Chapter 8: Neuropsychiatric aspects of epilepsy

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8.1. Introduction

a. An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive or synchronous neuronal activity in the brain.

b. Epilepsy is a disorder of the brain characterized by an enduring predisposition to generate epileptic seizures; it is also characterised by the neurobiologic, cognitive, psychological, and social consequences of this condition. The definition of epilepsy requires the occurrence of at least one epileptic seizure. (ILEA, 2017)

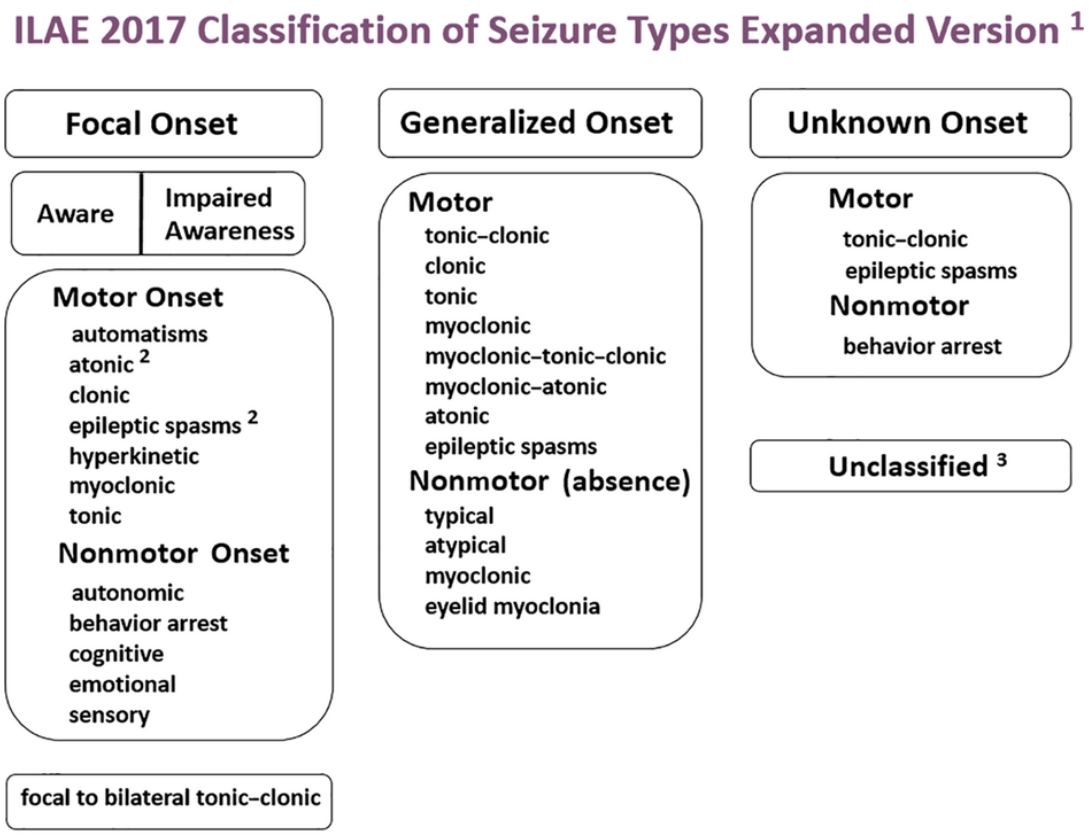
c. Epilepsy is one of the most common neurological disorders with more than 50 million people being affected worldwide.

