

## AN OVERVIEW ON NON EPILEPTIC SEIZURES

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### ABSTRACT

The brain is susceptible to many different types of disorders that strike at every stage of life. Developmental disorders such as autism and dyslexia first appear in early childhood. Psychiatric diseases such as depression and schizophrenia are typically diagnosed in teens or in early adulthood. Epilepsy is the fourth most common neurological disorder and affects people of all ages. Epilepsy is a group of related disorders characterized by a tendency for recurrent seizures that occur due to abnormal electrical discharges whereas Non Epileptic Seizures are not characterized by abnormal electric discharges in brain. Non Epileptic Seizures also possess greater impact on human life as that of normal epilepsy. This article aims towards discussing Non Epileptic Seizures in detail which includes the classification, epidemiology, types, causes, diagnosis, and treatment of Non Epileptic Seizures including treatment of Pediatric Non Epileptic Seizures.

**KEY WORDS:** Autism, Dyslexia, Depression, Schizophrenia, Epilepsy, Non Epileptic Seizures.

### Seizure

A seizure is a temporary loss of control often, but not always, accompanied by convulsions, unconsciousness or both. Most common are epileptic seizures, or seizures caused by sudden abnormal electrical discharges in the brain.<sup>[1]</sup> Epileptic seizures typically involve excessive firing and synchronization of neurons. This interrupts the normal working of the parts of the brain involved, leading to the clinical symptoms and epidemiology of the specific type of epilepsy.<sup>[2]</sup> The brain is made up of millions of nerve cells. These cells, called neurons, normally generate electrical discharges, sending messages to the body to produce thoughts, feelings and actions. A seizure is a disruption in the normal pattern of these discharges, caused by the neurons firing all at once and at a much faster rate.<sup>[3]</sup>

### Definitions

- A. **Seizure:** The clinical manifestation of an abnormal and excessive excitation and synchronization of a population of cortical neurons.
- B. **Epilepsy:** A disease characterized by spontaneous recurrent seizures.
- C. **Epileptogenesis:** It is the sequence of events that converts a normal neuronal network into an epileptic network.<sup>[4]</sup>

### Non-Epileptics

Non-epileptic seizures, on the other hand, are not accompanied by abnormal electrical discharges. They have been previously called pseudo seizures, but that

term is misleading. These seizures are quite real, and people who have them do not have conscious, voluntary control over them. Non-epileptic seizures have no identifiable physical cause, but they are believed to be physical reactions to psychological stresses. Non-epileptic seizures resemble epileptic seizures in outward appearance, even though their cause is very different. Non-epileptic seizures may appear to be generalized convulsions, similar to grand mal epileptic seizures, characterized by falling and shaking. They also may resemble petit mal epileptic seizures, or complex partial seizures, characterized by temporary loss of attention, staring into space or dozing off.<sup>[1]</sup>

Non-epileptic seizures (NES) constitute an important differential diagnosis for epileptic seizures in all age groups. NES should be carefully considered and should be ruled out before making a diagnosis of epilepsy. Confident diagnosis of NES in children is often more challenging than making a positive diagnosis of epilepsy. A significant proportion of children suspected of epilepsy or even those who have been labeled with a definite diagnosis of epilepsy or even refractory epilepsy have never had an epileptic seizure.<sup>[5]</sup>

Non-epileptic seizures (NES) are a descriptive term for a diverse group of disorders that refer to paroxysmal events that can be mistaken for epilepsy, but are not due to an epileptic disorder. "Non-epileptic seizure" is the preferred term. As confirmed by Steven Schechter, MD in his 1966 survey of American epileptologists, the majority of respondents consider this to be the preferred

term as opposed to many other anachronistic and pejorative terms, which have been suggested. These include “hysteroepilepsy, hysterical seizures, pseudo seizures, pseudo-epileptic seizures, non-epileptic pseudo-seizure, hysterical epilepsy, and non-epileptic attack disorder.” All of these terms have significant demeaning overtones, or, quite frankly, are inaccurate in terms of the pathophysiology.<sup>[6]</sup>

### Classification of seizures

#### Partial seizures

- ✓ Simple partial seizures (with motor, sensory, autonomic, or psychic Signs)
- ✓ Complex partial seizures
- ✓ Partial seizures with secondary generalization

