Surgical Interventions in Rasmussen's Encephalitis

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KEYWORDS

Rasmussen's encephalitis. Surgical treatment, Chronic focal encephalitis, Hemispherectomy

ABSTRACT

Rasmussen's encephalitis (RE) is a rare, devastating neurological condition characterized by chronic unihemispheric brain inflammation, refractory epilepsy, and progressive neurological decline and hemiplegia with an etiology that remains elusive and a pediatric-skewed epidemiology. The deleterious nature of RE on the patient's neurocognitive development necessitates early medical intervention. RE is diagnosed on the basis of clinical features, MRI, EEG and biopsy obtained after surgery. While medical management often proves ineffective, surgical intervention has shown durable seizure freedom and control. This review comprehensively explores the surgical techniques in the management of RE including the steps involved in modified functional hemispherectomy, peri-insular, vertical-parasagittal and endoscopic hemispherotomies. We have summarized how each procedure aims to disconnect the affected hemisphere from the healthy hemisphere through different corridors of approach. Hemidecortication procedures offer good functional and cognitive outcomes overall despite the expected hemianopia, hemiplegia and loss of fine motor skills. We also review the importance of selecting appropriate candidates for surgery, as well as comprehensive pre- and postoperative management, along with the most likely outcomes of surgery.

1. Introduction

First recorded in 1958 (1), Rasmussen's encephalitis (RE) is a rare acquired neurological condition involving severe chronic holohemispheric inflammation of the cerebral cortex (2). The clinical picture of the disease involves three stages: patients will typically first experience a prodromal stage, characterized by mild, nonspecific symptoms like headaches, infrequent seizures, and/or mild hemiparesis, before progressing to an acute stage, which contrastingly exhibits frequent intractable focal seizures with motor symptoms on one side of the body (3). These seizures are pharmacoresistant and increase in frequency and severity over time, even progressing to become epilepsia partialis continua in 50% of patients (2). As seizures continue, patients commonly present with symptoms of neurological decline, including hemiparesis/hemiplegia, hemisensory loss, homonymous hemianopia, language deficits (if the condition presents on the dominant hemisphere(DH)), and intellectual disability. Unilateral hemispheric atrophy eventually manifests as inflammation worsens (4). This decline may continue for months to years before a patient enters the residual stage, where they may experience static hemiplegia and residual focal motor seizures. Patients could live many years following the termination of the acute phase of the disease, with varying qualities of life depending on the damage inflicted throughout it. If seizures continue, however, RE often proves fatal (3).

Overall, RE has a mean age of onset of about 6.8 years, though cases of adult manifestations have been recorded (5). A study of its prevalence in Germany concluded a nationwide occurrence of about 2.4 cases per 10 million individuals under the age of 18 per year, making it quite uncommon (6). It furthermore shows no gender predilection. Even though its etiology remains largely unknown, the progressive course of the inflammation involved in RE is consistent with immune-mediated diseases (7).

The core targets of RE treatment are to decrease seizure severity and frequency, while preserving motor and cognitive performance (5). Medication often has a modest effect on RE: antiepileptic drugs may decrease the severity of seizures but commonly have a limited or refractory effect, while immunosuppressive/immunomodulatory drugs could help slow neurological decline but have no effect on seizures (8). Surgery, usually involving resection or disconnection of the effected hemisphere, is the standard treatment; however, the decision of performing the surgery is a therapeutic dilemma and must be done after careful deliberation from both physician and patient (5).

This paper presents a brief review of the surgical management of RE; it outlines important preoperative considerations, surgical techniques, and postoperative possibilities and discusses its future prospects.

2. Clinical features

RE is progressive and is characterized by focal epilepsy that is drug-resistant, progressive hemiplegia, cognitive impairment, and unihemispheric brain atrophy. The disease is rare and mostly affects children and young adults, but can range from infancy to adulthood, with the median age of onset being 6 years. The typical clinical presentation is in 3 stages. Stage 1 or prodromal phase is distinguished by a non-specific low seizure frequency and, in rare cases, some degree of hemiparesis, lasting an average of 7.1 months (ranging from 0 to 8.1 years) and much longer in teenage and adult patients. Stage 2 or acute stage is distinguished by frequent simple partial motor seizures, with epilepsia partialis continua in 69% of patients. The median duration of this stage is 8 months (ranging from 4-8 months). During this stage, the neurological deficits appear, of which are progressive hemiparesis, cognitive impairment and aphasia if it affects the DH. Stage 3 or the residual stage is distinguished by ongoing seizures with a decrease in seizure frequency, particularly with permanent and stable neurological disability. (9)

2.1 MRI and EEG

Neuroimaging is crucial in the diagnosis and management of the disease. Typical MRI findings indicative of RE include unilateral enlargement of the cerebrospinal fluid (CSF) compartments, particularly noticeable in the insular and peri-insular areas. There is also increased signal intensity in the cortical and subcortical regions(10). Additionally, MRI scans frequently show extensive inflammation, white matter atrophy, and enlargement of the ventricles, all confined to a single hemisphere, which are key indicators supporting the diagnosis of RE. EEG findings in patients with RE typically show abnormal slow-wave discharges, delta activity, irregular spike-and-wave patterns, and significant inflammation in the affected hemisphere(11).

