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**REVIEW ARTICLE** 

# **Ecological Dynamics: An Inspiration for Triggering Epilepsy**

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### ABSTRACT

Epilepsy is a rigorous transmission of electrical impulses across neurons of the brain and reported more prevalent in lower-income countries. A systematic literature review has been performed to implicate the impact of environmental variables on the occurrence of epilepsy using the following keywords: Epilepsy or environmental risk factors or seizures. More than 500 genes have been reported to involve in epilepsy potentially. Moreover, family history with neurological disorders, sleep apnea, depression, alcohol, stress, diet, gestational period of mother, and social involvement are among the risk factors which can reliably predict onset and severity of the disease. Hence, minimizing these factors along with recommended therapies, counseling, and awareness could be a miracle in the life of epileptic patients and can improve societies.

## INTRODUCTION

Epilepsy refers to a group of disorders that result in eliciting the rapid discharge of electrical impulses across the motor, sensory, and associated brain neurons and leads to convulsions and unconsciousness. It is a neurological disorder in which the clusters of neurons transmit electrical impulses 500 times more sharply than the normal ones [1]. The rate of seizure incidence varies from two seizures in less than 24 hours to one seizure in two days [2]. In the world, more than 50 million people have suffered from epilepsy. About 90% epilepsy has been recognized in developing countries. The mentioned disease is more prevalent in Asia, as it has affected about 23 million Asians as compared to 3.3 million Africans and 1.2 million sub-Saharan Africans [3]. New cases of epilepsy have been reported among infants and elderly people. In the United States, one out of hundred has been diagnosed with epilepsy for which 75-80% can be treated with modern medicines and surgical techniques [4]. In France, 22.5% patients possess drug resistant epilepsy. In Pakistan, rural population is more affected (10/1000 per year) than the urban population [5].

#### GENETICS

A number of genetic defects (in almost 500 genes) have been found tied with epilepsy like mutations in Cystatin B gene, HNRNPU, IQSEC2, CACNA1A, CHD2, MTOR GABRB, GABRA1, GRIN2B, NEDD4L, PCDH7, GRIN1, ALG1, and FLNA genes. Some of these are involved in neuronal signaling like PCDH7 variants causes disruption of protocadherin 7, a molecule involved in neuronal cell-cell adhesion during synapse development. HCN1 variants also implicate ion channel disturbance in humans [6]. A number of other genes involved in ion flow are SCN1A (Generalized epilepsy with febrile seizures), SCN2A (Generalized epilepsy with febrile and a-febrile seizures), SCN1B (Generalized epilepsy with febrile seizures), KCNQ3 (Benign familial neonatal convulsion epilepsy), GABRA1 (Juvenile myoclonic epilepsy), GABRG2 where distorted pore forming alpha ( $\alpha$ ) subunits or accessory beta ( $\beta$ ) subunits cause these channels to pass neuronal impulses inappropriately

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leading to seizures [7,8]. Another gene on X-chromosome, Fgf13 (fibroblast growth factor 13), codes for auxiliary protein of voltage-gated Na<sup>+</sup> channels. Reduced expression in Fgf13 mRNA reveals decreased inhibitory and increased excitatory synapses in hippocampal neurons [9]. These genes run in families and produce a characteristic seizure. These are much more diverse than their similar ones. SLC2A1 gene which encodes glucose transporter 1 (GLUT1) is responsible for regulating the movement of glucose in the brain. A number of brain disorders like microcephaly, developmental delay, Non-Acquired Focal Epilepsy (NAFE), and generalized epilepsy are caused due to mutations in SLC2A1 gene. In July 2017, 200 patients were studied with NAFE out of which 126 were with temporal lobe epilepsy. Ten exons and their splice site regions were amplified by Polymerase Chain Reaction (PCR) and sequenced by Sanger Sequencing but no variants were detected, which concluded less contribution of GLUT1 mutation in NAFE [10]. Micro-deletion on gene CHRNA7 chromosome 8q, DOK5 on chromosome 20q13 and PCYTIB genes have been found responsible for Electrical Status Epilepticus (ESES) [11].