#### Primarilygeneralized Seizures

- A. Absence (petit mal)
- B. Tonic-clonic (grand mal)
- C. Tonic
- D. Atonic
- E. Myoclonic

#### Unclassified Seizures

- A. Neonatal seizures
- B. Infantile spasms
- C. Non-Epileptic<sup>[7]</sup>

### Epidemiology

Nearly half of all people brought in to hospital with suspected serious epilepsy turn out to have Nonepileptic seizures instead. Unfortunately, the true statistical prevalence of NES is unknown. Nonetheless, we do know from the results of surveys performed in the United States and in Europe that NES patients account for 20% of tertiary care epilepsy unit admissions.<sup>[8]</sup> Scott has estimated the incidence in an outpatient epilepsy clinic at 5%.<sup>[9]</sup>

The NES population is quite heterogeneous, and very importantly, the economic impact of the disorder is likely to be very costly to society. Many of these patients are inappropriately treated with antiepileptic medications.

In adults, repeated studies demonstrate a fairly consistent 4:1 female: male ratio for psychogenic non-epileptic seizures. In the pediatric population, however, a 2:1 female: male ratio appears to exist under the age of ten, the ratio is probably more of a 1:1.6 The coincidence of non-epileptic seizures and epilepsy is a further confounding variable for definitive diagnosis and treatment. 30% of patients admitted to tertiary care epilepsy units have co-incidence disorders. Though there is a considerable estimated range of between 10-50%, again, no formal epidemiological study has ever been performed.<sup>[10]</sup>

The prevalence of epilepsy is estimated to be 4- 5/1000 children in the European and North American population. Up to 30% of these individuals may have a

misdiagnosis. The rate of misdiagnosis in epilepsy in adults is estimated to be 25% in one study.<sup>[11]</sup> There is no data to provide an estimate of rates of misdiagnosis in children but at an enquiry of a tertiary pediatric neurology service in the UK, the misdiagnosis rate was found to be 32%. A significant proportion of misdiagnoses comprise NES which are mislabeled as epileptic seizures.<sup>[12]</sup> Psychogenic seizures are more prevalent in females (75%) and typically in late teens. Common causes of misdiagnosis are; poor history taking, diversity of presentation of epileptic events, no sensitive or specific diagnostic tests available for epilepsy and many imitators that are confused with the diagnosis of epilepsy.

### Causes of non-epileptic seizures (nes)

Stressors or trauma in a person’s life usually cause NES – without that person’s conscious awareness of their cumulative effect. The underlying dynamics of stress threaten the person’s security, and NES helps to relieve anxiety by opening a channel of expression. Cumulative stressors could be any life changes that affect the person. Common stressors are loss of a relative/friend, pet, friendship, relationship difficulties, and significant family conflicts, change of school/job, abuse, teasing, or learning difficulties. NES are not faked, and the term ‘pseudo seizure’ should not be used to describe this condition. A person who fakes a seizure has a different psychological diagnosis that requires different management.<sup>[13]</sup>

Unlike epileptic seizures, non-epileptic seizures are not caused by physical disorders of the brain. Rather, Nonepileptic seizures may result from traumatic psychological experiences or unusual stresses, sometimes even those in the forgotten past. It has been known since ancient times that emotional or psychological stresses can produce physical symptoms in a person with no apparent physical illness.

Almost everyone has blushed in embarrassment or been nervous and anxious as part of a “stage-fright” reaction. Such illnesses are called psychosomatic, or mind-body, illnesses. Examples include forms of acne, allergy, angina (chest pain), asthma, headache, ulcer, obesity, rheumatoid arthritis and ulcerative colitis.

The medical term for these symptoms is somato form, meaning they take form in the body. Examples include forms of paralysis, blindness and even the inability to speak. These disorders differ from psychosomatic illnesses in that both their causes and treatments are primarily psychological.

Non-epileptic seizures represent such a disorder. No underlying physical cause is known to be responsible. It is important to remember, however, that somatoform disorders, including non-epileptic seizures, are real conditions that arise in response to real stresses.