RE is predominantly unilateral, but there have been rare cases of bilateral involvement. Bilateral clinical and imaging involvement in RE is an exception rather than the norm, with majority of the cases presenting as unihemispheric(12). However, the contralateral hemisphere may not be entirely unaffected. Morphometric MRI findings indicate potential structural changes, challenging the concept of the spared, healthy hemisphere(13).

2.2 Histopathology

The histopathological features currently looked for in the diagnosis of RE include T-cell-dominated inflammation, microglial activation and nodule formation, neuronal loss, and astrocytic activation. Recently, astrocytic apoptosis and subsequent loss have been identified as distinctive characteristics of this condition. A potential mechanism for astrocytic degeneration in RE could be a targeted attack by cytotoxic T lymphocytes(14).

2.3 Surgical Indications & Contraindications

Criteria for selecting patients for surgery in RE are essential to ensure optimal outcomes. Surgery is typically considered for those with drug-resistant epilepsy, worsening neurological deficits, and persistent seizures linked to the condition. Procedures like hemispherectomy are often recommended for patients who do not respond well to medication or have contraindications to medical treatment(15). The European consensus on RE highlights the importance of early diagnosis to identify an optimal treatment window, as initial brain damage is driven by T cells and microglia (16). When early surgery is not possible or in cases of slower disease progression, immunomodulatory treatments are used as an alternative(17). Nonetheless, surgical options such as functional hemispherectomy(FH) have proven effective for drug-resistant seizures in RE (18). However, there are certain contraindications to surgery for this condition. One such contraindication is the presence of severe seizures that do not respond to antiepileptic drugs and immunosuppressants, as surgery may not be effective in these cases(19). Additionally, the decision to proceed with surgery should carefully weigh the potential cognitive outcomes, especially when the DH is involved, since cognitive functions, including language recovery, can be affected after surgery(20,21).

3. Presurgical Workup

The presurgical workup involves a multimodal evaluation conducted by a multidisciplinary epilepsy team.

Phase one consists of comprehensive history-taking, semiology and neurological examination. Neurophysiology testing uses non-invasive video electroencephalography. An anatomical imaging with a standard epilepsy protocol is performed. Functional neuroimaging with FDG-PET or functional MRI (fMRI) is also obtained along with somatosensory cortex mapping (22,23). Lastly, as part of neurophysiological testing, patients 4 to 6 years of age undergo Wechsler Preschool and Primary Scales of Intelligence (WPPSI); ages 6 to 13 undergo Wechsler Intelligence Scale for children-revised (WISC-R); ages 14 and above are administered Weschler Adult Intelligence Scale (WAIS)(23).

Phase 2 is intracranial EEG, obtained when the ictal focus is not clear-cut and difficult to localize(22). Infrequently, Invasive long-term EEG monitoring is also performed, need based, implanting subdural grid electrodes (24).

The DH for language should be established using preferably fMRI or Wada (i.e. invasive intracarotid Amytal injection). The DH has to be localized in order for functional prognostication and counselling postoperatively(22).

3.1 Anesthesia

With the highest prevalence of RE in children, understanding pediatric dosage of anesthetics is crucial for their young age and small body size along with understanding of the pediatric cerebral physiology(22,25). In case of intraoperative neurophysiological monitoring (IONM), patients are placed under total intravenous anesthesia to facilitate somatosensory and motor evoked potentials. IONM can also provide valuable information on the safety of the contralateral hemisphere during corpus callosotomy or dissection of the mesial temporal lobe(24).

The surgical strategy is decided unanimously through a multidisciplinary case conference, according to Bien's RE diagnostic criteria in which the concordance between clinical and anatomical and EEG data has been established(23,24). Surgery is hence tailored to the individual patient's case presentation (24). Treatment plans are according to the patient and family (23).

4. Surgical techniques

The aim of disconnection surgery is disrupting all inter- and intra- hemispheric epileptic propagation, thus all surgical techniques discussed below follow this principle(22).

4.1 Anatomical Hemispherectomy(McKenzie)

Anatomical hemispherectomy was initially the accepted surgical intervention to treat severe medically refractory epilepsy. The procedure involved removing the entire affected cerebral hemisphere, leaving a void in the area formerly occupied by the cerebral hemisphere to be filled with CSF. In spite of the immediate success of AH, superficial cerebral hemosiderosis and delayed hydrocephalus were frequent complications, in almost a third of patients, rendering the procedure obsolete. In the 1970s, Rasmussen recognized the extensive cerebral tissue resection and the volume of the residual surgical cavity to be the stem of the complications associated with anatomical hemispherectomy. Thence, to avoid the former complications, he proposed a more conservative technique known as functional hemispherectomy(FH), involving the removal of minimal brain tissue while completely disconnecting the affected hemisphere from the healthy one. Since FH, refinements in the procedure resulted in smaller craniotomies giving rise to the more neuroprotective functional hemispherotomies(22). Figure 1 is a schematic representation of anatomical hemispherectomy.