In January 2016, one of the girls in identical twins experienced nocturnal or night sleep seizures [12,13] and generalized seizures at the age of 6 years whereas her identical twin was found normal, which suggested that environmental factors are responsible to induce epilepsy [14]. Epigenetics have been reported to cause ESES in monozygotic twins resulting in 75% cases of epilepsy [15].

Epilepsy also develops as a result of other brain disorders like brain tumors, Alzheimer's disease, sleep apnea, head injuries, lead poisoning and mal-development of the brain [16]. Conditions like hydrocephalus, AIDS, heart attacks, meningitis, strokes, viral encephalitis and other infectious diseases deprive the oxygen ( $O_2$ ) from the brain cells and lead to develop epilepsy with the passage of time [16] especially in older people [17]. Down's Syndrome (DS), which is a main genetic cause of mental retardation, presents 1–13% patients with epilepsy. DS patients have better control on seizures as compared to infantile spasms when early treatment is started. Heart attacks and strokes have also been observed as a stimulus of epilepsy in the people of age over 45 years.

Neurocysticercosis (NCC) is a brain infection of humans and pigs that is caused by a parasite Taenia solium. Frequency of NCC among epileptic patients is estimated around 30% from 12 different studies conducted in America, Africa and South East Asia [18]. Autism Spectrum Disorder (ASD) is a group of disorders characterized by problems in social behaviors and communications in children. Epilepsy and ASD are associated with each other since a long time [19,20]. In ASD patients, prevalence of epilepsy is 10–30% as compared to the normal population where it is 2–3% [20]. Patients with ASD and epilepsy are more associated with social problems, incontinence, language problems and behavior disorders. Patients with cerebral palsy and ASD are at a greater risk for epilepsy [21]. Epileptic encephalopathies refer to conditions in which neurologic deterioration impairs sensory, motor and cognitive functions resulting paroxysmal epileptic activity [22].

In Dravet Syndrome, patient faces seizures from the age of six months to severe status epilepticus at the end. Neurologic deterioration has also been seen in Rassumen Syndrome due to epilepsy. In West Syndrome, Ohtahara Syndrome and Myoclonic Encephalopathy, continuous spike waves are discharged as a result of sub-continuous paroxysmal interictal activity [23].

#### Seizures categories on the basis of Etiology

Some types of epilepsy are confined to particular stages of life but it cannot be considered as a single disorder because of its different symptoms with multiple seizures (Figure 1) all involving abnormal neuronal activity in brain [23].

Seizures in the mature brain cause more cell death as compared to immature brain, triggering irreversible adverse effect on neuronal activity of the brain [24].

#### Seizure categories on the basis of the brain area

Seizures are categorized into four main types, generalized seizures, focal seizures, Unknown and focal to bilateral seizure (Figure 2) on the basis of area of the brain from which seizures begin [25–51] as given in table 1.

In childhood, febrile seizures are the most common type occurring in 2–5% children in initial five years of age [52]. Febrile seizures usually occur before or after onset of fever and increase with the child's temperature [53]. In identical twins generalized and febrile seizures are found more prevalent than partial ones [54].

Epilepsy is categorized on the basis of underlying causes as Idiopathic (genetic causes) or symptomatic (cause known) or cryptogenic (cause unknown). Different types of epilepsy are also known as generalized or partial on the basis of the brain area involved as listed in table 2.

Epilepsy can also be categorized as temporal and parietal depends on whether seizures originate from temporal lobe or parietal lobe of brain. Temporal Lobe Epilepsy (TLE) is one of most common types of partial onset epilepsies in adults [59]. TLE is one of the most common types of Partial Epilepsies (PE) which account for 60% adult epilepsy cases. In TLE patients, conflicts in processing and inhibition of response have been observed. In TLE patients, right hemisphere frontal lobe, right frontal junction, middle frontal, superior frontal and inferior frontal showed more activation as compared to control ones [60]. In these patients, neuro-cognitive effects have been observed when the disease onset was early and duration was long. Pathological state of hippocampus has been found linked to executive functions in 70% patients [61].