A specific traumatic event — such as physical or sexual abuse, incest, divorce, death of a loved one or other great loss or sudden change — can be identified in many patients with non-epileptic seizures.

Often the underlying trauma has been blocked from consciousness. Many patients can recall the event only with considerable support from a trained therapist. The unconscious processes that give rise to Nonepileptic seizures also may cause or contribute to other conditions, such as depression and anxiety, which need to be identified and treated.

Non-epileptic seizures differ from other psychogenic disorders in one important aspect: Non-epileptic seizures can be shown with great certainty to be of psychological origin. With the appropriate tests, the accuracy of the diagnosis is comparable to that of diagnosing a broken bone with an X-ray. Such certainty is not possible for other psychogenic symptoms, such as pain, blindness or paralysis. This confidence in the diagnosis allows proper treatment and greatly increases the chances of complete recovery.<sup>[1]</sup>

### Types of NES

Non-epileptic seizures (NES) can be divided into two types:

1. Organic non-epileptic seizures
2. Psychogenic seizures.

#### 1. Organic NES

These seizures have a physical cause (relating to the body). They include fainting (syncope) and seizures with metabolic causes such as diabetes. Because organic NES have a physical cause, they may be relatively easy to diagnose and the underlying cause can be found. For example, a faint may be diagnosed as being caused by a physical problem in the heart. In these cases, if the underlying cause can be treated the seizures will stop.

#### 2. Psychogenic NES

Some NES have a psychological cause and are called 'psychogenic seizures' because they are caused by the impact of thoughts and feelings on the way that the brain works.

Psychogenic seizures include:

- **Dissociative seizures** are involuntary and happen unconsciously. The person has no control over them and they are not 'put on'. This is the most common type of NES.
- **Panic attacks** are a psychiatric condition. They can happen in frightening situations, when remembering previous frightening experiences or in a situation that the person expects to be frightening.
- Panic attacks can cause sweating, palpitations (being able to feel your heartbeat), trembling and difficulty breathing. The person may also lose consciousness and may shake (convulse).

- **Factitious seizures** happen under some conscious control. An example of this is when seizures form part of Munchausen's Syndrome, a rare psychiatric condition where a person is driven by a need to have medical investigations and treatments.

### Dissociative Seizures (DS)

Dissociative seizures (DS) are often caused by traumatic events such as:

- An accident
- Severe emotional upset (such as the death of a loved one)
- Psychological stress (such as a divorce)
- Difficult relationships
- Physical or sexual abuse
- Being bullied.

It can be hard to find the cause of someone's DS. For some, they start shortly after a specific event. For others, they may not start until years later or they may start suddenly for no apparent reason. Once DS have started, they might be triggered or brought on when the person is stressed or frightened. Or they might happen spontaneously in situations that are not stressful or frightening. Sometimes, even the fear of having a seizure can, itself, trigger a seizure.

Seizures caused by a delayed response to a very stressful event or situation, for example, being in a war or a disaster, are a response to post-traumatic stress disorder (PTSD) - a condition that sometimes happens after a traumatic event. During the seizure the person may cry, scream or have flashbacks (sudden, vivid memories of the event). They may not remember the seizures afterwards.

### Classification of Non-Epileptic Seizures:<sup>[14]</sup>

**Table 1: Classification of NES based on System.**

System	Conditions
Cardiac	1.Long Qt syndrome 2.Ventricular tachy arrhythmias 3.Heart blocks 4.Brugada syndrome
Vascular	1.Orthostatic syncope 2.Vaso-Vagal syncope
Respiration	1.Breathe holding attcks 2.Prolonged respiratory apnoeas
Neurological	1.Hypereclampsia 2.Episodic Atlaslas 3.Cata plexy
Psychological	1.Day dreams 2.Gratification 3.Out of the Body experience
GIT	1.Gastro oesophageal Reflux 2.Rectal pain syndrome
Sleep Related	1.Night terrors 2.Night Mares 3.Narcolepsy

