly curvilinear skin incision is made anterior to the tragus and above the zygoma. Neuronavigation is a helpful intraoperative tool to tailor the surgical approach. It is applied to navigate the optimal bony exposure over the cortical entry point. Throughout the procedure, neuronavigation helps in guiding the surgical pathway to the temporal horn and the posterior extent of mesial temporal resection. [16].

However, van Roost et al. found that neuronavigation can overestimate the extent of posterior hippocampal resection, which is related mainly to brain shift during the procedure. While neuronavigation is a useful adjunct, a thorough understanding of the anatomy is essential. On the other hand, intraoperative MRI was found to be helpful to ensure the completeness of hippocampal resection. [16].

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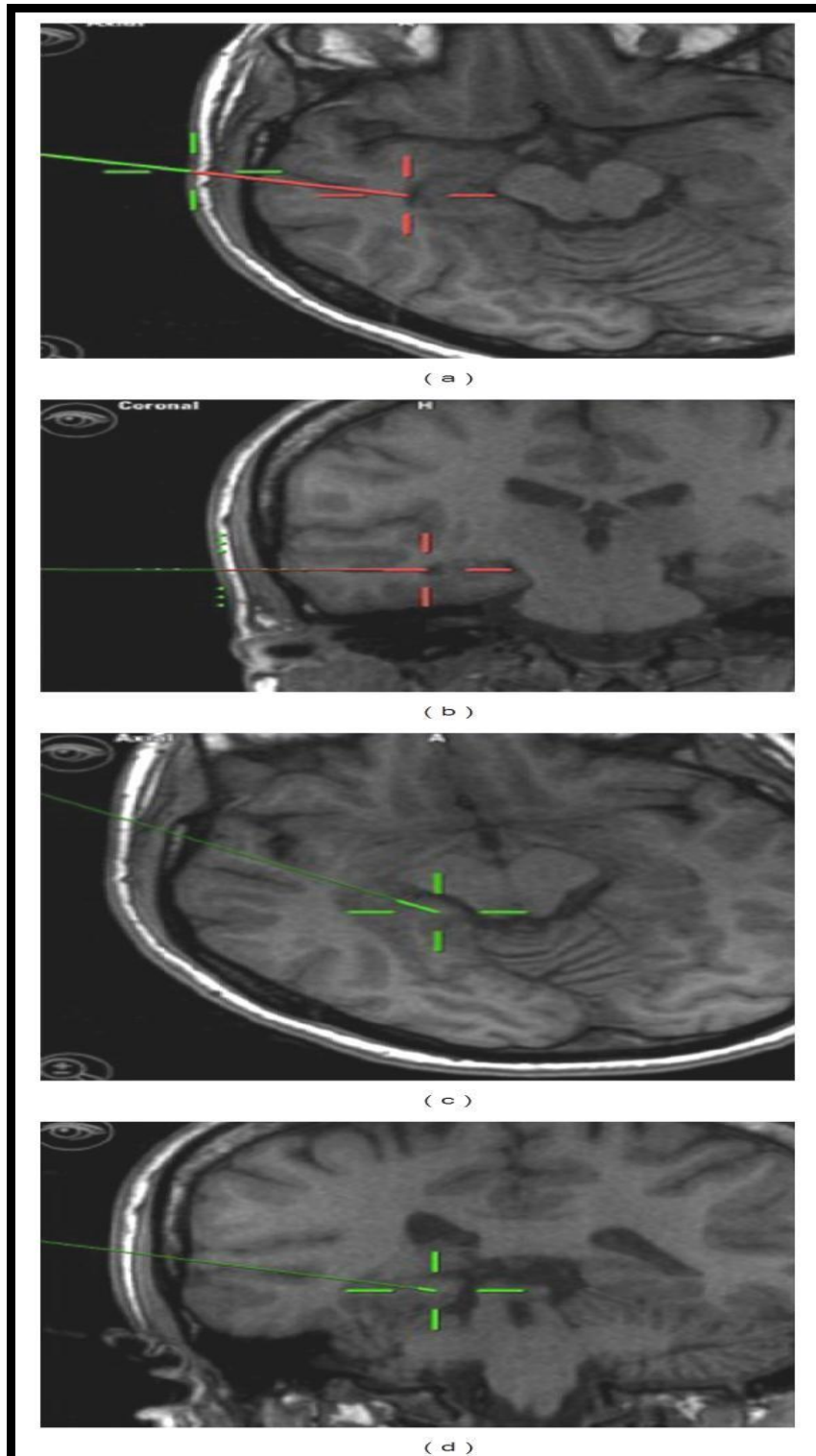


