



Under the Auspices of Indian College of Physicians, Academic Wing of Association of Physicians of India



Monograph

Epilepsy

Editors
Rajesh Shankar Iyer
Mugundhan Krishnan



Contents

1. **Epilepsy: Past, Present, and Future** 1
   Haseeb Hassan

2. **Epilepsy Classification: Seizures and Syndromes** 9
   Ajith Cherian, Divya KP

3. **Epilepsy Mimics** 18
   Suvasini Sharma, Harsh Patel

4. **Epilepsy Diagnosis** 26
   Shiva Kumar R

5. **Approach to the First Episode of Seizure** 47
   Rajesh Shankar Iyer

6. **Epilepsy Pharmacotherapy: The Anti-epileptic Drugs** 51
   Mugundhan Krishnan

7. **Epilepsy and Women** 67
   Neeraj N Baheti, Atma Ram Bansal

8. **Drug-resistant Epilepsy** 76
   Rajesh Shankar Iyer

9. **Status Epilepticus: The Current Status** 86
   Ramshekhar N Menon, Ashalatha Radhakrishnan

10. **Epilepsy Surgery** 104
    Biji Bahuleyan

4
CHAPTER

Epilepsy Diagnosis

Shiva Kumar R

INTRODUCTION

Various studies have shown that a significant proportion of epilepsy diagnosis made by nonspecialists (like general practitioners and physicians) are incorrect leading to physical, psychosocial, and economic implications for the patient along with unwanted investigations and exposure to antiseizure medications.[1-3] Diagnosis of epilepsy is difficult in the early stages, especially, if one does not have eye witness. Diagnosis of epilepsy is even more difficult in children with a learning disability and in elderly with multiple comorbidities.

An epilepsy specialist (epileptologist) has been defined as a trained doctor with expertise in epilepsy as demonstrated by training and continuing education in epilepsy, peer review of practice, and regular audit of diagnosis. Epilepsy must be a significant part of their workload (equivalent to at least one session a week) in their clinical practice.[4]

CLINICAL EVALUATION

One of main goals in the clinical evaluation of a person suffering from epilepsy is to identify the correct seizure type and to identify the correct epilepsy syndrome for appropriate selection of medications and prognosis. Commonly used terms in epilepsy are described in table 1. Recently, the International League Against Epilepsy (ILAE) updated seizure classification[5,6] and is described in detail elsewhere.

Important questions one has to answer during the diagnosis of epilepsy are:

- Are the paroxysmal events epileptic seizures?
- If epileptic, what type of epileptic seizures? Any specific precipitating and predisposing factors?
- What is the epileptic syndrome or epileptic disease?
- What is the cause (etiology)? Is there a treatable underlying cause?
- Disability associated with epilepsy. For example, driving, education, marriage, fertility, etc.

JAYPEE BROTHERS

TABLE 1: Commonly used terms in epilepsy

Term	Definition
Seizure	Seizure is an event caused by abnormal, excessive, and hyper-synchronous discharge from a group of neurons in the brain ("epileptic focus")
Epilepsy syndrome	Epileptic disorder characterized by a cluster of signs and symptoms occurring together, including seizure type, precipitating factors, age of onset, and severity
Drug-resistant epilepsy	Failure of adequate trials of two tolerated, appropriately chosen, and administered (at least 6 months) anticonvulsant drug (whether in monotherapy or in combination) to achieve seizure freedom

CLINICAL HISTORY

Diagnosis of epilepsy is almost always based solely on detailed clinical history. History should be obtained carefully from the patient, family member, and the available eye witnesses. In simple partial seizures, conscious patients can describe most of the details occurring during the seizures. However, if consciousness is impaired, history obtained from the eye witness or the family member is very important.

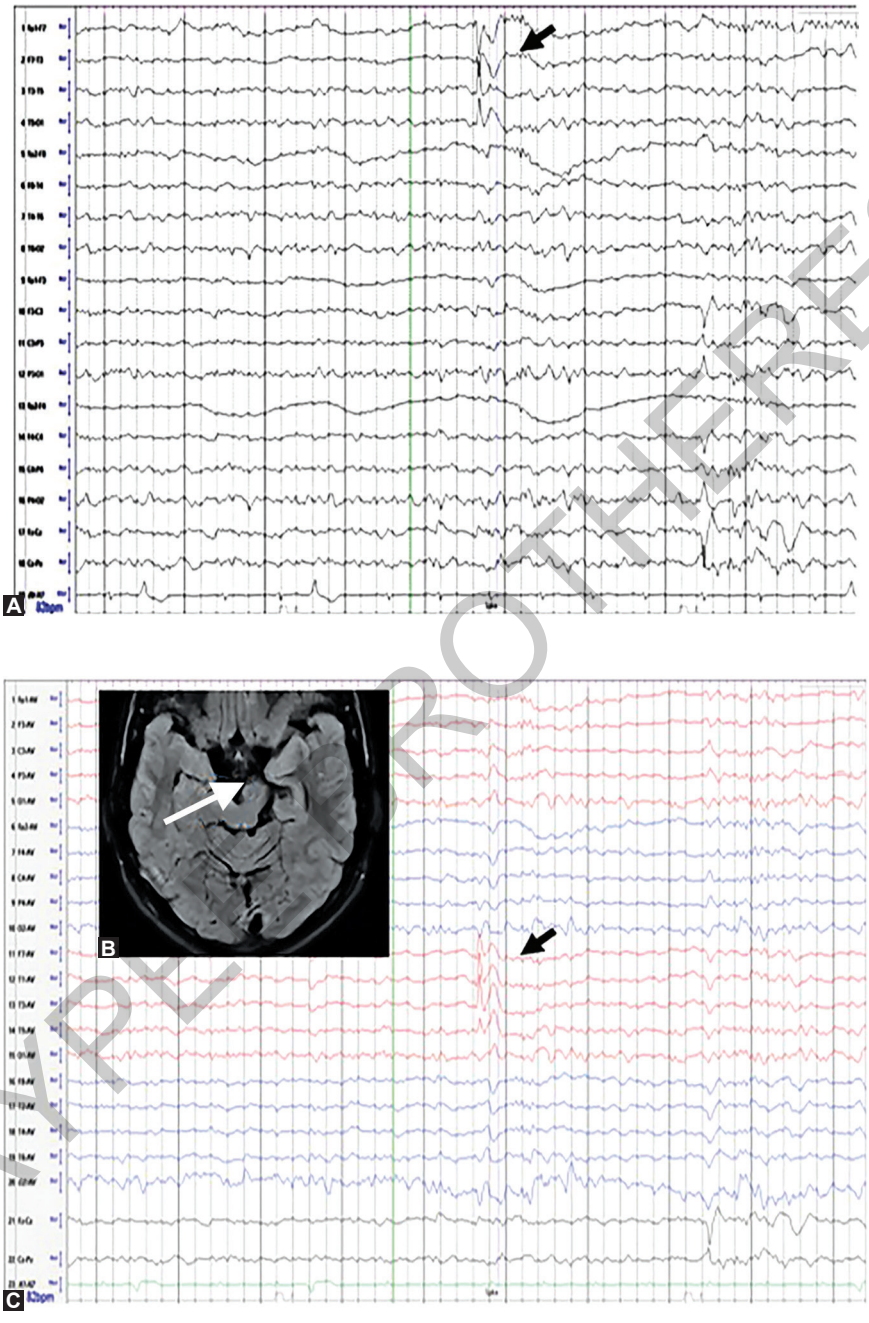
Sometimes, the diagnosis is easy based on the details provided by the patient or the eye witness. However, in situations, where clinical details are not available or inadequate, one has to enquire for other details like precipitating factors, circumstances leading to attacks, and for associated signs like incontinence, tongue bite, fractures, and joint dislocations. More difficult cases need video-electroencephalography (video-EEG) documentation.[7,8] Recording of events on the mobile phones and camcorders at home has reduced the need for video-EEG monitoring in recent times. Figure 1 shows video-EEG recording in a 34-year-old female presenting with episodes of confusion lasting for a minute without any automatisms, motor and sensory manifestations for about 2 years.