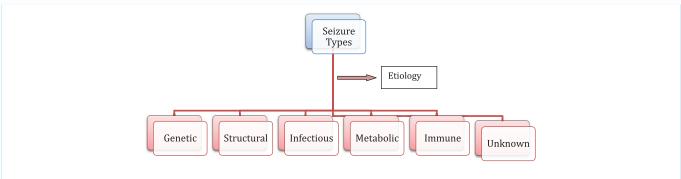
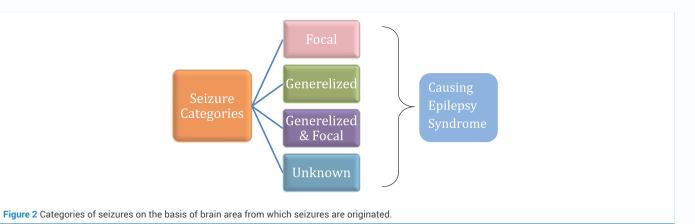


Figure 1 Seizure types on the basis of Etiology.



#### Table 1: Categories of Seizures

Generalized seizures Electrical impulses throughout the brain	Characteristics	Recommended Treatment	References	
Grand mal (Generalized tonic clonic)	Age dependent Valproic acid or Levetiracetam		[26]	
Typical absence	In childhood and adolescent	Ethosuximide and Valproic acid	[27]	
Atypical absence	Children	Levetiracetam and Rufinamide	[28]	
Myoclonic	Children	Sodium valproate	[29]	
Myoclonic absence	lctal automatisms	Valproate	[30]	
Myoclonic atonic	Childhood	Valproate	[31]	
Eyelid myclonia		Valproate	[32]	
Febrile or tonic clonic	Unknown eitology	Anakinra	[33]	
Focal or Partial Seizures Produced in a specific area of brain		Perampanel	[34]	
Occipital and parietal lobe seizures	Type of aura Focal resection		[35,36]	
Temporo parieto occipital junction seizures	Vertigo	Surgery	[36,37]	
Focal motor seizures	Management dilemma	nt dilemma Botulinum toxin		
ypical temporal lobe automatisms (mesial temporal lobe seizures)	Ablated volumes	Laser interstitial thermal therapy	[39]	
Hyperkinetic automatisms	Kicking, rocking		[40]	
Focal negative myoclonus	Centrotemporal spikes	Valproate and Levetiracetam	[41]	
Inhibitory motor seizures	Eyelid fluttering		[42]	
Gelastic seizures	Hypothalamus is epileptogenic zone	othalamus is epileptogenic zone Surgery		
Hemiclonic seizures	KCNQ3 mutation	Vaiproic acid		
Secondarily generalized	Seizures in cortex	Surgery	[45]	
Continuous seizure types				
Generalized status epilepticus	Glutamate mediate cytotoxicity		[46]	



Generalized tonic-clonic status epilepticus	Cognitive impairment	Perampanel	[47]
Clonic status epilepticus	-	-	
Absence status epilepticus	-	-	
Tonic status epilepticus	-	-	
Myoclonic status epilepticus	Cognitive decline		
Focal status epilepticus	Glycine receptor antibodies		[48]
Epilepsia partialis continua of Kojevnikov	Transcranial magnetic stimulation	Cortical stimulation	[49]
Aura continua	Visual aura	Indomethacin and topiramate	[50]
imbic status epilepticus (psychomotor status)	Mesial temporal lobes	AEDs	[51]

Table 2: Categories of Epilepsy.

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Types of Epilepsy	Generalized Epilepsy	Partial Epilepsy	References	
Idiopathic (genetic causes)	Childhood absence epilepsy, Juvenile myoclonic epilepsy, epilepsy with grand-mal seizures only	Benign focal epilepsy of childhood	[55,56]	
Symptomatic (cause known) or cryptogenic (cause unknown)	West syndrome Lennox-Gastaut syndrome	Temporal lobe epilepsy, Frontal lobe epilepsy	[57,58]	

Extra temporal abnormalities have been observed in white matter and grey matter in TLE patients due to which hippocampus creates alterations in orbito-medical, frontostriatal and tempo-frontal circuits as a result of which patients were no more able to use previously stored memory to use for future actions [61].