**Table 2: Classification according to symptoms of presentation.**

<b>Apnoeas</b> 1.Gastro esophageal reflux 2.Breathe holding attack Reflux anoxic seizures	<b>Brief Unresponsives</b> 1.Day Dreams
<b>Convulsive Seizures</b> 1.Syncope 2.Heart block	<b>Tonic Spasms</b> 1.Rectal pain syndrome 2.Breathe holding attacks
<b>Startle</b> 1.Sleep starts	<b>Psychic Status</b> 1.Out of body experience 2.Schizophrenia 3.Panic Attacks
<b>Weakness</b> 1.Periodic paralysis	<b>Sleep Phenomena</b> 1.Narcolepsy 2.Night Terrors 3.Night mares
<b>Varying</b> 1.Night terrors 2.Night mares	<b>Sensory Symptoms</b> 1.Migraine

**Ictal Characteristics and Diagnosis**

Ictal characteristics of non-epileptic seizures have been studied and there are some bedside parameters that can be of use to assist the clinician in determining whether an event is likely to be non-epileptic or epileptic.<sup>[15]</sup> For tonic-clonic resembling events, a high degree of confidence can be gained by observing out-of-phase upper extremity and lower extremity movements or vocalization at the start of the event, as opposed to 20-second into the event, when a true tonic-clonic seizure makes the tonic clonic transformation. Additional parameters of high amplitude forward pelvic thrusting and the lack of rigidity can also be useful for increasing the confidence of the clinical diagnosis to preclude inappropriate aggressive treatment with antiepileptic medication, assuming status epilepticus scenario.<sup>[15]</sup>

Ictal duration can also be of utility for assessing tonic-clonic resembling-events; a tonic-clonic seizure generally lasts 70 seconds, plus or minus 20- seconds. Any tonic-clonic resembling-event going beyond this point should raise the suspicion of possible non-epileptic seizures, though obvious care needs to be taken that a true status epilepticus scenario is not transpiring. Atypical complex partial events are often difficult to determine as to whether they are epileptic or non-epileptic. A blank state unassociated with any movement, in particular, is a difficult differentiation without concomitant video-EEG monitoring to observe any ictal pattern.<sup>[16]</sup>

Additionally, epileptic tonic-clonic and partial complex seizures most reliably elevate prolactins levels at approximately 20-minutes post start of the event. Similarly, convulsive syncope can elevate prolactins and have associated automatisms.<sup>[17,18]</sup> The significant number of patients (30% on average) having mixed epileptic and non-epileptic seizure disorders, reduction of

medication and further recording to exclude an underlying epileptic diathesis is important.<sup>[19]</sup>

Epileptic seizures have a clear threat of stereotypic, whereas the non-epileptic events are much more likely to have significant variation between them. Having videotaped examples of the events and having the opportunity to review them in close succession significantly facilitates the ability to make a definitive diagnosis.

**Ictal Video**

Video recording by parents on their mobile phone or on home video equipment assisted by community nurses or inpatient video telemetry can be an invaluable investigation in clinching the diagnosis of NES. Nowadays, most people have ready access to video technology to enable them to take a short high definition recording. In obtaining video records, seeking peer review and expert opinion is rewarding and worthy. Every paroxysmal condition should be analyzed with suspicion. When in doubt, even a few years down the line, clinicians should have no hesitation to revisit the diagnosis and seek peer review. Admitting patients for video monitoring of paroxysmal events has been a fruitful approach.<sup>[20]</sup>

**ECG**

In children and young adults a 12 lead ECG should be considered in cases of diagnostic uncertainty and should be undertaken in all children with suspected syncope. More extensive cardiac investigations such as echocardiogram, prolonged ECG recording (up to seven days), cardiac memo and tilt tablet testing may be indicated in individual cases of NES suspected to be of cardiovascular origin.

**EEG**

Since the EEG is a poorly sensitive and specific investigation in the diagnosis of epilepsy, it should be used with great caution in NES. EEG should not be performed in cases of probable syncope because of the possibility of false positive results. Ictal EEG with simultaneous video monitoring is an extremely useful investigation in psychogenic seizures. Video telemetry, if available, is more diagnostic in psychogenic seizures. Ambulatory EEG can be useful if a paroxysmal event can be captured within the time frame.

**Neuro-Imaging**

This is of limited help in establishing a diagnosis but could be indicated in suspected neurological conditions such as Arnold-Chiari malformation, suspected raised intracranial pressure and intracranial space occupying lesions.