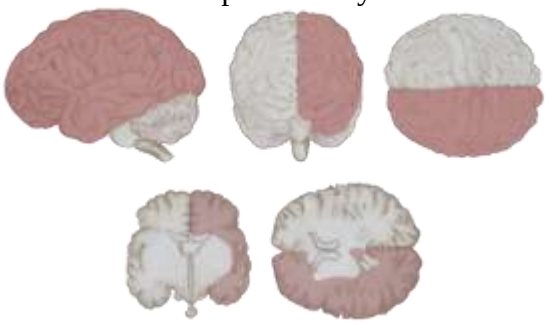

Figure 1: Anatomical Hemispherectomy

4.2 Modified functional Hemispherectomy (James Baumgartner)

The procedure is guided by neuronavigation throughout to confirm the anatomical landmarks, completeness of disconnection and to not breach the midline towards the healthy hemisphere. The patient is positioned supine with a shoulder bump under the ipsilateral shoulder and greater head rotation. A large question mark incision is made and the scalp is reflected anteriorly. Five to six screws are placed as neuronavigation points. A craniotomy is then made exposing the frontal, parietal and temporal lobes(26,27).

4.2.2. Frontotemporal topectomy

Guided by the operating microscope, the sylvian fissure(SF) is split, to view the superior and inferior SFs. Pia and arachnoid overlying the SF are separated and the separation is continued toward the midline until the parietal (P) and frontal (F) limits of the insula are reached. Lines P and F are joined antroposteriorly 4 cm to 6 cm from the midline(PF). Dissection through PF is then extended deep through frontoparietal tissue until the falx, approximately 1 cm from the pericallosal

vessels(PV). Lines P and F are extended until the falx as well. Then through the exposure created, PV are exposed subpially while disconnecting the body of the corpus callosum(CC) below.
Next, sylvian vessels are exposed in subpial resections until they are exposed to the superior insular fissure. A fourth line of dissection is then created from the superior insular fissure disconnecting until the ependyma of the lateral ventricle(LV). The block of tissue demarcated by the dissection is subsequently removed severing any points of connections(26,27).

4.2.3. Frontal disconnection

Again, subpial resections are used to expose the PV anteriorly, while disconnecting the genu of the CC along with the overlying white matter of the frontal lobe until the vessels curve rostrally reaching the A1 segment of the anterior cerebral artery(ACA). Subpially, the ACA is exposed at the floor of the frontal fossa, dividing the overlying white matter for ease of visualizing. Good exposure prevents complication of incomplete frontobassilar disconnection. Next, moving mesial to lateral, the pia of the floor of the frontal fossa is exposed along to the limit of the border of the sphenoid ridge, resecting the overlying white matter as needed for exposure.
Residual tissue within the limits of the lines of frontal and frontoparietal lines of disconnection is resected. Lastly, the sylvian vessels are exposed subpially at the anterior insular limit, mesial to lateral along the floor of the frontal fossa(26).

4.2.4. Posterior disconnection

In the subpial plane, the PV are exposed until the posterior limit of the splenium of the CC.
The posterior callosotomy severs the CC and all overlying white matter connections. Following the falx, dissection is continued subpially inferiorly and then anteriorly. At the posterior limit of the insula, the sylvian vessels are exposed. A cottonoid patty is then placed at the inferior limit of the disconnection(into ventricle to prevent hydrocephalus)(26,27).

4.2.5. Temporal lobectomy

Pia arachnoid is split lateral to the SF from the temporal tip to the posterior limit of the insula. Subpially, temporal tissue is resected from the inferior bank of the SF until the limit of the inferior insular sulcus. The resection is continued through the temporal stem inferiorly until just lateral to the hippocampus at the floor of the temporal fossa. Along the line of dissection pia and arachnoid are split antroposteriorly. Dissection is then taken laterally across the posterior limit of the temporal resection. Following the resection, the resected temporal cortex is rotated mesially to reveal the draining veins, which may vary individual to individual; the veins must be carefully exposed before the lateral temporal lobe can be safely removed. The now exposed choroid(Ch) fissure can be identified and amygdalohippocampectomy is performed subpially. Then, the posterior temporal resection is joined to connect with posterior inferior limit of the frontal disconnection(26,27).

The lines of disconnection are then explored for completeness of disconnection. Finally, the dura is sealed and the subdural space is filled with saline. Intraoperative MRI is obtained and reviewed by epileptology and neuroradiology. Any sites of incomplete disconnection are re-explored with the help of the neuronavigation points, then disconnected followed by a confirmatory MRI report(26).

4.2.6. Insular electrocorticography

Insular electrocorticography (ECoG) is obtained. Any epileptogenic activity warrants removal of insular tissue until the ECoG becomes quiet.

Dura is closed in a water-tight manner with a subdural drain placed in vivo until the CSF clears(26). Figure 2 is a schematic representation of a FH.

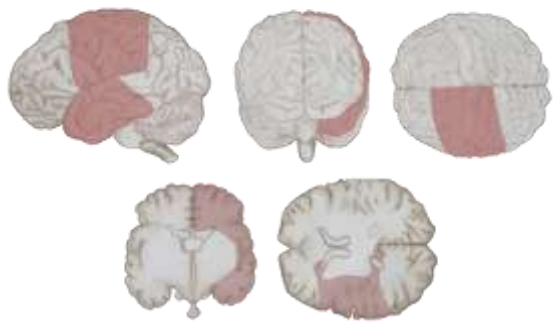

Figure 2: Functional Hemispherectomy

4.3. Peri-insular hemispherotomy (Jeffrey Blount, Johannes Schram's/ Villemure)

The patient positioning is supine with the head rotated laterally placing a contralateral shoulder bump. Neuronavigation is not necessary. The craniotomy is created centered over the SF, exposing the insula adequately(26).