"Reflex seizures" (which are the result of sensory stimulation caused by the environment) are triggered by visual stimuli (flashing lights or rapidly changing or alternating images as in clubs, around emergency vehicles), sunlight, reading, hot water, eating, and music. Figure 2 shows a video-EEG recording in a boy to document jerks noted while playing a game on mobile phone.

A person is considered to have epilepsy, if they meet any of the following conditions:[5]

- At least two unprovoked (or reflex) seizures occurring greater than 24 hours apart
- One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years

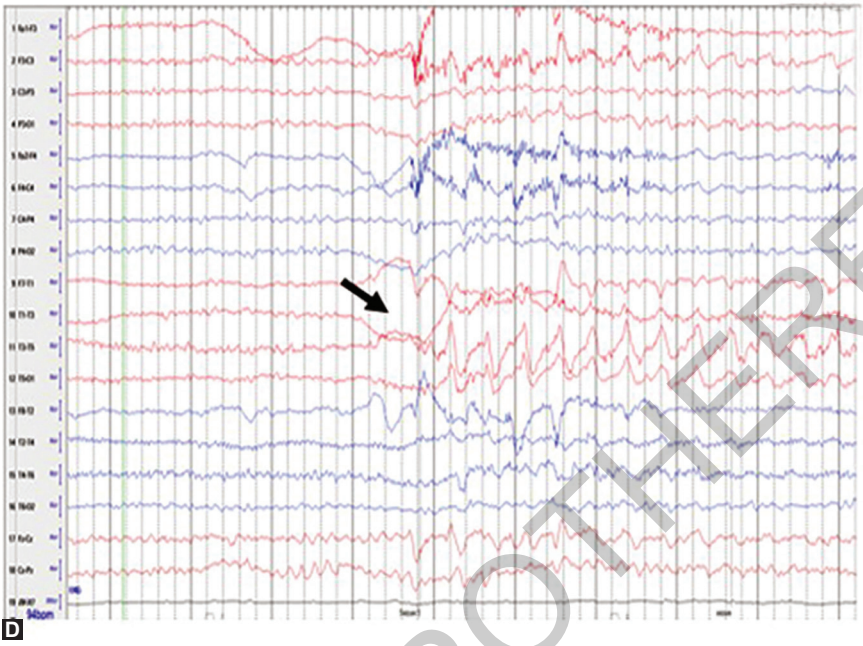
JAYPEE BROTHERS



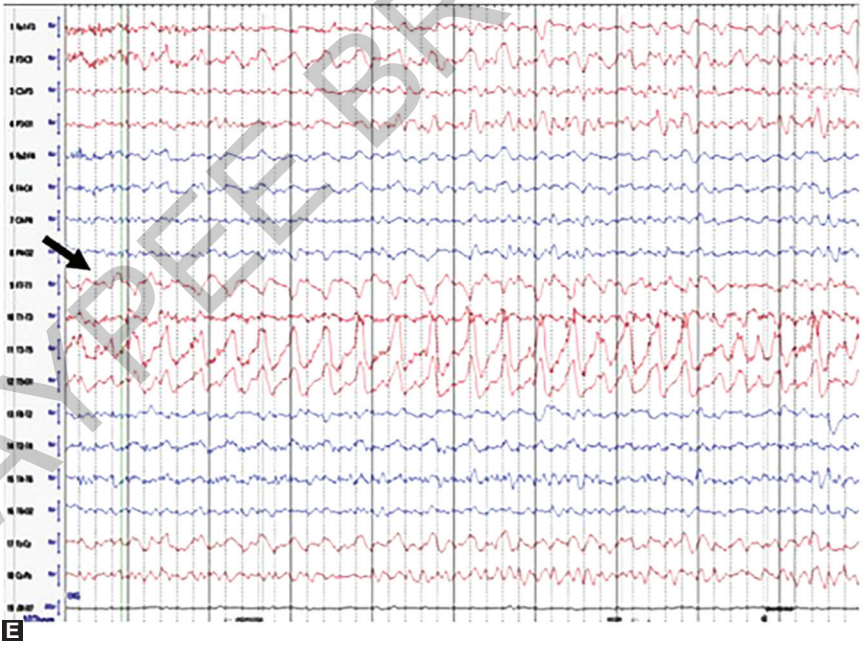
Continued

JAYPEE BROTHERS

Continued



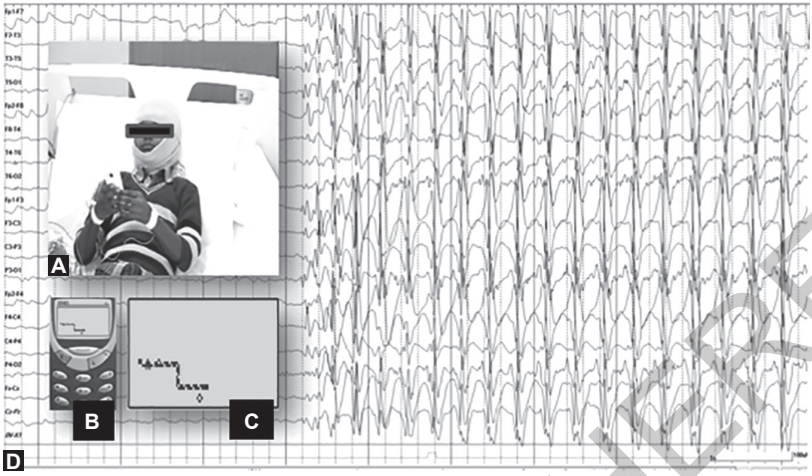
D

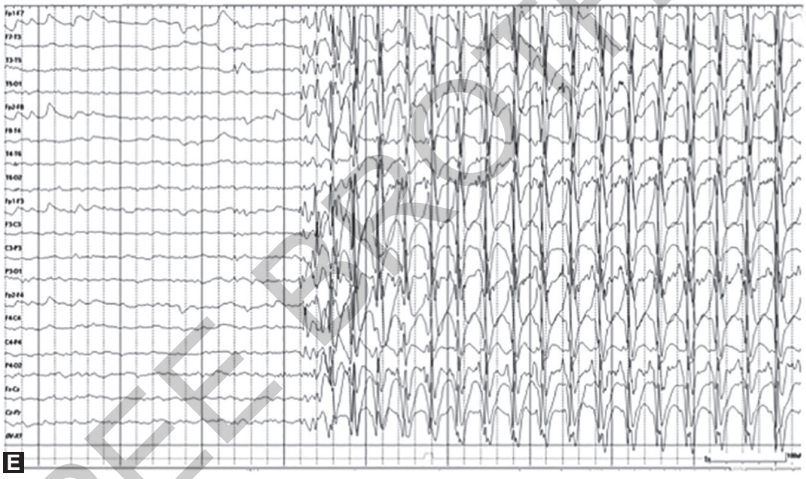


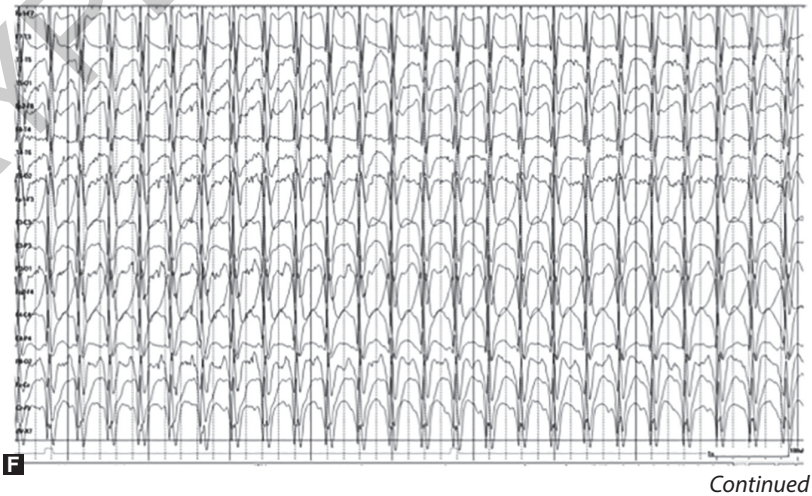
E

FIG. 1: Video-EEG in a 34-year-old lady with episodic confusion. EEG **(A and C)** showing left temporal sharp wave (pointed arrows). MRI **(B)** axial FLAIR sequence showing left hippocampal volume loss with signal changes (typical of mesial temporal sclerosis). EEG during a seizure **(D)** showing evolving ictal pattern over the left temporal region

JAYPEE BROTHERS







Continued

JAYPEE BROTHERS

Continued



FIG. 2: Video-EEG **(A)** in a boy done to document jerks noted while playing a "snake game" on Nokia mobile phone **(B and C)** showing rhythmic jerks in the neck and limbs. EEG during the jerks (**D, E, F and G**) showing 3 Hz generalized frontally dominant spike and wave discharges