**Sleep Studies**

Sleep studies are indicated in obstructive sleep apnoea; narcolepsy and REM/non-REM sleep disorders. These could be supplemented by video recording when nocturnal epilepsies e.g. Autosomal Dominant Nocturnal

Frontal Lobe Epilepsies (ADNFLE) can be identified and distinguished from NES.

### Genetics

Molecular genetic tests are gaining importance in establishing diagnosis of NES especially channelopathies<sup>[21]</sup> (Long QT syndrome, BPTI, BPVC, Episodic ataxias, Paroxysmal tonic up gaze and Hemiplegic migraine). Calcium, sodium, potassium channel genes will be supportive in strongly suspected cases.

### Symptoms

These are some other symptoms, which people with Non-epileptic seizures can sometimes experience as part of their illness. Often these symptoms have causes similar to Non-epileptic seizures.<sup>[22]</sup> The symptoms are: Numbness, tingling, Fatigue, Pain, Headache, Poor concentration, Memory problems, Poor sleep, Difficulty in speaking, Blurred vision, Feeling distant, Dizziness, Limb weakness, Frustration, anger, Low mood, Worry, Panic, Bladder problems.

### Treatment of non-epileptic seizures

Treatment for non-epileptic seizures takes time. Aftercare needs must be arranged with an identified therapist who clearly understands the diagnosis; and a smooth transition must be organized. Patients and their families must be advised that non-epileptic events may continue for a time, but once a more effective and culturally acceptable coping strategy has been initiated, they will eventually disappear. Humane treatment, however, has not always prevailed.<sup>[24]</sup> In severe attacks a moderate quantity only excites redoubled violence while a second gallon is more effectual than the first.” Alternately, “A much more convenient and effectual remedy than water is strong faradizations to the skin. Applied almost any where it will commonly quickly stop the attack.” Obviously these are anachronistic, extremely insensitive approaches to treat the patient suffering from non-epileptic seizures. Ultimately, to be effective, treatment must be patient-customized and based on DSM-IV diagnostic grouping, when available.<sup>[23]</sup> Hopefully soon, some well-designed, large prospective outcome studies of treatment modalities for the non-epileptic patient will be performed.<sup>[24]</sup>

### Pediatric Non-Epileptic Seizure Treatment

For pediatric patients, study sample sizes are small. The male to female ratio as previously discussed is 1:2, though probably 1:1 for children under 10 years of age. Co morbid epilepsy diagnosis in children is 22-38% as a consensus from the conference and from previous studies at 16-23%. Again, below average IQ not uncommon. School problems are reported in over 50% and history of sexual abuse is reported in 13-31%. Once psychosocial stressors are quantified, one or more stressors are present in 78-94% of pediatric patients and include parental marital discord, parental psychopathology/alcohol abuse, parent/child conflict, learning and attention problems and/or lack of adequate peer support. The assessment and

treatment of the child should be viewed differently than that of an adult, taking into consideration family dynamics, parental functioning, environmental issues, and especially school and relationship with peers.

### Non-epileptic seizures treatment consequences

Non-epileptic seizures are treatable, however there are only a few studies that have confirmed this, and further work in this area needs to transpire. Non-epileptic seizures are easier to treat than is epilepsy, in the sense that the condition is potentially curable without heroic intervention, such as surgery. The diagnosis of NES needs to be confirmed and, there is a need to rule-out co-existing disorders. It is important to present the diagnosis to the patient and family in a supportive, matter-of-fact fashion. Therapy needs to be directed to the underlying cause.

This includes appropriate treatment for depression, anxiety, psychosis and appropriately directed psychotherapy for issues of fear, rage, apathy and/or guilt. Non-epileptic seizures are common, though the actual prevalence is unknown. Patients comprise a heterogeneous population. Research in the area is quite embryonic, especially in the pediatric population. We need to direct research to formally study seizure sub-groups for prevention, treatment and prognosis of this condition.