Fig. (2): Snapshot from neuronavigation showing the entry point through the middletemporal gyrus and the trajectory toward the temporal horn ((a) and (b)).((c) and (d)) showed the posterior extent of mesial temporal structuresresection at the level of quadrigeminal plate.[17].

After exposure of the bone, neuronavigation can guide to center the craniotomy over the middle temporal gyrus., Olivier used image guidance to place the cortical incision at the T2, anterior to

the central sulcus on the nondominant hemisphere and anterior to the precentral sulcus on the dominant side .[18].

The pathway to the ventricle traverses the white matter. The lateral ventricular wall is usually found 2 mm above the fusiform gyrus. The white matter over the ventricle is resected from anterior to posterior in a slit-like fashion, Exposure of the intraventricular structures is performed by applying a retractor that elevates the upper ventricular wall and choroid plexus, . This movement exposes the fimbrial attachment to the ambient cistern arachnoid. An ultrasonic aspirator is used at a low setting to remove the parahippocampal gyrus using the endopial technique.[18].

The hippocampus is resected at the junction between the body and tail regions, followed by dissection of the fimbria from the arachnoid to allow the lateral elevation of the hippocampus. This procedure exposes the hippocampal sulcus and allows the coagulation of the hippocampal feeders. The uncus is removed beginning with the apex and followed by the regions of the amygdala that are posterior to the M1 segment of the MCA. The residual posterior hippocampus is resected extending to the level of the tectal plate. In this approach, Meyer's loop fibers can be affected by removal of the white matter located lateral to the temporal horn.[18].

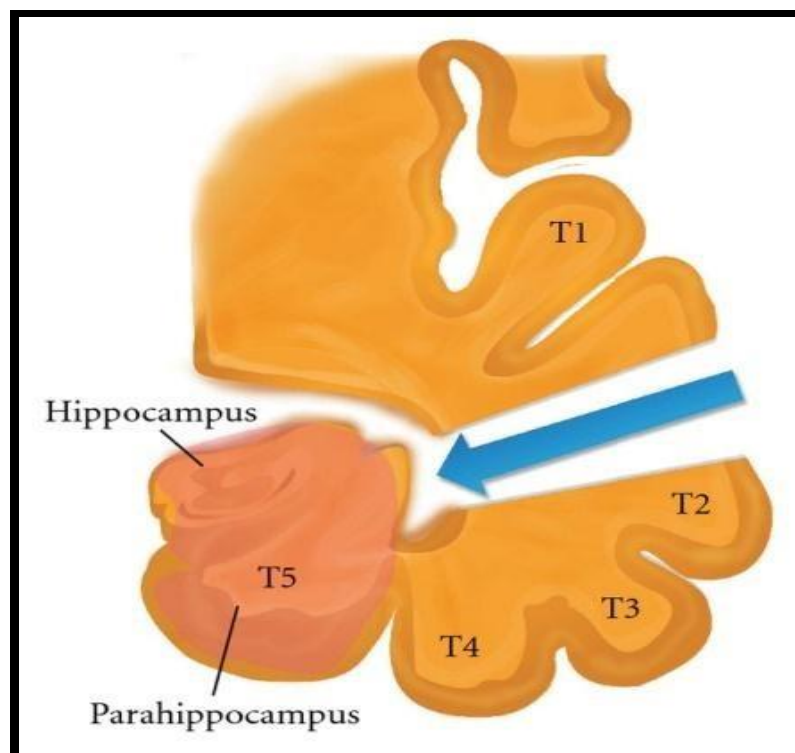


Fig. (3): Diagram representing transcortical selective amygdalohippocampectomy approach. [18].