- Diagnosis of an epilepsy syndrome
- Epilepsy is considered to be resolved for individuals who had an age-dependent epilepsy syndrome, but are now past the applicable age or those who have remained seizure-free for the last 10 years with no seizure medicines for the last 5 years.

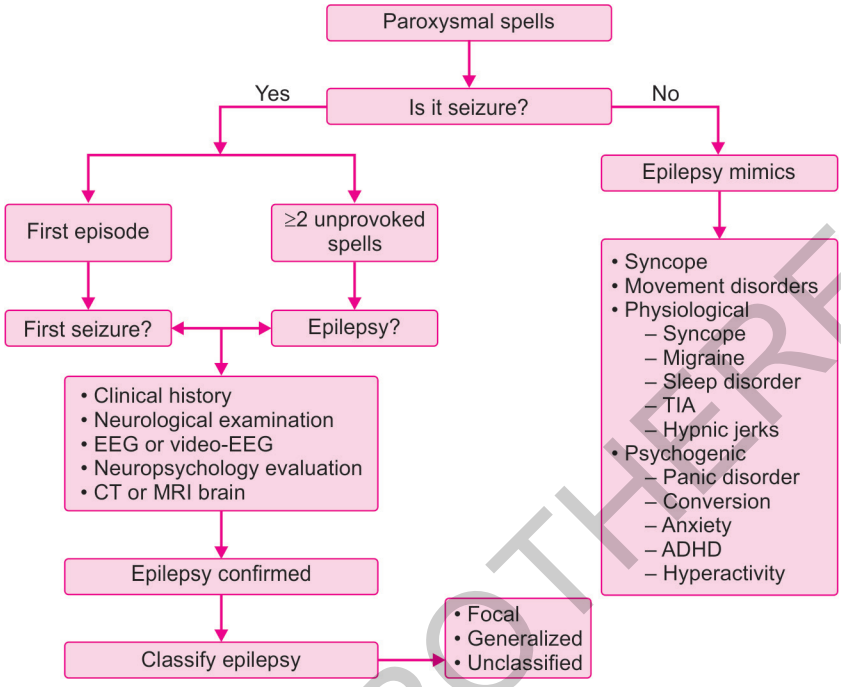
"That's It!" Phenomenon[9]

At times, it is necessary to ask the eye witness or the family member to imitate and physically demonstrate the events for clarification. Sometimes, it is necessary for the physician or a neurologist to imitate and demonstrate physically or when in doubt, to show video-EEG recorded examples of different epileptic or nonepileptic seizures in order to confirm the paroxysmal event as seizures: the "that's it!" phenomenon.

Description of Seizures: Seizure Semiology

Once we have confirmed that the paroxysmal event is genuinely epileptic, the next step is to define the type of seizure or seizures, which is mandatory for the correct diagnosis and management (Flowchart 1). A detailed description (seizure semiology) of what happens to the patient before a seizure (prodrome and aura), during the seizure (ictus or ictal), and after the seizure (postictal) is very important. Video recording of the events at home will be valuable for correct description of seizure semiology.

