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Review Article

A Review on Focal Epilepsy: Clinical Features, Diagnostic Challenges, and Treatment Approaches.

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Abstract

Focal epilepsy, the most common type of epilepsy in adults, is distinguished by seizures that originate in a single area of one hemisphere of the brain. This study examines the clinical characteristics, underlying causes, and therapeutic options for focal epilepsy. The syndrome causes a variety of seizure forms, including focal aware seizures, focal seizures with decreased awareness, and subsequent generalized seizures. The aetiology is frequently complex, with structural brain abnormalities such as cortical malformations, traumatic traumas, infections, and vascular lesions being discovered. Despite breakthroughs in neuroimaging, a considerable minority of patients continue to be idiopathic. Anti-seizure drugs are the primary form of management, while surgical options are considered in pharmacoresistant patients. This review emphasizes the importance of understanding the complexities of focal epilepsy.

Keywords: - Focal Epilepsy, Focal Seizure, EEG, ILAE

Introduction

Epilepsy is a common and serious neurological disorder characterised by recurring, spontaneous seizures caused by abnormal, excessive, or synchronised neuronal activity in the brain. Although not all seizures are indicative of epilepsy, epilepsy does include seizures. Epilepsy affects people of all ages, but it is most common in children, accounting for 75% of cases because the developing brain is more susceptible to epileptic activity. According to the 2017 International League Against Epilepsy criteria, epilepsy is diagnosed when a person has an apparent epileptic condition, two unprovoked seizures 24 hours apart, or one unprovoked seizure with a high probability of recurrence within the next 10 years. Epilepsy affects more than 1% of the global population, with an annual incidence rate of about 50 new cases per 100,000 people, posing significant challenges for both patients and healthcare providers.(1). Approximately one-third of epilepsy patients have refractory seizures that do not respond to current treatments.(2). Neuroinfection (neurocysticercosis), neurotrauma, and birth traumas are the main causes of secondary epilepsy in India.(3).Seizure classification plays an important role in epilepsy diagnosis and treatments. The International League Against Epilepsy (ILAE) recommends a three-tiered system: identifying the type of

seizure, determining the type of epilepsy (focal, generalised, mixed, or unknown), and attempting to diagnose a specific epilepsy syndrome while accounting for comorbidities and etiological factors at each stage.(4).

Seizures in a particular area of the brain are the hallmark of focal epilepsy, which presents special difficulties as well as therapeutic potential. The symptoms of focal seizures vary depending on which part of the brain is affected. Because focal epilepsy symptoms are minor and readily misinterpreted, diagnosing the condition can be challenging(5). Determining the focal site of a seizure requires accurate patient history, eyewitness accounts, and the use of contemporary diagnostic tools such as electroencephalography (EEG) and neuroimaging. Anti-seizure drugs are essential for treating focal epilepsy, as they try to improve the patient's quality of life by reducing seizure frequency and adverse effects.(6). When drugs are ineffective, surgical or neuromodulator therapy may be tried to remove or change the brain tissue that causes seizures, which can be effective for some people.(2). It is essential to comprehend and manage focal epilepsy to improve overall epilepsy care and deepen our knowledge of how the brain works. The complexities of focal epilepsy, such as its clinical traits, issues with diagnosis, and treatment options, are covered in detail in this review.

Methods

This review covers research on focal epilepsy conducted in the past ten years, with an emphasis on the diagnosis, treatment, and classification of seizures. Based on keywords like "focal epilepsy" and "seizure classification," studies were selected from PubMed, Scopus, and Web of Science. Peer-reviewed articles about focal epilepsy were accepted; non-peer-reviewed material and studies into generalised epilepsy were not. The primary concerns were new classifications of ILAE seizures, difficulty with diagnosis, and treatment results.

Classification of seizure

Seizure Type	Description	Key Features
Focal Seizures	Starts in one part of the brain and may spread to other areas.	Symptoms depend on the affected brain area. May spread to both hemispheres, becoming bilateral tonic-clonic seizures.
Generalized Seizures	Involves both hemispheres of the brain from the start.	Includes motor seizures (like tonic-clonic) and non-motor seizures (like absence seizures).

Unknown Onset Seizures	Seizures where the beginning is not observed, make classification hard.	Often occurs when the person is alone or asleep.
Unclassified Seizures	Seizures were suspected but not enough information for a clear diagnosis.	Lack of detailed information to definitively categorize

Table 1. Simplified classification of seizure types with key features(7)**.**

Focal Epilepsy

Focal epilepsy is defined according to the patient's state of awareness during a seizure, which can be impaired, preserved, or unknown. Consciousness is assessed by awareness and reactivity. The information is gathered from either history or behaviour assessment. It is ineffective to ask about awareness directly rather than recall and responsiveness to seizure occurrences. Impaired consciousness can occur even when the patient appears to be interacting normally. If a seizure affects awareness or responsiveness, it is classified as impaired consciousness.(7). It is important to rule out other conditions, such as epileptic amnesia and ictal paresis.

