Movement Disorders and Other Functional Neurosurgery

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Abstract: Functional neurosurgery is not usually a life-saving surgery; it is typically used in certain neurological conditions, including intractable or resistant-to-medical-therapy forms. It includes (but is not limited to) surgery for movement disorders (i.e., Parkinson's disease, tremor, and dystonia) in the form of deep brain stimulation (DBS) or lesioning (ablative procedures) in the brain; surgery for spasticity and torticollis; MVD (microvascular decompression for neurovascular compression syndromes, i.e., trigeminal and glossopharyngeal neuralgia, hemifacial spasm, spasmodic torticollis, etc.); surgery for psychiatric disorders; intractable pain surgery; etc. The principles of surgical management of extreme or resistant forms of these conditions will be discussed in abstract form.

Abbreviations

AAD	atlantoaxial dislocation	AICA	anterior inferior cerebellar artery
AVM	arteriovenous malformation	CBD	corticobasal degeneration
CBZ	Carbamazepine	CNS	central nervous system
CRPS	complex regional pain syndrome	CSF	cerebrospinal fluid
CSPTC	cortico-striato-pallido-cortical	CT	computed tomography
CVA	cerebrovascular accident	DRD	dopa-responsive dystonia
DBS	deep brain stimulation	ET	essential tremor
EMG	Electromyography	GKRS	gamma knife radiosurgery
GK	gamma knife	GTS	Gilles de la Tourette's syndrome
GN	glossopharyngeal neuralgia	HIFU	high-frequency focal ultrasound
HFS	hemifacial spasm	MDD	major depressive disease
IPG	implanted pulse generator	MS	multiple sclerosis
MSA	multiple system atrophy	MRgFUS	MR-guided focus ultrasound
MVD	microvascular decompression	NPD	neurosurgery for psychiatric disorders
MRI	magnetic resonance imaging	PD	Parkinson's disease
OCD	obsessive compulsive disorder	PSP	progressive supranuclear palsy
PICA	posterior inferior cerebellar artery	RF	Radiofrequency
REZ	root entry/exit zone	SCM	Sternocleidomastoid
SCA	superior cerebellar artery	TBI	traumatic brain injury
STN	subthalamic nucleus	TENS	transepidermal neurostimulation
TDPD	tremor-dominant Parkinson's disease	TS	Tourette's syndrome
TN	trigeminal neuralgia	VA	vertebral artery
UE	upper extremity		

1. Movement Disorder Surgery

1.1. Introduction

Medication, in conjunction with rehabilitative treatments such as physiotherapy, occupational therapy, and even psychotherapy, is the prime therapy for movement disorders. As the condition advances, these techniques may fail or have unfavorable outcomes, necessitating surgery. In movement disorders such as essential tremor (ET), Parkinson's disease (PD), and dystonia, surgery has become a well-established type of treatment. Other movement disorders, such as tremors linked with multiple sclerosis as well as tics observed in Tourette's syndrome, seem to benefit from surgery (TS). Although surgery cannot cure movement disorders, it does significantly reduce symptoms and, therefore, improve quality of life.

We will give an overview of numerous movement abnormalities in this chapter, with a focus on those that may benefit from neurosurgical intervention. We will also go over the indications, outcomes, and drawbacks of several surgical approaches for movement disorders.

1.2. Definition of Movement Disorders

Movement disorders are defined by impairments in movement planning, control, or execution and are genetically, pathologically, and clinically heterogeneous. Hypokinetic and hyperkinetic disorders are the two most

common types. Paucity or slowness of movement (bradykinesia) and an involuntary increase in muscular tone characterize hypokinetic diseases (rigidity). Parkinson's disease and various kinds of parkinsonism are examples of hypokinetic illnesses. Hyperkinetic disorders are characterized by excessive involuntary movement, either spontaneously or in reaction to a voluntary movement or another stimulus. Hyperkinetic disorders can sometimes have a voluntary element. Tremor, tics, dystonia, chorea, myoclonus, and ballismus are all hyperkinetic disorders.

1.3. Parkinson's Disease

PD is an age-linked disease with a progressively growing prevalence beyond the age of 50. It is anticipated that up to 2% of adults over the age of 60 will get the disease (Tanner and Aston 2000). PD is marked by bradykinesia, postural instability, and resting tremor that develops slowly and asymmetrically (Lang and Lang 1998). It progresses slowly and has a long-term response to dopaminergic medicines. The loss of melanin-laden dopaminergic neurons in the substantia nigra zona compacta causes depigmentation of the substantia nigra.

Patients with PD experience a wide range of symptoms of the nonmotor type, including fatigue, depression, cognitive decline, anxiety, visual dysfunction, behavioral disorders, dysautonomia, weight loss, sleep irregularities, aberrant sensations, and pain, in addition to motor dysfunction (Chaudhuri et al. 2006). These nonmotor signs may appear earlier in the disease, but they become increasingly disabling as the disease progresses, contributing mostly to a reduction in quality of life.

Atypical parkinsonism can mirror PD in its early stages, but there are typically "red flags" that point to a different diagnosis. The response to levodopa in atypical parkinsonism is poor from the start, transient, or unsustainable. Progressive supranuclear palsy (PSP), multiple system atrophy (MSA), and corticobasal degeneration are examples of atypical parkinsonisms (CBD).

Medical treatments are effective in the early stages of PD. Patients become less sensitive to treatments as the condition progresses, and medication-related problems occur. These are the patients who have benefited greatly from surgical operations.

1.3.1. Treatment of PD

1. Medical therapy: available medications include levodopa, dopamine agonists (pramipexole and ropinirole), anticholinergics (e.g., trihexyphenidyl), amantadine, MAO-B inhibitors (e.g., rasagiline), COMT inhibitors (e.g., entacapone), and many other. Levodopa is the main medication, in combination with add-on drugs from other groups.
2. Occupational and physiotherapy
3. Surgery
    a. Deep brain stimulation (DBS) to STN, GPi, VIM thalamus, and PPN;
    b. Ablative surgery: radiofrequency thalamotomy, pallidotomy, focus ultrasound thalamotomy, and gamma knife thalamotomy;
    c. Cell therapy;
    d. Gene therapy;
    e. Immunotherapy.

1.4. Tremor

In clinical practice, tremor is one of the most frequent movement disorders. It has been defined as a rhythmic, involuntary, and sinusoidal oscillation of one or more parts of body caused by synchronous or alternating muscle contractions.

Tremors are defined as resting or action tremors, in clinical terms. Postural, kinetic, and intention tremors are the three types of action tremor. When a limb is in a resting position, its weight is completely supported against gravity and it develops a resting tremor. It is common in PD and other parkinsonian disorders, as well as midbrain and rubral tremor. An active contraction of the muscles involved is implied by action tremor. A postural tremor takes place when the body maintains a posture against gravity, such as when the arms are stretched out in front of it. A voluntary movement of the extremity causes a kinetic tremor, such as a tremor in the upper extremity during the finger-to-nose technique. When approaching a target, the amplitude of the intention tremor increases.

Differential diagnosis of tremor includes:

1. Physiologic tremor;
2. Essential tremor;

3. Orthostatic tremor;
4. Task specific tremor;
5. PD and other parkinsonian syndromes;
6. Wilson's disease;
7. Multiple sclerosis;
8. Stroke;
9. Holmes tremor;
10. Neuropathic tremor;
11. Palatal tremor;
12. Dystonic tremor.

Essential tremor (ET) is the most prevalent type of action tremor, which can be postural or kinetic in nature and primarily affects the hands. With a frequency of 4–12 Hz, it is usually bilateral and symmetrical (Louis 2001). In around 95% of patients, the distal arms and hands are afflicted, followed by the head (34%), lower limbs (20%), voice (12%), face, and trunk (5%) (Elble 2000a).

When tremor of the head arises alone or before the beginning of hand tremor, dystonic tremor should be considered a possibility. The frequency of ET tremors diminishes over time, while the magnitude may increase (Elble 2000b).

Because ET frequently has an insidious onset, it is difficult for patients to memorize the exact age of onset. The majority of instances begin after the age of 40. The disease's family manifestations are more likely to manifest at an earlier age.

Although the results differ between studies, the majority suggest a crude prevalence of 4% or greater in those aged 60 and up, with both sexes being equally affected.

The incidence appears to increase exponentially as people become older (Louis 2019).

Apart from physiological tremor, essential tremor is the most prevalent type of tremor. In 50% of patients, a significant reduction in tremor occurs in reaction to a small amount of alcohol, which may aid in diagnosis (Mostile and Jankovic 2010).

Tremor is thought to affect roughly 25–60% of persons with multiple sclerosis. Postural and intention tremors are the most common symptoms of MS. The limbs, head, neck, voice cord, and trunk are all affected by the tremor. The tremor is thought to be cerebellar in origin and to be associated with additional sensory, cerebellar, and corticospinal dysfunction. The symptoms are frequently severe, humiliating, and difficult to manage (Koch et al. 2007).

Holmes' tremor, midbrain tremor, rubral tremor, and Benedikt's syndrome are all terms for a condition that affects the proximal limbs. It is a tremor with a slow frequency (less than 4.5 Hz) with a rest element that becomes worse with postural maintenance and even worse with motion.

The common etiology includes stroke, head injury, demyelinating diseases, infection, and vascular malformation. An MRI study usually discloses structural lesions occurring in the upper brain stem, cerebellum, or thalamus. The most common symptoms/signs associated with HT are hemiparesis, ataxia, hypoesthesia, dystonia, cranial nerve palsy, and dysarthria.

Treatment of Tremor

(i) Medical therapy: propranolol and primidone are two highly effective and widely used drugs for ET. Medical treatment of MS tremor and Holmes' tremor are very unrewarding. Isoniazid, levodopa, ondansetron, clonazepam, and some other drugs are used in these condition, in addition to the drugs used for ET.
(ii) Intramuscular injections of botulinum toxin.
(iii) Surgery:

- Deep brain stimulation (DBS) to the VIM thalamus;
- Ablative surgery: radiofrequency thalamotomy, focus ultrasound thalamotomy, and gamma knife thalamotomy.

1.5. Dystonia

Dystonia is a type of movement disorder that results in abnormal postures, typically repetitive abnormal motions, or both. Dystonic motions are structured, tremulous, and twisting in nature. Dystonia is frequently

sparked or exacerbated by deliberate effort and is associated with an overflow of muscular activation (Albanese et al. 2013).

One of the most disabling movement disorders is Parkinson's disease. Its pathogenesis is a network condition engaging the basal ganglia, sensorimotor cortices, and cerebellum that is defined by an abnormal input versus output sensorimotor or plasticity mismatch (Cury et al. 2018).

Dystonia syndromes are classified along three main axes: age at onset, etiology, (childhood onset and adult onset), and body distribution (focal, segmental, multifocal, generalized, and hemidystonia) (Fahn 2011).

Dystonia that starts in childhood has more chance to have a known cause and move from a focal to a widespread form, whereas dystonia that starts beyond the age of 25 commonly affects the craniocervical group of muscles, remains segmental or localized, and is generally non-progressive (Bressman 2004).

Primary dystonia, secondary dystonia, paroxysmal dystonia, and dystonia-plus syndromes are the etiological categories (Fahn et al. 1998).

Primary dystonias are idiopathic, with the exception of genetic alterations in rare cases, and are not accompanied by additional neurologic abnormalities other than tremor and myoclonus. Primary generalized dystonia is uncommon and usually begins in childhood. Primary focal dystonias are more frequent and almost always strike adults in their forties or fifties. These can affect the neck, arm, or face, but leg involvement is uncommon.

Cervical dystonia, the most common kind of focal dystonia, typically manifests itself between the ages of 30 to 50, with restricted head mobility, neck stiffness, and aberrant head postures, as well as irregular tremor of the head. Sensory tactics, such as lightly caressing the chin or face, are widespread and especially effective early in the disease course; this phenomenon is also called the geste antagoniste (Prakash and Lang 2009).

Cranial dystonia: A variety of face, oropharyngeal, and jaw muscles are involved in cranial dystonia. It is frequently linked with cervical muscle involvement (craniocervical dystonia) and occasionally with laryngeal involvement (spasmodic dysphonia). Blepharospasm is a condition in which the orbicularis oculi muscles contract abnormally, causing excessive blinking as well as forced eyelid closure, which can lead to functional blindness (Prakash and Lang 2009).

Oro-mandibular dystonia is characterized by aberrant activity in the lower face, tongue, pharyngeal, and jaw muscles, which can make speaking and swallowing difficult. Spasmodic dysphonia is a vocal cord dystonia; improper adduction, which results in a strangled, strained voice, is more common than abduction, which results in a whispered, breathy voice (Prakash and Lang 2009).

Brachial dystonia: Another type of focal dystonia is brachial dystonia, which is most commonly associated with writing (writer's cramp). Similar issues might arise with pianists and string players. This type of "task specific focal dystonia" can impact a wide range of extremely complicated skills (Prakash and Lang 2009).

Dystonia-plus syndromes are neurological illnesses that include symptoms such as parkinsonism or myoclonus (Prakash and Lang 2009).

Dopa-responsive dystonia (DRD) is a type of generalized dystonia that begins in childhood. As a result of mutations in the gene that codes for GTP cyclohydrolase I, the disorder usually starts in the first decade of life with foot dystonia, gait irregularity, and hyperreflexia. The illness eventually progresses to generalized dystonia with considerable postural instability and gait difficulty. With peak difficulty late in the evening, considerable diurnal variability is a unique trait. A significant, prolonged, and straightforward response to low to moderate dosages of levodopa is the characteristic of this condition (Prakash and Lang 2009).

1.5.1. Treatment Options for Dystonia

1. Medical therapy: available medication includes anticholinergics (e.g., trihexyphenidyl), baclofen, levodopa, benzodiazepines (clonazepam and diazepam), and dopamine depletors (tetrabenazine).
2. Local botulinum toxin injections.
3. Surgery:
    (a) Baclofen pump infusion;
    (b) Deep brain stimulation (DBS) to the GPi and VIM thalamus;
    (c) Ablative surgery: radiofrequency thalamotomy and pallidotomy (Cloud and Jinnah 2010).
4. 'Ruth Chiles Brain spotting technique' for cure of focal dystonia: The author claimed with cases of evidence in her book 'The focal dystonia cure' that most of the focal dystonia can be cured by this technique (Chiles 2022).

1.6. Stereotactic Neurosurgery

The *xx*-axis, *yy*-axis, and *zz*-axis are three mutually perpendicular coordinate axes that make up the Cartesian coordinate system. As a result, x, y, and z values can be used to define any point in space. A Cartesian coordinate system is used in stereotactic surgery. By using a computed tomography (CT) scan, magnetic resonance imaging (MRI), and Cartesian-coordinate-based stereotactic frame, anywhere deep in the brain could be reached/approached in a minimally invasive, precise, and reproducible manner. Modern stereotactic planning software helps in MRI and CT scan image fusion and trajectory planning and reduces surgical complication significantly.

Indications for intracranial stereotactic surgery:

1. Biopsy;
2. Radiosurgery;
3. Deep brain stimulation;
4. Radiofrequency ablation;
5. lacement of depth electrode;
6. Aspiration of hematoma or abscess.

1.7. Surgery for Movement Disorders

A variety of surgical treatments such as resection, ablation, stimulation, cell therapy, gene therapy, immunotherapy, and others have been utilized to manage cases with movement disorders. Currently, deep brain stimulation (DBS), with its inherent character of adjustability and reversibility as well as strong advocacy and marketing from industry, is the most common surgical procedure for PD, ET, and dystonia. Radiofrequency thalamotomy and other ablative procedures are also performed in selected patients. There have been a number of animal studies and clinical trials of gene therapy, tissue transplantation, and immunotherapy. While these trials have shown the safety of the procedure, clinical benefits have been less encouraging.

1.7.1. Deep Brain Stimulation

Deep brain stimulation (DBS) is basically stereotactic implantation of an electrode leading to a specific part of the brain (Figure 1). An internal pulse generator (IPG) is placed in the chest wall and can deliver the stimulus current pulses. An extension wire passes subcutaneously from the scalp area to the chest wall, thereby connecting the lead to the IPG. DBS applies high-frequency electrical stimulation in the subcortical brain. The selection of an appropriate patient and appropriate target is critical for satisfactory outcomes. The precise placement of a DBS lead in its target of interest is the main challenge of the procedure.

DBS has complicated electrical effects on individual neurons and neuronal networks, affects neurotransmitter concentrations and dynamics, and shapes the microenvironment, which includes astrocytes, microglia, and endothelial cells. DBS also affects neuroplasticity and may cause neurogenesis and neuroprotection (Jakobs et al. 2019).

Targets for DBS

1. Subthalamic nucleus: PD;
2. VIM thalamus: essential tremor, other tremor, and tremor-dominant PD;
3. Globus pallidus interna: dystonia and PD with dyskinesia;
4. Pedunculopontine nucleus: PD with gait instability.

The ideal candidates for DBS among PD patients should fulfill the following criteria (Enslin 2016):

1. Appropriate neuroimaging to exclude possible differential diagnosis;
2. Realistic expectations on the potential result of DBS;
3. No cognitive abnormality and motivated patient and family;
4. Duration of PD more than 5 years;
5. Disabling drug-resistant tremor;
6. Proof of dopamine responsiveness (at least 30% improvement in motor score with dopamine);
7. Problematic dyskinesia and motor fluctuations, in spite of appropriate drug therapy;
8. $\leq$70 years of age;
9. No atypical parkinsonism;
10. Good medical health.