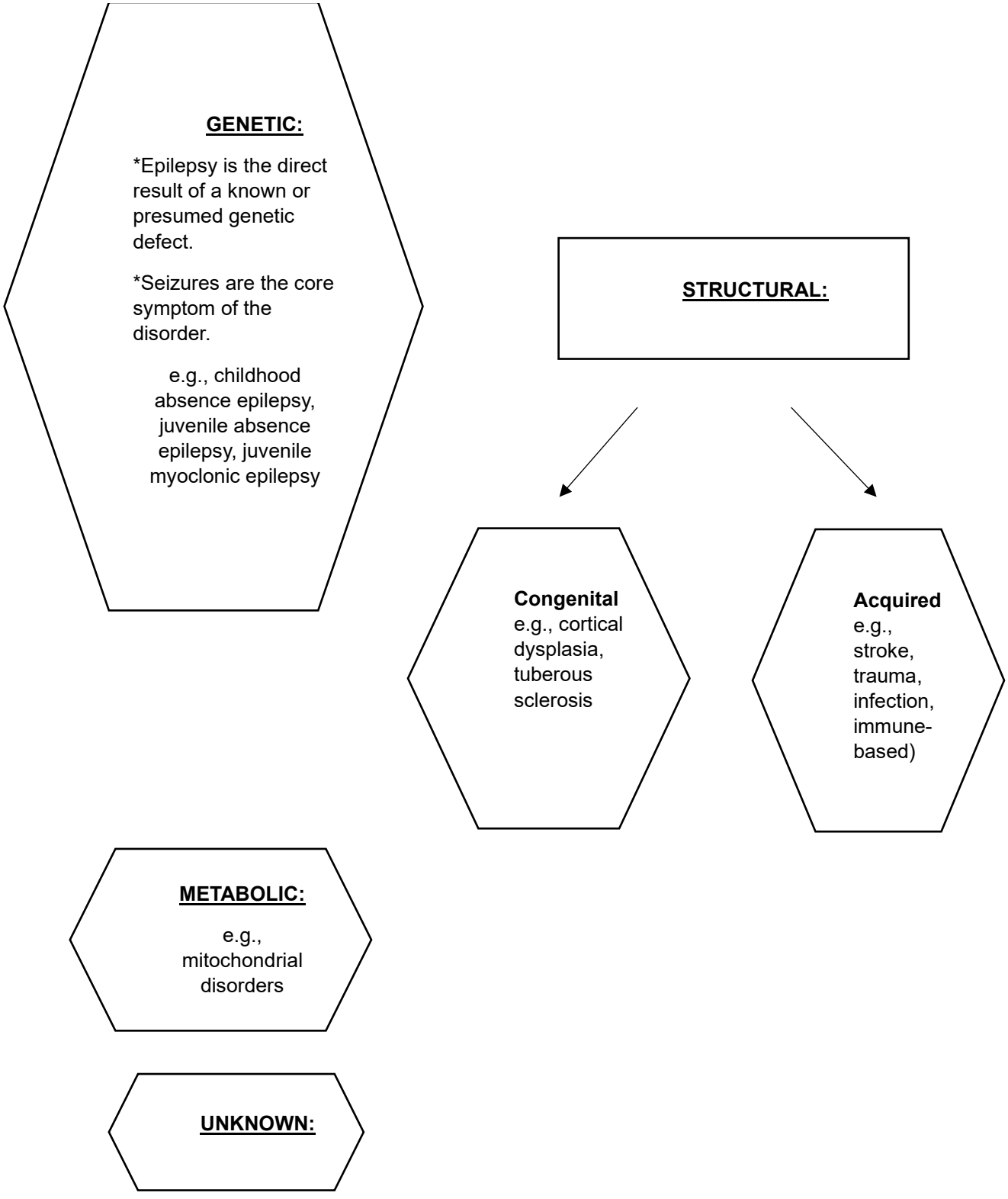
The classification of epilepsies according to the International League Against Epilepsy (ILAE) was updated in 2017. The classification approach is now an operational/practical classification. The classification system has three levels: Seizure type (see Figure 23), Epilepsy type and Epilepsy syndrome. Changes to the diagnostic classification include:

- ❖ The term 'complex' as in 'complex partial' has been removed from the new classification and is replaced by 'focal impaired awareness'. Whereas 'simple partial' is now defined as 'focal aware'.
- ❖ Aura has been removed in the new classification; it is now considered part of the seizure as there are associated changes on EEG.
- ❖ The term convulsion has been removed as well, as it implies a motor component.
- ❖ Aware versus impaired awareness added, and loss of consciousness has been removed.
- ❖ A separate subtype is focal to bilateral tonic-clonic seizures, which replaces the prior term 'secondarily generalized tonic-clonic'.