Category	**Subtype**	**Description**
1. Focal Seizures		Seizures originate in one specific area or network in the brain.
1.1 Focal Aware Seizure		(Previously Simple Partial Seizure) The person remains fully aware during the seizure.
	1.1.1 With observable manifestations	Seizures with clear symptoms such as motor, sensory, or autonomic signs (e.g., jerking of a limb).
	1.1.2 Without observable manifestations	Seizures where symptoms are not easily noticeable.
1.2 Focal Impaired Awareness Seizure		(Previously Complex Partial Seizure) A person's awareness is impaired during the seizure.
	1.2.1 With additional observable manifestations	Seizures with impaired awareness and visible signs like motor movements or other symptoms.

	1.2.2 Without additional observable manifestations	Seizures with impaired awareness but without clear physical symptoms.
1.3 Focal Seizure with Unknown Awareness		Awareness during the seizure is unknown.
	1.3.1 With observable manifestations	Seizures with visible symptoms, but it's unclear if consciousness is impaired.
	1.3.2 Without observable manifestations	Seizures without clear symptoms, and it is unknown whether awareness is affected.
1.4 Focal-to-Bilateral Tonic-Clonic Seizure		(Previously Secondary Generalized Seizure) Seizures start as focal and spread to both sides of the brain, leading to tonic (stiffening) and clonic (jerking) movements.
	1.4.1 Semiology descriptors in chronological sequence	Includes specific semiology (seizure signs) and somatotopic modifiers (which body parts are involved).

Table no.2 *the following table summarizes the classification of focal epilepsy, with seizure types and characteristic features.*(7).

Focal Epilepsy by Lobe of Seizure Occurrence

Focal is distinguished by the lobe of the brain where the seizures occur. Below is a breakdown of focal epilepsy by brain lobe involved:

Temporal Lobe Epilepsy (TLE) - Temporal Lobe Epilepsy (TLE) is a kind of focal epilepsy in which seizures originate in the temporal lobe of the brain, which is responsible for emotional processing and memory. It accounts for almost 60% of all cases of focal epilepsy. Complex partial seizures impair consciousness with automatisms and sensory disruptions, whereas simple partial seizures cause sensory or motor symptoms like tingling or hallucinations. Many people experience auras before seizures, such as deja-vu or sensory experiences. Memory impairment is common, particularly when seizures affect the hippocampus, and psychological symptoms such as worry or rage may coexist with seizure activity. Stress,

sleep deprivation, and hormone fluctuations are all potential causes of seizures in TLE patients(8).

Frontal Lobe Epilepsy (FLE) -FLE is a type of focal epilepsy that starts in the frontal lobe, which is crucial for language, memory, motor control, problem-solving, spontaneity, social and sexual behaviour, and recollection. A wide range of motor activities, behavioural problems, and brief motor seizures are all possible with FLE seizures. Frontal lobe seizures often occur during nighttime, are vocalized, tend to cluster, and are usually brief. Significant motor features include simple clonic movements, tonic posturing, eye deviation, and more complex actions such as cycling, rocking, or grimacing.(9).

Seizures originating in the primary motor cortex are characterized by the "Jacksonian march," where ictal activity spreads across the motor cortex. This typically manifests as clonic, tonic, or myoclonic movements affecting one side of the body (contralateral unilateral), which may spread to adjacent areas. Involvement of the supplementary motor area can lead to asymmetric bilateral tonic posturing, often seen as a "fencing posture." This includes flexion of the ipsilateral upper limb and extension of the contralateral upper limb, accompanied by distinctive head and eye deviation. The fencing response is commonly demonstrated with one arm extended forward and the other elbow flexed, externally rotated, and abducted at the shoulder.(10).

Parietal Lobe Epilepsy (PLE)- The parietal lobe, which plays a crucial role in sensory processing, spatial orientation, and bodily awareness, is where seizures originate in Parietal Lobe Epilepsy (PLE), a less common type of focal epilepsy. Symptoms associated with PLE include somatosensory experiences such as tingling, discomfort, burning sensations, numbness, or a feeling of pins and needles. Alongside these sensory symptoms, PLE can present with additional auras like the perception of limb movement, body tilting or swaying, twisting sensations, or even the sensation of a missing limb. Patients with PLE may also encounter vertigo and visual illusions, where objects might appear larger, disappear, or appear to approach unexpectedly.(11).

Occipital lobe epilepsy (OLE)- Occipital lobe epilepsy (OLE) is characterized by seizures that originate in the brain's occipital lobes. Focal aware seizures (FAS) that involve visual symptoms are the most recognized manifestation of occipital lobe seizures. These seizures are often present with primary visual hallucinations described as geometric shapes moving within the visual field, sometimes in a direction opposite to the viewer, or as flashing coloured lights. Complex visual hallucinations, such as seeing recognizable faces or people, can also occur. Individuals experiencing occipital lobe seizures may report negative symptoms with a loss of half of their visual field or may describe Ictal blindness, where all areas of their visual field appear blind.(12).