4.3.1. Fronto-parietotemporal topectomy

Under the operating microscope, the SF is split. Subsequently, frontal, temporal and parietal opercula are resected to expose the circular sulcus(26).

4.3.2. Lateral disconnection

From the circular sulcus dissection is begun, and exposing through the white matter, dissection is carried into the frontal horn of the LV followed by the temporal horn. Accessing through the circular sulcus ensures disconnection of the frontal stem of the corona radiata at the frontal lobe and temporal stem at the temporal lobe, hence completely disrupting all ipsilateral neocortical projection fibers. All the tissue lateral to the ventricular system along the plane of the c-shaped arc of the circular sulcus is resected. Caution must be taken at the back of the insula which may house large branches of the middle cerebral artery(MCA). Bipolar cautery can be used to cauterize or divide, otherwise small aneurysm clips can be used, in case of unusually large branches, to achieve hemostasis. The residual frontal cortex is unstable and should be supported by retractor blades or through cotton packing of the ventricles. Now, access to the amygdala and hippocampus is created. Navigation is often dispensable, especially when the ventricles are enlarged(26,27).

4.3.3. Mesial temporal disconnection

Next, the fornix is divided at the point where the hippocampus tapers into the fimbria along with the hippocampus and amygdala. Then, the ventricles are packed with cotton balls saturated with Lactated Ringer's solution to support the remaining cortex. Thus, limbic outflow and descending neocortical projections have been disrupted(26,27).

4.3.4. Corpus callosum

Through the superomedial roof of the frontal horn of the LV, corpus callosotomy is begun. The falx is used as a neuronavigational landmark due to its fixed position. To start, a point is chosen on the medial wall of the LV, two-thirds to three-fourths of the way up the wall. Then the trajectory traverses the ependyma aiming superomedially at 60 degrees to reach the falx. Ultrasound,

neuronavigation or finger palpation is used to find the free wall of the falx to gauge the angle of the trajectory.
Upon exposing the falx, the PV underneath are exposed subpially and followed as an important landmark distally, to disconnect the distal CC. The CC commonly thins out distally around the body and splenium, hence close attention must be given. Failure to disconnect at the distal end of the CC is a common cause of incomplete disconnection in peri-insular hemispherotomy.
Next, to achieve proximal callosotomy the ipsilateral pericallosal artery is followed subpially proximally until the A1 segment of the ACA all the way up to the bifurcation of the internal carotid artery(26,27).

4.3.5. Insular resection

Finally, the insula is decorticated across the long and short gyri while sparing the candelabra branches of the distal MCA.
The craniotomy is closed conventionally but with an in vivo subdural drain. It is also preferred to lay a ventriculostomy catheter into the LV secured by a figure-of-eight stay stitch for easy removal(26). Figure 3 is a diagrammatic representation of the technique.

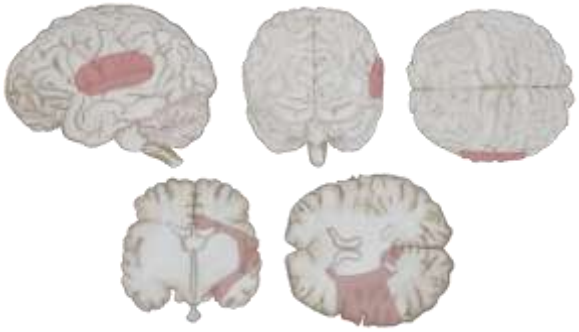

Figure 3: Peri-insular hemispherotomy

4.4. Parasagittal Hemispherotomy (Thomas Blauwblomme)

Patient positioning is supine with the head in neutral, and flexed at 30 degrees while being held in the pin head holder. Neuronavigation is used to compensate for brain dysmorphia. Upon a longitudinal frontoparietal incision 1.5 to 2cm lateral to the midline, a paramedian bone flap of 3 to 4cm width and 5 to 6cm in length is lifted about a third in front and two thirds behind the coronal suture(26).

4.4.1. Operative technique

Under the operative microscope, interhemispheric disconnection is performed, few bridging veins can be coagulated need wise. Both pericallosal arteries are dissected to allow for better visualization of the CC, which is transversely divided with the ultrasonic aspirator allowing for extraventricular exposure of the septum pellucidum. Dividing the septum pellucidum completes the callosotomy anteriorly until the anterior communicating arteries are visible below the rostrum subpially and the vein of Galen below the splenium.
The ventricle is then unroofed and the Ch identified and followed posteriorly until the atrium of the ventricle. The crus of the fornix is dissected just below the splenium and behind the thalamus again using the ultrasonic aspirator. Using a cavitron ultrasonic aspirator the peri thalamic dissection is done lateral to the Ch plexus in a posteroanterior direction making the junction between the temporal and frontal lobes.
Upon reaching the choroidal point, the posterior communicating, carotid and anterior communicating arteries are followed subpially creating a junction between the choroidal point and the frontal horn anteriorly to the foramen of Monroe. Thus, the anterior part of the internal capsule

and anterior commissure is disconnected. A biopsy can be obtained at the superior frontal gyrus at the start or end of surgery for histopathological examination(26,27). Figure 5 is a representation of the procedure.