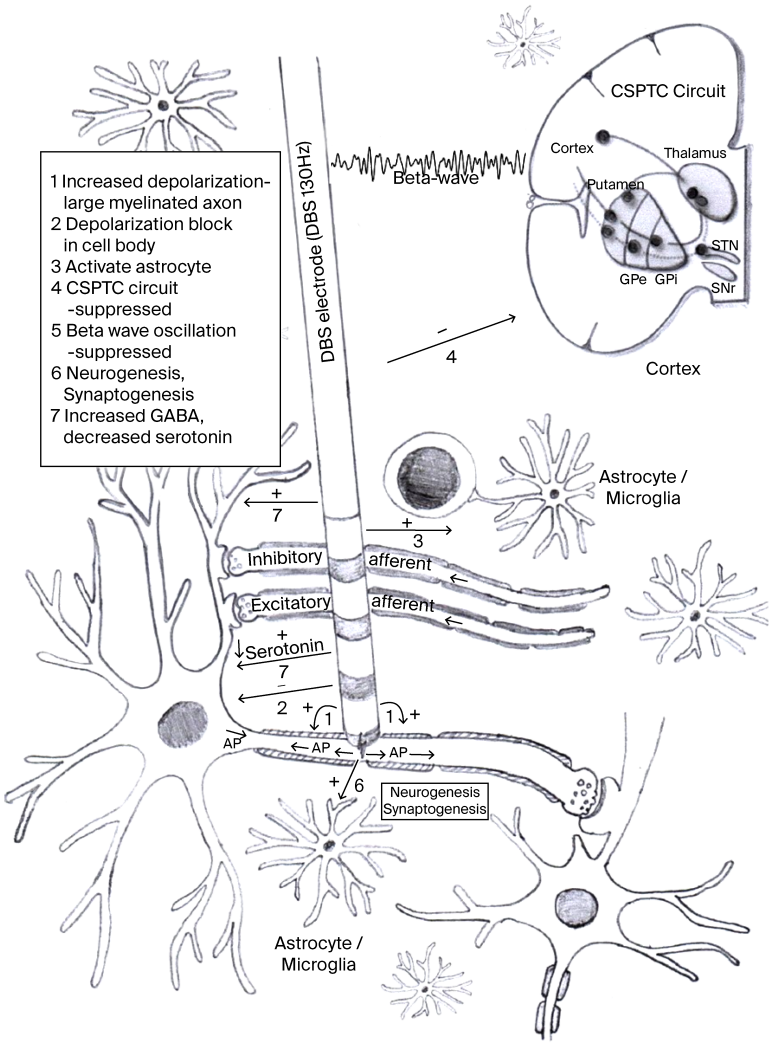

Figure 1. Illustrations showing possible mechanism of action of deep brain stimulation (DBS). CSPTC—cortico-striato-pallido-thalamo-cortical. Source: Figure by authors.

DBS in PD patients has shown long-term improvement in cardinal motor symptoms like tremor, bradykinesia, and rigidity. GPi DBS demonstrated long-term efficacy in the management of generalized and segmental dystonia. Efficacy is more pronounced in primary dystonia than secondary dystonia. Thalamic stimulation seems to be highly effective in TDPD, ET, and dystonic tremor with modest efficacy in Holmes tremor and MS tremor.

Complication of DBS Surgery

1. Intracranial hemorrhage;
2. Infection;
3. Fracture of DBS electrode, lead migration, failure of extension wire, IPG malfunction, and erosion of skin;
4. Dyskinesia, worsening of symptom, speech dysfunction, and dysarthria (Rezai et al. 2008).

1.7.2. Ablative Procedures

Currently, three main ablative procedures that are utilized for movement disorders are RF thermo-ablation, gamma/cyber knife radiosurgery, and high-frequency focused ultrasound (HIFU) thermal ablation. All these surgeries have their foundation in stereotactic principles.

The radiofrequency thermal ablation procedure involves heating a lesion with an intracranial electrode connected to an RF generator to create a lesion. Except at the tip, where the active electrode is placed, this electrode is electrically isolated.

External ablative treatment mode stereotactic radiosurgery offers a large single dose of radiation to a small intracranial target volume while sparing surrounding tissue. Lars Leksell developed gamma knife radiosurgery (GKRS), which takes advantage of gamma rays emitted by excited cobalt nuclei.

Thermal ablation with MR-guided focused ultrasound (MRgFUS) is a promising, noninvasive technology. Using a hemispheric phased array of transducers mounted to the skull, high-frequency focused ultrasound (HIFU) beams are targeted to an intracranial region. This permits ultrasonic waves to flow through a vast area of the skull, preventing overheating and brain injury. Ultrasonic mechanical energy is absorbed and transformed to heat within the focal target volume, causing tissue damage locally at the focus (ter Haar and Coussios 2007).

Radiofrequency for cases with ET and tremor-dominant PD and VIM thalamotomy have been demonstrated to provide considerable tremor control (TDPD). The majority of side effects with RF thalamotomy are temporary due to perilesional edema that goes away with time; nevertheless, persistent ataxia, dysarthria, and motor/sensory deficiency might develop. With bilateral lesions, the chance of dysarthria is much higher. As a result, RF thalamotomy is usually only performed unilaterally (Franzini et al. 2019).

GK thalamotomy and transcranial MRgFUS thalamotomy are noninvasive techniques that eliminate the risk of cerebral hemorrhage and infection associated with open surgery. In patients with TDPD and ET, both of these techniques revealed significant tremor (Witjas et al. 2015; Chang et al. 2018). While GK radiosurgery takes a long time to lesion, MRgFUS allows for rapid lesioning.

RF of the globus pallidus internus pars interna (GPi) was used to treat PD, PD with dyskinesia, and dystonia. In PD, a unilateral pallidotomy is performed on the side that is more symptomatic. Primary dystonic patients, on the other hand, frequently receive bilateral lesioning because they have bilateral extremities and axial symptoms and are more capable of tolerating bilateral lesioning. The cardinal motor symptoms of Parkinson's disease, including tremor, stiffness, and bradykinesia, have been demonstrated to be improved with posteroventral pallidotomy. Pallidotomy may also help with dyskinesias caused by levodopa (Franzini et al. 2019).

2. Surgery for Spasticity

Upper motor neuron pathway lesions cause spasticity in limbs and the trunk. The lack of inhibitory impulse on alpha motor neurons and on gamma motor neurons (intrafusal fibers) results in alpha spasticity and gamma spasticity, respectively. Increased muscle tone, myoclonus, and (sometimes) involuntary movements are the clinical findings in spasticity (Greenberg 2010).

2.1. Etiologies

- Cerebral insult (e.g., stroke, tumor, and vasculitis).
- Spinal cord lesions (cord injury rostral to the conus medullaris, tumor, and vasculitis).
- Multiple sclerosis and congenital abnormalities (e.g., spinal dysraphism and cerebral palsy).

2.2. Clinical Features

- History of etiological event (such as stroke, trauma, etc.).
- Elevated resistance to passive movements.
- Exaggerated deep tendon reflexes.
- Activation of antagonistic muscles simultaneously.
- Characteristic postures (i.e., hyperflexion of thighs or scissoring of legs).
- Pain (sometimes).
- It may confound the patient's ability to sit in a wheelchair, lay in bed, drive modified vehicles, sleep, etc.
- May also foster development of decubitus/contracture ulcers.
- Urge incontinence of bladder.

2.3. Grading Spasticity (The Ashworth Scale)

Assessment should be performed with patient supine and relaxed (Table 1).

Table 1. Ashworth scorer.

Score	Degree of Muscle Tone
1	Normal muscle tone
2	Slight (mild) increase; slight "catch" in flexion and extension
3	More marked (moderate) increase; passive movements easy
4	Considerable increase; difficult passive movements
5	Affected part rigid inflexion and extension

Source: Authors' compilation based on data from Ashworth (1964).

2.4. Treatment

2.4.1. Conservative

- Regular physiotherapy.
- Drugs: benzodiazepines, baclofen, and dantrolene.

2.4.2. Surgical

Reserved for spasticity that is refractory to medical management or where side effects of medications are intolerable. Generally, either orthopedic (e.g., tendon release operations (tenotomies) of heel cord or hamstrings, iliopsoas myotomies, etc.) or neurosurgical (e.g., nerve blocks, neurectomies, myelotomy, etc.).

A. Non-lesional procedures

1. Intrathecal baclofen (baclofen pump)—widely used where baclofen is administered intrathecally through a subcutaneously implanted reservoir. Other indications include: CVA (Meythaler et al. 2001), cerebral palsy, TBI, dystonia, and stiff-man syndrome.
2. Intrathecal morphine.
3. Electrical stimulation through epidural electrodes (Richardson et al. 1979).

B. Lesional procedures, with preservation of potential for ambulation

Motor point block (Scott et al. 1985) (intramuscular phenol neurolysis): sensations and remaining voluntary functions are preserved.

Time-consuming phenol nerve block: Akin to motor point block but utilized for more severe spasticity. Here, complete blocking of muscles is desired (Herz et al. 1990).

(i) Selective neurectomies (Scott et al. 1985)

1. Sciatic nerve neurectomy (Herz et al. 1990).
2. Obturator nerve neurectomy: useful for strong hip adductor spasticity that causes scissoring.
3. Pudendal nerve neurectomy: helpful if excessive detrusor dyssynergy interferes with bladder function.

(ii) Percutaneous radiofrequency foraminal rhizotomy

(iii) Midline "T" myelotomy

It intercepts the reflex arc from sensory to motor units without disturbing connections from the corticospinal tract to anterior horn cells (Cury et al. 2018).

(iv) Selective dorsal rhizotomy (Privat et al. 1976)

Intraprocedural EMG and electrophysiological stimulation are used to cut the sensory rootlets engaged in "handicapping spasticity". It may be temporary but seems to work for a minimum of 5 yrs. In cerebral palsy children, it may improve gait in ambulatory cases; in nonambulatory children, their gait is improved, but they may not be able to walk.

(v) Stereotactic thalamotomy or dentatotomy

It may be helpful in cerebral palsy. Usually used for unilateral dystonia, especially shoulders or hips. It should not be utilized if the situation is swiftly progressive.

C. Lesioning procedures, with sacrifice of potential for ambulation (such as in complete cord injuries where Nona lesioning procedures are not indicated as there is no motor function to recover). Utilized in failed percutaneous rhizotomy and "T" myelotomy.

(i) Intrathecal injection of 6 mL of 10% phenol (by weight) in glycerin mixed with 4 ml of iohexol;

(ii) Selective anterior rhizotomy: results in flaccid paralysis and atrophy of muscles;

(iii) Neurectomies plus/minus tenotomies;
(iv) Intramuscular neurolysis by phenol;
(v) Cordectomy (reserved only for patients who do not respond to any other measure; it results in total flaccidity) (Greenberg 2010; Ashworth 1964; Meythaler et al. 2001; Richardson et al. 1979; Scott et al. 1985; Herz et al. 1990; Privat et al. 1976).

3. Torticollis (Wry Neck)

A special type of dystonia due to failure to maintain the head position.

3.1. Etiology

- Congenital torticollis;
- Spasmodic torticollis (Idiopathic)—the sternocleidomastoid (SCM) muscle is shortened in spasm;
- Hemorrhage into the sternocleidomastoid muscle (scaring);
- Extrapyramidal lesions: usually improve by lying down; EMG usually shows abnormal, grouped electrical activities of muscles;
- Psychogenic;
- Torticollis from atlantoaxial rotatory instability—SCM may be in continuous spasm state (unlike that of spasmodic torticollis) (Figure 2);
- Neurovascular compression of the 11th nerve;
- Infection of the cervical spine, i.e., Tuberculosis;
- Cervical adenitis;
- Chari malformation;
- Syringomyelia/syringobulbia;
- Cerebellar tumors in children;
- Bulbar palsies;
- Diplopia from extraocular muscles weakness (Greenberg 2010).

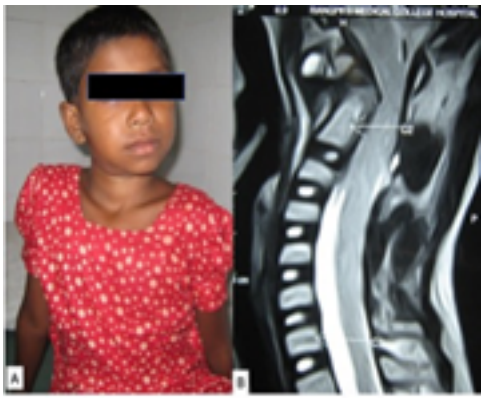

Figure 2. (**A**) Torticollis due to atlantoaxial dislocation (AAD) in a pediatric patient. (**B**) MRI of cervical spine showing AAD. Source: Figure by authors.

3.2. Investigations

1. MRI of brain in accessory and lower cranial nerve protocol and MRI craniovertebral junction;
2. CT scan of cervical spine and craniovertebral junction;
3. EMG of neck muscle.

3.3. Treatment

3.3.1. Conservative

Relaxation training, stretching, physiotherapy, and transepidermal neurostimulation (TENS).

3.3.2. Surgical Procedures

Usually advised for disabling, intractable cases. Options are as follows:

1. Dorsal cord stimulation;
2. Local injection of botulinum toxin—less effective for torticollis;

3. Selective rhizotomy and spinal accessory neurotomy;
4. MVD of accessory nerve root entry zone;
5. Stereotactic lesioning of Forel's H1 field;
6. Sectioning SCM;
7. Treatment of specific etiology, such as Chiari malformation, AAD, etc.;
8. Torticollis of accessory nerve origin.

- Transection of the anastomotic branches between the 11th nerve and the upper cervical posterior root (C1 anastomotic branch is sensory only);
- MVD of the 11th nerve (most cases caused by VA, but PICA compression is also described; symptoms relieved a few weeks after operation) (Greenberg 2010; Shima et al. 1988).

4. Trigeminal Neuralgia (TN)

4.1. Introduction

Trigeminal neuralgia (TN) is a condition marked by recurrent, unilateral, short, electric-shock-like pains that are sudden in onset and termination, localized to one or more divisions of the trigeminal nerve, and caused by harmless stimuli. Moreover, there might be simultaneous continuous pain of moderate intensity within the distributions of the involved nerve division/s.

4.2. Diagnostic Criteria

A. Recurrent paroxysms of one-sided face pain in one or more divisions of the fifth nerve, with no radiation beyond, while meeting criteria B and C.

B. Pain manifests itself in all of the following ways:

(1) Lasting anywhere between a fraction of a second and two minutes;
(2) Extreme severity;
(3) The quality is electric-shock-like, sharp, shooting, or stabbing.

C. Triggered by seemingly harmless stimuli in the involved trigeminal distribution;

D. Not adequately explained by another condition (International Headache Society 2018).

4.3. Classification of TN

1. Classical trigeminal neuralgia: vascular compression seen on MRI or during surgery with morphological alterations of the fifth nerve root.
2. Secondary trigeminal neuralgia occurs when a neoplasm in the cerebellopontine angle, multiple sclerosis, or an arteriovenous malformation causes pain (International Headache Society 2018).
3. Idiopathic TN: there are no diagnostic tests that can confirm a lesion or condition that could cause trigeminal neuralgia (International Headache Society 2018).

4.4. Incidence and Pathophysiology

TN is a rare condition, with a yearly incidence of 4.3–27 per 100,000 people. Women are more likely to be affected, and the risk rises with age. In classic TN, the average age of onset is 53 years, while in secondary TN, it is 43 years (Maarbjerg et al. 2017).

The transition from peripheral Schwann cell myelination to central oligodendroglia myelination occurs within the root entry zone (REZ). This area is especially prone to compression by a blood vessel or tumor, which causes demyelination and morphological changes such distortion, indentation, flattening, or atrophy (Maarbjerg et al. 2014). Sensory nerve fibers that have been demyelinated turn hyperexcitable and are capable of producing ectopic impulses, which present as spontaneous pain (Devor et al. 2002). Touch-evoked pain may be caused by ephaptic links between demyelinated A and A fibers (Magerl and Treede 2004).

4.5. Causes

Classical TN caused by microvascular compression by:

- Superior cerebellar artery (SCA—the most frequent);
- Anterior inferior cerebellar artery (AICA);
- Elongated PICA;

- Ectatic vertebrobasilar artery (EVBA) (Figure 3);
- Veins.

Secondary TN caused by:

- Mass lesion epidermoid (Figure 4), schwannoma, meningioma, etc.;
- Multiple sclerosis and white mater plaque.

Idiopathic.

- There is no microvascular compression or other pathology.

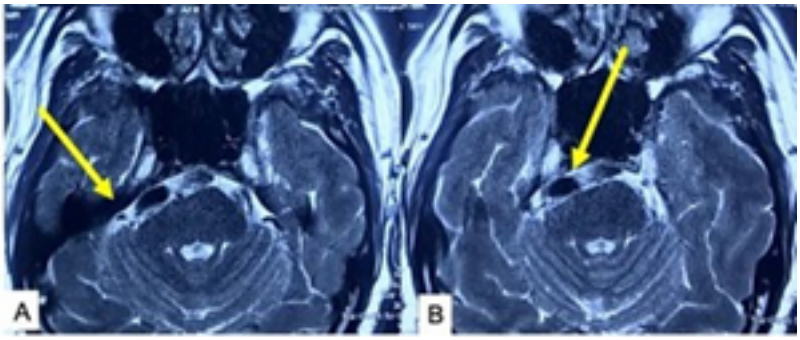

Figure 3. (**A**,**B**) MRI of brain T2W images: axial views showing REZ compression of right 5th nerve (arrow marked) by an ectatic vertebrobasilar artery (EVBA) causing trigeminal neuralgia. Source: Figure by authors.