Focal seizures of Insular Cortex origin

Patients with insular cortex seizures may have a variety of symptoms. Subjective symptoms include difficulty breathing, tingling in the mouth or other parts of the body, laryngeal discomfort, and epigastric or thoracic feelings.(13). Objective symptoms that are frequently noted include dysphonia, and dysarthria, which can sometimes develop into full muteness and hypersalivation.

Childhood Focal Epilepsies: Etiology and Mechanisms

Focal epilepsy makes up over two-thirds of pediatric epilepsy cases, making it the most common variety. When determining the cause of this illness, three primary factors must be used. Mutations can cause moderate epilepsy with centrotemporal spikes or more severe disorders such as Dravet syndrome. Common reasons include congenital brain abnormalities such as cortical dysplasia, tuberous sclerosis, and periventricular nodular heterotopia. In addition, acquired disorders such as encephalitis infections, prenatal brain injury, and post-traumatic brain injury all contribute to the development of localised epilepsy in children. It has also been determined that immunologically mediated encephalitis and metabolic disorders are important etiological contributors(14). There are three main types of causes of focal epilepsy syndromes in children.

Self-limited focal epilepsy syndromes	**Focal epilepsy of known cause**	**Focal epilepsy of unknown cause**
Self-limited neonatal epilepsy (KCNQ2)	Structural, developmental (malformations of cortical	
Self-limited infantile epilepsy (PRRT2, SCN2A, SCN8A)	development; possible genetic origin: e.g., DEPDC5 and TSC1/TSC2)	
Self-limited epilepsy with autonomic seizures	Structural and/or acquired	
Self-limited epilepsy with centrotemporal spikes	• Perinatal brain injury • Hypoxic-ischemic injury • Stroke • Trauma • Tumor • Vascular malformation	

	• Post-infectious • Hippocampal injury/FS • Immune-mediated (anti-NMDAR)	

Table. 3. Summarizes the most common causes of focal epilepsy syndromes in children.(1).

Self-limited focal epilepsy syndromes

The ILAE recently recognized self-limiting focal epilepsy syndromes for newborns, and infants Self-limited focal epilepsy syndromes are an uncommon group of disorders that primarily affect infants, children, and newborns. These diseases are identified by specific clinical signs and are transient. Children with self-limited neonatal epilepsy frequently have localized tonic or clonic seizures within the first week of life, which typically resolve by the age of six weeks. Mutations that damage the KCNQ2 gene are usually associated with this type of epilepsy. Benign epilepsy with centro-temporal spikes (BECTS) is characterized by focal seizures that occur primarily at night or in the morning. Prestigious centrotemporal spikes on the electroencephalogram (EEG) are the hallmark of this illness, which has a typically good prognosis with seizures that abate by puberty.(15).

Another type of self-limiting focal epilepsy that typically affects children between the ages of three and six, panayiotopoulos syndrome, also presents with pallor and vomiting as symptoms.This syndrome normally goes away by adolescence; however PRRT2, SCN2A, and SCN8A variants have been related to it through genetic investigations. The importance of EEG findings and genetic testing in the identification and management of pediatric epilepsy is highlighted by several disorders(1). Though these patients' imaging scans are frequently normal, research on the underlying mechanisms and potential treatments for these self-limited focal epilepsy syndromes is still ongoing.

Pathophysiology

Seizures can occur when hyperexcitability is caused by a disturbance in the neuronal membrane's integrity. Hyponatremia, for example, reduces the intracellular to extracellular gradient and affects neuronal stability, perhaps leading to hyperexcitability. When certain drugs (such as alcohol, benzodiazepines, and barbiturates) are abruptly discontinued, the inhibitory neurotransmitter GABAA becomes hypersensitive, resulting in

seizures and neuronal hyperexcitation. Hypoglycemia disrupts neuron metabolism and affects subcellular processes. Seizures can be caused by any dysfunction in a specific cell, network, brain area, ion, receptor, or other component of the central nervous system.

Children with Focal Epilepsy of Unknown Cause

Though extensive testing, including brain MRI, is performed on about 50% of children diagnosed with childhood-onset focal epilepsies who do not fit the profile for one of the recognized self-limiting syndromes, no clear explanation is found. The prognosis for seizures in these patients is usually positive despite the difficulties in diagnosis. Studies based on population-based long-term data show that 81% of these kids have no seizures, and 68% of them have successfully stopped taking anti-seizures(16). When a child reaches typical developmental milestones and has a standard neurological assessment, the likelihood of a satisfactory outcome is high. This suggests that, even though the cause of their epilepsy is unknown, their general brain development and health have a significant bearing on their prognosis. In addressing focal epilepsy of unknown origin, the large percentage of children who achieve seizure freedom highlights the importance of ongoing monitoring and supportive care.

Focal epilepsy with a known cause

There are known underlying causes for around half of childhood focal epilepsies that do not fit into a specific self-limited epilepsy diagnosis. Children who have these identified causes are more likely to develop medication-resistant epilepsy and are less likely to go through an epileptic remission. Apart from children who meet the criteria for a self-limited epileptic illness, the most known causes of focal epilepsy in children are structural abnormalities. This emphasizes the significance of a high-quality brain MRI employing the epilepsy protocol for the investigation of all such patients. This imaging procedure is essential for detecting structural lesions or anomalies that may be the cause of epilepsy since it will help with seizure control and the long-term outcomes for affected children(17).