JAYPEE BROTHERS



EEG, electroencephalography; CT, computed tomography; MRI, magnetic resonance imaging; TIA, transient ischemic attack; ADHD, attention-deficit hyperactivity disorder.

FLOWCHART 1: Algorithm for epilepsy diagnosis and management

Manifestations of seizures range from the dramatic events of a generalized tonic-clonic seizure (GTCS) to the mild flickering of the eyelids or unawareness or automatisms of the mouth. Minor events also called as small seizures by the patient or family members are often overlooked in the history and are in fact more important than a GTCS in the diagnosis of epilepsies. The same patient may suffer from different types of minor and major seizures, independently or evolving from one to the other.

People with epilepsy are unlikely to report minor seizures because they do not appreciate their significance

Physician's responsibility is to detect minor seizures and evaluate them.

The examiner must note the following details in seizure history:

- Age of onset of first seizures along with detailed description of the first event[10]
  - Age of onset is diagnostically useful as many causes of epilepsy and most specific epilepsy syndromes are age related
- Detailed note of different types of seizures the patient has experienced (for example: in juvenile myoclonic epilepsy presenting with GTCS, a detailed history should be taken to uncover previous myoclonic jerks and absence seizures)[11,12]

JAYPEE BROTHERS

- Age of onset, frequency, and evolution of seizures over time should be determined
  - Evolution of symptoms may also suggest progression of the underlying pathophysiological process (for example: enlarging epileptogenic lesion such as neoplasm or degenerative disease)
- Antiseizure drug history:
  - Complete list of all medications tried in the past
  - Highest doses and the length of time each medication tried
  - Efficacy and side effects of each medication
  - Reason for termination of antiseizure medications should also be noted.

Improper use or unnecessary termination of effective drugs is a frequent cause of apparent medical intractability (pseudorefractory epilepsy).

Prodrome

- Presence of prodrome and aura should be determined in every epilepsy patient
- Prodrome is a preictal phenomenon and is not a seizure. Prodrome is a subjective clinical alteration (e.g., ill-localized sensation or agitation) that precedes the onset of an aura and epileptic seizure, but does not form part of it.

Aura

- Aura is a subjective ictal phenomenon that may precede an observable seizure. Rarely auras can occur after seizures (postictal auras)
- Consciousness is preserved during aura and one is aware of the surroundings
- Auras can be in the form of olfactory, visual and auditory hallucination, lightheadedness, Deja vu, abnormal taste, abdominal sensation, and indescribable sensation
- Duration of aura (varies from few seconds to more than 5 minutes) and the consistency with which it precedes the seizure should be noted
- Auras can occur in isolation without any seizure (only auras = simple sensory seizure)
- Often presence of aura indicates that the seizure is focal in origin
- Once recognized as a reliable warning, auras and prodromal symptoms often provide an opportunity for the patient to avoid injury or embarrassment during an epileptic attack.

Ictal Phase

The clinical manifestations during a seizure are known as ictus and have to be described in detail from the onset to the end by a reliable eye witness. The description should include temporal sequence of any arrest of movement, autonomic changes and alteration in consciousness, the part of the body and

JAYPEE BROTHERS

the side involved in jerks, or tonic or clonic movements. Degree of consistency from one seizure to another is very important in seizure description (stereotypy). Based on clinical manifestations and EEG findings, seizures are classified as focal (also called as partial) and generalized.

Generalized Seizure (Primary or Secondary)

In generalized seizures consciousness is impaired at onset due to simultaneous involvement of both cerebral hemispheres and with bilateral motor manifestations. EEG changes are bilateral at onset and widespread over both hemispheres (Fig. 3). Generalized seizures may be convulsive or nonconvulsive. Generalized seizures may be primary or secondarily generalized. **Primarily** generalized seizures or *idiopathic* are generalized from the onset. **Secondary** generalized seizures are partial (focal) at onset and then spread over both hemispheres triggering a generalized fit.[12,13]

Focal (Partial) Seizure

A seizure is partial when the initial clinical and electrographic manifestations indicate an origin in one cerebral hemisphere (Fig. 4). What happens to the person during the seizure depends on part of the brain involved during a seizure. Depending on impairment of consciousness focal seizures are classified as simple and complex partial seizures.

- Simple partial seizures may manifest with motor signs, somatosensory or special sensory symptoms, autonomic signs or symptoms, or with

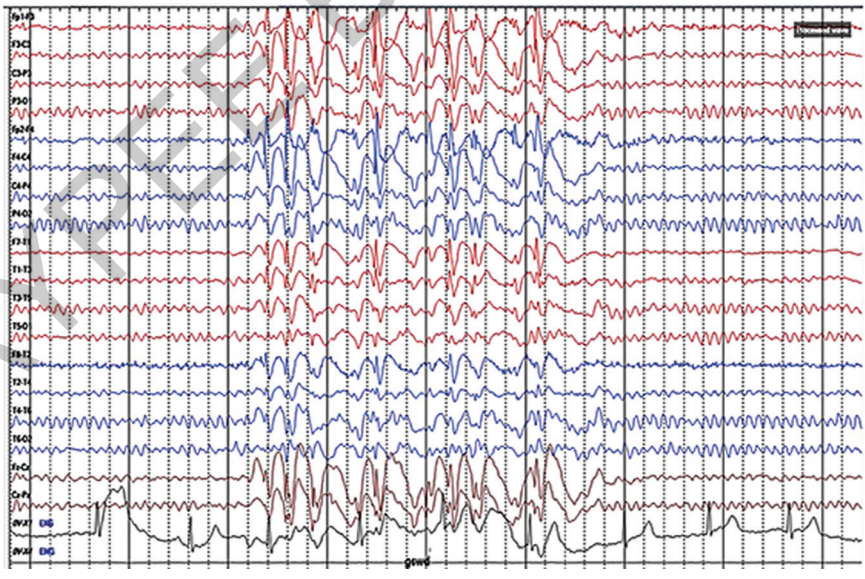


FIG. 3: Electroencephalography of a 10-year-old girl with poor academics showing generalized atypical, fast frontally dominant 3.5–4 Hz spike, and wave discharges suggestive of primary generalized epilepsy