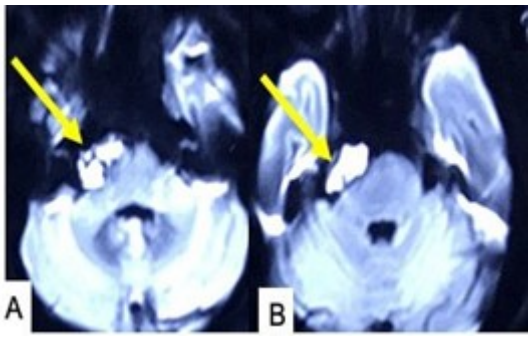

Figure 4. (**A**,**B**) MRI of brain axial DW images showing sided small epidermoid in right cerebellopontine angle (arrow marked) causing TN. Source: Figure by authors.

Intraoperatiive picture of MVD in hemifacial spasm (right side) is shown in Figure 5.

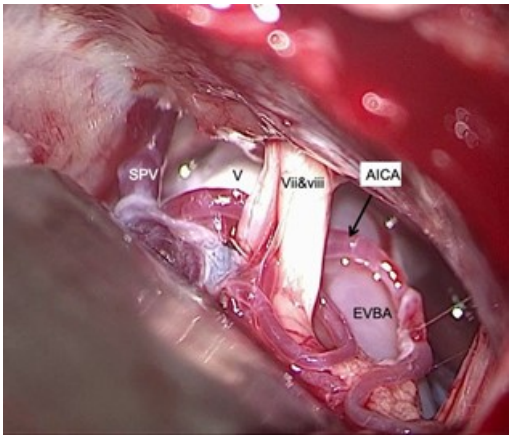

Figure 5. Peroperative picture after right-sided retrosigmoid retromastoid craniotomy showing compression of REZ of 7th (Vii) nerves by ectatic vertebrobasilar artery (EVBA) and anterior inferior cerebellar artery (AICA), causing hemifacial spasm. The patient also had REZ compression of 5th (V) nerves (not in picture) by superior cerebellar artery, causing TN as well. Viii—vestibulo-cochlear nerves. Source: Figure by authors.

4.6. Clinical Features

Short-lasting, paroxysmal, stabbing, shooting, or electric-shock-like pain is characteristic of trigeminal neuralgia. However, 14–50% of cases also have a simultaneous, continuous, dull-aching pain of low intensity (Maarbjerg et al. 2014). Mild autonomic features, such as nasal congestion, lacrimation, rhinorrhea, sweating, and miosis might be present.

The second and/or third trigeminal divisions are most commonly afflicted by TN, and the right side is more involved than the left. Bilateral illness is extremely uncommon and should raise concerns of subsequent TN (Maarbjerg et al. 2017). Innocuous sensory stimulation such as mild contact, chatting, chewing, tooth brushing, and washing the face can all trigger discomfort (Bendtsen et al. 2020).

4.7. Diagnosis

A clinical diagnosis of trigeminal neuralgia exists. Physical and neurological exams are generally normal. Any aberrant neurological results should trigger additional testing to rule out other causes. Three-dimensional (3D) T2-weighted, 3D time-of-flight, and MR angiography, in combination with 3D T1-weighted gadolinium, have proven to be dependable in finding vascular contact and estimating the severity of root compression [MRI of the brain in the TN protocol]. Diffusion tensor imaging and tractography give information about the brain structure that traditional imaging techniques cannot capture (Bendtsen et al. 2020).

Differential diagnosis includes glossopharyngeal neuralgia, painful post-traumatic trigeminal neuropathy, post-herpetic neuralgia, persistent idiopathic facial pain, a cluster headache, a cracked tooth, a primary stabbing headache, and caries or pulpitis.

4.8. Treatment

4.8.1. Medical Treatment

Sodium channel blockers (carbamazepine and oxcarbazepine) are first-choice drugs and were shown to be most effective according to one very-high-quality meta-analysis (McQuay et al. 1995). Zakrzewska and Linskey have demonstrated rates of 100% symptom relief in 70% of patients (Zakrzewska and Linskey 2014). Lamotrigine, baclofen, pregabalin, or gabapentin are used as add-on drugs with CBZ or oxcarbazepine, when the later drugs are ineffective or poorly tolerated.

4.8.2. Surgical Treatment

Microvascular decompression (MVD) is the most effective, albeit most invasive, surgical treatment. It is a nondestructive surgery with a low risk of sensory disturbances, as well as being a good choice for otherwise healthy persons. This procedure results in lasting pain relief in 70% of cases (Tronnier et al. 2001). Here, the offending vessel (usually the superior cerebellar artery) is freed from the REZ by arachnoid dissection and displacement and is kept away from the REZ by Teflon, surgical, cotton, fascia, or muscle. In the case of an ectatic artery, "slinging of artery" may be needed. Common complications are hearing loss, tinnitus, imbalance, facial weakness and facial sensory loss, diplopia (fourth nerve palsy), hemorrhage, infarction, meningitis, seizure, CSF fistula, etc. (Greenberg 2010). MVD cures up to 80% of cases, 10% of cases improve, and 10% fail (mostly due to failure to detect the offending vessel peroperatively, and so re-exploration is needed). Options for failed MVD or recurrent cases are reoperation (MVD), neurectomy, rhizotomy, high cervical spinal tract of trigeminal nerve tractotomy, DBS, thalamotomy, anterior cingulotomy, and motor cortex stimulation (Greenberg 2010; Henderson and Lad 2006).

Percutaneous rhizotomy is a minimally invasive surgical option that involves the selective lesioning of A-delta and C pain nerve fibers with intent to preserve A-alpha as well as beta sensory nerve fibers. Rhizotomy has three types:

(1) Percutaneous balloon compression rhizotomy;
(2) Percutaneous retrogasserian glycerol rhizotomy;
(3) Percutaneous radiofrequency rhizotomy.

The pathway to the trigeminal ganglion for all these techniques is through the foramen ovale. Percutaneous procedures offer variable degrees of pain relief for up to three years (Jones et al. 2019).

4.8.3. Gamma Knife Radiosurgery (GKRS)

It is utilized as a surgical option for patients who are not good surgical candidates or who refuse to undergo more intrusive treatment. This is a stereotactic, outpatient operation that uses high doses (70–80 Gy) of submillimeter radiation beams directed at the trigeminal root entrance zone to promote necrosis, which reduces pain signals over time. A systematic review found a 69% success rate after one year and a 52% success rate after three years (Jones et al. 2019).

5. Hemifacial Spasm (HFS)

5.1. Introduction

Hemifacial spasm (HFS) is a pathological condition of painless, involuntary, intermittent, spasming of facial muscles supplied by the seventh cranial nerve solely in one side. In typical HFS, it commonly starts from the orbicularis oculi and progresses to half of the face (due to compression on the anterio-inferior part of the REZ); the frequency of the spam increases with time, which may impair the vision of the involved side. In atypical forms of HFS, spasms start from the buccal muscle and spread upward over the face (due to compression on the upper or posterior part of the REZ) (Greenberg 2010; Wilkins and Rengachary 1985). Some patients may have hyper-lacrimation of the involved side. HFSs may be restricted to the upper or lower part of the face only.

5.2. Etiopathophysiology

5.2.1. Causes of HFS

1. Neurovascular compression syndrome at the root exit zone (REZ) is the most common cause of HFS (Figures 5–7).

Culprit vessels may include the following:

- AICA (most common; either pre- or post-meatal);
- An elongated PICA;
- SCA (a tortuous EVBA);
- The cochlear artery;
- A dolichoectatic basilar artery;
- AICA branches;
- Aneurysm or an arterio-venous malformation (AVM);
- Veins (rarely).

2. Idiopathic or unknown cause.
3. Posterior fossa tumor compressing the fascial nerve.

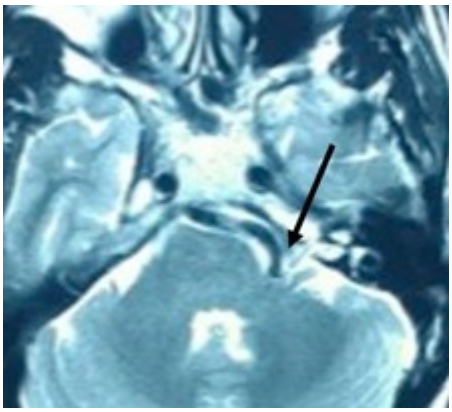

Figure 6. MRI of brain axial view T2W image showing REZ compression of left 7th nerve (arrow marked) by an EVBA, causing intractable HFS. Source: Figure by authors.

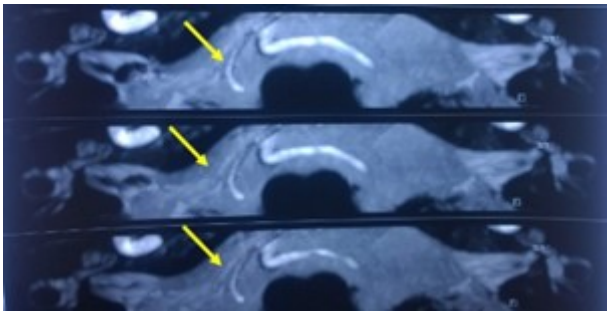

Figure 7. Focused MRA of brain showing compression of REZ of right 7th nerve (arrow marked), causing HFS. Source: Figure by authors.

Here, there is no short-circuit (ephaptic) conduction at the REZ; rather, the facial motor nucleus is engaged secondarily due to compression of the REZ via the kindling phenomenon. HFSs persist during sleep (like palatal myoclonus and unlike all other movement disorders that disappear during sleep). HFS is more common in women than men and the left side is more affected than the right. It may be associated with vestibulo-cochlear nerve dysfunction (hearing loss, vertigo, and tinnitus). Differential diagnoses include blepharospasm and facial myokymia (Greenberg 2010; Wilkins and Rengachary 1985; Yeh et al. 1981; Chowdhury et al. 2018).

5.3. Investigations

HFS is a clinical diagnosis like TN. Any unusual neurological finding(s) requires additional investigations to exclude secondary etiology. Three high-resolution sequences, three-dimensional (3D) T2-weighted, 3D time-of-flight, and MR angiography, as well as 3D T1-weighted gadolinium, may be used to detect vascular contact at the REZ [MRI of the brain in HFS protocol].

5.4. Treatment

5.4.1. Conservative

HFS is usually a neurosurgical condition. Carbamazepine and phenytoin generally do not work. Local injection of botulinum toxin may work temporarily (Greenberg 2010; Moller and Jannetta 1983).

5.4.2. Surgical Management

MVD is the procedure of choice. Techniques include that of TN. Here, the culprit vessel is put away by arachnoid dissection and by placing surgical Teflon, fascia, muscle, etc. (Greenberg 2010). Sometimes, slinging may be needed. Postoperatively, HFS starts to decrease 2–3 days after MVD. Severe spasms that do not improve suggest failure to accomplish satisfactory decompression, and re-exploration should be considered. Complete cure of HFS occurs in about 80% patients. A total of 10% partially improve and 10% provide no response (Moller and Jannetta 1983). Recurrence occurs in 10% of cases within 2 years (Greenberg 2010). Complications include tinnitus, hearing loss, facial weakness, ataxia, etc.

Some ablative techniques are useful for HFS where MVD has failed such as sectioning of divisions of the facial nerve with some paresis.

6. Glossopharyngeal Neuralgia (GN)

GN is often misdiagnosed due to its rarity. The incidence of GN is very low and 70 times lesser than TN (Youmans 1982).

6.1. Pathophysiology

Most GN cases seem to be a manifestation of the compression of a ninth cranial nerve at the REZ by the vessels, usually by PICA or VA. But, GNs can also be due to compression of the nerve by a mass lesion (Chowdhury et al. 2020).

6.2. Clinical Features

GN pain is a very severe, lancinating, pricking pain most frequently involved (in the distribution of the ninth and tenth nerves) in the throat and base of the tongue, which usually radiates to the ear. GN can be associated with occasional salivation, coughing, hypotension (Weinstein et al. 1986), syncope (Ferrante et al. 1995), and cardiac arrest. It may be precipitated by swallowing, chewing, and talking. Trigger zones are rarer.

6.3. Investigations

MRI of the brain is usually normal. MRI in cranial nerve protocol (GN) may show the culprit vessel at the REZ of the glossopharyngeal $\pm$ vagus nerve.

6.4. Treatment

6.4.1. Conservative

Pain may be reduced by cocaine application on tonsillar pillars and fossa. Anti-epileptic drugs (carbamazepine and phenytoin) are less responsive.

6.4.2. Microsurgery

Patients with drug intolerance, refractoriness, or both require microsurgery. Presently, MVD is a highly efficacious treatment and should be utilized as the first therapy in drug-resistant GPN with aberrant vessel compression. Surgical therapies for medically intractable GPN that involve the destruction of glossopharyngeal and vagus nerve fibers (neurectomy) are becoming less common. Transection of the preganglionic glossopharyngeal nerve (IX) and upper third of the vagus (X) nerve: IX is easily recognized as it is the dural exit zone in the jugular foramen, where it is separated from the vagus nerve by a dural septum. Early postoperative dysphagia commonly resolves. Cardiovascular events following vagal nerve section are alarming and warrant close monitoring for at least 24 h (Youmans 1982; Chowdhury et al. 2020; Weinstein et al. 1986; Ferrante et al. 1995).

7. Psychosurgery

7.1. Introduction

The management of mental diseases has improved, thanks to advances in medication, psychotherapy, and cognitive behavioral intervention. However, a significant number of individuals do not react to treatment, do not maintain their response, or have intolerable side effects. For more than a century, surgery for psychiatric disorders (NPD), also known as psychosurgery, has been used to address these treatment-resistant individuals. Indiscriminate patient selection, initially crude techniques, and a high incidence of complications made psychosurgery one of the most controversial topic in medical science (Neumaier et al. 2017). Over time, a better understanding of pathophysiology has led to more targeted approaches and eventually morbidity and mortality dropped significantly. Contemporary indications for neurosurgery are major depressive disorder (MDD), obsessive compulsive disorder (OCD), and Gilles de la Tourette syndrome (GTS), with level-two evidence of safety and efficacy. Neurosurgical intervention for anorexia nervosa, post-traumatic stress disorder, and addiction are still at the experimental stage (Neumaier et al. 2017).

7.2. Prerequisites for NPM

1. Diagnosis should be based on structured interviews.
2. Candidates for surgery should fulfil generally accepted clinical criteria for chronicity, severity, disability, and drug management refractoriness.
3. Patient with OCD should receive at least 20 sessions of cognitive behavior therapy prior to considering surgery.
4. Major depressive disorder should have been found to be nonresponsive to electroconvulsive therapy. Similarly, patients should be administered at least twelve sessions of evidence-based psychotherapy.
5. Informed consent must be obtained from the patient.
6. It is acceptable to take surrogate consent only when the patient is deficient of decision-making capacity. Hospital ethical committee approval for DBS in psychiatric disorders is needed.

7. Patient selection, preoperative evaluation, choice of procedure, and the surgical target should be decided by an expert multidisciplinary team composed of trained functional and stereotactic neurosurgeons working together in a team with neurologists, psychiatrists, and neuropsychologists (Neumaier et al. 2017; Doshi et al. 2019).

7.3. Surgical Procedures

Stereotactic thermal or gamma knife lesioning of various brain targets has been conducted since 1950. In the 21st century, deep brain stimulation has been replacing ablative techniques in developed countries.

Anterior cingulotomy represents radiofrequency or gamma knife lesioning of the anterior cingulate gyrus and the cingulate bundle. In the United States, Scotland, and South Korea, it is the most commonly reported psychosurgical procedure (Ferrante et al. 1995). Cingulotomy has the best results for intractable MADs and, to a lesser extent, OCD and GTS (Nuttin et al. 2014; Leiphart and Valone 2010).

Lesioning of the anterior limb of the internal capsule (Anterior Capsulotomy) is the more favorable ablative technique for OCD. It is the most frequent lesion surgery in Spain, Sweden, Brazil, Canada, China, and Mexico (Ferrante et al. 1995).

Limbic leucotomy represents a summation of bilateral cingulumotomy and subcaudate tractotomy. Use of this procedure is declining.

Bilateral Stereotactic RF ablation of nucleus accumbens has been conducted in China and some other countries for addiction and intractable anorexia nervosa (Li et al. 2013; Wang et al. 2013).

Deep brain stimulation has been popularizing for its inherent reversibility and adjustability. The anterior limb of the internal capsule, the ventral capsule/striatum, the subgenual cingulate, the inferior thalamic peduncle, and the nucleus accumbens are all targets for DBS. The thalamic nuclei anteromedial globus pallidus internus (amGPi) and centromedian–parafascicular (cmPf) complex are two of the most common DBS targets in GTS (Servello et al. 2008; Baldermann et al. 2016).