There are two main structural causes of epilepsy in children: acquired and developmental. Developmental irregularities, such as hemimegalencephaly and focal cortical dysplasia (FCD), result from disrupted brain growth and often lead to drug-resistant epilepsy. Hemimegalencephaly can begin with infantile spasms and progress to focal seizures, while FCD may cause epilepsy later in childhood or adulthood. Hippocampal

sclerosis, often linked to prolonged fever episodes in early childhood, can develop into mesial temporal sclerosis, treatable with epilepsy surgery. Early detection and treatment are crucial for improving outcomes. Advances in neuroimaging, genetic testing, and understanding of neurodevelopmental disorders enhance our ability to manage childhood epilepsy. Multidisciplinary care and individualized treatment plans are essential. Acquired causes include perinatal brain injuries like hypoxic-ischemic injury in term infants and intraventricular haemorrhage in premature newborns, leading to seizures that may reappear as focal seizures or epileptic spasms. Other acquired structural changes, such as stroke, trauma, and tumours like dysembryoplastic neuroepithelial tumours (DNETs) and gangliogliomas, can occur at any age. Post-infectious brain damage from diseases like encephalitis or meningitis also contributes to epilepsy in children(18).

Somatic mutations and mosaicism can cause brain abnormalities in children, resulting in epilepsy. Common causes include genetic changes that affect pathways such as mTOR, SLC35A2, Sturge-Weber disease, and tuberous sclerosis complex. If the seizures are localized, surgery may be a possibility. Metabolic illnesses are frequently associated with generalized seizures, although rare immune-mediated epilepsies, such as anti-NMDA receptor encephalitis, are distinguished by sudden seizures and decreased movement. When MRI findings are consistent with clinical complaints, infectious illnesses such as neurocysticercosis should be explored(19). Imaging and genetic testing advancements will lead to earlier detection and more targeted treatment.

Adult Focal Epilepsies: Etiology and Significance

Adults with epilepsy include those who develop the condition later in life as well as those who have it since childhood or adolescence. Focal epilepsy has multiple etiologies, some of which are increasingly common as people age. The 2017 ILAE position paper revised the epilepsy categorization to emphasize etiological features, which are essential for predicting outcomes and guiding therapy. Epilepsy in adults is frequently caused by structural issues such brain tumors or strokes, genetic factors (ion channel mutations), metabolic abnormalities, autoimmune diseases, and infectious diseases (neurocysticercosis)(20). A precise diagnosis, made possible by contemporary imaging and genetic testing, is essential for the implementation of customized care choices intended to manage seizures and improve quality of life.

TABLE 4. Most Common Etiologies of Focal Epilepsy Syndromes in Adults.

Structural	Genetic	Infectious	Metabolic	Immune-mediated	Unknown
Stroke Hippocampal sclerosis Hypoxic–ischemic injury Neurodegeneration (Alzheimer's disease) Tumors (primary – high-grade glioma, meningioma – or metastatic) Brain trauma Malformation of cortical development (HME, PMG, FCD, MOGHE) Vascular malformations (cavernoma, meningeal angiomatosis)	Familial temporal lobe epilepsy Autosomal dominant sleep-related hypermotor epilepsy (CHRNA4, CHRNB2, CHRNA2)	Viral encephalitis Parasitic infections (malaria, neurocysticercosis) Bacterial meningitis, encephalitis, e.g., brain abscess or meningoencephalits Fungal infections (candida,aspergillus, cryptococcus)	Mitochondrial Acute intermittent porphyria Adrenoleukodystropy Wilson's disease	Anti-LGI1 Anti-NMDAR Anti-GABA-B Anti-Caspr2	

The structural causes

Adult epilepsy is primarily caused by structural brain abnormalities acquired over time, such as trauma, stroke, infections, neoplasms, vascular malformations, and genetic disorders. These variables can result in focal epilepsy, which is characterized by seizures that originate in specific brain regions. Epilepsy prevalence increases with age, particularly among the elderly, who are more susceptible to acquiring illnesses such as Alzheimer's disease and cerebrovascular disease(21). Cerebrovascular disease is responsible for 50-70% of adult epileptic episodes, with neurodegenerative diseases contributing to 10-20%. Seizures are a common manifestation of brain tumours, affecting 30 to 50 percent of patients. Tumour characteristics including location and histology influence epilepsy risk. For example, involvement of the RAS-RAF-MAP-Kinase pathway in neuroglial tumors promotes the development of seizures as well as tumor progression. In comparison to primary brain tumours, brain metastases typically have a less infiltrative development pattern and less influence on neuronal excitability(22).