In addition to characterizing, and therefore classifying the type of seizure and epilepsy, an attempt to understand cause is helpful. The majority of seizures fall into genetic, structural (congenital or acquired), and metabolic groups. A significant number, though, will remain of unknown cause.

Figure 23: Classification of seizure types according to the International League Against Epilepsy (ILAE) (Fisher et al., 2017)




GENETIC:
*Epilepsy is the direct result of a known or presumed genetic defect.
*Seizures are the core symptom of the disorder.
e.g., childhood absence epilepsy, juvenile absence epilepsy, juvenile myoclonic epilepsy
STRUCTURAL:
Congenital
e.g., cortical dysplasia, tuberous sclerosis
Acquired
e.g., stroke, trauma, infection, immune-based)
METABOLIC:
e.g., mitochondrial disorders
UNKNOWN:

8.2. Neuropsychiatry and Epilepsy

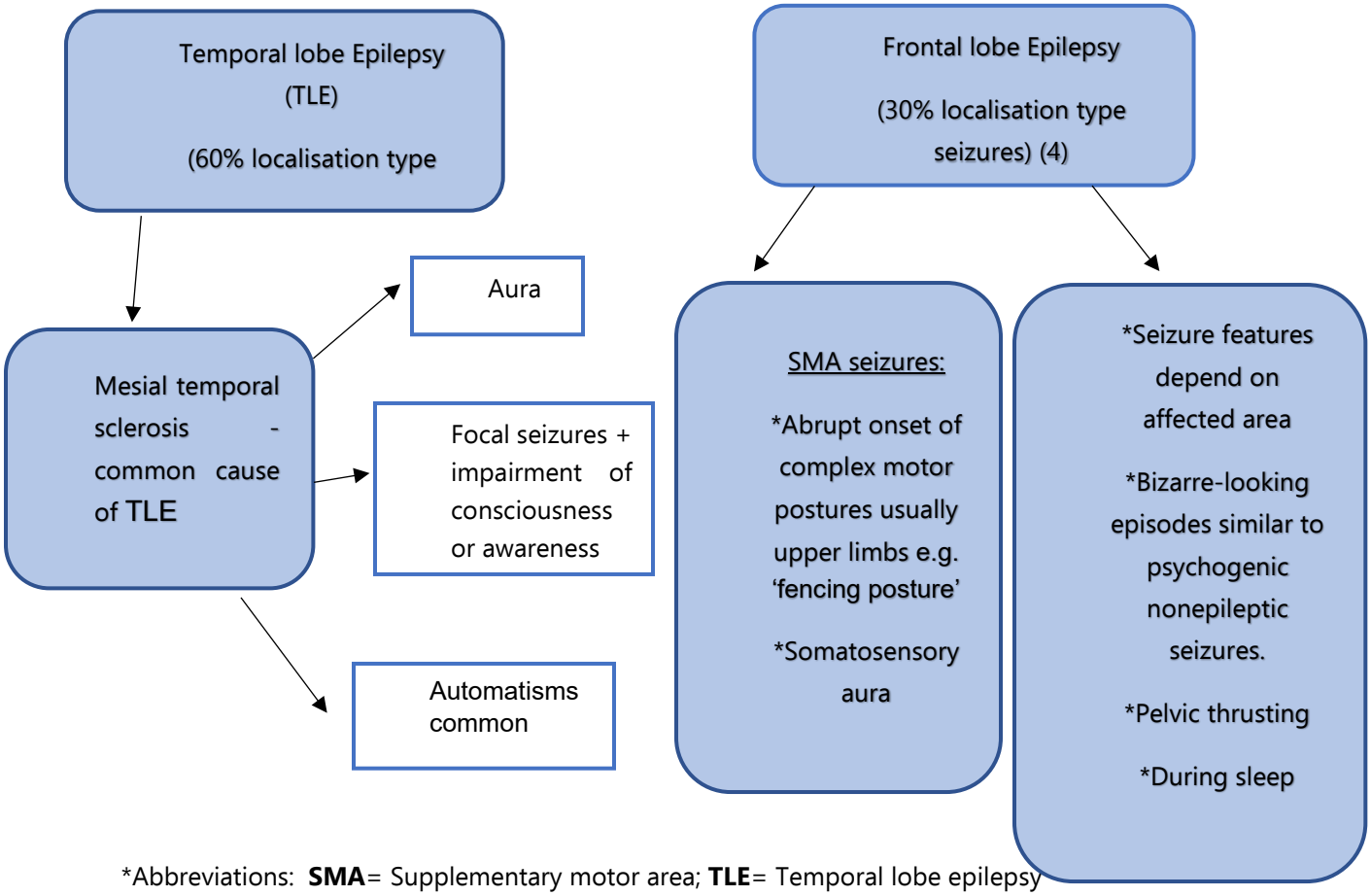
8.2.1. Co-morbidities

Psychiatric comorbidities are overrepresented in people with epilepsy and represent a poor prognosis marker as well as having a major effect on quality of life. Around 30- 50% people with epilepsy experience psychiatric, behavioral, or social difficulties (Lin et al.,2014). Depression is the most frequent psychiatric comorbidity in people with epilepsy (PWE) with lifetime prevalence rates ranging between 30 and 35%.

There is evidence from population-based studies of a bidirectional relationship between epilepsy and neuropsychiatric conditions. For example, not only are PWE at greater risk of developing depression, but patients with depression have a three- to seven-fold higher risk of developing epilepsy (Hesdorffer et al., 2006). Irrespective of the cause and duration, any form of epilepsy can have neuropsychiatric implications. Neuropsychiatric comorbidities, are more prevalent in the following instances:

- Where there is temporal lobe epilepsy