8. Intractable Pain Surgery

8.1. Introduction

Chronic pain is defined as pain that persists for longer than six months. It can be classified as nociceptive, neuropathic, or cancer-related. Peripheral pain receptors, as well as A-delta and C fibers, are activated in nociceptive pain. Pain signaling or the nervous system's processing of sensory input is distorted in neuropathic pain. Cancer pain is linked to the evolution of the disease, including tissue injury and nervous system impairment, which can cause both nociceptive and neuropathic symptoms. There are two forms of surgical pain treatments: ablative (or, more accurately, destructive) techniques and neuromodulation. Medical therapy must be trialed in maximum dose before consideration for pain surgery.

8.2. Options of Pain Surgeries

8.2.1. Pain Surgeries Particular to Trigeminal Neuralgia and Glossopharyngeal Neuralgia

These includes MVD, rhizotomy, spinal tractotomy of the trigeminal nerve, thalamotomy, cortical stimulation, DBS, and cingulotomy.

8.2.2. Pain Surgeries for Other Intractable Pains

1. Electrical neurostimulation
    (a) Deep brain stimulation: targets include the thalamus and periaqueductal or periventricular gray matter;
    (b) Spinal cord stimulation (Figure 8).

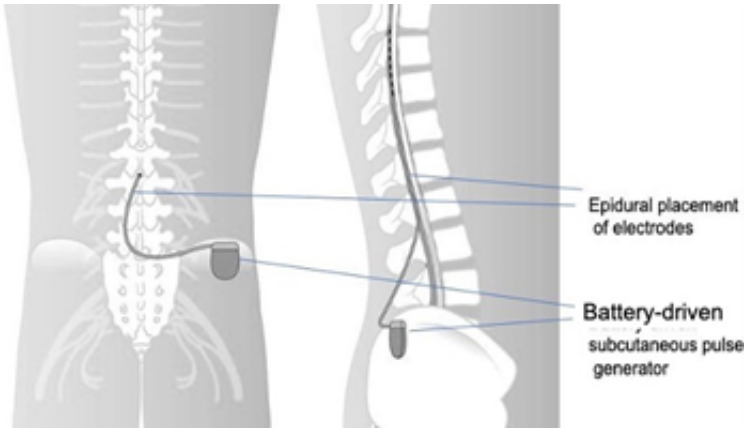

Figure 8. Illustration showing placement of spinal cord stimulator. Source: Figure by authors.

2. Direct administration of drugs into the CNS: epidural, intrathecal, or intraventricular administration of local anesthetics and narcotics.
3. Intracranial ablative/destructive surgeries:
    (a) Bilateral cingulotomy: diminishes the unpleasant effect of pain, sans eliminating the pain (pain persists without bothering the patient).
    (b) Stereotactic medial thalamotomy: controversial—may be useful for some nociceptive malignant pain.
    (c) Stereotactic mesencephalotomy: for one-sided head, face, neck, and/or UE pain. (Radiofrequency is utilized to produce lesion 5 mm lateral to the sylvian aqueduct at the level of the inferior colliculus.)
4. Spinal ablative surgical procedures
    (a) Cordotomy:
        (i) Open;
        (ii) Percutaneous.
    (b) Cordectomy.
    (c) Commissural myelotomy: for bilateral pain.
    (d) Punctate midline myelotomy: for relief of visceral malignant pain.
    (e) Dorsal root entry zone lesion.
    (f) Dorsal rhizotomy: not useful for large areas of involvement.
    (g) Dorsal root ganglionectomy (an extradural/extraspinal procedure).
    (h) Sacral cordotomy: for patients with pelvic pain who have had colostomy and ileostomy. A ligature is tied around the dural sac below the Sl nerve roots.
    (i) Sympathectomy: possibly for causalgia major and complex regional pain syndrome (CRPS).
5. Peripheral nerve procedures
    (a) Nerve block: injection of neurodestructive agents e.g., phenol or absolute.
    (b) Neurectomy: such as intercostal neurectomy in infiltration of the chest wall by malignancy.
    Types:
        (i) Open;
        (ii) Percutaneously with radiofrequency lesion.
    (c) Peripheral nerve stimulators: very rarely mentioned (Greenberg 2010; Burchiel and Raslan 2019; Young et al. 1985; Marshall 1996; Krieger and Rosomoff 1974).

Because about one-third of patients with advanced cancer suffer from medically refractory and intractable pain, and fear of pain outnumbers fear of death in many of these cases, surgical management of intractable pain should be a top priority. Procedures are available to help these individuals, and the existing data, at least in the case of cordotomy, suggest that neurosurgery should play a bigger role in their care (Burchiel and Raslan 2019).

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Epilepsy and Epilepsy Surgery

Jalal Uddin Mohammod Rumi and Forhad H. Chowdhury

Abstract: Epilepsy affects approximately 50 million people throughout the world, making it one of the most common neurological disorders. Around 60–70% of epilepsy patients react to treatment, whereas 30–40% become resistant to anti-epileptic drugs. Patients not responding to medical treatment are supposed to undergo evaluation for surgical intervention. Not all cases of drug-resistant epilepsy (DRE) are remediable by surgery. Worldwide, 10.1 million persons with active epilepsy could benefit from surgery every year. Methodical, careful, and skillful presurgical evaluation to select appropriate candidates for surgical intervention and choosing an appropriate procedure are the most critical parts of epilepsy surgery. A short synopsis of epilepsy, including definitions, diagnostic criteria, etiology, classification, and differentials of epilepsy, is given in first part of the chapter. Epilepsy surgery is discussed in the later part of the chapter and includes principles of presurgical evaluation, tools for presurgical evaluation, epileptic conditions remediable by epilepsy surgery, and common surgical procedures for epilepsy.

Abbreviations

AEDs	anti-epileptic drugs	AKA	also known as
AMTL	anteromedial temporal lobectomy	CNS	central nervous system
CT	computed tomography	DNET	dysembryoplastic neuroepithelial tumor
DRE	drug-resistant epilepsy	ECoG	electrocorticogram
ECS	electrical cortical stimulation	EEG	electroencephalogram
EZ	epileptogenic zone	FCD	focal cortical dysplasia
FDA	food and drug administration	FDG-PET	flurodeoxyglucose PET
fMRI	functional MRI	HME	hemimegaencephaly
ILAE	international league against epilepsy	IEEG	intracranial EEG
IVIG	intravenous immunoglobin	LGS	Lennex–Gastaut syndrome
LKS	Landau–Kleffner syndrome	MEG	magnetic encephalography
MTLE	mesial temporal lobe epilepsy	MRI	magnetic resonance imaging
MTS	mesial temporal sclerosis	PET	positron emission tomography
RNS	responsive neurostimulation	SAH	selective amygdalohippocampectomy
SEEG	scalp EEG	SPE CT	single photon emission CT
SRT	stereotactic radiofrequency thermocoagulation	TIA	transient ischemic attack
TLE	temporal lobe epilepsy	VEM	video EEG monitoring
VNS	vagus nerve stimulation		

1. Introduction

Epilepsy affects approximately 51.7 million people worldwide, making it one of the most common neurological disorders. Every year, 4.6 million people are diagnosed with epilepsy for the first time. Epilepsy is more common in LMICs (low- and middle-income countries), with 104 per 100,000 person-years in low-income countries and 78 per 100,000 in middle-income countries, compared to 51 per 100,000 person-years in HICs (High-income income countries). According to various studies, 60–70% of epilepsy patients react to treatment, whereas 30–40% become resistant to anti-epileptic medicines (AEDs) (Kalilani et al. 2018; Kwan and Brodie 2000). Patients not responding to medical treatment are supposed to undergo evaluation for surgical intervention. Not all cases of drug resistance epilepsy (DRE) are suitable for remediation by surgery. Worldwide, 10.1 million persons with active epilepsy could benefit from surgery, and 1.4 million new surgically treatable epilepsy patients are diagnosed each year, potentially increasing the number of surgical candidates (Vaughan et al. 2019). Methodical presurgical evaluation to select appropriate candidates for surgical intervention and choosing an appropriate procedure are the most critical parts of epilepsy surgery.

Definition of epilepsy (ILAE n.d.): Epilepsy is a brain disorder characterized by one or more of the following criteria:

- At least two spontaneous (or reflex) seizures that occur within 24 h.

- One spontaneous (or reflex) seizure, with a danger of subsequent seizures analogous to the overall recurrence risk (at least 60%), following two unprovoked seizures over the next 10 years.
- An epilepsy syndrome is diagnosed.

Individuals who have stayed seizure-free for the last 10 years with no anti-epileptic drug for the last 5 years are regarded as having resolved epilepsy if they had age-based, self-limited epilepsy syndrome but have now past the applicable age.

Definition of Seizure (ILAE n.d.): A seizure is a brief episode of symptoms and/or indications in the brain caused by abnormally high or synchronized neuronal activity. Unless the criteria for epilepsy diagnosis are met, a seizure event does not essentially suggest the presence of epilepsy.

The following are the different forms of epileptic seizures:

- Unknown-onset seizures;
- Focal (localized)-onset seizures;
- Generalized-onset seizures.

1.1. ILAE (International League against Epilepsy) Classification of Seizure Types, Expanded Version

ILAE Classification of Seizure Types is shown in Figure 1.

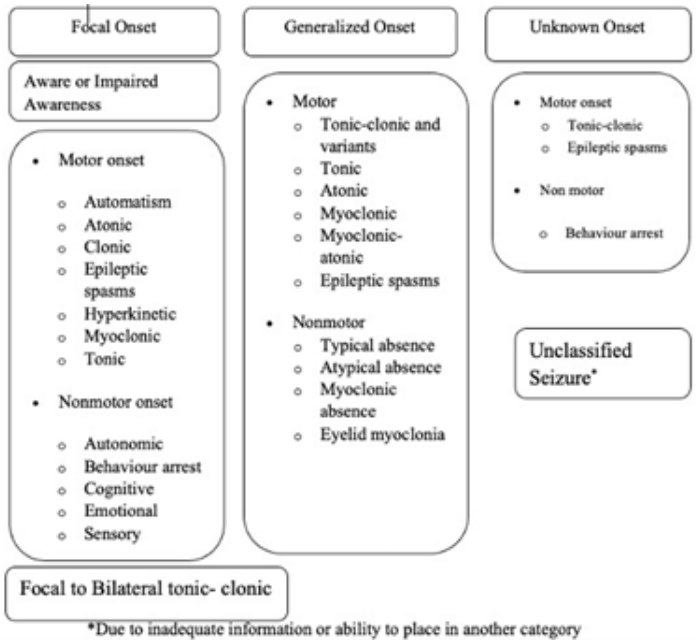

Figure 1. ILAE (International League against Epilepsy) Classification of Seizure Types, Expanded Version. Source: Authors' compilation based on data from Fisher et al. (2017).

1.1.1. Generalized Onset Seizure

A generalized seizure is thought to start somewhere within bilaterally dispersed networks and spread very quickly. Cortical and subcortical structures can be included in bilateral networks, but they do not always contain the entire cerebral cortex. Individual seizure onsets may appear isolated, yet their lateralization and location vary from one seizure to the next.

1.1.2. Focal Onset Seizure

Focal seizures are thought to originate in networks that are restricted to one hemisphere. They could be concentrated in one area or widely spread. Focal seizures could be caused by subcortical structures. Ictal initiation is uniform from one seizure to the next one for each seizure type, with ipsilateral and/or opposite hemispheres showing preferred propagation patterns. During a seizure, semiology (symptoms/signs) can be utilized to determine the specific brain region, lobe, or hemisphere that is engaged in seizure onset and propagation.

1.1.3. Unknown Onset Seizure

Unknown onset seizures are those that cannot be characterized as either generalized or focal in onset seizures. Seizures with uncertain initiation can be characterized as motor (tonic–clonic and epileptic spasm) and nonmotor (behavioral arrest, for example).

1.2. Classification of Epilepsy

Epilepsies are categorized as follows:

- Focal epilepsy;
- Generalized epilepsy;
- Combined generalized and focal epilepsy;
- Unknown epilepsy (ILAE n.d.).

1.2.1. Generalized Epilepsy

Generalized epilepsy patients have a generalized type of seizure, which might involve ictal and/or interictal EEG irregularities (such as generalized spike and wave). A family history of epilepsy or generalized seizures is beneficial.

1.2.2. Focal Epilepsy

Focal epilepsy patients have specific seizure types, which may include ictal and/or interictal EEG abnormalities (for example, focal sharp waves or focal interictal slowing). Patients with hereditary causes and normal imaging can have localized epilepsy; however, imaging that reveals a focal structural brain anomaly may be useful. Unifocal, multifocal, and hemispheric epilepsies are the three types of focal epilepsies.

1.2.3. Combined Generalized and Focal Epilepsy

Patients may have both focal and generalized seizures, as well as interictal and/or ictal EEG irregularities. Patients with Dravet syndrome and Lennox–Gastaut syndrome can experience both generalized and localized seizures.

1.2.4. Unknown Epilepsy

The term "unknown" is utilized when it is impossible to tell whether a patient has focal, generalized, or a combination of focal and generalized epilepsy. This can happen when there is not enough information to define epilepsy, such as when the EEG is normal/uninformative.

1.3. Epilepsy Syndrome

An epileptic syndrome is a collection of signs and symptoms that makes up a distinct epilepsy condition with varied causes (Daroff et al. 2015). A typical age at which seizures begin, distinct seizure types with EEG features, and other criteria, when combined, allow the detection of a specific epileptic conditions. The detection of an epilepsy syndrome is beneficial since it indicates which underlying causes should be explored as well as which antiseizure medication(s) may be most effective (ILAE n.d.). Some epilepsy syndromes are inherently intractable and long trials with medication before considering surgical evaluation seem unwise. Some other syndromes, i.e., Benign Childhood Epilepsy with Centrotemporal Spikes (BECTS), may have poor control of seizures with medication but will ultimately remit and do not need surgery. Surgically remediable epilepsy syndromes will be discussed later.

2. Etiology of Epilepsy

Advances in contemporary neuroimaging (Figure 2) and genetic testing have contributed to a major increase in explaining the underlying causes of epilepsies in recent years (ILAE n.d.). As a result, terms like "idiopathic," "cryptogenic," and "symptomatic" are no longer employed.

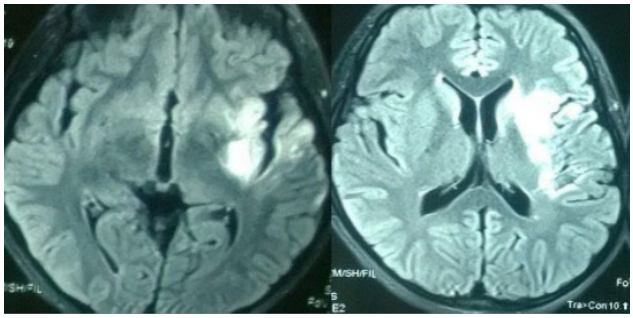

Figure 2. MRI of brain axial views showing insular cortical dysplasia (CD). Source: Figure by authors.

2.1. Etiology Genetic

4p–syndrome, Angelman syndrome, inversion duplication 15 syndrome, Miller–Dieker syndrome, ring chromosomes 14 and 20, terminal deletions of chromosome 1q and 1p, and ring chromosomes 14 and 20 are chromosomal abnormalities with a high association with seizures.

2.2. Structural Etiology

Common structural brain abnormalities associated with epilepsy, including cavernoma-causing, drug-resistant TLE:

- Developmental malformation of the cortex (Figure 2);
- Malformations of blood vessels (Figure 3);
- Sclerosis of hippocampus (Figures 4 and 5);
- Structural abnormalities from hypoxia +/ischemia (Figure 6);
- Head injury (Figure 7);
- Neoplasms (Figures 8 and 9) and porencephalic cysts;
- Cerebral gliosis (Figure 10).

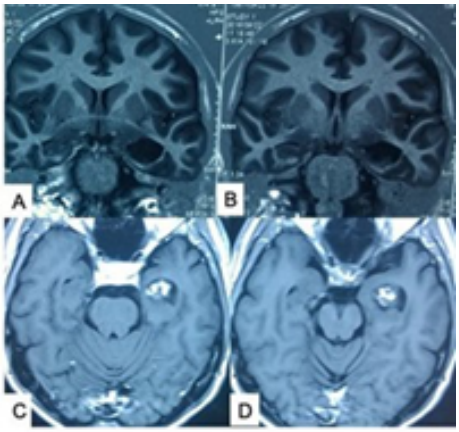

Figure 3. MRI of brain: (**A**,**B**) coronal views and (**C**,**D**) axial views showing hippocampal head. Source: Figure by authors.

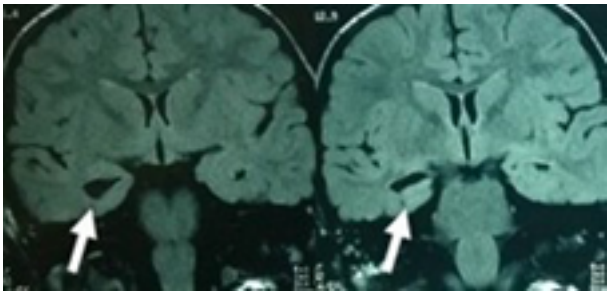

Figure 4. MRI of brain coronal views showing right-sided (arrow indicated) MTS (mesial temporal sclerosis). Source: Figure by authors.