Status Epilepticus (SE) has been found acute symptomatic with bimodial distribution having peaks in children less than age of one year and elderly people. Short term mortality rate is 7.6–22% and long-term mortality rate is 43%. Aetiology and patients age are determinants of mortality [62]. Reflex Epilepsy (RE) is characterized in which generalized and myclonus convulsive and non-convulsive seizures and partial seizures are prevalent among children and adolescents [63].

During a seizure, a person can perform a number of semi purposeful activities like wandering around aimlessly, lip smacking and television watching [64]. Epilepsy can be associated with a number of behavioral issues, social competence, emotional problems and disturbed academic achievements [65]. Factors that led to the onset of seizure or epilepsy are referred as "seizure triggers" or Triggering Factors (TF) (Figure 3). Imbalance of neurotransmitters causes epilepsy, which can be excitatory or inhibitory. Epileptogenesis is a process of converting normal brain to epileptic one by lesions or excite toxicity by some pesticides. One of the most studied inhibitory neurotransmitters is Gamma Amino Butyric Acid (GABA) [64]. It is the root cause of epilepsy in some patients; in others, it can accelerate the rate of seizures recurrence.

# **ENVIRONMENTAL FACTORS**

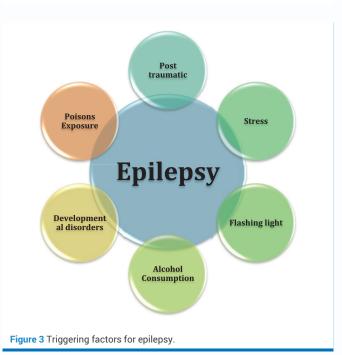
Some other recounted dynamics which can hasten the onset of seizures are listed below:

#### **Alcohol consumption**

Heavy intake of alcohol, use of morphine and caffeine are TFs for epilepsy (Figure 1). Nicotine in cigarettes excites Acetyl Choline neurotransmitter in the brain by increasing neuronal firing, which triggers the inward and outward movement of ions causing seizures [66].

#### **Developmental disorders**

Head traumas during an accident with other developmental disorders accelerate epilepsy to a greater extent [67]. Prenatal injuries are also found epileptogenic. When a mother is suffering from infection and mal nutrition, deficiency of oxygen leads to cerebral palsy which is a leading cause of seizures in 20% children [17]. Autism and Downs's syndrome are also leading causes of epilepsy [68].





#### **Flashing light**

Flashing lights flickering in photosensitive epilepsy lead to tonic-clonic or myoclonic seizures. These seizures are triggered by watching TV, playing video games, riding during day light or driving [17].

#### Stress

Glutamate is excitatory neurotransmitter in brain increases in case of stress, mal-nutrition and sleep apnea, triggering neuronal signal transmission through inter neuronal junctions [17].

#### Post traumatic epilepsy

Post-traumatic seizure studies have become more prevalent in the last 40–50 years. Traumatic Brain Injury (TBI) is identified as a major cause of epilepsy in recent years [69]. It has been found that 4–53% seizures are posttraumatic. If a person has one seizure after TBI then 86% chances of second seizure are there in the next two years with 25–40% remission rates. Significant risk factors of developing seizures are acute intracerebral hematoma, especially subdural hematoma, severe brain injury, >65 years age and brain contusion [70].

## POISONS EXPOSURE

Excessive exposure to lead, carbon monoxide, street drugs, and over-dose of anti-depressants are important TFs for seizures [17].