Molecular biomarkers, such as MGMT promoter methylation, BRAF V600E mutations, and IDH1 mutations, are critical for therapy selection. High-grade gliomas are common at age 60, but low-grade gliomas typically appear in the third and fourth decades of life. Metastatic tumors and meningiomas, which are generally

benign, can also produce seizures in the elderly. Focal cortical dysplasias (FCDs) are prevalent epileptogenic anomalies, particularly in children undergoing epilepsy surgery. Arteriovenous malformations (AVMs) and cavernomas, which frequently induce seizures, highlight the importance of early detection and treatment, made feasible by advances in neuroimaging and genetic testing. Cavernomas, on the other hand, have been linked to genetic changes in genes including CCM1/KRIT1, CCM2/MGC4607, and CCM3/PDCD10. They could be sporadic or familial. Seizures, the most common clinical sign of cavernomas, affect half of all patients and are typically caused by lesions in the temporal lobe(23). Traumatic brain injury (TBI) accounts for around 30% of epilepsy cases in young adults, and post-traumatic epilepsy is often medication-resistant. Understanding the mechanisms of epileptogenesis is crucial for successful prevention(24).

Infectious causes

Adults with central nervous system diseases are equally susceptible to seizures and epilepsy as children. Estimates place the risk of post-infectious epilepsy at up to 26% in low-income areas and 8% in wealthier countries(25). The kind of pathogen, level of cortical involvement, and inflammatory response all influence epilepsy progression. Treating infections as soon as possible is crucial for lowering the prevalence of epilepsy. High-risk illnesses that can result in epilepsy include parasitic disorders like neurocysticercosis and malaria, as well as viral encephalitis, which can cause considerable cortical damage and an intense inflammatory response(26). Although uncommon, bacterial meningitis has the potential to cause chronic epilepsy.

Genetic causes

Genetic factors are becoming more important in the research and management of focal epilepsy, however genetic testing is not yet widely used for diagnosis. Genetic variations linked to epilepsy have been identified with considerable advancement over the past two decades. Autosomal dominant sleep-related hypermotor epilepsy (ADSHE) and familial temporal lobe epilepsy (FTLE) can both result from gene mutations in CHRNA4, CHRNB2, CHRNA2, and KCNT1. Furthermore, Type 2 focal cortical dysplasia (FCD) and epilepsy are associated with loss-of-function mutations in the GATOR1 complex gene DEPDC5(27). Genetic testing can help develop more tailored approaches to treating epilepsy by enabling medical professionals to forecast the severity of a patient's condition, how well a patient will respond to treatment, and if a patient

will require surgery in cases when medication is not working.

Metabolic causes

There are approximately 600 different forms of metabolic abnormalities associated with epilepsy, most of which are caused by genetic enzyme deficits that disrupt biochemical pathways. Adult metabolic epilepsies, including MERRF, MELAS, POLG-related disorders, and primary mitochondrial abnormalities, are prevalent. While MELAS can produce status epilepticus during stroke-like episodes, POLG mutations cause mitochondrial epilepsy in people of all ages. Early adulthood MERRF is characterized by myoclonic and focal seizures, which are frequently associated with the m.8344A>G mutation. Acute intermittent porphyria, adrenoleukodystrophy, and Wilson disease are other metabolic epilepsies that can affect adults. These conditions are linked to abnormalities in the metabolism of heme, very long-chain fatty acids, and copper buildup, respectively(28).

Immune causes

Autoimmune epilepsy, despite increasing awareness, is predominantly caused by neural autoantibodies against intracellular or cell surface antigens. To diagnose this illness, serum or spinal fluid must be tested for these antibodies. Some antibodies suggest an increased risk of cancer, prompting screening. Anti-NMDAR antibodies, for example, are connected with a 50% increased risk of ovarian cancer, whereas GABA-B receptor antibodies are linked to small cell lung cancer. Patients with NMDAR antibodies are often in their twenties, whereas those with GABA-B, LGI1, and Caspr2 antibodies are usually in their sixties or older(29). Early identification and adequate screening are critical for optimal management of autoimmune epilepsy.

Unknown cause

Even though testing and imaging techniques have advanced greatly, the precise etiology of epilepsy remains unknown in certain cases. Shortage of resources in the medical field, such as brain MRI access and long-term video-EEG monitoring, might make it more difficult to diagnose and treat epilepsy properly. The goal of this precision medicine era is to find the cause of focal epilepsy since it will help with focused seizure treatment and customized counselling. If an epileptic patient is diagnosed correctly and early on in their condition, treatment outcomes may be improved and quality of life increased.

Diagnostic Workup for Focal Epilepsies

Focal epilepsy is diagnosed by imaging, neurophysiology, and neuropathology. A high-resolution MRI, a complete medical history, and physical tests can all assist reveal structural problems. Regular and extended video-EEG surveillance is critical for detecting epileptiform discharges and linking clinical events to EEG data. Genetic testing helps to discover underlying genetic disorders, whilst laboratory studies rule out metabolic reasons. Functional imaging techniques such as PET and SPECT are used to find seizure foci. Neuropsychological tests assess cognitive and behavioural impacts. Epilepsy specialists provide comprehensive care, including possibly surgery for medication-resistant instances. Early and correct diagnosis, achieved through extensive evaluation, improves patient outcomes**.**