JAYPEE BROTHERS

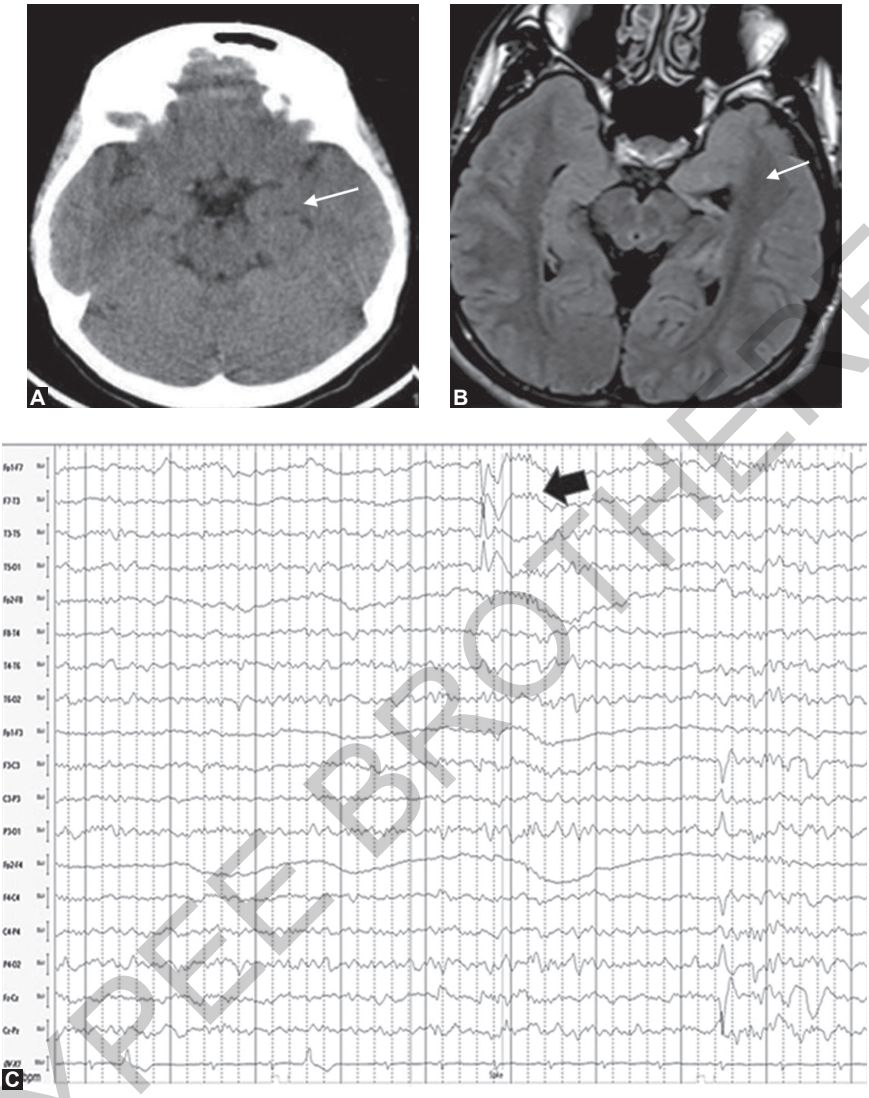


FIG. 4: A 25 year old girl with febrile seizures in childhood and medically refractory focal (complex partial seizures) epilepsy. **A,** Computed tomography scan. brain normal. **B,** Magnetic resonance imaging brain shows hyperintense signals in the left amygdala, uncus, and hippocampus with atrophy and dilated temporal horn (hippocampal sclerosis) classical of mesial temporal sclerosis (arrow). **C,** Electroencephalography show left temporal sharp waves (arrow)

psychic symptoms. Somatosensory or special sensory symptoms vary depending on the region of cortical involvement and are generally positive phenomenon. Primary somatosensory seizures are felt as tingling or as pins or needles sensations and can spread (Jacksonian march) along

JAYPEE BROTHERS

regions subserved by the sensory homunculus. Autonomic activity may in the form of goose bumps, flushing, pallor, sweating, and change in heart rate, breathing, and blood pressure.

A Jacksonian seizure is a type of simple focal motor seizure characterized by abnormal movements that begin in one group of distal muscles and progress to adjacent groups of muscles. If these focal motor seizures are unremitting then they are called as epilepsia partialis continua.

Impaired consciousness is defined as the inability to respond normally to external stimuli by virtue of altered awareness and/or responsiveness. Complex partial seizures can evolve either from simple partial seizures or they can begin with impaired consciousness *de novo*. Simple partial seizures that begin at onset are considered as auras and they are generally forgotten as a part of perictal amnesia.

Complex partial seizures can be further classified into seizures with and without automatisms. Automatisms are complex release behaviors that emerge with impairment of consciousness. Automatisms are learned behaviors and can manifest in the form of chewing, speaking, gesturing, walking, or making facial expressions.

Postictal Phase

Following a seizure, the person enters into the postictal state. Various postictal phenomenons are frequently noted and include fatigue, drowsiness, headache, confusional state, Todd's paresis, and psychosis. Duration of postictal period may vary from few minutes to days and should not be confused with ictal duration, which rarely lasts for more than 40–60 seconds in generalized seizure and a minute or two in complex partial seizures.

Todd's paresis (Todd's palsy) is focal weakness in a part of the body and typically affects appendages. It usually subsides completely within 48 hours. Todd's paresis may also affect speech, eye position (gaze), or vision. Postictal psychosis and aphasia have lateralizing value in diagnosis of epilepsy.

Other History in Diagnosis of Epilepsy

- Circumstances under which seizures have occurred:
  - Timing of seizures (circadian distribution—nocturnal, on awakening or diurnal)
  - Standing or sitting (helps to differentiate from epilepsy mimics like syncope)
  - At rest or during exercise
  - Possible triggering, precipitating, or facilitating factors (has implications in treatment):
    - Watching television and playing video games (Fig. 2)
    - Exposure to sunlight and flickering lights
    - Sleep deprivation and working in shifts
    - Stress, febrile illness, and fasting during festivals

JAYPEE BROTHERS

    - Missing medications
  - Frequency of seizures:
    - Seizure diary helps in knowing frequency of each type of seizure and assessing epilepsy disability and effectiveness of therapy
- Past medical history—provides clues to etiology:
  - Complications during gestation, birth trauma, postictal intracranial infections, and serious head injury are common causes of epilepsy
  - Febrile seizures or febrile status lasting for more than 30 minutes
  - Development history in children to differentiate between progressive degenerative neurological disorder and a static lesion
  - Medications history
- Social history:
  - Level of education, occupation, and living arrangements
  - Marital status and use of contraceptives
  - Driving
  - Nicotine, caffeine, alcohol, and recreational drug use
- Family history:
  - History of febrile seizures and epilepsy in family (genetic epilepsy with febrile seizure plus)
  - Left handedness in the absence of a family history of sinistrals and raises suspicion of early injury to the left cerebral hemisphere
- Epilepsy related comorbidities:
  - Headache (migraine); depression, suicidal ideations; quality of life in epilepsy (QOLIE)
  - In children-learning disabilities, anxiety, and attention deficit hyperactivity disorder.