Transsylvian Selective Amygdalohippocampectomy

Wieser and Yasargil introduced the transsylvian SAH approach for resecting the mesial temporal structures through the sylvian fissure corridor without compromising the adjacent temporal neocortex. The patient's position is different from that in other temporal procedures: the head is

tilted such that the malar eminence is the highest point. A curvilinear skin incision exposes the frontal and temporal bones above and below the sylvian fissure [19].

The sphenoid ridge is flattened to the anterior clinoid process. The dura is opened in a curvilinear fashion and reflected onto the sphenoid ridge. Next, the sylvian fissure is opened from the level of the carotid artery bifurcation through the bifurcation of the MCA, exposing the anterior insular cortex, limen insulae, mesial uncus, and temporal pole. A 15-mm incision is made in the temporal stem at the level of the limen insulae. The temporal horn is entered, and the uncus is removed using an ultrasonic aspirator. This step is followed by the removal of the amygdala, anterior parahippocampus, and entorhinal cortex. The choroid plexus and choroidal point are identified, and the hippocampus is disconnected from the lateral regions in an anterior to posterior manner using (preferably) an ultrasonic aspirator until the collateral sulcus is reached. The fimbria is dissected from the mesial arachnoid using a dissector. The hippocampus is dissected laterally, exposing the hippocampal sulcus, followed by the coagulation of the hippocampal feeders. Finally, a posterior hippocampal resection is performed to remove the hippocampal tissue, hemostasis is secured, and closure is performed.[19].

Subtemporal Selective Amygdalohippocampectomy

Subtemporal SAH was first described in 1993 by Hori et al. This technique involves removing the fusiform gyrus to access the temporal horn and cutting the tentorium to minimize retraction onto the temporal lobe. [20]

Later, the same group modified the subtemporal approach, opting for retrolabyrinthinepresigmoidtranspetrosal access to resect the mesial temporal structures .[18].

In general, the rationale for using this approach is the avoidance of an incision into the temporal stem and the preservation of the temporal neocortex. This approach, however, risks damaging to the vein of Labbe caused by temporal retraction. Moreover, the limited exposure of the amygdala and uncus limits resection.[20].

Extratemporal Lobe Epilepsy Resection:

Surgical management of extratemporal lobe epilepsy is mainly applicable for patients who had drug-resistant epilepsy induced by cortical dysplasias, accompanied with tumor, ischemic change, and vascular malformation, etc.[21].

The surgical management of extratemporal lobe epilepsy is more common in children due to the prevalence of progressive cortical dysplasia associated with diffuse epileptogenic zones .Epileptogenic zones are often distributed in the cortex, but vary from person to person, and sometimes may reside in the deep structure of the brain. So, an accurate positioning of the epileptogenic zones is a major challenge for the successful implementation of lateral temporal lobe epilepsy surgery. [21].

Cortical Resection in the Central Region:

The surgical treatment of epilepsy in the central region or rolandic cortex presents special challenges to neurosurgeons. Not only does the central region provide essential somatomotor

and somatosensory control of the contralateral face and limbs, this region of the brain is highly epileptogenic. Lesions in this region often produce disabling and treatment refractory seizures, which can frequently result in episodes of focal status epilepticus. [22].

Seizures of the Central Region

The clinical semiology of seizures originating in the central region is much more stereotyped than focal epilepsy of the frontal, temporal, or parietal lobes. Seizures of the central region are rarely characterized by auras with subjective or emotional accompaniment. [23].

The majority of the attacks are heralded by primary somatomotor or somatosensory symptoms or signs. Seizures typically begin with clonic movements\ of the face, arm, or leg with no alteration of consciousness.

The clonic movements may remain localized to the affected region or may spread and secondarily generalize.[23].

If the seizure spreads along the sensory or motor strip, the patient or clinician may observe progression of the clonic motor movements to involve more of the affected extremity or face and then spread to contiguous areas. This so-called Jacksonian march is the clinical accompaniment of the spread of epileptic discharges along the rolandic cortex.[23].

The seizure may stop at this point or may go on to a secondary generalized tonic-clonic convulsion. If the seizures involve the inferior portion of the motor strip where face and tongue are represented, the patient often experiences a speech arrest. [24].