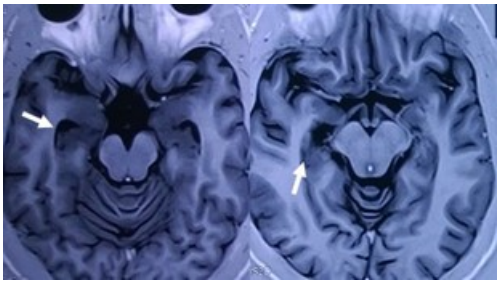

Figure 5. MRI of brain axial views showing right hippocampal head sclerosis (arrow indicated). Source: Figure by authors.

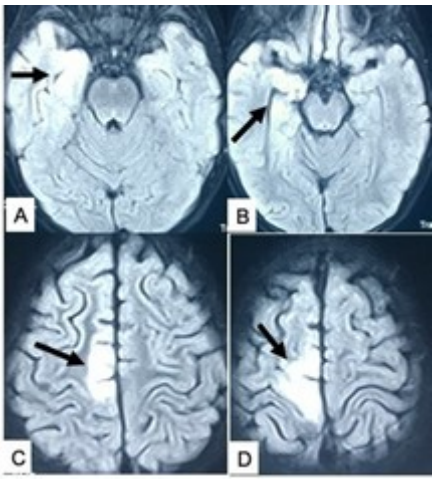

Figure 6. MRI of brain axial views in a 7-year-old girl with a history of birth asphyxia with intractable focal seizures: (**A**,**B**) showing right MTS (arrow indicated) and (**C**,**D**) showing right superior frontal focal CD (arrow indicated). Source: Figure by authors.

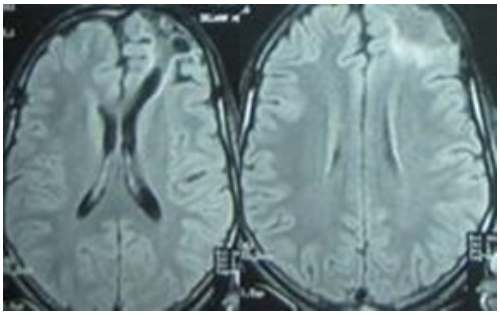

Figure 7. MRI of brain axial views showing post-traumatic left fronto-polar gliosis causing drug-resistant focal seizures. Source: Figure by authors.

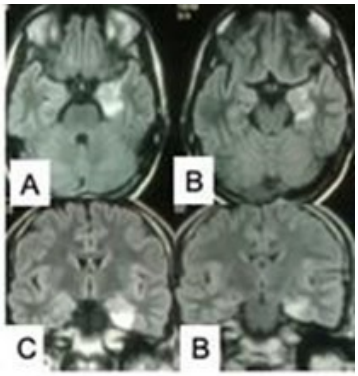

Figure 8. MRI of brain: (**A**,**B**) axial and (**C**,**D**) coronal views showing left amygdalo-hippocampal DNET causing TLE. Source: Figure by authors.

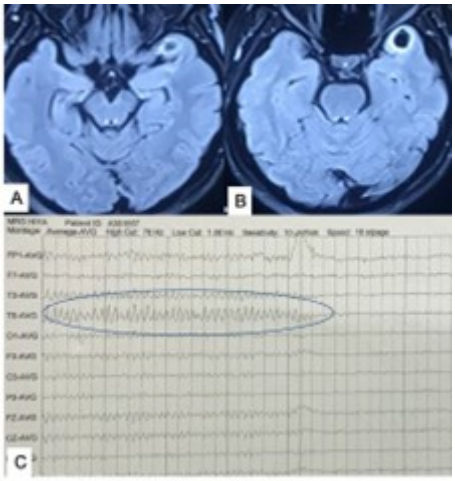

Figure 9. (**A**,**B**) MRI of brain axial views showing left temporal polar cystic lesion causing complex partial seizures. (**C**) Scalp EEG tracing showing left temporal focal discharges. Source: Figure by authors.

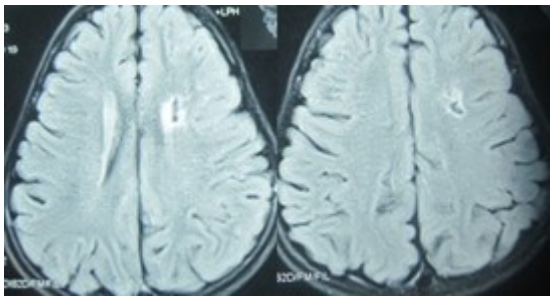

Figure 10. MRI of brain FLAIR axial views showing left frontal subcortical gliosis causing focal seizures. Source: Figure by authors.

2.3. Metabolic Etiology

- Creatine problems;
- Deficiency in cerebral folate;
- Deficiency in biotinidase and holocarboxylase synthase;
- Glucose transporter 1 (GLUT1) deficiency;
- Pyridoxine-dependent epilepsy/PNPO deficiency;
- Mitochondrial disorders;
- Folinic acid responsive seizures;
- Peroxisomal disorders.

2.4. Immune Etiology

- Antibody mediated etiologies;
- Rasmussen syndrome.

2.5. Infectious Etiology

Infectious disease is the most common etiology of epilepsy throughout the world, particularly in developing nations. Infections of the CNS may result in both acute symptomatic epilepsy and seizures (both are linked to the time of the initial infection). HIV, Tuberculosis, cerebral malaria, cerebral toxoplasmosis, subacute sclerosing panencephalitis, and neurocysticercosis are all infectious etiologies.

2.6. Unknown Etiology

The term "unknown" is meant to be taken in a neutral manner and used to indicate a type of the underlying etiology of epilepsy which is still unclear; it could be a basic genetic abnormality or a distinct, undiagnosed condition.

3. Epilepsy Imitators

There are a number of disorders linked to recurring paroxysmal occurrences that can mimic epilepsies and lead to misdiagnosis. Epilepsy misdiagnosis rates are high all throughout the world. Video recordings are quite important in determining a precise diagnosis. Epileptic and non-epileptic episodes can coexist under certain circumstances. Common epilepsy imitators are reflex anoxic seizures, syncopal attack, breath-holding attacks, psychogenic non-epileptic seizures, parasomnias, narcolepsy–cataplexy, stereotypies, paroxysmal kinesigenic dyskinesia, paroxysmal nonkinesigenic dyskinesia, hyperekplexia, migraine, shuddering attacks, and TIA (ILAE n.d.).

4. Drug-Resistant Epilepsy

Drug-resistant epilepsy, also called refractory epilepsy or intractable epilepsy, may be defined as "the failure of 02 tolerated and correctly designed and utilized AED regimens (whether as mono or combination therapy) to get persistent seizure independence" (Kwan et al. 2010). Seizure freedom lasting at least three times the longest seizure-free period previous to a new therapeutic intervention is defined as a treatment response in these criteria.

Factors associated with the risk of DRE include early-onset epilepsy, symptomatic generalized epilepsy, the presence of neuropsychiatric disorders, abnormal neuroimaging test results, abnormal EEG, focal EEG slowing, high initial seizure frequency, and a history of febrile seizures (Kalilani et al. 2018; Ko and Holmes 1999).

5. Epilepsy Surgery

5.1. Introduction

Despite much improvement in understanding the pathophysiology of epilepsy, improved imaging facilities, and the availability of newer-generation AEDs, the prevalence of DRE (0.30%) has been somewhat similar over decades. Surgical intervention could assist 10.1 million people with active epilepsy worldwide, and 1.4 million new epilepsy patients per annum could potentially be surgical candidates (Vaughan et al. 2019). Methodical presurgical evaluation to select appropriate candidates for surgical intervention and choosing appropriate procedures are the most important part of epilepsy surgery.

5.2. Principle of Presurgical Evaluation

Presurgical evaluation aims to detect and define the epileptogenic zone, its function, and spatial relation with eloquent brain, as well as to determine the best surgical procedure for that particular case. The following questions should be addressed:

1. Does the person truly have epilepsy? It is quite common that epilepsy imitators are misdiagnosed as epilepsy and treated with AED with ultimate failure and referral to a comprehensive epilepsy management program.
2. Is the epilepsy truly refractory? The selection of an appropriate AED and treatment with the maximum tolerable dose is needed before considering surgery.
3. What is the underlying etiology? Surgery has little effect in a patient with epilepsy secondary to an underlying progressive metabolic or degenerative condition.
4. Is remission still a possibility? Benign rolandic epilepsy patients may have difficult-to-control seizures but ultimately will recover.

5.2.1. Definition of Cortical Zones

The epileptogenic zone (EZ) is an area of the brain that is essential for epileptic seizures to begin. It may contain a "potential epileptogenic zone," which is a region of cerebral cortex that may induce seizures once the presurgical seizure onset zone has been removed, as well as an actual EZ, which is the cortical region producing seizures prior to surgery.

When stimulated by an epileptiform discharge, the symptomatogenic zone of the cortex generates ictal symptoms. It is defined by a thorough examination of seizure semiology, which includes either a detailed history or an examination of ictal video records.

Interictal electrographic spikes are generated in the irritative zone, which is characterized as a region of cortical parenchyma. Interictal spikes trigger EEG (invasive or scalp), functional MRI (fMRI), or

magnetoencephalography (MEG) to quantify the irritative zone. This irritative zone, which is frequently greater than the EZ, encompasses all regions where the epileptic focus could potentially be found.

In contrast to the EZ, which is required for the development of epileptic seizures, the seizure start zone is the region of the cerebral cortex from which clinical seizures are (actually) produced. Either calp EEG or invasive EEG techniques are often utilized to locate the seizure onset zone.

A radiographic lesion that causes epileptic episodes is called an epileptogenic lesion. High-resolution MRI is the best way to define this now. However, not all lesions detected in epileptic seizure patients are epileptogenic. It is possible that some radiographic abnormalities have nothing to do with the clinical seizures.

In the interictal stage, the functional deficit zone is mentioned as the area of cortex that is functionally unusual. This dysfunction could be a direct outcome of the lesion's destructive effect, or it could be functionally mediated, i.e., aberrant neuronal transmission affecting cerebral function either locally or far away from the epileptogenic tissue. The functional deficiency zone can be measured using a variety of techniques; some examples include a neurological exam, cognitive testing, EEG evaluation, [^{18}F]fluorodeoxyglucose-PET (FDG-PET) scan, and interictal SPECT.

The eloquent cerebral cortex is the part of the brain that has a specific critical clinical role. The eloquent cortex refers to primary sensory, primary motor, memory, or language skills in the context of epilepsy surgery (Rosenow and Luders 2001).

5.2.2. Modalities/Tools in Presurgical Evaluation

1. History and clinical examination;
2. Neurophysiological assessment;
3. Structural neuroimaging;
4. Functional neuroimaging;
5. Neuropsychological assessment;
6. Intracarotid amobarbital procedure (Wada test);
7. Electrical cortical stimulation.

History and Clinical Examination

Presurgical evaluation starts with detailed clinical history and general and neurological examination. History details include the age of onset of seizures and frequency. The sequence of incidents at the time of a seizure should be obtained from the patient and also from one or more witnesses and compared with videotaped seizures recorded at home and in an epilepsy monitoring unit. The past medical history should include birth history, history of febrile seizures, significant head trauma, and CNS infections. Medication trials and their adverse effects should be noted. Family history of febrile/afebrile seizures and other neurological illness should be taken. Most patient's neurological examinations reveal no findings. In children, the skin should be examined for signs of neurocutaneous disorders. Any focal weaknesses or asymmetric reflexes might have a lateralizing value.

The semiology of seizures is an important aspect of the epilepsy surgery examination. Clinicians can benefit from a thorough examination of seizure semiology. In three-quarters of patients, semiology locates and lateralizes seizures (Elwan et al. 2018).

The following are characteristics that indicate lateralization of the seizure. These characteristics support the idea of lateralization (ILAE n.d.):

- Ictal dystonia or unilateral ictal clonic activity indicate lateralization of the seizure to the opposite hemisphere. The initial forced-head version alludes lateralization to the cerebral hemisphere opposite the head version direction, i.e., if the head rotates to the right side, the seizure initiation is in the left hemisphere.
- Ictal speech does lateralize to the cerebral hemisphere—it is not dominant.
- The dominant hemisphere is affected by ictal aphasia.
- The dominant hemisphere is affected by postictal dysphasia.
- During ictal automatisms, awareness is preserved and lateralized to the non-dominant cerebral hemisphere.
- After ictal nose-wiping, the hemisphere ipsilateral to the nose-wiping hand lateralizes.
- Unilateral eye-blinking does lateralize to the hemisphere on the opposite side.
- The non-dominant hemisphere is affected by ictal vomiting.

However ictal semiology is also an area fraught with pitfalls. Seizures may arise from a "silent" or non-eloquent cortex and then spread to a functional area and express its manifestation. Thus, semiology would

indicate the site of seizure propagation instead of the site of seizure onset. Generally, the late features of seizure semiology reflect ictal spread and have less localizing value.

Neurophysiological Assessment

Electroencephalography (EEG): EEGs record the electrical activity of the brain in real time. An interictal scalp EEG (also known as a routine EEG) is used as the initial investigation for seizure disorders. It is a simple, noninvasive procedure where EEG electrodes are put on the scalp according to a standard, international 10/20 system. Recording is conducted for 30 to 60 min. Digital EEG recordings allow reformatting of EEG montages with judicious utilization of filters to improve reporting, hence it is adopted by most epilepsy centers. Routine EEGs very rarely record actual seizures, except generalized absence seizures. The main positive findings of routine EEGs are interictal epileptiform activity, which includes spikes and sharp waves and focal slowing. Both spikes (duration < 70 ms) and sharp waves (duration 70–200 ms) have pointed peaks of negative polarity, in most cases. Epileptiform discharges tend to have aftercoming slow waves. Sharp and spiked waves and focal slowing on the interictal EEG indicate the irritative zone and the functional deficit zone, respectively (Figure 11). Even without an epileptogenic lesion, subtle background asymmetries may be significant for localization and lateralization.

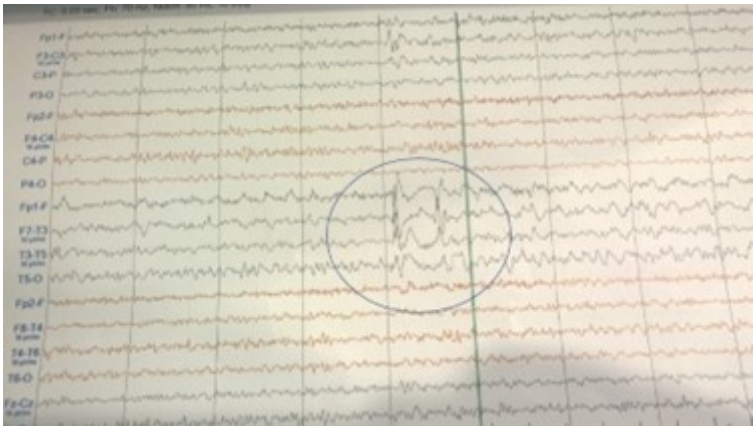

Figure 11. Interictal scalp EEG tracing showing focal electrical discharge from left frontotemporal regions. Source: Figure by authors.

However routine EEGs have important limitations. The electrical activity detected by a scalp EEG is attenuated by the impedance of intervening tissue. Epileptiform discharges are detected only if more than a 6 cm^2 area of cortical surfaces is involved in synchronized activity (Cooper et al. 1965). Interictal activity originating from the midline or deep area do not show up in scalp recordings. Therefore, the yield of the first routine EEG is normal in 50% of patients. With multiple recordings, epileptiform EEGs detected abnormality in more than 90% of epilepsy patients (Salinsky et al. 1987).

Prolonged video EEG monitoring (VEM) is considered a cornerstone of presurgical evaluation. Anti-epileptic drugs are tapered or withdrawn to capture 4–10 habitual seizures. The ictal onset zone is detected by electrographic discharge and clinical manifestations that reflect the symptomatic zone. Placement of additional electrodes increases the precision of localization of the ictal onset zone. Ictal EEG activity should be analyzed in the background of time-locked symptoms and signs. Most video recordings at home miss the initial events, which are more important. VEM provides better opportunities for analysis of seizure semiology. The interpretations are more accurate when ictal events are analyzed in conjunction with simultaneously recorded EEGs. VEM is a sensitive tool to exclude pseudoseizures.

The scalp EEG recorded at the start of the seizure can take at least five different forms (Fisher et al. 2014):

1. Rhythmically evolving frequencies in the theta, delta, or alpha bands;
2. Rhythmic spiking;
3. Spike–wave patterns;
4. Electrodecremental patterns;
5. No change in the scalp EEG.