GENERAL PHYSICAL EXAMINATION

Detailed general examination helps in finding specific physical signs or malformations that cause epileptic seizures. Evidence for systemic side effects of antiseizure medications may also be noted during examination. For example, phenytoin can cause coarse facial features, hirsutism, gingival hyperplasia, and rickets in children. Simple bedside hyperventilation can trigger absence seizures in children.

- Vital parameters like heart rate, blood pressure, and detailed cardiac examination may help to differentiate convulsive syncope from epileptic seizures
- Dermatological abnormalities—axillary freckling, nevus anemicus and café au lait spots associated with neurofibromatosis; Port Wine stain of Sturge-Weber syndrome; ash-leaf spots, facial sebaceous adenoma, and shagreen patch of tuberous sclerosis
- Funduscopic examination helps to look for retinal abnormalities that may be seen in association with brain malformations or storage disorders

JAYPEE BROTHERS

- Dysmorphic facial and body features provide clues to presence of brain malformations
- Head circumference for micro- or macrocephaly in infants and children
- Auscultation of the head for bruits for vascular malformations
- Abdominal examination for hepatosplenomegaly seen in children with storage disorders.

NEUROLOGICAL EXAMINATION

Neurological examination is often normal in patients with epilepsy. Abnormal neurological findings suggest either diffuse or focal structural or metabolic abnormalities and provide useful localizing and lateralizing information. Specific motor and sensory deficits can be seen with disturbances in the primary cortical regions. Visual field defects indicate lesion in the posterior cortex (posterior temporal and parieto-occipital region).

INVESTIGATION IN THE DIAGNOSIS OF EPILEPSY

Electroencephalography

- Electroencephalography remains the sinlge most noninvasive test in the diagnosis of epilepsy and is often misused
- Overinterpretation of EEG is the most common cause of unwarranted diagnosis of epilepsy
- Unnecessary EEG procedures result in unavoidable expense and inconvenience
- Electroencephalography is not a substitute for good history. But can add value to the diagnosis of epilepsy
- An EEG should be obtained in all patients with epilepsy to provide baseline data that can be used if clinical picture changes
- Electroencephalography can be of help to:
  - Confirm the diagnosis of epilepsy
  - Classify the type of epilepsy and epilepsy syndrome
  - Localization of epilepsy
  - Effectiveness of treatment in epilepsy
  - Predicting the risk of recurrence after first seizure
- Yield of EEG is higher if done within 48 hours of the seizure or epilepsy.[14]

"Normal EEG does not rule out the possibility of epilepsy"

Video-electroencephalography Monitoring in Diagnosis and Classification

- Video-EEG monitoring refers to continuous EEG recorded for a prolonged period with simultaneous video recording of the clinical manifestations

JAYPEE BROTHERS

- Having a correlation of the recorded behavior (video) and the EEG activity, the diagnosis of seizures or nonepileptic seizures can be made definitely in nearly all cases
- Video-EEG helps to classify seizure types, assess seizure frequency, identifies seizure triggers, and localize seizure onset in refractory focal epilepsies
- Additional physiologic parameters like electrocardiogram, heart rate, electrooculogram, electromyogram, and respiratory function can be monitored, which helps in differentiating physiologic nonepileptic disorder associated with paroxysmal clinical events
- Video-EEG monitoring is essential in determining the localization of the epileptogenic zone (i.e., the site of seizure onset and initial seizure propagation) in adult patients being considered for surgical-ablative procedures.[14]

"When clinical information and standard investigations do not allow a confident diagnosis, referral for the recording of attacks should be considered."

Ambulatory Electroencephalography

- 24–72 hours of EEG recorded in a special recorder worn over the wrist
- During the test, one has to keep a diary of what you do during the day and if you have had any seizures or other symptoms.

Neuropsychological Tests

- To evaluate memory and language functions and help to lateralize to right or left hemisphere
- Help lateralization and localization of areas of brain that are abnormal
- Baseline assessment before like epilepsy surgery for its risk on memory and cognition.

Neuroimaging in Epilepsy[15]

Imaging of brain is indicated in almost all patients suspected of having seizures and aid in syndromic and etiological diagnosis. Scans must be interpreted in the context of entire clinical situation. A specialist in neuroimaging, who has training and expertise in the neuroimaging of epilepsy, must review the images.

- Computed tomography (CT) scan brain—can only detect gross lesions and calcifications
- Magnetic resonance imaging (MRI) brain (ideally 1.5 Tesla and 3 Tesla)—imaging modality of choice:
    - Superior to CT scan in identifying lesional epilepsies (hippocampal sclerosis, malformations of cortical development, vascular malformations, tumors, granulomas, trauma and strokes) (Figs 5 and 6)

