



ANXIETY DISORDERS IN ADULTS WITH EPILEPSY

Anxiety disorders are, together with depressive disorders, the most frequent psychiatric disorders in people with epilepsy (PWE). In fact, one in every three people with epilepsy are expected to have suffered from an anxiety disorder in the course of their life. Anxiety disorders can have a negative impact on the life of PWE at several levels: they can worsen quality of life, interfere with tolerance of antiepileptic drugs, increase suicide risk, and increase health care costs. Therefore, it is essential that symptoms of anxiety (and its frequent comorbid condition, depression) should be identified during ongoing care of every patient to minimize those risks cited above.

Types of Symptoms and Anxiety Disorders in Epilepsy

Psychiatric symptoms in epilepsy are the expression of:

1. An interictal anxiety disorder. This is the most frequently recognized type of anxiety symptoms and they are independent of seizure occurrence.
2. A side effect caused by medications used to treat epilepsy, or symptoms occurring after epilepsy surgery. These are known as iatrogenic symptoms.
3. A peri-ictal symptom and /or episode, that is symptoms or episodes that are temporally related to seizure occurrence. These are categorized as pre-ictal (they precede seizures by up to two to three days), ictal (they are the expression of the actual seizure, also known as aura) and postictal, in which case they occur a few hours to up to 5 days after seizures. While peri-ictal symptoms are relatively frequent, they are often unrecognized. Of note, the same patient may experience interictal, peri-ictal and iatrogenic anxiety symptoms / episodes.
4. Anxiety symptoms may also be an expression of a reactive process to the diagnosis of epilepsy and the limitations associated with it and /or may be associated with the fear of seizure occurrence.

Recognizing the type of anxiety symptom is essential, as the treatment differs by type. For example, remission of peri-ictal symptoms requires control of seizures, while a change of antiepileptic medication is necessary to eliminate iatrogenic symptoms. Interictal anxiety disorders will respond to pharmacologic therapy and /or psychotherapy.

- Interictal anxiety disorders are the expression of several symptoms that meet specific criteria described in the Diagnostic and Statistical Manual-5 (DSM-5) anxiety disorders chapter. In people with epilepsy, the most frequent anxiety disorders include:
 - Generalized anxiety, in which the predominant symptoms include constant worrying (without a cause), often associated with feelings of restlessness.
 - Social anxiety disorders present with an apprehension to meet new people.
 - Panic attacks consist of recurrent episodes of 5 to 20 minutes duration, during which the patient experiences a sensation of impending doom, shortness of breath, palpitations, diffuse sweating and a variety of physical symptoms that can include pressure in the chest, tingling sensations on one side of the body, or other symptoms.

- Simple Phobia, which consists of an intense and illogical fear to specific object(s) (e.g., insects, needles, etc.) or situations (e.g., heights, close spaces).

Epidemiology

- Approximately 20% to 30% of adults with epilepsy have anxiety disorders (compared to 9-10% in the general population).
- Estimates of anxiety disorder prevalence in PWE vary widely.
 - Clinical evaluation only: Anxiety disorder prevalence 8%
 - Structured clinical interview: Anxiety disorder prevalence 27%

This variation may be due to differences in HOW anxiety disorders were diagnosed, and suggests lack of recognition of anxiety in PWE with typical clinical evaluations.

- The prevalence of anxiety disorders in PWE is NOT associated with duration of epilepsy diagnosis, seizure control (or lack thereof), use of multiple seizure medications.
- Factors that *may affect* the prevalence of anxiety disorders in PWE: Employment status, social support and felt stigma.

Screening for and Diagnosing Anxiety

- Although collaboration amongst epileptologists, psychiatrists, and psychologists (along with other mental health professionals) optimizes diagnosis and treatment, epilepsy or neurology clinics may be the frontline for identifying/recognizing anxiety and anxiety-related disorders in PWE and offering an initial treatment plan. Proposed AAN quality measures specify that screening for anxiety, along with comorbid depression, should be performed at each visit.
- Ictal anxiety, also known as ictal fear or ictal panic, is particularly common among patients with temporal lobe epilepsy and is frequently confused with panic attacks. Yet, a careful history can easily help distinguish the two conditions. Key characteristics of ictal anxiety in contrast to a panic attack include: sudden onset and offset, duration typically less than 30 seconds and occasionally up to 1 to 2 minutes (vs 5 to 20 minutes for panic attacks), symptoms awakening the patient from sleep at night, and the occurrence of other symptoms and signs seen in seizures of mesial temporal lobe origin, such as feelings of déjà-vu, epigastric discomfort, excessive salivation and confusion.
- It may be helpful to assess for:
 - the impact of psychosocial issues (e.g. being unable to drive, stigma related to having epilepsy), and the timing of symptoms with regard to ictal phenomenon (i.e. are the symptoms peri-ictal or ictal?).
 - possible contributions from concurrent substance or medication use, e.g., initiation of AEDs, negative side-effects of AEDs, recent withdrawal of AEDs with mood stabilizing and /or anti-anxiety properties, and withdrawal from antidepressant psychotropics (anxiety is a symptom associated with discontinuation syndrome), as well as a positive family history of anxiety and depressive disorders in first degree relatives.
- Anxiety disorders may be identified using DSM-5 based clinical interviews, including structured and semi-structured interviews, and open questionnaires. Rating scales are often used to identify symptoms of anxiety, but they are mostly used to screen for the “possible” existence of an anxiety disorder and by themselves, they do not establish a diagnosis.
- There are screening instruments that have been validated in PWE. Of these, the Generalized Anxiety Disorder-7 (GAD-7) and Neuro-QOL Anxiety Scale are freely available¹.