Because of the lower threshold for epileptic discharges, seizures involving the central region can frequently result in focal status epilepticus or epilepsia partialis continua (EPC). These episodes of focal status epilepticus are often associated with very small, discrete and restricted lesions in either the somatomotor or somatosensory cortex and can be very difficult to control pharmacologically.[24].

Gliosis and post-inflammatory changes have been implicated in genesis of EPC especially in Rasmussen's encephalitis.[24].

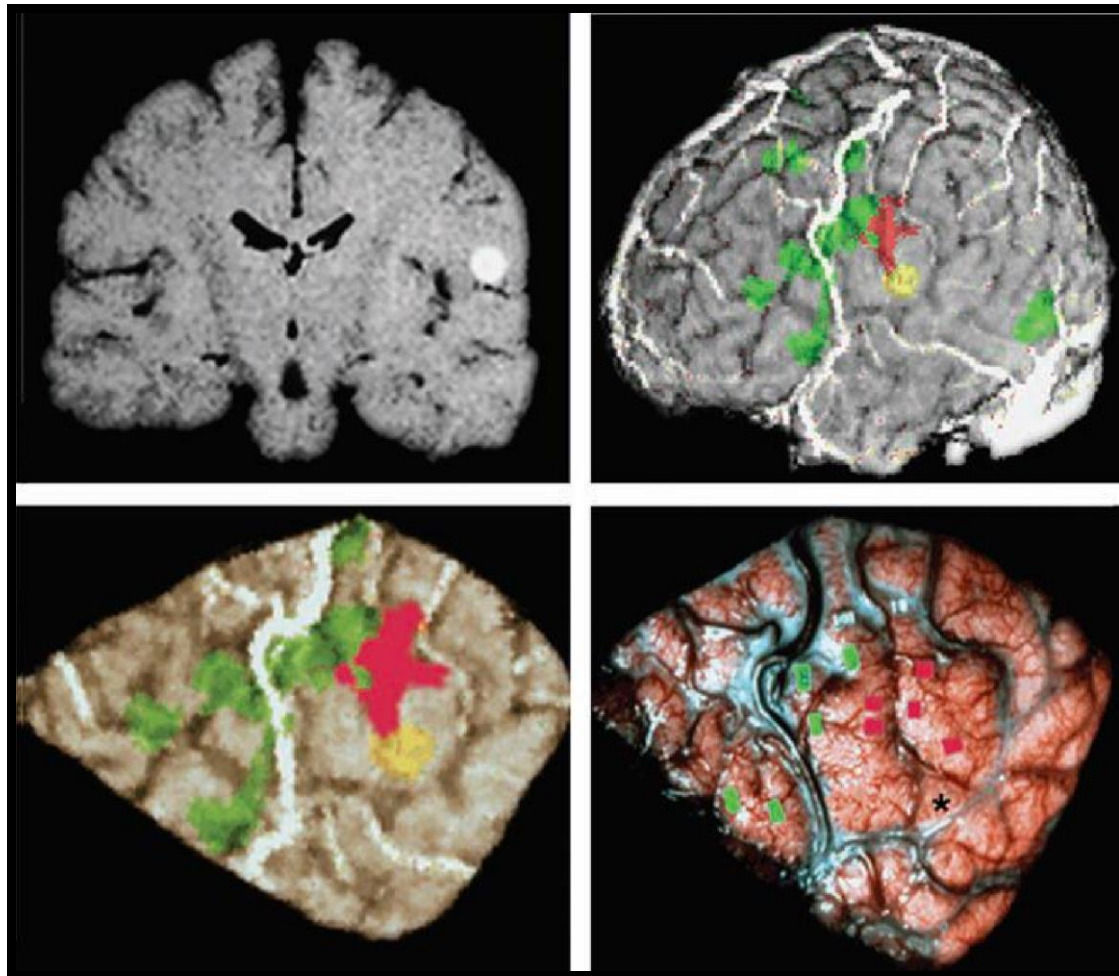


Fig. (4): fMRI. (A) Coronal view, contrast-enhanced MRI shows angiolipoma in the left-frontal lobe. **(B)** Brain lateral surface reconstruction with fMRI activity during a series of language and sensorimotor tasks mapped onto figure. Green indicates areas active during a verb-generation language task. Red indicates primary motor cortex active during tongue movements. Yellow indicates the tumor. **(C)** Detailed view of (B). **(D)** Intraoperative view of the left lateral brain surface, with veins and brain surface exposed. Green tags indicate areas where direct cortical electrical stimulation elicited speech arrest. Red tags indicate cortical areas that created either tongue movement or sensations with stimulation. Asterisk indicates brain tumor.[24].