JAYPEE BROTHERS

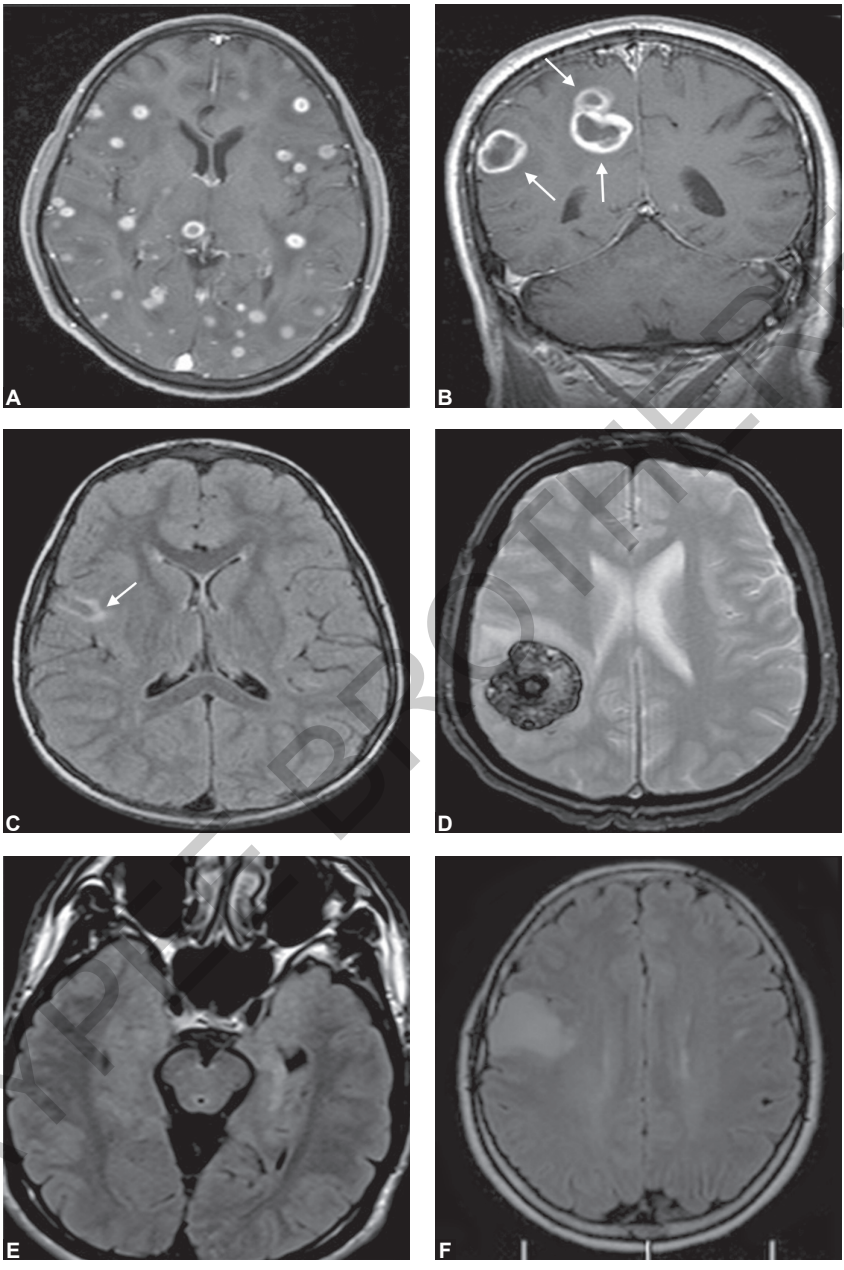


FIG. 5: **A,** Magnetic resonance imaging (MRI) contrast showing ring enhancing lesions (cysticercosis); **B,** MRI contrast showing ring enhancing lesions (tuberculomas); **C,** MRI showing malformations of cortical development (dysplasia); **D,** MRI showing right frontal cavernoma; **E,** MRI showing volume loss and left hippocampal hyperintensity; **F,** MRI showing focal cortical dysplasia in the right frontal

JAYPEE BROTHERS

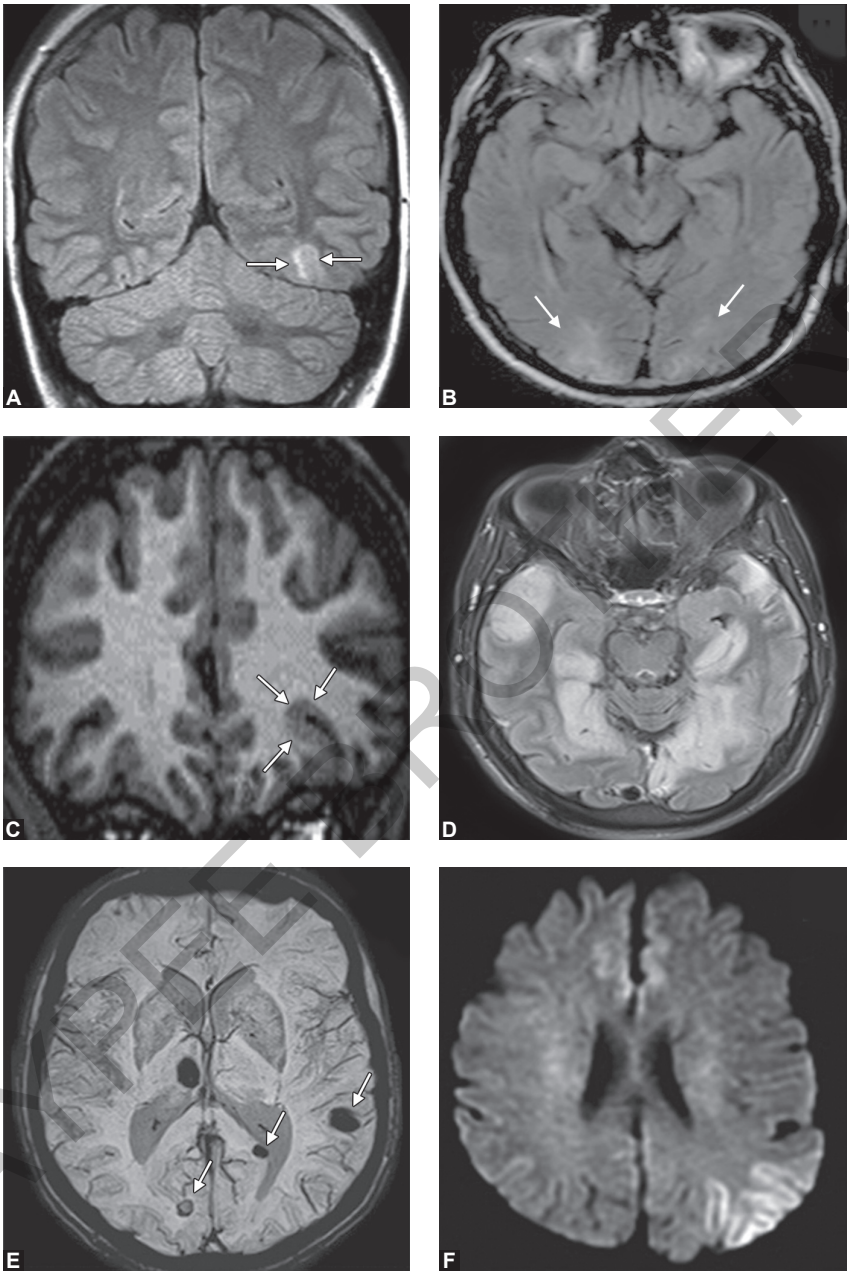


FIG. 6: A, coronal fluid-attenuated inversion recovery (FLAIR) showing focal cortical dysplasia; **B,** axial FLAIR showing bilateral occipital gliosis; **C,** coronal T1 images showing sulcal depth cortical dysplasia; **D,** coronal FLAIR showing temporal lobe changes in herpes simplex virus encephalitis; **E,** susceptibility weighted imaging showing calcific lesions; **F,** diffusion MRI showing acute left parietal infarct and seizures

JAYPEE BROTHERS

- T1-weighted, T2-weighted, fluid attenuation inversion recovery sequences, three-dimensional coronal and axial sequences, susceptibility weighted images, and T2 relaxometry are usual recommended sequences

- Functional MRI:
  - For localizing motor and sensory cortex and lateralizing language functions (Fig. 7)
- Positron emission tomography (PET) scans:
  - Positron emission tomography scan may be used to locate the part of the brain causing seizures
  - Positron emission tomography scan is usually done in the interictal state and shows hypometabolism in the areas of the brain producing seizures. Ictal PET can show hypermetabolism and can help in localization of seizure focus (Fig. 8).