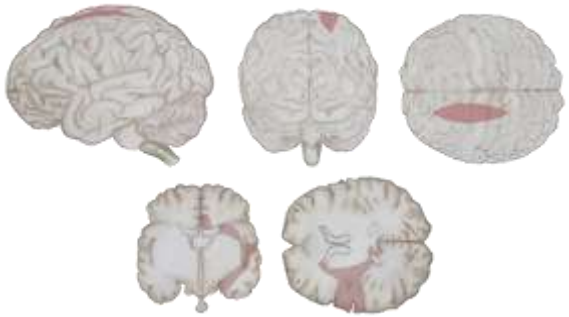

Figure 4: Parasagittal Hemispherotomy

4.5. Endoscopy-assisted hemispherotomy (P. Sarat Chandra)

A transverse incision is made across the coronal suture, followed by raising a 4x3cm bone flap lateral to the midline. Neuronavigation is then used to register the bone flap and avoid large draining veins(26).

4.5.1. Operative technique

The procedure is done is three stages: complete corpus callosotomy, anterior and middle disconnection and posterior disconnection.

Upon opening the dura , the medial margin of the hemisphere is retracted. The is head maintained at 30 degrees with mannitol infusion and cisternal CSF drainage to relax the brain. Endoscope used is a rigid 0-degree high-definition (HD) endoscope held by a rigid endoscope holder. Standard microsurgical instruments, extra-long bipolar instruments and self-irrigating bayonetted bipolar are used in parenchymal dissection. Under endoscopic guidance, starting from the falx, the medial edge of the hemisphere is dissected and the CC is entirely exposed(26,28).

4.5.2. Complete corpus callosotomy

The CC is exposed antroposteriorly and disconnection is done from the splenium to the genu, while keeping the corpus callosotomy closer to the ipsilateral ventricle(26).

4.5.3. Anterior and middle disconnection

Just posterior to the ACA, the genu is disconnected and extended laterally in a horizontal plane until just anterior to the caudate nucleus. The disconnection is then taken inferiorly until the skull base in level with the lesser wing of sphenoid in the subarachnoid plane. Then, the disconnection continues until the posterior part of the gyrus rectus. The anterior cerebral vessels and the optic nerve should now be visible through the arachnoid. The anterior disconnection hence finishes disconnecting the frontal lobe.

The middle disconnection is picked up at the lateral end of the anterior disconnection, and resection is continued posteriorly to open into the body of the LV and through the lateral horn dissection ends lateral to the choroidal fissure at the atrium, just lateral to the thalamus. The MCA should now be visible at the sphenoidal ridge(26,28).

4.5.4. Posterior disconnection

Lastly, in posterior division, a remaining posterior part of the fornix, which falls between the Ch plexus at the atrium and the posterior-most part of the splenium is separated until the arachnoid

beneath taking caution not to inadvertently damage the Galenic veins underneath. A small piece of tissue underneath the Ch plexus is sometimes missed, hence a 30-degree scope can be used to visualize it. The posterior disconnection completes the separation of the temporal lobe(26).

Each of the approaches to hemispherotomy are most successful at the hands of experienced surgeons performing on the specific patient. The targeted disconnection of each surgery is described in table 1(26). The main limitations and advantages of each technique are discussed in table 2.

Table 1: Disconnection targets in hemispheric disconnection procedures (26)

	Procedure	Structures	Disconnection target	Useful anatomic landmarks
Modified functional hemispherectomy	Fronto-parietal topectomy	Sylvian fissure White matter of the frontal and parietal tissue Corpus callosum(anterior part)	Corona radiata Interhemispheric fibers	Sylvian fissure Falx Pericallosal vessels Superior insular fissure
	Frontal disconnection	Corpus callosum(genu)	Interhemispheric fibers	Pericallosal vessels until A1 segment of the anterior cerebral artery
	Posterior disconnection	Corpus callosum(splenium) White matter of the parietal lobe(posterior)	Interhemispheric fibers Parietal lobe tissue	Pericallosal vessels falx
	Temporal lobectomy	White matter of temporal lobe Hippocampus and amygdala	Temporal lobe tissue, amygdala, hippocampus Internal capsule	Temporal tip Sylvian fissure Choroid fissure
	Insular electrocorticography	Insular tissue	Insular cortex	
Peri-insular Hemispherotomy	Fronto-parietotemporal topectomy	Frontal, temporal and parietal opercula		Sylvian fissure
	Lateral disconnection	White matter of the temporal lobe	Frontal stem of corona radiata Temporal stem of corona radiata	Lateral ventricle C-shaped arc about the circular sulcus
	Mesial temporal disconnection	fornix	Limbic circuit	-

			Neocortical projections	
	Corpus callosotomy	Corpus callosum	Interhemispheric fibers	falx Pericallosal artery until A1 segment of anterior cerebral artery
	Insular resection	Long and short gyri of the insula	Insular cortex	Long and short gyri of the insula
Parasagittal Hemispherotomy		Corpus callosum fornix Perithalmic tissue Tissue between choroidal point and frontal horn	Interhemispheric fibers Fornix internal capsule, anterior commissure	Anterior communicating arteries Vein of Galen Choroid Lateral ventricle Foramen of Monroe Posterior communicating arteries Carotid Anterior communicating arteries
Endoscopy-assisted hemispherotomy	Corpus callosotomy	Corpus callosum(spleniu m to genu)	Interhemispheric fibers	Falx
	Anterior and middle disconnection	Subcallosal gyrus Thalamus, basal ganglia, insula claustrum Hippocampus	Anterior temporal lobe, amygdala, fronto-orbital fibers Fibers of corona radiata, internal capsule, anterior temporal connections, and orbitofrontal connections Hippocampal projections and association fibers	Anterior cerebral artery Lateral ventricle