Feature	**Seizure**	**Transient Ischemic Attack (TIA)**	**Migraine**	**Syncope**	**Transient Global Amnesia (TGA)**	**Psychogenic Non-Epileptic Seizures (PNES)**	**Parasomnia (e.g., Somnambulism, Sleep Talking, Night Terrors)**
Age of Onset	Any age, often younger	Typically elderly	Younger age, more common in women	Any age, often younger	Older age, typically between 25 and 45 years	Younger age	Childhood tends to disappear in adolescence
Clinical Clues	Positive symptoms: Abnormal body movements, eye and head deviation, loss of consciousness, tongue biting (side), incontinence. Visual aura with coloured circles. Negative symptoms may develop postictally	Negative symptoms: numbness, visual loss, paralysis, ataxia, vertigo, dysarthria. High-grade stenosis or occlusion of the internal carotid artery linked with limb-	Visual auras are usually present as scintillating scotomas or fortification spectra. Headache follows with nausea, vomiting, photophobia, phonophobia	Lightheadedness, graying of vision, nausea, pallor, cold sweating, decreased alertness, transient loss of consciousness	Anterograde memory loss without other cognitive impairment, ability to engage in complex activities	Abnormal movements of upper and lower extremities are out-of-phase, absence of vocalization or vocalization at the start, pelvic thrusting, side-to-side head movement, biting the tip of the lip or the	Verbalization, vocalization, motor activity that may be aggressive (e.g., punching, kicking), moving out of bed

		shaking TIAs				tongue	
Duration	Less than 2 minutes	Usually over 2 minutes, mostly less than 1 hour; limb-shaking TIAs typically <5 minutes	Typical aura lasts 5–60 minutes	Usually less than 30 seconds	Episodes last for hours and resolve within 24 hours	Last for 3 minutes to hours	Last 5-15 minutes, onset within 2 hours of sleep onset
Triggers	Sleep deprivation, stress, fatigue, fever, flickering light, menstruation	Precipitated by rising or exercise	Stress, fasting, bright or flashing lights, loud sounds, strong smells, food	Prolonged standing, micturition, defecation, or cough	Emotional stress, pain, Valsalva maneuver	Emotionally triggered attacks	Triggers include sleep deprivation, febrile illness, anxi

Neuroimaging and Diagnostic Workup of Focal Epilepsies

Neuroimaging plays a crucial role in diagnosing focal epilepsy, aiding in both emergency evaluations and ongoing management. To diagnose epileptic syndromes and determine the reason behind recurrent seizures, early neuroimaging is essential(20,30). MRI and CT scans are essential for identifying structural abnormalities like tumors and guiding treatment decisions. Recently, the ILAE Neuroimaging Task Force approved the "HARNESS" MRI technique (Harmonized Neuroimaging of Epilepsy Structural Sequences). To detect a range of epileptogenic lesions with the least amount of scanning time, this procedure includes both required and optional sequences. This process uses isotropic 3D MRI acquisition without an interslice gap and recommends high-resolution imaging to reduce partial volume effects. Important tests include 3D T1 and susceptibility-weighted imaging with gadolinium enhancement for greater sensitivity and 2D T2-weighted imaging for evaluating the hippocampal region(31). Sometimes tiny structural abnormalities like focal cortical dysplasias (FCDs) can go undetected at first, even with the greatest imaging tools. Post-processing techniques in MRI analysis are crucial for detecting small lesions that visual inspection alone may

miss. These methods use computers to examine morphological data such as sulcal depth, cortical thickness, and gray-white matter contrast. By comparing the aberrations to healthy controls, these measurements provide objective evidence of structural abnormalities, assisting in the diagnosis of disorders such as localised cortical dysplasia. Artificial intelligence and visual analysis combine to greatly boost sensitivity, even when routine MRI scans initially produce normal results(32). PET and SPECT provide additional localization information, measuring brain metabolism and perfusion, respectively, which is vital for surgical planning, especially in non-lesional cases(33). Functional imaging modalities like MEG and fMRI map brain function, guiding surgical approaches to minimize functional deficits post-surgery(34). Despite their limitations, these imaging techniques enhance the precision of focal epilepsy diagnosis and improve patient outcomes by tailoring treatment strategies effectively.

Neurophysiology and focal epilepsy diagnosis workup

Neurophysiological evaluations are essential to the diagnostic process for focal epilepsies because they offer vital information on the location and nature of epileptic activity in the brain. Electroencephalography (EEG), video-EEG monitoring, and invasive monitoring with intracranial electrodes are important neurophysiological procedures.