### Other methods to treat non-epileptic seizures

#### A. Medicines

1. **Anti-anxiety therapy:** this medicine is given to decrease anxiety and help you feel calm and relaxed.
2. **Anti-depressant:** this medicine is given to decrease the symptoms of depression

#### B. Psychosocial therapy

- a. **Cognitive behavioral therapy:** with a therapist, you will learn to face the feared object or situation slowly and carefully. You will also learn to control the mental and physical reactions of fear.
- b. **Psychotherapy:** your therapist may include your family or people who are close to you during these talks.
- c. Paradoxical injunction therapy.<sup>[25]</sup>

#### Anti-anxiety

An anxiolytic (also antipanic or antianxiety agent)<sup>[25]</sup> is a medication or other intervention that inhibits anxiety. This effect is in contrast to anxiogenic agents, which increase anxiety. Together these categories of psychoactive compounds or interventions may be referred to as anxiotropic compounds/agents. Some recreational drugs such as ethanol (alcohol) induce anxiolysis. Anxiolytic medications have been used for the treatment of anxiety disorders and its related psychological and physical symptoms. Bright light therapy and other interventions have also been found to have an anxiolytic effect.<sup>[26]</sup>

**Benzodiazepines**

- Alprazolam (Xanax)- panic, generalized anxiety, phobias, social anxiety.
- Clonazepam (Klonopin) - panic, generalized anxiety, phobias, social anxiety
- Diazepam (Valium) - generalized anxiety, panic, phobias
- Lorazepam (Ativan) - generalized anxiety, panic, phobias
- Oxazepam (Serax) - generalized anxiety, phobias
- Chlordiazepoxide (Librium) - generalized anxiety, phobias

**Tricyclic Antidepressants**

- Imipramine (Tofranil) -panic, depression, generalized anxiety, PTSD
- Desipramine (Norpramin, Pertofrane and others) - panic, generalized anxiety, depression, PTSD
- Nortriptyline (Aventyl or Pamelor) - panic, generalized anxiety, depression, PTSD
- Amitriptyline (Elavil) -panic, generalized anxiety, depression, PTSD
- Doxepin (Sinequan or Adapin) - panic, depression
- Clomipramine (Anafranil) - panic, OCD, depression

**Other Antidepressants**

- Trazodone (Desyrel)-depression, generalized anxiety.

**Monoamine oxidase inhibitors (MAOIS)**

- Phenelzine (Nardil) - panic, OCD, social anxiety, depression, generalized anxiety, PTSD
- Tranylcypromine (Parnate) - panic, OCD, depression, generalized anxiety, PTSD

**Selective serotonin reuptake inhibitors (SSRIS)**

- Fluoxetine (Prozac) - OCD, depression, panic, social anxiety, PTSD, generalized anxiety
- Fluvoxamine (Luvox) - OCD, depression, panic, social anxiety, PTSD, generalized anxiety
- Sertraline (Zoloft) - OCD, depression, panic, social anxiety, PTSD, generalized anxiety
- Paroxetine (Paxil) - OCD, depression, panic, social anxiety, PTSD, generalized anxiety
- Escitalopram oxalate (Lexapro) - OCD, panic,depression, generalized anxiety, social anxiety, PTSD, generalized anxiety
- Citalopram (Celexa) - depression, OCD, panic, PTSD, generalized anxiety.

**Serotonin-norepinephrine reuptake inhibitors (SNRIS)**

- Venlafaxine (Effexor) - panic, OCD, depression, social anxiety, generalized anxiety
- Venlafaxine XR (Effexor XR) - panic, OCD, depression, social anxiety, generalized anxiety
- Duloxetine (Cymbalta) - generalized anxiety, social anxiety, panic, OCD.

**Mild Tranquilizer**

- Buspirone (buspar) - generalized anxiety, OCD, panic.

**Anticonvulsants**

- Valproate (Depakote) - panic
- Pregabalin (Lyrica) -generalized anxiety disorder
- Gabapentin (Neurotin) - generalized anxiety, social anxiety

**Selective Serotonin Reuptake Inhibitors**

Selective serotonin reuptake inhibitors or serotonin-specific reuptake inhibitor(SSRIs) are a class of compounds typically used as antidepressants in the treatment of depression, anxiety disorders, and some personality disorders.