#### Localization related epilepsy

Simple partial seizures change to complex partial seizures and if it remains untreated, it may further evolve into generalized tonic-clonic seizures. This type of epilepsy referred as localization related epilepsy for which several epilepsy surgery is beneficial [71]. Most common TFs are smoking (6.4%), fever (6.4%), missing meals (9.1%), fatigue (15.3%), sleep apnea (19.7%), emotional stress (31.3%) and missing medication (40.9%) [72] (Figure 4).

Almost 25% epilepsy is characterized as symptomatic in which causes are head trauma, brain infections, injuries, and strokes [73].

#### **Epilepsy and pregnant women**

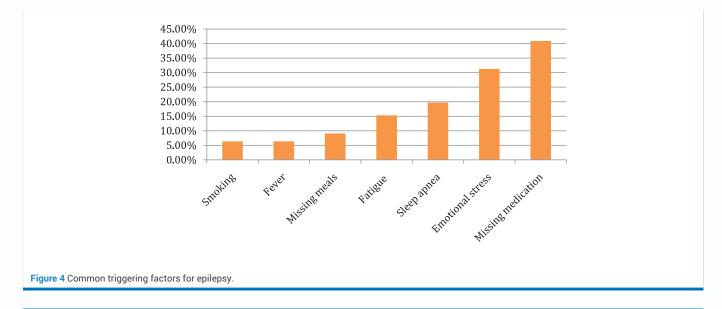
Rate of epilepsy in untreated epileptic women's offspring is not higher as compared to non-epileptic mothers, whereas mothers who receive Antiepileptic Drugs (AEDS) have more chances of malformations in their children than normal ones. Women With Epilepsy (WWE) taking AEDS have no risk of premature labor, delivery or premature contractions, but remaining seizure free prior nine months is essential [74].

Risk factors of febrile seizures include neonatal exclusion after 28 days, developmental delay, daycare attendance, vaccinations, iron zinc deficiencies, severe viral infections, and family history of febrile seizures [75].

# DIAGNOSIS AND TREATMENT

For patients with first unprovoked seizures, routine parameters are used of which EEG is considered as a primary parameter. The most common and reliable method performed to check status of epilepsy is EEG [76]. Brain imaging like Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are reported to be useful for 15% patients. Laboratory tests like Blood Hemoglobin (Hb) count, blood glucose level and level of electrolytes could be useful parameters for epilepsy [77].

In some of the cases, seizures stop when the disease is treated, but becoming seizure-free is uncertain and depends on affected brain area, the extent of brain damage, type of antiepileptic medication, and type of seizures [78].





Since biblical times, fasting was recommended as a safe treatment for epilepsy but with the advent of AEDs, it is much reduced [2]. Its hypotheses focus on detoxification of gut due to production of ketones which reduce seizure reoccurrence. Ketogenic diet was recommended in 4:1 fat carbohydrates ratio by Pfeifer and Thiele [79,80]. Effectiveness of ketogenic diet in children for the reduction of seizure onset has been reported but it may cause growth retardation, kidney stones, constipation and dehydration [80]. Statistical analysis has shown >50% seizure reduction in 1084 patients staying on the ketogenic diet. In others with the cessation of the diet, seizure reduction was<50%. Diet restriction was seen in 16.4% patients and side effects was observed in 13.2% patients [81,82].

Vagus Nerve Stimulator (VNS) under chest skin deliver short bursts of electrical discharges in the brain and reduces seizures onset by 20–40% but creates coughing, shortness of breath, muscle pain, hoarseness, and tingling along with throat pain. In refractory epilepsy, VNS therapy is found effective for the reduction of seizure frequency and seizure severity. Before and after VNS, data for EEG should be taken 3–5 day on Epilepsy Monitoring Unit (EMU) around ictogenic zones [83].