EEG

Neurophysiological evaluations need electroencephalography (EEG), which uses scalp electrodes to capture brain electrical activity. It is crucial for confirming or refuting suspicions of focal epilepsy and can support an electroclinical diagnosis. However, a few factors limit its applicability as a supplemental diagnostic tool. First and foremost, EEG records low-amplitude, continuous biosignals that require expert interpretation. Because data reflect brain activity over a large region, there is heterogeneity among interpreters and a high signal-to-noise ratio. Either reading minor epileptiform abnormalities too little or normal variants too much can lead to misinterpretation. This heterogeneity necessitates a balanced approach to interpretation, balancing sensitivity and specificity(35). Second, 4% of school-age children who do not have epilepsy may have anomalies related to epilepsy; these conditions are more common in people with neurodevelopmental disorders or learning disabilities. Therefore, the diagnostic yield of EEG, which includes fresh data to improve diagnostic precision, is largely dependent on prior clinical likelihood. To increase the diagnostic

efficacy of EEG, tactics, like repeat testing during or after sleep deprivation to identify particular patterns, is crucial(35). While ambulatory EEG can capture lengthier episodes, its limitations may result in the inability to detect brief or moderate seizures(36). Long-term video-EEG monitoring in specialized units remains the gold standard for comprehensive epilepsy assessment because it provides information on both background and seizure-related brain activity. The diagnosis of epilepsy benefits from the use of interictal EEG results, which help with classification and therapy choices. Although their presence can help with diagnosis, particularly in cases of moderate clinical suspicion, their absence does not rule out epilepsy.

EEG In Diagnosis Syndromes

EEG is essential for diagnosing focal epilepsy, classifying epileptic syndromes, estimating prognoses, and guiding further investigations. Self-limited focal epilepsies account for around 25% of juvenile epilepsies, and they are often distinguished by unique EEG patterns that imply a benign course(37). Under the right treatment conditions, these unique qualities can lessen the need for neuroimaging, which is especially important in settings with low resources.

The EEG presentation of self-limited epilepsy with centrotemporal spikes (SeLECTS) is characterized by high-amplitude (≥200 μV), bi/triphasic spike/sharp-slow wave discharges with maximum negativity in the centrotemporal region and frontal positivity, notably during drowsiness(7). On a standard EEG, these discharges can occasionally only show up on one side, even though they are often independent and bilateral. Interictal-focused slowing, unilateral discharges on many EEGs, and only diurnal discharges are rare for SeLECTS and may indicate an underlying structural brain disorder; hence, an alternative diagnosis should be explored. Multifocal, high-amplitude, sleep-activated epileptiform discharges on an electroencephalogram are a feature of autonomic seizures associated with self-limited epilepsy (SeLEAS). These discharges are initially more common in the posterior head areas of children, although they can eventually be seen throughout the scalp. Brief focal conscious seizures and postictal headaches are the hallmarks of childhood-onset visual epilepsy, which often affects children between the ages of 8 and 9. In these conditions, the EEG displays both centrotemporal spikes and sleep-predominant occipital discharges(38). When focal slowness and unifocal discharges are present, both SeLEAS and childhood-onset visual epilepsy should be treated with a different diagnosis.

Developmental and epileptic encephalopathies (DEE) or epileptic encephalopathies (EE) with spike-and-wave activation in sleep (EE-SWAS and DEE-SWAS) may arise from focal epilepsy syndromes such as SeLECTS, SeLEAS, or other structural focal epilepsies. Their EEGs show nearly continual spike-and-wave complexes when they sleep, and they exhibit regression in motor, behavioural, verbal, and cognitive abilities. Under these circumstances, EEG can guide treatment and monitor patient responses(39).

Interictal EEG is also used to categorize individuals who may benefit from early epilepsy surgery, such as neurostimulation. Studies reveal that early surgery improves quality of life and increases seizure independence more than ongoing medical therapy for patients with drug-resistant temporal lobe epilepsy. For patients with unilateral temporal lobe discharges on EEG and concordant MRI lesions, early surgical referral is strongly advised(40).

In addition, EEG manages focal epilepsy by identifying patients who can safely be weaned from antiseizure medication following an extended seizure-free period. According to a meta-analysis, aberrant EEG contributes to relapse risk despite disagreements on the nature of the association between abnormal EEG and risk of relapse.

Focal Epilepsy Diagnostic Workup and Neuropathology

Epileptologists, neurosurgeons, and neuropathologists work together to produce the best results when it comes to the histopathology evaluation of brain tissue samples from epilepsy surgery. Nonetheless, the neuropathology laboratory must supervise the standardization of brain tissue procurement from any neurosurgical procedure. Standard operating procedures (SOPs) for the neuropathology workup, which include the examination, distribution, and handling of brain tissue that is epileptogenic, have been created by the ILAE. These standard operating procedures (SOPs) are designed to reduce sampling errors, guarantee optimal histological assessment, and facilitate research and brain banking endeavours(41).

Long-term tissue storage and archiving have become even more important with the development of novel molecular assays, such as those that test for mutations in the SLC35A2 gene or the mTOR signalling pathway in focal cortical dysplasia (FCD) or the BRAF V600E and IDH1 variants in low-grade epilepsy-associated tumors (LEAT)(42). After performing previous epilepsy procedures on patients, doctors are more likely to request additional tissue sample testing or follow-up studies. Using advanced frozen storage facilities, meticulous documentation, and procedures for microscopic analysis of frozen samples will increase the

diagnosis accuracy. The current classification systems require that histopathology reports match anatomical characteristics and orientation precisely to make a histological diagnosis(43).