¹ http://www.phqscreeners.com/sites/g/files/g10016261/f/201412/GAD-7_English.pdf
<http://www.healthmeasures.net/explore-measurement-systems/neuro-qol>

Clinicians who do not wish to use structured questionnaires may ask questions such as: Over the last couple of weeks have you been feeling nervous, on edge, maybe even fearful that something bad is going to happen? Have you tried and not been able to stop worrying about things?

Treatment

Several therapeutic modalities are available to treat anxiety disorders in PWE. Treatment strategies do not differ from those used in non-epilepsy patients. Controlled studies are needed to develop tailored treatment strategies specific for PWE.

Psychotherapy Approaches to Treating Anxiety in PWE

- Available evidence indicates that cognitive-behavioral therapy (CBT) is the preferred psychotherapeutic intervention when treating most anxiety-related disorders in PWE.
- Other psychotherapy treatments include: behavioral therapy (e.g., conditioning, relaxation training, biofeedback, and systematic desensitization), psychoeducational approaches, and mindfulness.

Pharmacologic Treatment of Anxiety in PWE

- There are no controlled trials for the psychopharmacologic treatment of anxiety-related disorders within PWE; therefore, treatment should be individualized.
- The proposed treatment strategies for the treatment of anxiety in PWE do not differ from those available for patients without epilepsy
- Selective serotonin reuptake inhibitors (SSRIs) and serotonin and norepinephrine reuptake inhibitors (SNRIs) should be considered as first line pharmacologic treatment, given their favorable side-effect profile and absent seizure propensity when used at therapeutic doses, bearing in mind that certain agents may lead to an increase in AED levels through their enzyme-inhibiting effects (Kerr et al., 2011).
- The following table summarizes recommendations for pharmacologic treatment of anxiety disorders in epilepsy (Mula, 2013, 2016) and in the general population (Katzman et al., 2014). To better appreciate first-line/second-line treatments and level of evidence, please refer to these articles and other references. This information is not meant to limit potential alternative pharmacologic interventions, especially in light of the increased number of psychotropics now available in each drug class and the use of adjunctive therapies.

Pharmacologic Treatments for Common Anxiety Disorders

Type of Anxiety Disorder	Pharmacologic Treatment
Social anxiety disorder	SSRIs (sertraline, escitalopram, paroxetine), SNRIs (venlafaxine, duloxetine), MAOI (monoamine oxidase inhibitor, phenelzine), benzodiazepine (clonazepam), buspirone (serotonergic anxiolytic), and AEDs (pregabalin, gabapentin)
Generalized anxiety disorder	AED (pregabalin), SSRIs (escitalopram, paroxetine, sertraline), SNRIs (duloxetine, venlafaxine), benzodiazepines, imipramine (tricyclic antidepressant [TCA]), quetiapine (atypical antipsychotic), buspirone (serotonergic anxiolytic), and hydroxyzine
Panic disorder	SSRIs (citalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, escitalopram), SNRI (venlafaxine), benzodiazepines, TCAs (clomipramine, imipramine), mirtazapine (antidepressant), and reboxetine (antidepressant)

(Table is modified from Mula M. *Treatment of anxiety disorders in epilepsy: an evidence-based approach*. *Epilepsia*, 2013; 54(Suppl 1):13-8, with permission from Wiley and The International League Against Epilepsy.)

References

- Fiest, KM, Patten, SB, & Jetté, N. Screening for depression and anxiety in epilepsy. *Neurologic Clinics* 2016; 34:351-361.
- Kanner AM. Anxiety disorders in epilepsy: the forgotten psychiatric comorbidity. *Epilepsy Curr* 2011; 11:90-1.
- Katzman, MA, Bleau, P, Blier, P, Chokka, P, Kjernisted, K, Van Ameringen, M et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress, and obsessive-compulsive disorders. *BMC Psychiatry* 2014; 14(Suppl 1):S1.
- Kerr MP, Mensah S, Besag F, de Toffol B, Ettinger A, Kanemoto K, et al. International consensus clinical practice statements for the treatment of neuropsychiatric conditions associated with epilepsy. *Epilepsia* 2011; 52:2133-8.
- Mula M. Treatment of anxiety disorders in epilepsy: an evidence-based approach. *Epilepsia*, 2013; 54(Suppl 1):13-8.
- Mula M. Using anxiolytics in epilepsy: neurobiological, neuropharmacological and clinical aspects. *Epileptic Disord* 2016; 18:217-27.
- Mula M, Kanner AM. Introduction--Treatment of psychiatric disorders in adults with epilepsy: what every epileptologist should know. *Epilepsia* 2013; 54(Suppl 1):1-2.
- Scott AJ, Sharpe L, Hunt C, Gandy M. Anxiety and depressive disorders in people with epilepsy: A meta-analysis. *Epilepsia* 2017; 58:973–982.
- Tang V, Michaelis R, Kwan P. Psychobehavioral therapy for epilepsy. *Epilepsy Behav* 2014; 32:147-155.

Websites on anxiety which may be helpful to children, teens and parents:

“Anxiety Disorders” from Cleveland Clinic <https://my.clevelandclinic.org/health/articles/anxiety-disorders>

“Epilepsy, anxiety and depression” from www.beyondblue.org.au
<http://resources.beyondblue.org.au/prism/file?token=BL/0835>

AnxietyBC® <https://www.anxietybc.com>

Disclaimer: This information sheet is designed to serve as a quick reference resource for clinicians. It is not intended to establish a community standard of care, replace a clinician's medical judgment, or establish a protocol for all patients. The clinical conditions contemplated by this information sheet will not fit or work with all patients. Approaches not covered in this information sheet may be appropriate.