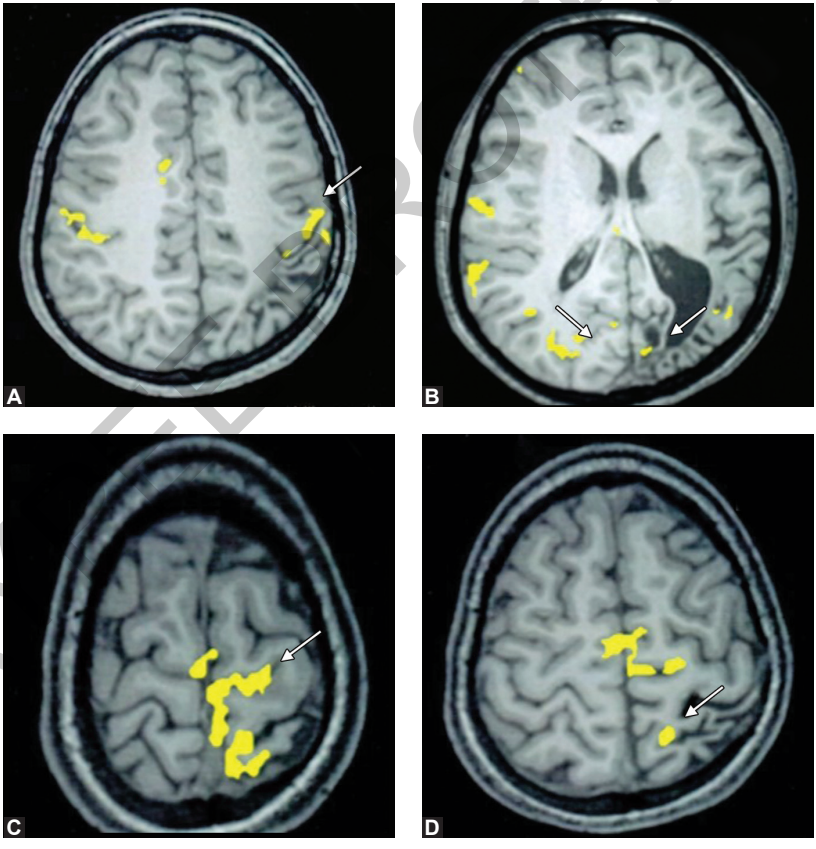


FIG. 7: Functional magnetic resonance imaging images showing blood oxygen level dependent response (yellow maps) **A,** during language **B,** visual cues; **C,** right toe tapping; **D,** right hand motor in a patient with left parieto-occipital gliosis

JAYPEE BROTHERS

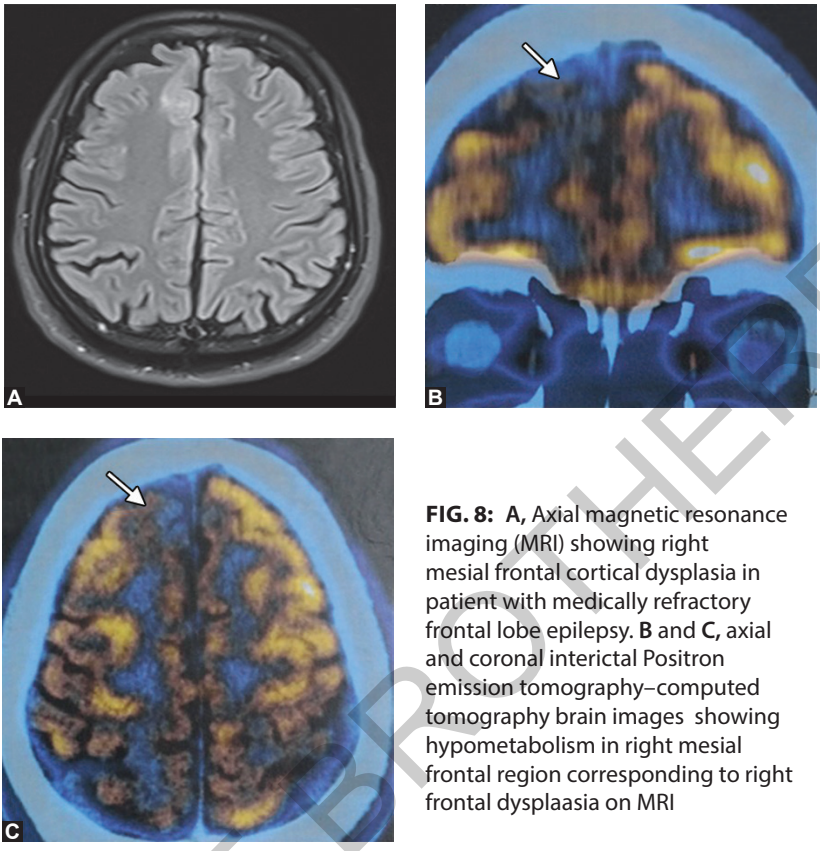


FIG. 8: A, Axial magnetic resonance imaging (MRI) showing right mesial frontal cortical dysplasia in patient with medically refractory frontal lobe epilepsy. **B** and **C,** axial and coronal interictal Positron emission tomography–computed tomography brain images showing hypometabolism in right mesial frontal region corresponding to right frontal dysplaasia on MRI

- Single-photon emission computed tomography (SPECT):
  - Functional nuclear imaging technique performed to evaluate regional cerebral perfusion, which is linked to neuronal activity. Pre- and postseizure SPECT scan helps in detection and resection of seizure focus in drug-resistant epilepsy (Fig. 9)
- Magnetoencephalography (MEG):
  - In the evaluation of epilepsy, MEG is used to localize the source of epileptiform brain activity, which most likely is the source of seizures
- Wada test (Amytal study):
  - Also known as the intracarotid sodium amobarbital procedure (ISAP) where sodium amytal or propofol is injected in to the right or left internal carotid artery by placing a catheter and each hemisphere is put to sleep and the contralateral hemisphere, if tested, for memory and language by a neuropsychologist
  - For localization of memory and to lateralizes the language function.

JAYPEE BROTHERS

Available at all medical bookstores
or buy online at www.jaypeebrothers.com

JAYPEE BROTHERS
Medical Publishers (P) Ltd.
www.jaypeebrothers.com
Join us on facebook.com/JaypeeMedicalPublishers

Shelving Recommendations
MEDICINE, NEUROLOGY

ISBN 978-93-86261-42-7