Similar to routine EEGs, ictal recording of scalp EEGs comes with limitations in detecting deep foci and very focal small partial seizures, which explain the fifth pattern of ictal EEGs mentioned above. Furthermore, signals are obscured by muscle and movement artifacts in tonic–clonic seizures. In the presence of substantial

atrophy on the side of the epileptogenic focus, false lateralization of the ictal EEG might occur. The reliability of scalp ictal EEG recordings appears to be contingent on the presence of enough brain in the epileptogenic focus area to provide an amplitude signal that can be distinguished from the surface. Furthermore, the amplitude of the ictal EEG signal from the non-diseased hemisphere surpasses that of the atrophic side during bilateral ictal propagation, resulting in a falsely lateralized image (Chang et al. 2007). Invasive intracranial monitoring is frequently required when MRI and EEG data are inconsistent. Intracranial electroencephalography (IEEG) is an invasive procedure and is utilized only when noninvasive tools fail to define EZ adequately. ILAE-recommended general indications for IEEG are as follows (Jayakar et al. 2016):

1. To properly identify the EZ when noninvasive data are equivocal;
2. To reconcile noninvasive data divergence pointing to two or more areas;
3. To correctly map eloquent cerebral cortical functions;
4. Secondary indications: to confirm the EZ or offer prognostic information by targeted ablation of active areas with thermocoagulation.

There are subdural grid and strip electrodes and depth electrodes of multiple configurations for IEEG. Intracranial EEGs may be recorded intraoperatively or extraoperatively. Craniotomy and placement of subdural and depth electrodes and recording of electrical activity intraoperatively is known as electrocorticography (ECoG) (Figure 12). ECoG records interictal epileptiform discharge and background abnormalities, thus defining the irritative zone. In lesional epilepsy, ECoG-based stepwise resections of tumors and the peritumoral irritative zone improve outcomes significantly (Mikuni et al. 2006). ECoG is unlikely to capture ictal events. Thus, for more complex cases, after the placement of electrodes, IEEGs are recorded extraoperatively.

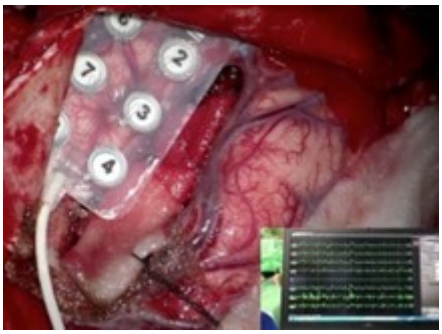

Figure 12. Peroperative electrocorticogram (ECoG). Source: Figure by authors.

Strips can be inserted through burr holes. Craniotomy is needed for grid placement. Depth electrodes could be placed through the burr, via craniotomy, or under neuronavigation guidance but are more commonly placed using the stereotactic method. Some centers practice only stereotactically placed, bilateral multiple electrodes for chronic invasive recording, known as an SEEG. Based on noninvasive evaluations, a hypothesis was to made of a presumptive EZ. Electrodes are placed to cover the EZ and irritative zone and adjacent EC. Cortical stimulation mapping could be conducted through IEEG electrodes after EEG recording is completed. AEDs should be restarted before ECS.

Magnetoencephalography is a promising noninvasive tool for defining the epileptogenic cortex and to delineate the eloquent cortex as well. The MEG signal is generated using the same neurophysiological process as the EEG signal (Barth 1993). Extracranial magnetic fields created by intracellular neuronal currents are detected using an MEG recording device made up of highly sensitive bio-magnetometers. MEG signals, unlike EEG signals, are unaffected by inhomogeneous tissue conductivity. Magnetic source imaging is the co-registration of MEG-determined source localization of epileptic spikes and evoked responses with MRI (MSI). As a result, in extratemporal localization epilepsy, presurgical assessment of MEG spike sources (MEGSS) and evoked responses on MSI is very reliable (Çataltepe and Jallo 2019). MEGSS in temporal lobe epilepsy is not precise enough to locate the source of interictal epileptiform discharges (Ebersole 1997).

Magnetoencephalography is also useful in the localization of the sensory motor cortex, primary auditory cortex, and language area. However, the establishment of an MEG recording system is very expensive and it has a very large running cost. Hence, despite encouraging results in clinical trials, its use in routine clinical set-ups is limited to a few centers. For a minority of patients with intractable localization-related epilepsy, improved clinical application of MEG has the potential to replace invasive subdural and depth electrode recordings.

Structural Neuroimaging

MRI is the mainstay investigation for epilepsy. The ILAE recommends MRI evaluation for all patients who have experienced their first seizure, except patients with genetic generalized epilepsy. Radiologically detected epileptogenic lesions help in syndromic classification and are a predictor of poor seizure freedom with medication and better outcomes following surgery. However, the presence of a lesion does not necessarily mean that it is responsible for seizures. Moreover, multiple lesions do not confirm that the epilepsy is multifocal. The concordance of a radiological lesion with seizure semiology and/or an EEG is to be established. Common pathological indications for DRE include hippocampal sclerosis, malformation of cortical development, epilepsy-associated tumors, Rasmussen encephalitis, hypothalamic hamartoma, arteriovenous malformation, and cavernoma.

The neuroimaging task force of the ILAE recommend the "Harmonized Neuroimaging of Epilepsy Structural Sequences (HARNESS-MRI) protocol" for the evaluation of seizures (Bernasconi et al. 2019). Key features of the HARNESS–MRI protocol are as follows:

1. High-resolution, 3D, T1-weighted MRI in gradient echo sequence with isotropic millimetric voxel resolution; slice thickness of 1.5 mm or less; and no interslice gap.
2. Acquisition of a high-resolution, 3D, fluid-attenuated inversion recovery (FLAIR) sequence in the turbo spin with isotropic millimetric voxel resolution and no interslice gap.
3. High in-plane resolution, 2D, coronal, T2-weighted MRI with sub-millimetric voxel resolution and no interslice gap obtained perpendicular to the long axis of the hippocampus.
4. Available in 1.5 T and 3 T scanners.

In children with FCD, MRI conducted at one year of age is more sensitive as subsequent myelination may hide the features of dysplasia on later scans. MRI should be repeated for patients with DRE if the available scan is not optimized or normal.

Computed tomography (CT) scanning has low sensitivity for identifying small cortical lesions and basal lesions and, therefore, is not a primary imaging modality in epilepsy. However, CT scans should be considered in new-onset seizure patients presenting in the emergency room to rule out intracerebral hemorrhage, subarachnoid hemorrhage, or brain abscess. Furthermore, CT scans may be followed to identify any area of focal calcification, when MRI shows tuberous sclerosis, Sturge–Weber syndrome, or an epilepsy-associated tumor.

Functional Neuroimaging

Blood flow and metabolism in the epileptic zone and eloquent cortex are different from adjacent brain tissue. The epileptic region shows hypometabolism and hypoperfusion in the interictal period and the reverse in the ictal period. During a particular task, blood flow and oxygenation levels increase in the corresponding functional cortex. Functional neuroimaging was developed based on these physiological phenomena (So and Ryvlin 2018).

Functional MRI (fMRI) is a noninvasive and widely available tool for presurgical evaluation of cognitive function and the motor cortex. Functional mapping in fMRI is performed by calculating the blood-oxygen-level-dependent (BOLD) signal change in T2-weighted images while patients engage in functional tasks. fMRI is comparable with IAT for determining hemispheric dominance for language and speech. But, fMRI detects both essential and nonessential language regions. fMRI-based motor cortex mapping is performed when the presumed EZ is adjacent to the motor cortex.

During seizures, blood flow in the epileptic zone (EZ) increases up to three times. For ictal SPECT, patients remain admitted in the video EEG monitoring unit. At the onset of a seizure, ethylene cysteine dimer (ECD) or hexamethyl propylene amine oxime (HMPAO) labeled with 99 mTc is injected. HMPAO/ECD crosses the BBB and is trapped within the neuron in proportion to regional cerebral perfusion during a seizure. Trapped radiotracers emit gamma rays, which are then detected by a rotating camera. The exact timing of the radiotracer is crucial and ictal SPECT is less feasible in very-short-lasting seizures such as myoclonic epilepsy. In SPECT, the EZ displays hyperperfusion. Interictal SPECT depicts normal perfusion or hypoperfusion in the epileptic region and is compared with the ictal image. Interictal SPECT is subtracted from ictal SPECT and the resulting image is co-registered to an MRI (SISCOM). SISCOM improves ictal SPECT's specificity and sensitivity.

In positron emission tomography (PET), various biological substrates leveled with a radioisotope such as ^{18}F, ^{11}C, or ^{15}O are injected intravenously. ^{18}Flurodeoxyglucose (FDG) is the most commonly used radiotracer. FDG is taken up by brain tissue and phosphorylated to FDG-6-phosphate and becomes trapped within the cell. FDG-6-phosphate trapped in the body emits gamma rays, which are identified by a PET camera and used to

rebuild quantified tomographic pictures, which are then combined with CT images. As metabolism is low in the epileptic region in the interictal period, FDG PET shows reduced radiotracer uptake in the EZ. The area of hypometabolism detected by PET extends far beyond the EZ; thus, it is less precise for defining EZ. However, PET reliably lateralizes the EZ and, thus, a hypothesis could be made of a presumed EZ for subsequent placement of IEEG electrodes. The FDG-PET findings may guide reviews of MRI images retrospectively and reveal the pathology. Moreover, concordant findings on PET increase confidence in subtle MRI findings (So and Ryvlin 2018).

Neuropsychological Testing

It is standard practice that all epilepsy surgery candidates should receive a presurgical outpatient neuropsychological evaluation. It provides a baseline neurocognitive profile for comparison after surgery. The domains of neuropsychological testing include verbal memory and nonverbal memory, expressive and receptive language skills, verbal fluency, semantic fluency, visuospatial function, general cognitive ability, and higher executive functions. The location of the epileptic focus, the age at which the seizures began, the epilepsy syndrome, and the brain's plasticity all influence the pattern of cognitive deficits. For example, a person with dominant temporal lobe epilepsy would have remarkable language and verbal memory problems.

An identical type of seizure arising on the right (non-language-dominant) side, on the other hand, would usually result in visual memory problems (Bell and Davies 1998). Thus, neuropsychological test findings have lateralizing and localizing value, especially useful in MRI-negative epilepsy to further confirm—or argue against—the assumed epileptogenic zone. Patients with a similar cognitive profile have a better seizure result, while those with a lower baseline intellectual profile have worse postoperative seizure control. Memory and language tests help determine the ipsilateral lobe's functional capacity and the contralateral lobe's functional reserve.

Memory deficit is a common complication of anteromedial temporal lobectomy. Patients with better preoperative memory and language function (i.e., suggesting better functional integrity of the parenchyma to be removed) have a higher risk of postsurgical memory and language deterioration than those with lower scores in this category.

Intracarotid Amobarbital Injection Procedure (IAP, Wada Test)

Dr. John Atsushi Wada developed the procedure in 1949 and it has since been further modified by others. It is the gold standard for determining language and speech hemisphere dominance. The Wada test's more delicate function is to assess memory function in each hemisphere as well as the functional adequacy of the contralateral hippocampus in supporting memory following ipsilateral mesial temporal lobe resection. Additionally, the Wada test aids to predict seizure freedom following surgery.

Anterior circulation feeds the anterior two-thirds of the cerebrum. Short-acting barbiturate introduced into the ICA (internal carotid artery), thus, will induce temporary disruption in the function of the anterior two-thirds the of cerebrum, including the temporal lobe. Prior to the procedure, an angiogram is performed to assess anatomical variation and the extent of cross flow. Then 100–150 mg of sodium amobarbital is injected into one ICA at a time and cognitive ability and language function for each hemisphere are assessed in isolation.

However, the Wada test is an invasive procedure and has potential minor and major complications (Loddenkemper et al. 2008). More importantly, this technique is not standardized and there are reports of false positive and false negative results. At present, in most centers, the Wada test is replaced by noninvasive fMRI (Binder 2011).

Electrical Cortical Stimulation (ECS)

The encroachment of the epileptic zone on the eloquent cortex necessitate precise mapping using cortical stimulation to ensure adequate removal of potential epileptogenic tissue without creating new functional deficits. Extraoperative ECS is performed at the end of IEEG by stimulating subdural and depth electrodes. Intraoperative ECS is performed after ECoG. During stimulation, clinical responses and electrocorticographic changes are monitored. Cortical stimulation at primary and supplementary motor areas produce tonic or clonic movements. Sensory responses are elicited at sensory cortex stimulation. Stimulation of motor or sensory speech areas causes

speech arrest (Çataltepe and Jallo 2019). With the availability and increasing accuracy of noninvasive tools such as fMRI, ECS is reserved for MRI-negative epilepsy and complex cases of malformation near eloquent cortex.

5.2.3. Epilepsy Remediable by Epilepsy Surgery

Malformations of Cortical Development

Cortical malformations occur when neuronal proliferation, migration, or cortical structures are disrupted during the development of the cortex (Jamuar and Walsh 2015; Barkovich et al. 2012). The disruption of any of these processes can raise the risk of seizures and neurodevelopmental delays in children (Jamuar and Walsh 2015). Malformations may be focal or multifocal such as focal cortical dysplasia, polymicrogyria, schizencephaly, and hypothalamic hamartomas, which require focal, lobar, or multilobar resection. Malformation may involve most or all of one hemisphere (e.g., hemimegalencephaly), making these patients ideal candidates for some form of hemispherectomy. Less commonly, malformation may be widespread and bilateral, e.g., lissencephaly and subcortical band heterotopia, and not amenable to surgery.

Hemimegalencephaly (HME)

This is a spontaneous congenital brain deformity that is extremely rare. It can be found on its own or in conjunction with a neurocutaneous syndrome. The abnormal growth of a significant piece of one hemisphere, a whole hemisphere, or a hemisphere and part of the opposite side characterizes HME. There may be ipsilateral cerebellar and brainstem hypertrophy, as well as cranial expansion.

Mental retardation, contralateral hemiparesis, intractable epilepsy, macrocephaly, and hemi-anopsia are common clinical characteristics. Motor function and linguistic impairment are typically worse in persons with localized cortical dysplasia. Partial-onset seizures, epilepsia partialis continua, infantile spasms, and drop attacks are all examples of seizures (Terra-Bustamante et al. 2006).

An enlarged cerebrum (proportion or entirety) with a broad gyrus, thicker cortex, neuronal heterotopia, aberrant gray–white matter differentiation, ventricular asymmetry, and internal capsule and basal ganglia abnormalities are all seen on post-natal MRI. The damaged hemisphere may shrink as the disease progresses, and it may not be greater than the contralateral, unaffected hemisphere during imaging. Cortical tubers may or may not exist in the non-HME hemisphere (Terra-Bustamante et al. 2006).

Slow, rhythmic, or rapid activity, as well as multifocal bilateral or unilateral high-amplitude spikes and spike–wave complexes, are all examples of interictal EEG abnormalities. Generalized or independent bilateral discharges are possible. Ictal abnormalities might be made up of a build-up of unilateral or widespread fast rhythmic activity or bilateral independent activity (Terra-Bustamante et al. 2006).

Histopathologic changes include abnormal gyrification, dyslamination, neuronal heterotopia, marked gliosis, and balloon cells (Terra-Bustamante et al. 2006).

For intractable epilepsy, hemispherotomy or functional hemispherectomy is the technique of choice. Following hemispherectomy, patients with HME had a dramatically improved seizure load and quality of life, although less than patients with Rasmussen's encephalitis or congenital vascular anomalies (Ikeda and Mirsattari 2017).

Focal Cortical Dysplasia

Localized patches of cortical lamination disruption characterize focal cortical dysplasias (FCDs), which are frequently linked to epilepsy in both adults and children (Figure 2). In children receiving epilepsy surgery, FCD is the most frequent pathogenic condition (Wyllie et al. 1998). The ILAE Task Force recommends a three-tiered clinicopathological classification system for FCD. Isolated lesions of the neocortex that show as radial (FCD Type Ia) or tangential (FCD Type Ib) dyslamination, microscopically diagnosed in one or more lobes, are referred to as FCD Type I. Cortical dyslamination as well as dysmorphic neurons without (Type IIa) or with balloon cells describe FCD Type II (Type IIb). Cortical dysplasia develops in FCD Type III in conjunction with hippocampal sclerosis (FCD Type IIIa) or epilepsy-related malignancies (FCD Type IIIb) (Blümcke et al. 2011).

MRI characteristics of FCD include cortical thickening, blurring of the gray matter–white matter junction, an enhanced signal on T2-weighted imaging, a radially oriented linear or conical T2 hyperintensity stripe, cortical thinning, and regional brain atrophy. Unfortunately, none of these indicators are dependable or constant (Blümcke et al. 2011).

On MRI, FCD can sometimes go undetected, especially in type I. Furthermore, possible epileptogenic zones are often bigger than lesions shown by MRI, necessitating the use of additional technologies for precise surgical resection planning (Kabat and Król 2012). Extratemporal FCDs are more prevalent, and they have a tendency to encroach on the eloquent cortex. IEEG improves the accuracy of both ictal and interictal data, making it easier to distinguish the EZ. Electrical stimulation using the implanted electrodes can also be used to perform functional mapping.

A discrete epileptogenic focus is removed via focused resection. When the ictal area is big, lobectomy or multilobar resections are considered. When a lesion encroaches into the functional cortex, partial resection combined with multiple subpial resection for the rest of the EZ is the safest surgical strategy.