	Posterior disconnection	Fornix Posterior part of splenium Residual tissue between choroid at the atrium and posterior end of splenium	Fibers of posterior column of fornix	

Table 2: Limitations and advantages of disconnection approaches (26)

Surgical Approach				Limitations	Advantages
Anatomical		Hemispherectomy	Anatomical	Large amount of tissue resection requiring long operative time. The procedure frequently causes massive blood loss, hydrocephalus and superficial hemosiderosis.	Patients with previous failed functional hemispherectomy/ hemispherotomy.
Functional	Lateral		Modified Functional	Relatively time consuming, with highest blood loss, and greater risk of post-hemispherectomy hydrocephalus in comparison to hemispherotomies. Risk of incomplete disconnection.	Most suitable for dysmorphic brains such as in advanced cases of RE with cerebral atrophy in which large craniotomies are better tolerated for brain retraction during surgery.
		Hemispherotomies	Peri-insular	Difficult anatomical orientation to operate in. Risk of incomplete disconnection.	Does not necessitate neuronavigation. The technique also has a simpler postoperative course with an external drain left in place for 3-4 days and removed at bedside.
			Parasagittal		

	Vertical			Is contraindicated in patients with hemispheric pericallosal arteries in order to avoid inadvertent damage during the sagittal approach. It can be challenging to perform as the slight retraction of the brain has to performed through a small craniotome. Risk of incomplete disconnection.	Relatively small craniotome. Suitable for hemispheric atrophy in cases of RE. Avoiding corticectomy allows for easy closure and avoids the complication of subdural collections. In addition, no postoperative external ventricular drain is required.
			Endoscopic-Assisted	Requires a steep-learning curve for less experienced surgeons in hemispherectomies. Surgery requires the availability of appropriate endoscopes, holders and integrated neuronavigational systems. Risk of incomplete disconnection.	Fastest operating time with the lowest blood loss, smallest craniotome.

5. Postoperative management

After surgery the patient is admitted into the intensive care unit (22). All tests performed preoperatively are repeated postoperatively (29). Postoperative care also includes pain and seizure management, infection prophylaxis, and rehabilitation(16). Gross and fine motor interdisciplinary rehabilitation is started early on to ensure good functional recovery(30). Lastly, regular follow-ups are required to monitor the patient's condition(22).

6.Complications

Hemispheric disconnection procedures come with a number of complications. Major complications postoperatively include perioperative bleeding, aseptic meningitis, hydrocephalus, fever of central origin, sepsis, postoperative brain abscess, meningitis, superficial hemosiderosis, coagulopathy, venous infarcts and subdural hematoma requiring decompressive craniotomy. Minor complications include chronic hypogammaglobulinemia, anemia and metabolic

imbalances. The mortality rate reported due to hemispherotomy remains as low as 0-5%. Both functional and anatomical hemispherectomies have been reported to cause very few complications and very few deaths have been reported in the literature overall(24,31,32).

7. Outcomes

Surgical outcomes are divided into primary (frequency and severity of seizures) and secondary (AEDs therapy, cognition, language, speech, behavior, and quality of life) outcome measures. All the hemidecortication procedures show comparable outcomes but differ in the postsurgical complications.

Hemispherotomy is effective in completely controlling seizures in 73% to 80% of patients(29,31). Postural control, balance and ability to walk in handicapped patients improve. However, hemianopia, hemiparesis, loss of fine motor skills and aphasia are inevitable. Cognition is improved in 68.7% to 90% of patients notably due to the absence of the burden of debilitating seizures. Improvement in cognition after surgery has also been shown to be inversely proportional to disease duration, hence it is recommended to perform surgery before disease spreads to the healthy hemisphere(31). Post surgically, language improved in 83 % of patients with DH disease. Receptive language has been said to improve markedly more than expressive language with common residual deficits in expressive function(33). Studies have also reported improvements in functional independence and disruptive behavior(29). Furthermore, following surgery, steroids are tapered before being completely withdrawn in 63%; AEDs are simplified in seizure-free patients and 76% patients are drug-free. Overall, the drug load is reduced (31,33).

According to Bellamkonda, hemispheric decortications should be taken as palliative measure rather than a remedy for RE-related seizures (34). The surgical approaches often maintain the functional abilities these patients had before surgery, even when the left hemisphere is affected. Despite its inherent risks, hemispheric surgery consistently leads to positive seizure outcomes, significantly improving the overall quality of life.

8. Recent advances in hemispheric disconnection surgeries

A bloodless technique for minimally invasive robotic thermocoagulative hemispherotomy (ROTCH), was proposed by the founders of the Endoscopic-Assisted Hemispherotomy. The technique employs a robot arm which can cover multiple trajectories in a short time along with an O-arm, which allows for co-registration, and radiofrequency ablation. Resulting in a mean total blood loss of less than 5ml in the pilot study(35).