SSRIs are primarily classified as antidepressants and typically higher dosages are required to be effective against anxiety disorders than to be effective against depression; nevertheless, most SSRIs have anxiolytic properties. They can, however, be anxiogenic early on in the course of treatment due to negative feedback through the serotonergic auto receptors. For this reason in some individuals a low dose concurrent benzodiazepine therapy might be beneficial during the early stages of serotonergics therapy to counteract the initial anxiogenic effects current serotonergics antidepressants. Examples include imipramine, doxepine, amitriptyline, and the unrelated trazodone. Monoamine oxidase inhibitors (MAOIs) are very effective for anxiety, but due to drug dangers, are rarely prescribed. Examples include: phenelzine and tranylcypromine.

A reversible MAOI, which has none of the dietary restrictions associated with classic MAOI's, moclobemide is used in severe SSRI's and SNRI's caused SSRI discontinuation syndrome, an often overlooked and damaging syndrome which is objectively and subjectively as bad or, for some, even worse than Benzodiazepine withdrawal syndrome.

**Mebicar**

Mebicar (mebicarum) is an anxiolytic produced in Latvia and used in Eastern Europe. Mebicar has an effect on the structure of limbic-reticular activity, particularly on hypothalamus emotional zone, as well as on all 4 basic neuro mediator systems –  $\gamma$  aminobutyric acid (GABA), choline, serotonin and adrenergic activity. Mebicar decreases the brain noradrenaline level, exerts no effect on the dopaminergic systems, and increases the brain serotonin level.

**Afobazole**

Afobazole is an anxiolytic drug launched in Russia in the early 2000s. Its mechanism of action remains poorly defined, with GABAergic, NGF and BDNF release promoting, MT1 receptor antagonism, MT3 receptor antagonism, and sigma agonism all thought to have some

involvement. It has yet to find clinical use outside of Russia.

### Selank

Selank is an anxiolytic peptide based drug developed by the Institute of Molecular Genetics of the Russian academy of sciences. Selank is a heptapeptide with the sequence Thr-Lys-Pro-Arg-Pro-Gly-Pro. It is a synthetic analog of a human tetra peptide tufts in. As such, it mimics many of its effects. It has been shown to modulate the expression of interleukin-6 (IL-6) and affect the balance of T helper cell cytokines. There is evidence that it may also modulate the expression of brain-derived neurotropic factor in rats.

### Bromantane

Bromantane is a stimulant drug with anxiolytic properties developed in Russia during the late 1980s, which acts mainly by inhibiting the reuptake of both dopamine and serotonin in the brain, although it also has anticholinergic effects at very high doses. Study results suggest that the combination of psycho stimulant and anxiolytic actions in the spectrum of psychotropic activity of bromantane is effective in treating asthenic disorders compared to placebo.

### Emoxypine

Emoxypine is an antioxidant that is also an anxiolytic. Its chemical structure resembles that of pyridoxine, a type of vitamin B<sub>6</sub>.

### Azapirones

Azapirones are a class of 5-HT<sub>1A</sub> receptor agonists. Currently approved azapirones include buspirone (Buspar) and tandospirone (Sediel).

### Barbiturates

Barbiturates exert an anxiolytic effect linked to the sedation they cause. The risk of abuse and addiction is high. Many experts consider these drugs obsolete for treating anxiety but valuable for the short-term treatment of severe insomnia, though only after benzodiazepines or non-benzodiazepines have failed. They are rarely prescribed any more.

### Hydroxyzine

Hydroxyzine (Atarax) is an old antihistamine originally approved for clinical use by the FDA in 1956. It possesses anxiolytic properties in addition to its antihistamine properties and is also licensed for the treatment of anxiety and tension. It is also used to induce sedation after anesthesia. It has been shown to be as effective as benzodiazepines in the treatment of generalized anxiety disorder, while producing fewer side-effects.

### Pregabalin

Pregabalin's therapeutic effect appears after 1 week of use and is similar in effectiveness to lorazepam, alprazolam, and venlafaxine, but pregabalin has

demonstrated superiority by producing more consistent therapeutic effects for psychic and somatic anxiety symptoms. Long-term trials have shown continued effectiveness without the development of tolerance, and, in addition, unlike benzodiazepines, it does not disrupt sleep architecture and produces less severe cognitive and psychomotor impairment; it also has a low potential for abuse and dependence and hence preferred over the benzodiazepines.