Rasmussen's Encephalitis

Rasmussen's encephalitis is an uncommon neurological illness marked by inflammation of one cerebral hemisphere, persistent epilepsy, progressive hemiparesis and hemianopia, and cognitive decline. Rasmussen's encephalitis is most likely caused by a T-cell response to one or more antigenic epitopes, with autoantibodies playing a role as well. The inflammatory process in the brain is seen with MRI as T2/FLAIR hyperintensity in the cortical or subcortical region with ipsilateral caudate atrophy. The evolution of signal alteration and atrophy is usually visible on serial MRIs (Chiapparini et al. 2003; Yamazaki et al. 2011). In Rasmussen's encephalitis, seizures are localized and around half of the patients develop epilepsia partialis continuous. Electroencephalography shows continuous high-amplitude delta activity over the injured hemisphere within months of the seizure starting, but epilepsy partialis continua is not always associated with visually evident ictal surface EEG activity (So and Gloor 1991). Interictal aberrations in the non-affected hemisphere can indicate cognitive decline, but they do not appear to be suggestive of bilateral disease (Longaretti et al. 2012).

Choosing the correct time to transition from medical care to surgery is a significant therapeutic challenge for many patients, families, and clinicians, especially when the neurological damage is partial. The sole solution for seizures is anatomical or functional hemispherectomy, which comes at the cost of some functional constraints. Immunomodulatory therapy appears to reduce rather than stop the progression of Rasmussen's encephalitis, with no effect on the final result.

Corticosteroid and intravenous immunoglobulin are used as immunomodulators in Rasmussen's encephalitis, while AED is used to lessen seizure intensity and frequency. However, interventions have thus far merely addressed the symptoms rather than the underlying causes. Total disconnection of the afflicted hemisphere (hemidisconnection), either via hemispherotomy or functional hemispherectomy (Figures 13 and 14), is the only treatment for the convulsions due to Rasmussen's encephalitis (Varadkar et al. 2014).

Temporal Lobe Epilepsy

The commonest epilepsy surgically treated is temporal lobe epilepsy (TLE), which impacts the majority of patients with localization-related epilepsy observed in tertiary epilepsy centers (Téllez-Zenteno and Hernández-Ronquillo 2012).

Based on the anatomical area of seizure onset, TLE can be categorized into two categories. Lateral or neocortical epilepsy occurs when the epileptogenic zone is lateral to the collateral sulcus, while mesial temporal TLE occurs when the epileptogenic zone is medial to the collateral sulcus (MTLE).

The limbic regions that make up the temporal lobe's mesial part are strongly epileptogenic. The fornix connects the anteromesial frontal lobe to the anterior nucleus of the thalamus, and the uncinate fasciculus connects the mesial temporal lobe to the orbitomesial frontal lobe (Duvernoy et al. 2013). The mesial temporal structures are closely linked to the anterolateral neocortical temporal lobe. The two TLE groups frequently share seizure semiology due to the substantial linkages between the mesial temporal structures and the anterior and lateral temporal lobes, as well as other limbic regions (O'Brien et al. 1996; Burgerman et al. 1995).

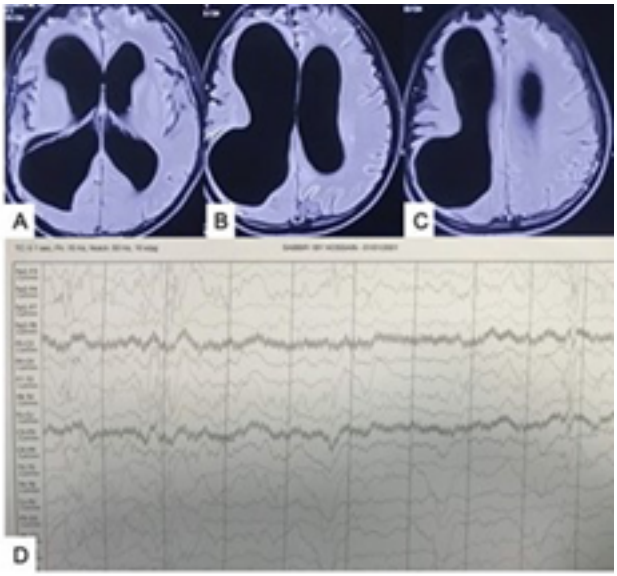

Figure 13. (**A**–**C**) MRI of brain axial views showing right hemispheric atrophy (with intractable left-sided focal convulsion to generalization). (**D**) Scalp EEG tracing showing multifocal electrical discharges mainly from right-sided leads. (But, left-sided lead spikes and sharps are more pronounced due to more parenchymal tissue-paradoxical affects.) Source: Figure by authors.

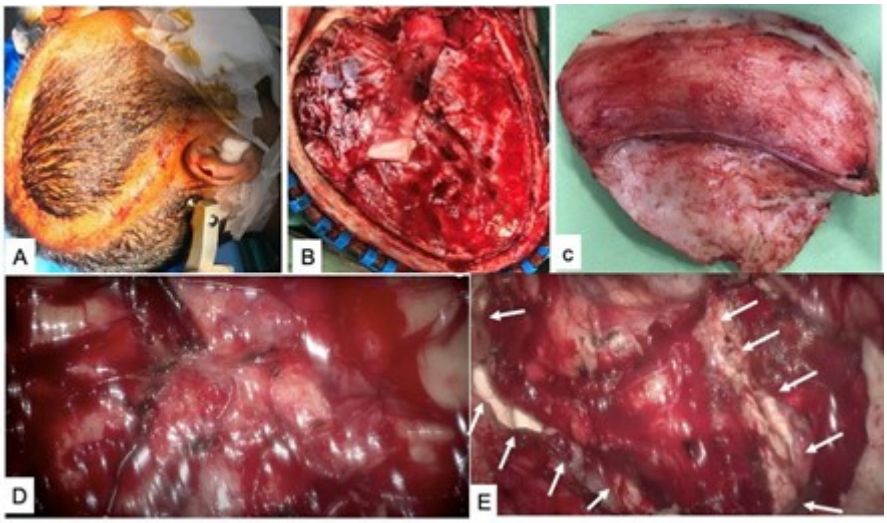

Figure 14. Peroperative pictures of right-sided functional hemispherotomy: (**A**) incision mark, (**B**) after craniotomy, (**C**) craniotomy bone flap, (**D**) right hemisphere before hemispherotomy, and (**E**) right hemisphere after hemispherotomy (arrows marked). Source: Figure by authors.

Behavioral arrest and reduced awareness are common symptoms of temporal lobe seizures. Automatisms, such as oral and/or manual automatisms, are common during seizures. There may be sensory (auditory), cognitive (déjà vu), emotional (terror), or autonomic (tachycardia, epigastric sensation, and color change) characteristics before the onset of diminished consciousness. Postictal confusion is very common.

Ictal speaking, spitting, the urge to urinate, vomiting, drinking, and automatisms with maintained consciousness reflect non-dominant temporal lobe seizure onset. A dominant temporal lobe seizure is indicated by postictal speech difficulties. Upper limb dystonia is a good lateralizing trait since it shifts the seizure to the other hemisphere. On the other hand, manual automatisms frequently occur on the ipsilateral side.

The most prevalent substrate for MTLE is mesial temporal sclerosis, which manifests in MRI as hippocampal atrophy and sclerosis, as well as elevated T2 and FLAIR signal intensity (Berkovic et al. 1991). FCD, cavernoma, epilepsy-associated tumors, and post-traumatic gliosis are some of the other indications for mesial or neocortical TLE.

Despite significant semiological overlap between the two types of TLE, noninvasive testing can usually pinpoint the seizure focus. In a limited number of people, intracranial electrode monitoring may be needed to

analyze the lateralization of seizure onset to a temporal lobe (So et al. 1989) or to verify temporal lobar localization in one hemisphere (Olivier et al. 2012).

The standard temporal resection accomplished at most epilepsy facilities is anteromedial temporal lobectomy (AMTL). It mainly entails removing temporal mesial tissues after anterior temporal neocortical resection.

Selective amygdalohippocampectomy (SAH) for MTLE has sparked a lot of attention since Yasargil et al. published their findings (Yasargil et al. 1985). SAH may have the advantage of selectively removing the seizure focus, preserving temporal lobe areas that are not actually epileptogenic.

The outcome on seizure independence is the same as for anteromedial temporal lobectomy at centers with experience in SAH (AMTL) (Little et al. 2009). SAH appears to have better cognitive outcomes than typical temporal resections (Kessels et al. 2004; Gleissner et al. 2004).

Epilepsy Associated Tumors

A neoplasm is the second most prevalent etiology of focal epilepsy (Englot and Chang 2014) among individuals considered for epilepsy surgery, and it is found in roughly 30% of cases intervened in for focal epilepsy (Tassi et al. 2009).

The risk of focal seizures differs based on the tumor's location and histological type. Low-grade neoplasms are, thus, frequently more epileptogenic compared to high-grade tumors (van Breemen et al. 2007).

The biologic activity of epileptogenic tumors is normally benign, yet certain tumors may recur or develop into cancer (Luyken et al. 2003). Gangliogliomas (Figure 15), dysembryoplastic neuroepithelial tumors (DNET), pleomorphic xanthoastrocytoma, diffuse astrocytoma, papillary glioneuronal tumor, oligodendroglioma, pilocytic astrocytoma, and angiocentric gliomas are all examples of epileptogenic tumors.

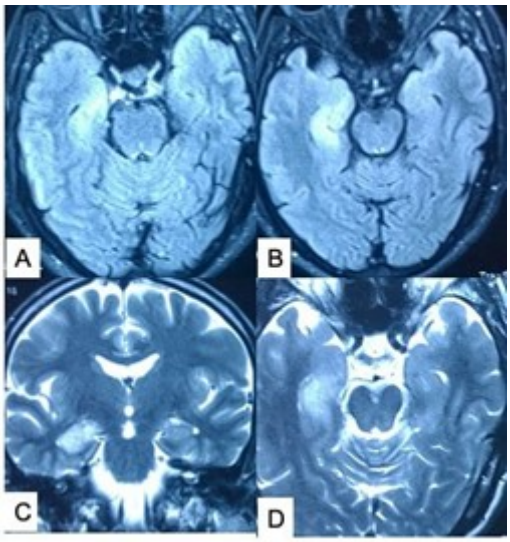

Figure 15. MRI of brain: (**A**,**B**) axial sections and (**C**,**D**) coronal sections showing right-sided medial temporal (hippocampal) ganglioglioma. Source: Figure by authors.

The most common and often only sign of malignant tumors that develops in young adulthood and adolescence is focal seizure.

As a result of the presence of a mixture of solid, calcified, and cystic elements, the MR signal of ganglioglioma is inhomogeneous and variable, with no contrast enhancement; an axial CT scan reveals the calcified element.

DNETs are multinodular, wedge-shaped, "bubbly" intracortical tumors that are usually mistaken for other LGGs. DNETs are more likely than GGs to have a multi-cystic shape and to stay the same size throughout time.

In around 30% of cases, contrast enhancement was discovered. The tumor presents on CT scana as a hypoattenuating cortical–subcortical mass with occasional calcifications. The surrounding inner table of the cranium may also have scalloping. On MRI, DNETs are most commonly seen as multinodular, pseudocystic cerebral cortical lesions that are hypointense on T1W images but hyperintense on T2W images, with or without circumferential vasogenic edema.

Anti-epileptic medicines are frequently ineffective in controlling epilepsy-related tumors, although surgery can provide great benefits (Clusmann et al. 2004). Lesionectomy, extended lesionectomy, and customized resection

are among the surgical strategies used. When a tumor is found in the mesial or neocortical temporal lobe, some authors recommend anterior temporal lobectomy.

When the tumor is extratemporal or in the temporal neocortex, most of the authors concur that lesionectomy alone delivers the best seizure reduction result (Cataltepe et al. 2005). However, the effects of temporomesial lesionectomy are debatable (Cataltepe et al. 2005). The involvement of temporomesial areas, according to some writers, may extend and complicate the epileptogenic zone.

Hypothalamic Hamartoma

A hypothalamic hamartoma (HH) is an uncommon, developing, disordered tissue mass that arises from the tuber cinereum and the bottom of the third ventricle and is found in the hypothalamus. Precocious puberty is associated with infraventricular HHs linked to the tuber cinereum. Intraventricular HHs are connected to the third ventricle's floor and cause seizures. Gelastic seizures (GSs) are the commonest type of seizure in pediatric patients; however, patients can also have dacrystic seizures, complicated partial seizures, or other types of seizures. Epilepsy linked to HH is pharmacoresistant and results in severe epileptic encephalopathy and infantile catastrophic epilepsy (Harvey and Freeman 2007).

Scalp electroencephalograms do not exhibit epileptiform discharge in gelastic seizures caused by HH, whereas depth electrodes implanted into the hamartoma clearly indicate epileptiform activity.

The suprasellar cistern and anterior third ventricle are obliterated on non-enhanced CT scans, and the nodule is iso- or hypodense compared to the grey matter. On high-dose, contrast-enhanced CT, HHs do not enhance. On T1WI, signal intensity is frequently isointense to normal gray matter, and on T2/FLAIR, signal intensity is usually isointense to slightly hyperintense. Following contrast injection, HHs do not improve (Saleem et al. 2007).

Surgery appears to be the best technique for acquiring seizure independence and preventing the steady loss of neurocognitive function in HHS patients who were resistant to AED. Surgical options include the transcallosal interhemispheric approach, endoscopic removal, stereotactic radiosurgery (Rosenfeld et al. 2004), and stereotactic radiofrequency thermocoagulation (SRT) (Wang et al. 2009).

The Lennox–Gastaut Syndrome

Lennox–Gastaut syndrome (LGS) is one of the most severe epileptic syndromes. It generally develops between the ages of 3 and 5, but it can also occur later in life, even into adulthood (Camfield 2011; Arzimanoglou et al. 2009). LGS is a clinical diagnosis marked by polymorphous epileptic seizures, primarily axial tonic, atypical absences, and atonic seizures; permanent psychological disturbances; and an electroencephalogram (EEG) that frequently shows either paroxysmal fast activity or slow spike–waves brought on by sleep when superimposed on a slow background (Camfield 2011; Arzimanoglou et al. 2009).

LGS is still difficult to treat and seizures are extremely pharmacoresistant. Patients with LGS who have not responded to pharmacological treatment may be candidates for surgery.

Neuroimaging studies in patients with LGS may have two patterns of findings. MRI may reveal a well-circumscribed lesion, the removal of which will lead to seizure freedom. More usual is that MRI reveals no epileptogenic lesion or lesions that are extensive, bilateral, diffuse, or not well defined and, thus, not removable. In the second situation, it is possible to perform a palliative operation such as corpus callosotomy or vagus nerve stimulation.

The Landau–Kleffner Syndrome

This is an epileptic encephalopathy with the EEG characteristic of continuous spikes and waves during slow sleep (CSWS). During a vital phase of language development, an epileptogenic lesion in the speech area (or that influences the speech cortex) causes the disease.

Neurocysticercosis, subpial gliosis, encephalitis, vasculitis, and neuronal migration disorder have all been recognized as pathologic entities in children with LKS (Cole et al. 1988). In most patients with LKS, however, standard neuroimaging reveals no structural abnormalities.

The onset of language disturbances is temporally linked to the onset of seizures. Seizures are typically low in severity, infrequent, and nocturnal. AEDs, steroids, high-dose benzodiazepines, and IV immunoglobulin have all been used to treat LKS (IVIG). Clinical seizures can be effectively treated with AEDs and other medical treatments; however, cognitive impairments and epileptiform discharge are treated differently.

Surgical options for LKS include lesionectomy, when appropriate, and multiple subpial transection (MST), when there is no identifiable lesion in MRI.

The target of epilepsy surgery for LKS is to obtain seizure freedom and remission of the language problems. AEDs can usually achieve the latter goal in most patients. As a result, the most common reason for considering surgery is to eliminate epileptiform discharge and thereby improve language function. There are reports of excellent outcomes following lesionectomy (Nass et al. 1993).

Morell and colleagues introduced MST for selected children with LKS who failed medical therapy, and the outcome of their series was encouraging (Morrell et al. 1995). A similar outcome was also published by Grote et al. (1999) and Irwin et al. (2001). However, Downes et al. found reason to recommend MST over medical therapy (Downes et al. 2015).

5.2.4. Classification of Epilepsy Surgery

The surgical approach and method in a case with refractory epilepsy is determined by the seizure type, location of epileptic focus, presence or absence of an identifiable pathology on MRI, and its proximity to eloquent brain and the patient's functional baseline. Epilepsy surgery is divided into two types: curative and palliative. Without the use of AEDs, the goal of curative surgery is to fully eliminate seizures and create long-term remission. When "curative" surgery is not an option, palliative surgery is considered. Resection of the epileptic zone, disconnection at the level of white fibers, and neurostimulation are the three basic techniques in epilepsy surgery.

Resective Surgery for Epilepsy

Anteromedial temporal lobectomy (AMTL) and its modifications are the most commonly accomplished surgeries for the management of refractory epilepsy.

In conventional resection (AMTL), the neocortical resection in the non-dominant and dominant temporal lobes is roughly 5 cm and 3.5 cm, respectively. The amygdala and the first 3 cm of the hippocampus are removed (Figure 16). A more extensive hippocampus resection was not linked to a higher risk of seizure freedom after surgery (Schramm et al. 2011). Selective amygdalohippocampectomy (SAH) was created for people with obvious hippocampal sclerosis to prevent the removal of lateral (neocortical) temporal tissue and has been demonstrated to be as effective in controlling seizures (Figure 17) (Tanriverdi et al. 2009). Yasargil advocated for a trans-sylvian route (Siegel et al. 1990), but the same surgery might be performed using an inferior temporal approach or a transcortical method through the middle temporal gyrus.