Benedictis proposed using three-dimensional(3D) rendering models and augmented realty simulators in optimizing anatomical awareness in presurgical planning, intraoperative orientation and educational training for epilepsy surgeries. These emerging technologies are widely used in various neurosurgical domains requiring high levels of accuracy, however their application in pediatric neurosurgery is relatively unreported (36).

9. Conclusion

In spite of the functional sacrifices, RE is a progressive debilitating condition with hemispheric disconnection surgery offering the only durable seizure control and freedom for a better quality of life for patients. Elaborate surgical procedures currently in use like anatomical hemispherectomy and functional hemispherotomies are shifting towards more conservative techniques with lower fidelities in line with advances in robotics and artificial intelligence. However, patient selection and time to surgery still remains a challenging decision in order to achieve the best functional outcomes.

Abbreviations

RE
: **Rasmussen's encephalitis**

CSF
: **cerebrospinal fluid**

DH
: **dominant hemisphere**

FH
: **functional hemispherectomy**

CC
: **corpus callosum**

PV
: **pericallosal vessels**

ACA
: **anterior cerebral artery**

SF
: **sylvian fissure**

LV
: **lateral ventricle**

Ch
: **choroid**

MCA
: **middle cerebral artery**

References

1. Rasmussen T, Olszewski J, Lloyd-Smith D. Focal seizures due to chronic localized encephalitis. Neurology [Internet]. 1958 [cited 2024 Jun 13];8(6):435–45. Available from: https://pubmed.ncbi.nlm.nih.gov/13566382/

2. Lim M, Gorman M. Autoimmune neurologic disorders in children. Handb Clin Neurol. 2016 Jan 1;133:485–510.

3. Britton J. Autoimmune epilepsy. Handb Clin Neurol. 2016 Jan 1;133:219–45.

4. Hammed A, Badour M, Baqla S, Amer F. Diagnosis and treatment of Rasmussen's encephalitis pose a big challenge: Two case reports and literature review. Annals of Medicine and Surgery [Internet]. 2021 Aug 1 [cited 2024 Jun 13];68:102606. Available from: /pmc/articles/PMC8358639/

5. Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet neurology [Internet]. 2014 Feb [cited 2024 Jun 13];13(2):195. Available from: /pmc/articles/PMC4005780/

6. Bien CG, Tiemeier H, Sassen R, Kuczaty S, Urbach H, Von Lehe M, et al. Rasmussen encephalitis: incidence and course under randomized therapy with tacrolimus or intravenous immunoglobulins. Epilepsia [Internet]. 2013 Mar [cited 2024 Jun 13];54(3):543–50. Available from: https://pubmed.ncbi.nlm.nih.gov/23216622/

7. Dupont S, Gales A, Sammey S, Vidailhet M, Lambrecq V. Late-onset Rasmussen Encephalitis: A literature appraisal. Autoimmune Rev. 2017 Aug 1;16(8):803–10.

8. Prayson RA. Pathology of Epilepsy. Practical Surgical Neuropathology: A Diagnostic Approach A Volume in the Pattern Recognition Series. 2018 Jan 1;617–32.

9. Li T, Gao Q, Luan G. Central Bringing Excellence in Open Access. 2016.

10. Jadhav SS, Dhok AP, Mitra KR, Ambhore AN. The Diagnosis and Treatment of Rasmussen's Encephalitis: A Case Report. Cureus. 2023 Jan 23;

11. Noordin NS, Deyo LJ, Ryon CW, Anderson WT. Atypical Presentation of Cerebral Palsy and Seizures: A Case Report on Rasmussen's Encephalitis in an Adolescent. Cureus. 2021 Mar 4;

12. Elavarasi A, Shukla G, Vibha D, Suri V, Bal C. Chronic T cell encephalitis responsive to immunotherapy. Ann Indian Acad Neurol. 2022;25(3):495.

13. David B, Prillwitz CC, Hoppe C, Sassen R, Hörsch S, Weber B, et al. Morphometric <scp>MRI</scp> findings challenge the concept of the "unaffected" hemisphere in Rasmussen encephalitis. Epilepsia. 2019 May 8;60(5).

14. Bauer J, Elger CE, Hans VH, Schramm J, Urbach H, Lassmann H, et al. Astrocytes are a specific immunological target in Rasmussen's encephalitis. Ann Neurol. 2007 Jul 14;62(1):67–80.

15. Sundar SJ, Lu E, Schmidt ES, Kondylis ED, Vegh D, Poturalski MJ, et al. Seizure Outcomes and Reoperation in Surgical Rasmussen Encephalitis Patients. Neurosurgery. 2022 Jul;91(1):93–102.

16. Bien CG. Pathogenesis, diagnosis and treatment of Rasmussen encephalitis: A European consensus statement. Brain. 2005 Jan 5;128(3):454–71.

17. Mir A, Almudhry M, Al-Ghamdi F, Bashir S. Successful treatment of epilepsia partialis continua with perampanel: two pediatric cases. Epileptic Disorders. 2021 Apr 15;23(2):385–91.