- Where the epilepsy is drug resistant or / and epilepsy is severe with polypharmacy
- In the face of co-morbid substance use and pre-existing psychiatric disorders

Figure 25: Epilepsy syndromes associated with neuropsychiatric symptoms



*Abbreviations: **SMA**= Supplementary motor area; **TLE**= Temporal lobe epilepsy

8.2.2. Psychiatric symptoms related to ictal phases

It is useful to consider neuropsychiatric symptoms related to epilepsy into:

>Pre-ictal,

>ictal,

>post ictal, and

Ictal / seizure-related

>interictal phenomena (Table 12).

NON- Ictal / seizure-

It helps to determine the primary intervention that is required. Pre-ictal, post-ictal and ictal phenomena require improved seizure control.

Inter-ictal neuropsychiatric symptoms are not directly related to the seizure and may thus require additional psychiatric treatment for the specific psychiatric symptom that has emerged.

For each "phase" of seizure phenomenon, it can be helpful to consider the broad categories of Neuropsychiatric Symptoms: Cognitive, Anxiety, Mood / Affective, Psychotic, Sleep / Vegetative.

Table 12: Psychiatric symptoms related to ictal phases.

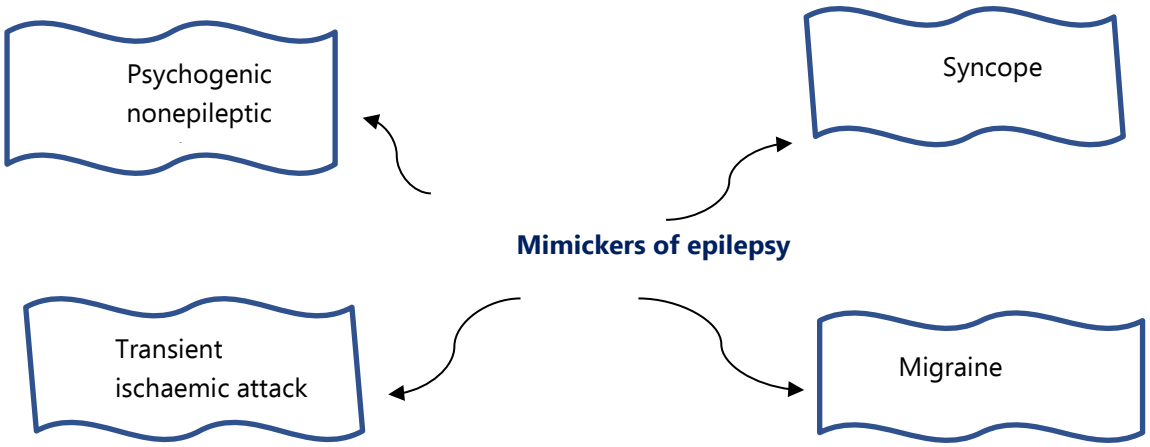
	Cognitive	Anxiety	Mood	Psychosis	Sleep & Vegetative	Other / Somatic
Pre-ictal "prodrome" (hours to days)			Irritability Dysphoria Depression			Headache Malaise
Ictal (including aura)		Ictal anxiety		Hallucinations- often incl non auditory		Relatively Stereo-typed
Post-ictal	Confusion common (<30min)		Anger and aggression common	Preceding lucid period (24 hrs), abrupt onset, agitation, behavioural disturbance	Drowsy	
Inter-ictal	Mild attention, executive function, or memory Dysfunction. Can be Progressive over years	Anxiety common (agora-phobia, GAD, social)	Depression common (irritability & somatic)	SCZ like psychosis: Associated with recurrent postictal psychosis	Hyposexuality common (medication, TLE)	Personality changes controversial