Cortical Resection:

Once the epileptic region has been accurately localized, the next objective is to completely excise the seizure focus without causing a neurological deficit. An important determinant of the risk of surgery is the relationship of the lesion to functionally important or —eloquentll brain regions because injury to these eloquent areas can cause irreversible neurological impairment. [24].

Because surgery in the central region is by definition in eloquent cortex, resections must be relatively focal and restricted or they will result in irreversible deficits. A variety of strategies have therefore been employed to optimize surgical resection while minimizing risk of injury to

functional cortex. Most surgery in the primary sensorimotor cortex is done under local anesthesia with intravenous sedation. This allows for direct electrical stimulation of the cortex using a handheld bipolar stimulator to map out sensory, motor, and language areas.[25].

Rarely, direct cortical stimulation can precipitate a patient's habitual seizures, which can be an important validation of the seizure focus. It also allows for the assessment of function during resection. The patient is carefully evaluated during the resection for loss of either motor or sensory function. If the patient has a longstanding preoperative motor or sensory deficit, then more aggressive resections can be considered. Rarely, minute lesions in these primary sensorimotor areas can be resected through a small transgyralcorticectomy without permanent deficits. In the inferior portions of the rolandic cortex, resections of the facial region can be performed, especially on the nondominant side.[25].

This will result in a 3- to 4-month period of dysarthria but minimal permanent deficits. The superior extent of resection should stop at the motor thumb area. On the dominant hemisphere, similar resections can be performed but special attention has to be paid to prevent encroachment on the deeper white matter pathways, that is, arcuate fasciculus, that connect essential language areas. [26].

After the resection strategy is decided upon, tissue removal is performed using subpial resection techniques. Cortical gray and white matter is carefully removed by bipolar cautery and suction or CUSA. So that the pia remains intact over the adjacent gyri. This tends to form a nonscarring barrier and preserves blood supply to the remaining cortex as well.[26].

Cortical Resection in Frontal, Parietal and Occipital Lobe.

Resection of the seizure focus in the frontal lobe, as with other sites, offers the greatest chance of a seizure-free outcome. Published series of frontal resection report a wide range of good outcome. Diagnostic imaging of the underlying pathological and pathophysiological substrate, often coupled with intracranial electrode investigation, enables tailored resection. [27].

The most common underlying pathological substrates for intractable frontal lobe epilepsy are focal cortical dysplasias, low grade tumors, and posttraumatic encephalomalacia. Subtle dysplasias are not always readily identifiable on routine MRI scanning and may require high field MRI scanning or special reformatting.[27].

Co-registration of preoperative studies with the operative field allows preoperative planning of these resective strategies and most importantly their accurate execution. In those instances with lesional substrates, completeness of resection of structural pathology has been associated with better seizure outcome. Actual resection follows standard microsurgical technique. Adequate exposure of the extent of intended cortical resection is essential, and in those patients in whom eloquent cortex—subserving language and motor function in particular with respect to the frontal lobe—is either involved or adjacent to the resection, recognition of that functional localization is critical.[28].

The gold standard of functional mapping has been intraoperative mapping by electrical stimulation technique. For language, this requires an awake craniotomy; for motor function, the ability to map in the anesthetized patient is commonplace.[28].

Patients in whom an intracranial electrode investigation has been performed using subdural grid electrodes may be mapped extraoperatively using those same grids, a practice advantaged by the greater ease and less constrained nature of the setting. Traditionally 5-second long 50 Hz stimulation is used for functional mapping intra- and extraoperatively. Due to the propensity for seizures and after-discharges functional motor mapping with high frequency pulse trains and electromyography (EMG) control can be of advantage for motor mapping..[26].

Co-registration of imaging studies, including both structural and functional investigations, enables additional localization to be incorporated into the surgical field.[26].

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