18. Haroon K, Taher T, Alam MS, Reza MA, Mia MAQ, Hossain SS. Functional Hemispherotomy in a Patient with Rasmussen's Encephalitis: A Case Report. Bangladesh Med Res Counc Bull. 2022 Sep 5;48(1):71–5.

19. Tekturk P, Erdogan ET, Kurt A, Kocagoncu E, Kucuk Z, Kinay D, et al. Transcranial direct current stimulation improves seizure control in patients with Rasmussen encephalitis. Epileptic Disorders. 2016 Mar 15;18(1):58–66.

20. Borne A, Perrone-Bertolotti M, Jambaqué I, Castaignède C, Dorfmüller G, Ferrand-Sorbets S, et al. Cognitive outcome after left functional hemispherectomy on dominant hemisphere in patients with Rasmussen encephalitis: beyond the myth of aphasia. Patient series. Journal of Neurosurgery: Case Lessons. 2022 Nov 28;4(22).

21. Bulteau C, Grosmaitre C, Save-Pédebos J, Leunen D, Delalande O, Dorfmüller G, et al. Language recovery after left hemispherotomy for Rasmussen encephalitis. Epilepsy & Behavior. 2015 Dec;53:51–7.

22. Young CC, Williams JR, Feroze AH, McGrath M, Ravanpay AC, Ellenbogen RG, et al. Pediatric functional hemispherectomy: operative techniques and complication avoidance. Neurosurg Focus. 2020 Apr;48(4):E9.

23. Guan Y, Chen S, Liu C, Du X, Zhang Y, Chen S, et al. Timing and type of hemispherectomy for Rasmussen's encephalitis: Analysis of 45 patients. Epilepsy Res. 2017 May;132:109–15.

24. Casciato S, Di Bonaventura C, Giallonardo AT, Fattouch J, Quarato PP, Mascia A, et al. Epilepsy surgery in adult-onset Rasmussen's encephalitis: case series and review of the literature. Neurosurg Rev. 2015 Jul 16;38(3):463–71.

25. Khandelwal A, Chaturvedi A, Kumar N, Jena B. A009 Perioperative Anesthetic Management in Rasmussen's Encephalitis: A Retrospective Analysis. In 2019.

26. Baumgartner JE, Blount JP, Blauwblomme T, Chandra PS. Technical descriptions of four hemispherectomy approaches: From the Pediatric Epilepsy Surgery Meeting at Gothenburg 2014. Epilepsia. 2017 Apr 7;58(S1):46–55.

27. Schijns OEMG, Delev D, von Lehe M, van Roost D, Rössler K, Theys T, et al. Functional hemispheric disconnection procedures for chronic epilepsy: history, indications, techniques, complications and current practice in Europe. A consensus statement on behalf of the EANS functional neurosurgery section. Brain and Spine. 2024 Jan 1;4.

28. Roldan P, Guizzardi G, Di Somma A, Valera R, Varriano F, Donaire A, et al. Endoscopic Anatomy of Transcallosal Hemispherotomy: Laboratory Study with Advanced Three-Dimensional Modeling. World Neurosurg. 2022 Aug 1;164:e755–63.

29. Pulsifer MB, Brandt J, Salorio CF, Vining EPG, Carson BS, Freeman JM. The Cognitive Outcome of Hemispherectomy in 71 Children. Epilepsia. 2004 Mar 18;45(3):243–54.

30. Varadkar S, Bien CG, Kruse CA, Jensen FE, Bauer J, Pardo CA, et al. Rasmussen's encephalitis: clinical features, pathobiology, and treatment advances. Lancet Neurol. 2014 Feb;13(2):195–205.

31. Granata T, Matricardi S, Ragona F, Freri E, Casazza M, Villani F, et al. Hemispherotomy in Rasmussen encephalitis: Long-term outcome in an Italian series of 16 patients. Epilepsy Res. 2014 Aug;108(6):1106–19.

32. Sarat Chandra P, Subianto H, Bajaj J, Girishan S, Doddamani R, Ramanujam B, et al. Endoscope-assisted (with robotic guidance and using a hybrid technique) interhemispheric transcallosal hemispherotomy: A comparative study with open hemispherotomy to evaluate efficacy, complications, and outcome. J Neurosurg Pediatr. 2019 Feb 1;23(2):187–97.

33. Hoffman CE, Ochi A, Snead OC, Widjaja E, Hawkins C, Tisdal M, et al. Rasmussen's encephalitis: advances in management and patient outcomes. Child's Nervous System. 2016 Apr 16;32(4):629–40.

34. Bellamkonda N, Phillips HW, Chen JS, Tucker AM, Maniquis C, Mathern GW, et al. Epilepsy surgery for Rasmussen encephalitis: the UCLA experience. J Neurosurg Pediatr. 2020 Oct;26(4):389–97.

35. Chandra PS, Doddamani R, Girishan S, Samala R, Agrawal M, Garg A, et al. Robotic thermocoagulative hemispherotomy: concept, feasibility, outcomes, and safety of a new "bloodless" technique. J Neurosurg Pediatr. 2021 Jun;27(6):688–99.

36. De Benedictis A, Marasi A, Rossi-Espagnet M, Napolitano A, Parrillo C, Fracassi D, et al. Vertical Hemispherotomy: Contribution of Advanced Three-Dimensional Modeling for Presurgical Planning and Training. J Clin Med. 2023 May 31;12(11):3779.