Until now, curing the epilepsy is not possible but thanks to medication by which its effects can be minimized [84]. In 30% epilepsy cases, seizures cannot be controlled even with the best available AEDs. The drug resistance mechanism is variable and multifactorial according to cause, drug type, drug mode of action, drug site of action, age of the patient, and patient health factor. Seizure free rate is more in older people than younger ones [5]. Resistance against AEDs is due to over-expression of genes and proteins particularly p-glycoprotein [85]. Anticonvulsant medications are the most reliable treatment for epilepsy. Some patients take medicine throughout their life and these medicines possess much influence on their quality of life. Their effectiveness, way of action and side effects vary according to the type of epileptic seizures. Toxicology and clinical pharmacology showed chlordiazepoxide, nitrazepam, clonazepam, flurazepam, oxazepam and diazepam as effective AEDs out of which flurazepam has not been tested experimentally. Benzodiazepines possess no effect on focal epilepsy but effective in stopping generalized seizures like myoclonic, infantile, absence, alcohol causing, and photosensitive. Sodium Di-Propylacetate (DPA) has found the most effective in the treatment of absence seizures. With its antiepileptic structure, this branched-chain carboxylic acid is used in the treatment of generalized tonic-clonic seizures and partial seizures [86-100]. Grand-mal is aggravated by these AEDs, but focal and partial seizures are reduced to some extent. Status epilepticus and ecliptic convulsions are reduced by the use of AEDs. Benzodiazepines are found most effective but orally their effectiveness is reduced and tolerance may also develop. Some of the treatments prescribed for different seizures are given in table 3.

Valproate, phenytoin, phenobarbital and other AEDS should be avoided during pregnancy, especially during the first trimester to avoid congenital malformations [74]. Remifentanil works in dose dependent manner and affects cortical spikes [101]. Mono-therapy in pregnancy possesses epileptic patient on a higher risk of congenital malformation. European and International Registry of Antiepileptic Drugs and Pregnancy (EURAP) show effects of four common AEDs phenobarbital, lamotrigine, valproic acid and carbamazepine up to 12 months after birth. Assessment is according to dose at the time of conception [4,5,61]. Lowest rates of congenital malformation are observed with lamotrigine (dose: less than 300 mg per day) whereas risks of malformations are higher with barbital, carbamazepine (dose: 400 mg per day) and valproic acid [102].

AEDs dose during prenatal exposure should be determined particularly due to teratogenicity associated with them [103]. If dose is increased gradually, then other side effects like drowsiness, ataxia and toxicity are minimized [61]. Depression, anxiety, fatigue, loss of coordination, dizziness, loss of bone density, inflammation to liver, pancreas and suicide are ultimate side effects of medication [85].

In some cases of brain damages, surgery is performed to avoid epileptic seizures. Surgical removal of ictogenic zones is necessary for patients with refractory epilepsy [104]. In the United States, there are 4 x 10<sup>5</sup> to 6 x 10<sup>5</sup> patients with refractory epilepsy and only 2-3% epileptic patients are offered surgery [105,106]. In 97-98% patients, it is difficult to localize ictogenic zone [83] whereas 66% patients are found seizure free after temporal lobe resections, 27% after frontal lobe resections and 46% after occipital and parietal resections [65]. With left sided temporal surgery, verbal memory was reduced to 44%, and verbal fluency was improved in 27% patients [107].Today our basic need is to improve epilepsy surgery by making it cost effective and using non-invasive biomarkers. High Frequency Neuromagnetic Signals (HFNS) and spikes are potential biomarkers for the localization of ictogenic zones and have improved seizure freedom rate [108]. The number of daily seizures is correlated with spikes in HFNS [109]. A patient in which ablative surgery is not recommended, bilateral hippocampal stimulation is useful [110].

# EPILEPSY AND EMPLOYMENT

Epileptic persons are at a higher risk for thinking and learning capabilities, attention, memory, skills, emotional and behavioral difficulties along with perception problems. National Institute for Health and Care Excellence (NICE) recommended that epileptic patients should have a regular medical checkup. To cope with epileptic after effects, this review should be performed on yearly basis for adults and children. This gives a chance to discuss seizures, their effects, treatment and any other questions [111]. Psychotherapy which includes group work, oriented therapy and cognitive behavior therapy is helpful with antidepressant medication.