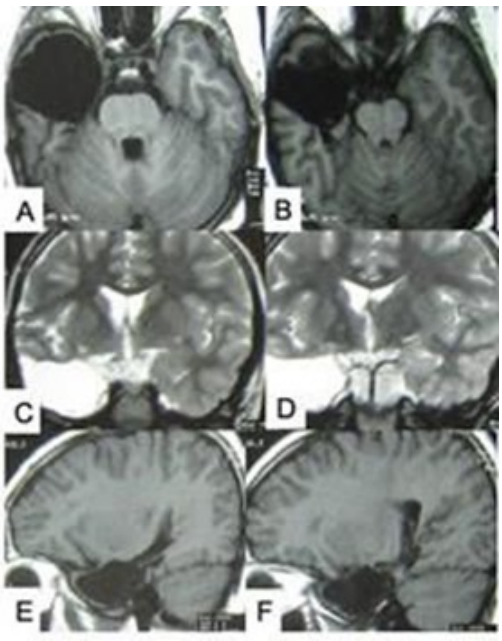

Figure 16. MRI of brain; (**A**,**B**) T1W axial, (**C**,**D**) T2W coronal and (**E**,**F**) T1W sagital postoperative images after right amygdalohippocampectomy plus standard anterior temporal lobectomy in a case of MTS. Source: Figure by authors.

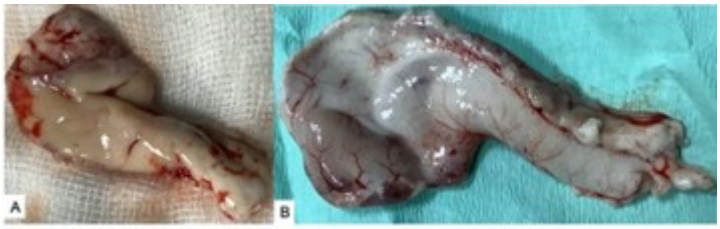

Figure 17. Resected specimens (**A**,**B**) of amygdala and hippocampus after selective amygdalohippocampectomy. Source: Figure by authors.

Approximately 70% of correctly selected patients achieve seizure-free status after ATL, and the majority of those who remain, benefit greatly from seizure reduction and increased quality of life (Engel 1996; Spencer et al. 1984).

When there is a well-demarcated structural lesion, such as a benign tumor, FCD (Figures 18–20), gliosis (Figures 21 and 22), or cavernous malformation, lesionectomy is a viable surgical option if seizure semiology and EEGs are in agreement. In general, removing the epileptogenic brain area completely increases the likelihood of seizure freedom. Overlap with the eloquent cortex makes adequate resection difficult. As a result, the extent of resection should be assessed against these risks and tailored to each individual instance.

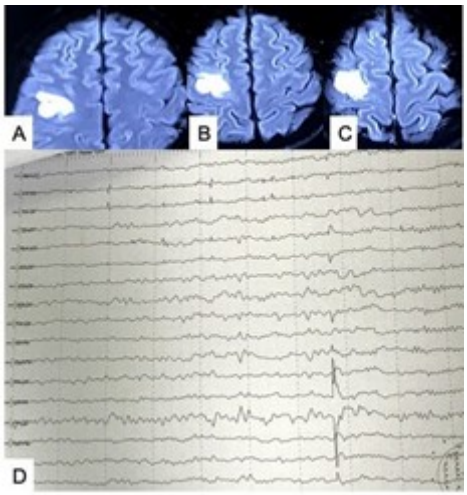

Figure 18. (**A**–**C**) MRI of brain axial sections showing right middle frontal gyrus FCD. (**D**) EEG showing right frontal focal discharge. Source: Figure by authors.

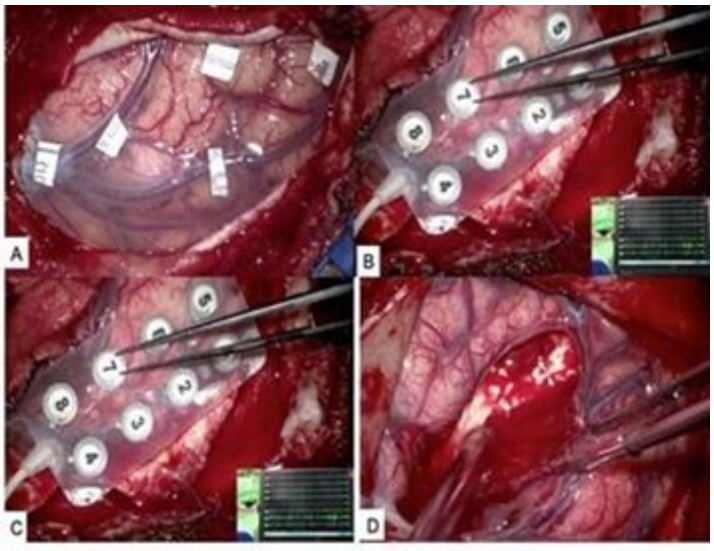

Figure 19. Peroperative (ECoG- and neuronavigation-guided excision) pictures: (**A**) before excision, (**B**,**C**) ECoG-guided excision, and (**D**) after excision. Source: Figure by authors.

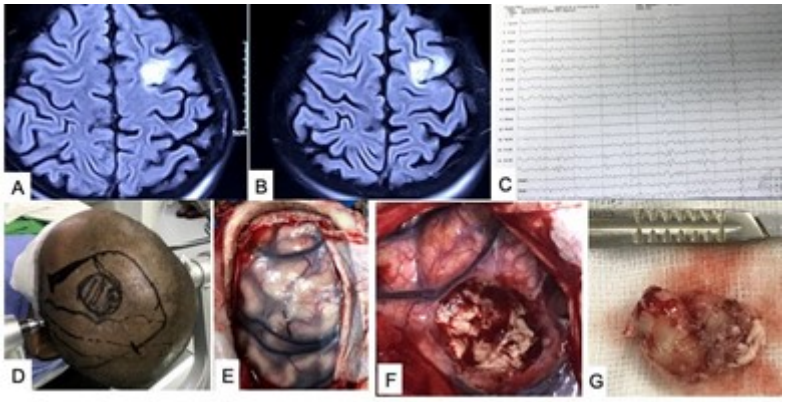

Figure 20. (**A**,**B**) MRI of brain axial sections showing left frontal FCD. (**C**) EEG showing abnormal electrical discharge concordant with lesion. (**D**–**F**) Peroperative pictures of focal excision of lesion. (**G**) Specimen after resection of lesion. Source: Figure by authors.

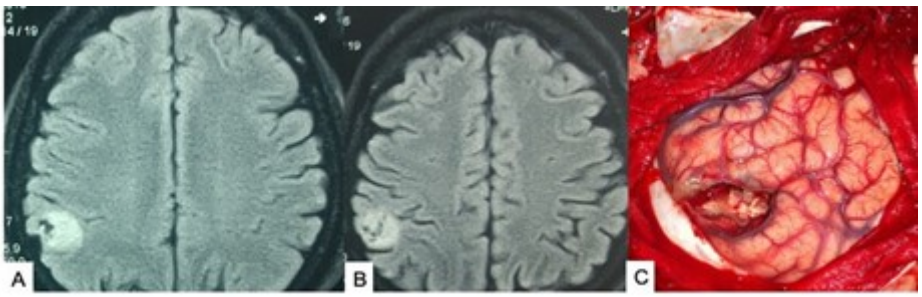

Figure 21. (**A**,**B**) MRI of brain showing right-sided parietal post-neurocysticercosis gliosis. (**C**) Peroperative picture of excision of lesion. Source: Figure by authors.

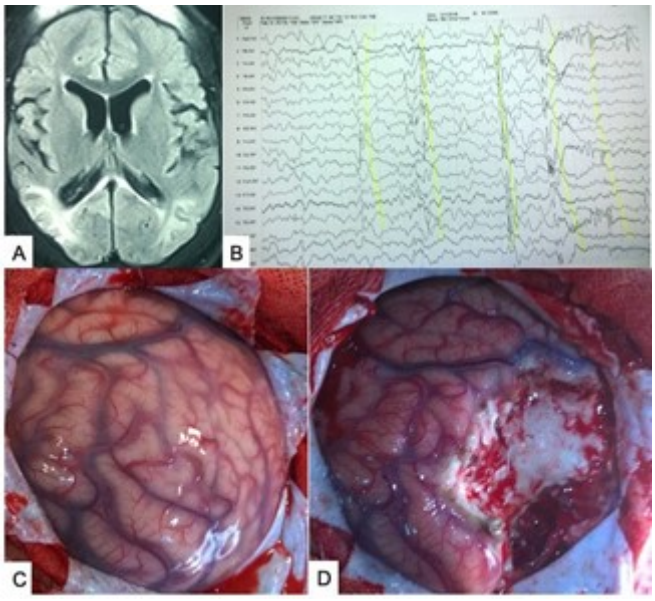

Figure 22. (**A**) MRI of brain axial view showing post-viral-infection occipital gliosis and atrophy (right > left) with resistance epilepsy with a history of repeated severe head injury due to falls. (**B**) EEG showing abnormal electrical discharges predominantly from the right occipital area. (**C**,**D**) Peroperative pictures of right occipital focal excision (patient was hemianopic). Surgical excision eased seizure control with drugs. Source: Figure by authors.

Removal of hemosiderin-stained tissue around the malformation is required in cavernoma. The use of intraoperative cortical mapping and intraoperative electrocorticography (ECoG) (Figure 19) (Van Gompel et al. 2009) and awake craniotomy with neuronavigation-guided (Figure 23) resection improves outcomes and reduces postoperative neurological deficits.

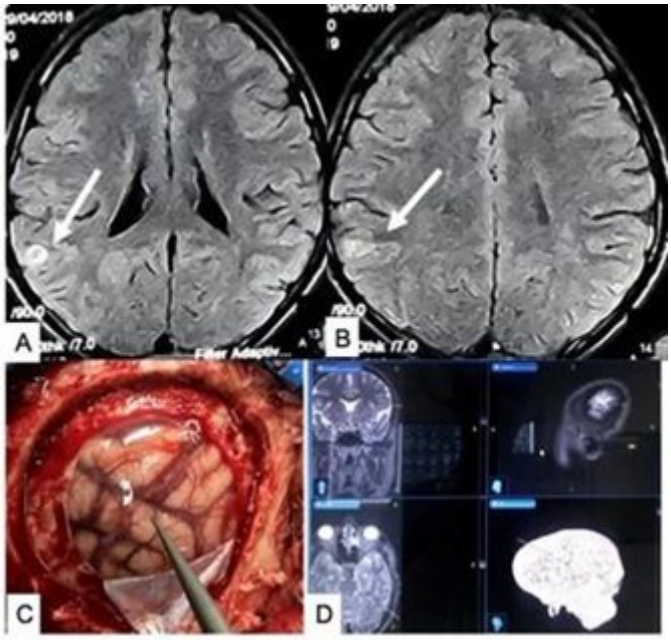

Figure 23. (**A**,**B**) MRI of brain axial sections showing right parietal small FCD. (**C**,**D**) Peroperative identification of lesion with neuronavigation guide. Source: Figure by authors.

After the ictal onset zone and cortical functions have been established using intracranial recordings, most typically utilizing subdural grids or SEEGs, MRI-negative epilepsy usually requires a customized resection.

While open brain resection has traditionally been the basis of surgical treatment, recent advancements have enabled less-invasive ablative treatments such as MRI-guided laser interstitial thermotherapy (LITT). Following is a brief rundown of the many technological approaches and procedures.

Recently, laser ablation under real-time MR thermographic guidance has been shown as an alternative to open resection in patients with hippocampal sclerosis (Willie et al. 2014). Its main advantages are decreased surgical morbidity and better cognitive outcomes (Drane et al. 2015). This approach can also be used for other small, deep epileptogenic lesions.

Laser Ablation Surgery

In both extratemporal and temporal lobe epilepsy, laser ablation surgery has recently been found to be successful in both non-lesional and lesional instances. MTS, FCD, unsuccessful prior open surgery, and deeper lesions relatively inaccessible to open surgery are all examples (Gonzalez-Martinez et al. 2014).

This approach has the advantage of precisely targeting seizure-causing lesions without the need for a craniotomy, leading to less pain as well as a shorter hospital stay. The goal of an MRIgLITT (MRI-guided laser interstitial thermal therapy) system is to use interstitial irradiation or thermal therapy to necrotize soft tissues while employing MRI guidance. This method has been used to treat MTS, cavernous angioma, hypothalamic hamartoma, cortical development abnormalities, and tuberous sclerotic lesions (Gross et al. 2016). MRIgLITT can also be used to treat mesial temporal epilepsy. It has been compared to open surgery in terms of safety, accuracy, and efficacy but provides reduced morbidity (Kang et al. 2016), especially in elderly patients (Waseem et al. 2015).

Corpus Callosotomy

Corpus callosotomy (CC) is a palliative surgical treatment that involves severance of the corpus callosum in the anterior two-thirds or its entirety. The treatment is most commonly utilized for drop attacks, with roughly three-quarters of patients benefiting and more than a third being free of drop attacks (Tanriverdi et al. 2009). Detaching the corpus callosum is thought to stop rapid bilateral seizure spread, which causes loss of consciousness or posture, and so lessens the intensity and frequency of secondary generalized seizures in people who are not surgical candidates. In seizure types that require bi-hemispheric synchrony for seizure expression, CC has the potential to eliminate clinical seizure symptoms. Patients with very refractory, generalized tonic–clonic seizures may benefit from CC in the case of IGE (Cukiert et al. 2009; Jenssen et al. 2006).

Multiple Subpial Transection Procedure

This approach, developed by Morrell in 1989, is largely used to treat refractory epilepsies in which resection is impossible due to the epileptogenic zone being close to, or overlapping, the eloquent cortex (Morrell et al. 1989). Ictal discharges frequently spread along horizontal fibers, whereas cortical activities tend to be organized vertically. Multiple vertical subpial transections are performed in 5 mm intervals of the cortex based on this principle, severing horizontal intracortical fibers but maintaining vertical connections. In an awake patient, MST on the eloquent cortex is frequently combined with the excision of neighboring nonessential cortex. Excision surgery has been found to be more successful than this method (Morrell et al. 1989).

Hemispherectomy

The most favored surgical strategy in the care of children with unilateral hemispheric epilepsy and hemisphere functions that are compromised or projected to become impaired is hemispherectomy (Figures 13 and 14) (Limbrick et al. 2009). Indications for hemispherectomy include Rasmussen syndrome, hemimegalencephaly, Sturge–Weber syndrome, infantile spasms, hemiconvulsion-hemiplegia-epilepsy (HHE) syndrome, multilobar cortical dysplasia, and congenital hemiplegia. In anatomical hemispherectomy, the entire abnormal hemisphere is resected, giving excellent seizure freedom. But, patients develop serious late postoperative complications including superficial cerebral hemosiderosis and hydrocephalus. With subsequent modifications, anatomical hemispherectomy has been almost completely abandoned and replaced by functional hemispherectomy and hemispherotomy. Current functional hemispherectomy surgery removes the temporal and centroparietal portions of the brain, keeping the frontal and occipital poles alive but isolated from the rest of the brain. Around three-quarters of patients have total seizure control after hemispherectomy, with the majority of the remaining patients having better seizure control (Limbrick et al. 2009). Seizure independence generally improves the function of the remaining hemisphere, resulting in enhanced cognitive function and behavior during follow-up.

Non-Resective Surgical Treatments: Neurostimulation

i. Vagus Nerve Stimulation (VNS)—The US Food and Drug Administration (FDA) approved VNS for refractory focal onset epilepsies with or without secondary generalization in cases aged 4 years and up. A battery generator is inserted in the left upper chest wall and tunneled beneath the skin to the vagus nerve in the VNS system. The device is set to send electrical stimulation to the brain via the left vagus nerve. The mean seizure frequency dropped by 26% after one year, 30% after five years, and 52% after 12 years, according to a retrospective assessment assessing the efficacy of VNS in 48 patients with intractable partial epilepsy (Uthman et al. 2004).

ii. Responsive Neurostimulation (RNS)—The FDA authorized RNS in 2013 for medically resistant focal epilepsy. In reaction to ictal discharges recorded by the RNS device, it gives cortical stimuli. This programmable neurostimulator is implanted in the brain and coupled to one or two depth and/or subdural cortical strip electrodes over seizure foci. In the final months of the two-year trial, the randomized investigation of 191 patients found a progressive decrease in the frequency of debilitating seizures in the treatment group (41.5%) compared to the control group (9.4%) (Heck et al. 2014).

iii. Deep Brain Stimulation (DBS)—DBS of the anterior nucleus of the thalamus has been licensed in the European Union as an adjunctive treatment for drug-resistant focal epilepsy in adults since 2010. It is also FDA-approved. In a multicenter trial, the treatment group experienced a 29% reduction in seizures in the first month, analogous to the control group, and at least a 50% seizure decrease in 54% of patients after two years (Fisher et al. 2010).

6. Conclusions

Drug-resistant epilepsy has a remarkable impact on cognitive development and life quality. Many of them can be addressed successfully with surgery. In managing patients with DRE, appropriate utilization of diagnostic tools to identify a patient's suitability for surgical management as well as to determine what type of surgical technique would be safer and most useful to the particular case is critical. Both presurgical examination and surgical approaches will improve as diagnostic and treatment technologies advance.

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