In the first revision of the consensus classification of FCD by the international community, an integrated and multilayered diagnostic methodology was recognized. The system offers a detailed genotype-phenotype relationship for an exact FCD subtype by supplementing the one-layer histopathological diagnosis with additional diagnostic results from techniques like MRI and genetic data. When patients do not recover from surgery and this moves the focus of treatment toward genetic mosaicism as a therapeutic target, or when histopathology reports do not explain or correlate with the clinical picture because samples are incomplete or accessory stainings are lacking, there will only be an enhanced need for an integrated approach. These scenarios could result in a decline in neurosurgical resections caused by thermocoagulation or laser ablation procedures(44).

During a postsurgical patient management conference, which the supervising epileptologist should arrange for the patient, the integrated diagnosis will be put together. Further, this conference should also include a fully integrated multidisciplinary review of all the available diagnostic results to come up with the most accurate and effective patient management plan.

Management

Managing focal epilepsy involves a strategic approach to treatment aimed at identifying the underlying cause and specific seizure type. Benign forms of focal epilepsy may resolve spontaneously without requiring ongoing treatment. When initiating therapy, it is essential to consider factors such as the type of seizure, epilepsy syndrome, patient demographics (age, gender, race), and any existing medical conditions. Monotherapy, using a single anti-seizure medication (ASM), is preferred whenever possible, with a gradual titration from a lower starting dose unless urgency dictates otherwise. According to guidelines from the National Institute for Health and Care Excellence (NICE), first-line treatments for focal seizures include medications like levetiracetam or lamotrigine, followed by options such as carbamazepine, oxcarbazepine, zonisamide, and lacosamide. Second-line therapies, including sodium valproate, brivaracetam, eslicarbazepine acetate, perampanel, and pregabalin, are considered if initial treatments prove ineffective(45). Special considerations are given for pregnant or lactating women in choosing appropriate medications. Regular individual assessments are crucial to assess the potential for seizure recurrence if ASM

withdrawal is contemplated after achieving two years of seizure-free status.

In special patient groups, such as women of childbearing age, careful consideration of anti-seizure medication (ASM) effects on hormonal contraceptives is essential. Certain ASMs can reduce the effectiveness of hormonal birth control methods, while estrogen-containing contraceptives may impact the efficacy of lamotrigine. Pre-pregnancy planning should address these concerns to optimize pregnancy outcomes(46). Levetiracetam and lamotrigine are associated with lower rates of major congenital malformations compared to other medications. Additionally, available data suggest that lamotrigine does not significantly affect neurodevelopmental outcomes, while levetiracetam and topiramate appear to carry a low risk based on current knowledge, though more research is needed(47).

For elderly patients with epilepsy, treatment considerations include changes in pharmacokinetics, polytherapy challenges (involving both anti-epileptic and non-epileptic drugs), and increased susceptibility to adverse effects. Studies have shown that lamotrigine and gabapentin may be better tolerated than immediate-release carbamazepine in newly diagnosed cases of geriatric epilepsy(47).

Non-drug therapies and supportive care play crucial roles in managing focal epilepsy, particularly for patients who do not respond adequately to medication. These interventions include epilepsy surgery, vagal nerve stimulator implantation, ketogenic diet, neurostimulation techniques, and palliative surgical options(48).

Epilepsy surgery becomes an option for approximately thirty-five per cent of individuals with focal-onset seizures who do not achieve satisfactory control with anti-seizure medications (ASMs). The most common site for epilepsy surgery is the mesial temporal lobe, specifically targeting the amygdalohippocampal region. Surgical procedures aim to either cure or palliate seizures. Selective amygdalohippocampectomy, a less invasive procedure with comparable seizure control outcomes, is suitable for patients with evident hippocampal sclerosis. Structural lesions like cavernous malformations or benign tumours may be treated with lesionectomy(49). Hemispherectomy is recommended when one hemisphere is significantly affected and the epileptogenic zone is well lateralized but extensive within that hemisphere(50). Advancements in minimally invasive neurosurgery techniques, such as stereotactic radiosurgery, MR-guided laser interstitial thermal therapy, and stereotactic intracerebral EEG-guided radiofrequency thermocoagulation, have improved safety and efficacy for delicate brain regions(51).

Conclusion

Clinical features, diagnosis problems, and therapeutic options of focal epilepsy have been mostly clarified by the gigantic efforts of clinicians and researchers. During the past years, one-size-fits-all concepts are outmoded by more tailored concepts, taking into account different symptoms and comorbidities linked to focal epilepsy. These pathologies often become difficult to diagnose and treat due to their very diverse and changeable symptoms. Despite these challenges, advances in neuroimaging and neurodiagnostic approaches have enhanced the precision of detecting and diagnosing focal seizures. Treatment for focal epilepsy has evolved also, placing greater emphasis on individualized therapeutic strategies. While ASMs remain one of the mainstays of management, new treatments in the form of surgical procedures and neuromodulation hold new hope for patients with drug-resistant epilepsy. Furthermore, recent genetic discoveries are providing the opportunity for new drugs that could improve treatment response and the quality of life of patients.

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