### Validol

Sublingual administration of Validol produces a sedative effect, and has moderate reflex and vascular dilative action caused by stimulation of sensory nerve receptors of the oral mucosa followed by the release of endorphins. Validol is typically administered as needed for symptom relief.

### Picamilon

It is a prodrug formed by combining niacin with GABA that is able to cross the blood-brain barrier and is then hydrolyzed into GABA and niacin. It is theorized that the GABA released in this process activates GABA receptors, with potential to produce an anxiolytic response. Picamilon is sold in the United States as a dietary supplement, while in Russia it is sold as a prescription drug.

### Chlorpheniramine

Diphenhydramine (Benadryl) have hypnotic and sedative effects with mild anxiolytic-like properties (off-label use). These drugs are approved by the FDA for allergies, rhinitis, and urticaria.

### Melatonin

It has anxiolytic properties, likely mediated by the benzodiazepine/GABAergic system. It has been used experimentally as an effective premedicant for general anesthesia in surgical procedures.

### Inositol

In a double-blind, controlled trial, *myo*-inositol (18 grams daily) was superior to fluvoxamine for decreasing the number of panic attacks and had fewer side-effects.

### Anti-Depressants

Depression is the most common psychiatric disorder in patients with epilepsy and a significant cause of morbidity. Reported rates of depression in epilepsy are 20–55% for patients with recurrent seizures, depending on the study. There is growing evidence of a biological link between depression and epilepsy, and depleted biogenic amines and gamma aminobutyric acid may be significant factors in the development of both disorders.

There is a high incidence of psychiatric comorbidity in people with epilepsy (PWE), particularly depression. The manifold adverse consequences of comorbid depression have been more clearly mapped in recent years.

Accordingly, considerable efforts have been made to improve detection and diagnosis, with the result that many PWE are treated with antidepressant drugs, medications with the potential to influence both epilepsy and depression.

Exposure to older generations of antidepressants (notably tricyclic antidepressants and bupropion) can increase seizure frequency. However, a growing body of evidence suggests that newer ('second generation') antidepressants, such as selective serotonin reuptake inhibitors or serotonin-noradrenaline reuptake inhibitors, have markedly less effect on excitability and may lead to improvements in epilepsy severity. The second section describes neurobiological mechanisms implicated in both antidepressant actions and in Epileptogenesis, highlighting potential substrates that may mediate any effects of antidepressants on the development and progression of epilepsy.

Newer antidepressants such as the selective serotonin reuptake inhibitors (SSRIs) appear safe for almost all epilepsy patients. These drugs include:<sup>[27]</sup>

- Fluoxetine (prozac)
- Paroxetine (paxil)
- Sertraline (zoloft)
- Citalopram (celexa)
- Escitalopram (lexapro)

### Cognitive Behavioral Therapy

Cognitive behavioural therapy (CBT) refers to a range of techniques which focus on the construction and reconstruction of people's cognitions, emotions and behaviours. Generally in CBT, the therapist, through a wide array of modalities, helps clients assess, recognize and deal with problematic and dysfunctional ways of thinking, emoting and behaving.<sup>[28]</sup>

### CONCLUSION

Seizures are very common but prolonged seizures may lead to epilepsy -a brain disorder, which is still in the "Dawn of Darkness" i.e though it is a severe brain disorder effecting a wide range of population all over the world, people have no awareness about it. But in contrast Non Epileptic Seizures which are not accompanied by abnormal electric discharges, both of which differs in their causes results in misleading of proper diagnosis of actual seizures that are likely to cause epilepsy. The present study reveals a brief description about various types of Non epileptic Seizures including the treatment involved. According to this, Anxiolytics and Anti-Depressants are used by patients with Non Epileptic Seizures. Moreover it would be better to follow the proverb "Prevention is Better than Cure". This can be achieved by practicing a hale & healthy food habits and thus one can lead a non epileptic as well as antiepileptic life by gaining awareness about seizures, non epileptic seizures, epilepsy & other mortality defining disorders for mankind.

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