Abbreviations:* **Cogn imp, cognitive impairment; **Esp**, especially; **GAD**, generalised anxiety disorder; **SCZ**, schizophrenia; **TLE**, Temporal lobe epilepsy

8.3. Differential diagnosis of epilepsy

It is important to consider a differential diagnosis for seizure like activity (*Figure 26)*. A notable differential diagnosis for the mental health practitioner is psychogenic non epileptic seizures (PNES).

Figure 26: Mimickers of epilepsy



8.3.1. Psychogenic non epileptic seizures (PNES)

PNES is an important consideration when any of the following are present:

- atypical seizures,
- associated emotional triggers preceding the seizure,
- poor response to adequate anti-epileptic treatment,
- pre-existing psychiatric history, or
- childhood trauma.

It is more common in the 20-40 years age group, with a female to male ratio of 3:1. Care needs to be taken not to over-diagnose this condition. Epilepsy can and does co-exist with PNES (approx. 30%). Inter-specialty input between neurology and psychiatry is the ideal. The gold standard investigation for diagnosis is 24-hour video electroencephalogram (EEG) monitoring. A multidisciplinary approach is vital, especially psychological interventions. Co-morbid psychiatric conditions should also be treated.

Table 13: Features that can help differentiate epileptic vs psychogenic seizures (adapted from R Duncan)

Sign	Epileptic	Psychogenic non epileptic seizures (PNES)
Duration	Usually brief (< 1-2 min)	Usually > 2 mins
Eyes	Usually, open	Often closed
Motor activity	Stereotyped, builds & progresses, synchronized	Variable, wax & wanes, pelvic thrusting, rolling side to side
Vocalization	Uncommon	May occur
Prolonged ictal atonia	Very rare	May occur
Incontinence	Common in convulsive seizures	Less common
Autonomic signs	Cyanosis & tachycardia common in major convulsions	Uncommon
Postictal symptoms	Headache common, confusion, drowsiness	Headache rare, can awaken & be fully orientated.

8.4. Assessment of Epilepsy and Neuropsychiatric Aspects

Epilepsy is a neurological condition and the diagnosis should ideally be made by a neurologist / epilepsy specialist, where available. The diagnosis of epilepsy remains a clinical diagnosis, with the vast majority of seizures being relatively stereotyped. The inclusion of witness history or video footage (nowadays using phones) is crucial, and often more valuable than further special investigations. Normal EEG's do not exclude epilepsy, and structural brain imaging may often not reveal focal changes. These investigations, however, often complete the work-up of cases.

8.4.1. Inter-ictal psychiatric disorders

A range of depressive and anxiety disorders may follow a diagnosis of epilepsy. Anxiety disorders are associated with generalized tonic-clonic seizure (GTCS) and with worse social functioning. Psychotic disorders in Persons with Epilepsy were found to be associated with longer duration of epilepsy (Gurgu et al 2021). CBT and supportive therapies can be very effective, and reduce the need for psychotropic treatment in depression and anxiety (see Choudhary, N. et al. 2024, for example).

The concept of an "epileptic personality" has been rejected. However personality changes have been documented, and these include:

- Hyper-religious: deepening of emotionality with serious, highly ethical, spiritual demeanour.
- Viscosity: particularly detailed, orderly, and persistent in speech and action.
- "Eternal adolescence": labile, suggestibility and immaturity.