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Туре	Cause	Symptoms	Age	Treatment	References
Pyridoxine dependent	Illness or high fever (Pipecolic acid elevation)	Intractable seizures	Newborn	B6 supplementation	[87]
Awakening grand mal	Sleep apnea	Tonic clonic grand mal seizures	20-60y	Sleep awake cycle	[88]
Reflex epilepsy	Idiopathic, visual stimuli	Myoclonic generalized convulsive or non- convulsive seizures	30y	With or without AEDs	[89]
Juvenile Absence (JAE)	Idiopathic generalized	Absence seizures, tonic clonic seizures	Prepubertal adolescence (3Hz)	Successful treatment by AEDs	[90]
Juvenile Myoclonic (JME)	idiopathic	Rapid isolated jerks in muscles, myoclonus	Teenagers (4-6Hz)	Anti-convulsant medications	[90]
Benign	Benign infantile encephalopathy	Benign neonatal convulsions	Childhood		[91]
Benign Rolandic (BRE)/ Benign Centro Temporal Lobe	Benign infantile encephalopathy	Jerking of face, limbs with memory loss and difficulty in phonologic processing	Children 3-13 years age	Regular sleep awake cycle	[91]
Status Epilepticus (SE)		Continuous seizures	adults	Death	[62]
SUDEP		Generalized tonic clonic seizures		Heart arrhythmias and death	[92]
Childhood absence		Rapidly blinking eyes, jerking arms	Before puberty		
Temporal Lobe (TLE)	Symptomatic	Focal seizures, Hippocampus shrinks	Late childhood and adolescence	Anticonvulsant medications, surgery	[81]
Neocortical	Brain cortex damages	Visual hallucinations, muscle spasms	Adults	Surgical treatment	[93]
ennox-Gastaut Syndrome (LGS)	idiopathic, symptomatic or cryptogenic	Tonic seizure, drop attacks, tonic seizures	Children (2Hz slow spike waves) (2-18y)	Anticonvulsants are not successful	[94]
Autosomal dominant nocturnal frontal lobe	idiopathic	Frontal lobe seizures, hand clenching, arm raising	Childhood	Carbamazepine	[95]
Benign Occipital (BOEC)	idiopathic	Scotoma, fortifications	3-10 years	CBZ, VAP	[96]
Catamenial (CE)	idiopathic	Sublte chewing, eye blinking	4-12 years	No specific treatment	[97]
Severe myclonic epilepsy of infancy(SMEI)/ dravets syndrome	Idiopathic (mutations in SCNA1 gene)	Unilateral convulsions	Starts in 1 <sup>st</sup> year and remains throughout life	No treatment	[98]
Female epilepsy without mental retardation	PCDH19 mutations	Tonic clonic, tonic, atonic seizures	6-36 months		[99]
Frontal lobe epilepsy	Symptomatic or cryptogenic	Seizures in frontal lobe		Surgery	[100]

In 2008 a campaign was started to create awareness in people regarding epilepsy and named as a Purple Day on March 26 [52,112].

The severity of seizures, stigma, and other variables like self-esteem, self-efficacy, coping style which are the determinants of employment may cause difficulties for epileptic patients. It is very difficult to maintain regular employment in epileptic patients [113]. Rate of underemployment and unemployment are much higher in epileptic patients especially with severe seizures. Employment impacts much to the quality of normal life [114]. In society, earning and acceptance by others give us confidence of living life [114]. Employment also helps gaining self-confidence. From more than three decades employment is considered a significant problem for epileptic persons [115]. In developing countries, epileptic persons are ignored and stigmatized. Epileptic persons are more prone to sexual difficulties and non-acceptance of self. Epilepsy can be associated with several behavioral problems, social competence, emotional disturbance and disturbed academic achievements even after surgery [116]. Inadequacy, social impairment, sporadic illness and recalcitrance increased above average in children with epilepsy [117].

# CONCLUSION

Genetics, as well as environmental factors play crucial role in the development of epilepsy. Therefore, current literature review highly recommend to adjust these environmental triggering factors to minimize the severity and occurrence of seizure attacks in epileptic patients.

# 😂 Liferature

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