Note that many anti-epileptic medications are associated with neuropsychiatric symptoms and must be considered in the differential diagnosis of any treatment-emergent syndromes.

8.4.2. PNES

In patients with suspected PNES, collaborative care between epilepsy specialists and mental health teams can be invaluable: not least because epilepsy and PNES can co-exist. Detailed childhood, personal and psycho-social history assists not only in assessing whether psychological factors are driving epilepsy or PNES, they will guide psychiatric management- ideally this will treat or mitigate the disorder.

8.5. General management principles

Optimise seizure control, refer to neurology for further workup and medication adjustment as indicated. Awareness of the commonly used antiepileptic drugs (AEDs) and their neuropsychiatric sequalae is important (see Table 3). Prescribers should keep potential drug-drug interactions with AEDs in mind when choosing psychotropic medication.

Table 14: Commonly prescribed AEDs & their neuropsychiatric implications (adapted from S Karceski)

Medication:	Mechanism of action	Type of epilepsy (Indication)	Neuropsychiatric indications	NB Drug-drug interactions	Neuropsychiatric Side-effects
Sodium Valproate (metabolised to valproic acid in GIT)	Indirectly increases GABA	Generalised tonic clonic (GTC); Absence	Bipolar disorder (for mania & depression); Aggression,agitation	Valproate can increase levels of TCAs, lamotrigine, quetiapine OCP co-admin can lower Na Valproate levels	Tremor, parkinsonism associated with cognitive decline
Lamotrigine	May affect neurons that synthesise glutamate & aspartate	Focal onset seizures; GTC seizures	Bipolar depression; impulsivity and behavior symptoms in borderline PD	Enzyme inducers (phenytoin, carbamazepine, phenobarbital, estrogen-containing OCPs, rifampin, protease inhibitors) can lower levels of lamotrigine	Neurotoxic side effects: dizziness and somnolence
Carbamazepine	Binds to voltage dependent Na channels	Focal and generalized seizures	Bipolar disorder and chronic pain syndromes e.g., trigeminal neuralgia.	Potent and broad-spectrum inducer of the CYP system	Sexual dysfunction, drowsiness, dizziness, blurred or double vision, lethargy, & headache
Phenytoin	Binds to voltage dependent Na channels	Focal & generalized seizures, status epilepticus Second-line agent for patients with mixed seizures	Nil	Potent inducer of CYP system	Confusion, slurred speech, double vision, ataxia, and neuropathy (with long-term use)

Levetiracetam	Unknown, in animals binds to the synaptic vesicle protein SV2A	Adjunctive therapy for focal-onset seizures Adjunctive therapy in treatingmyoclonic seizures; juvenile myoclonic epilepsy	Nil	Metabolism not related to CYP system	Fatigue, somnolence, dizziness

Co-admin, co-administration; **CYP,** Cytochrome P450**; GABA,** Gamma aminobutyric acid (GABA**); GIT,** gastrointestinal tract; **NA,** sodium; **NB,** important**; OCP,** oral contraceptive pill; **PD,** personality disorder; **SV2A,** Synaptic vesicle glycoprotein 2A**; TCAs,** tricyclic antidepressants.

Key Points

- *Epilepsy is one of the most common neurological disorders with more than 50 million people being affected worldwide.*
- *Seizures are commonly accompanied by emotional, cognitive and psycho-social features.*
- *Seizures are now classified according to onset (focal or generalized), presencemotor / non-motor, and awareness.*
- *Causes include genetic, structural and metabolic factors.*
- *Psychiatric comorbidities are very common, with depression occurring in a third of Persons with Epilepsy.*
- *Psychogenic Non-epileptic seizures and dissociative attacks are a common event in both confirmed and unconfirmed epilepsy.*
- *Diagnosis of epilepsy rests on clinical assessment especially witness accounts.*
- *Psychotropics and psycho-therapies are both effective and should be used when indicated.*
- *Many anti-epileptic drugs may produce neuropsychiatric symptoms and must be considered in differential diagnosis.*

8.6. References

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