EPILEPSY FOUNDATION®
END EPILEPSY® TOGETHER

The Intersection of Epilepsy and Psychiatric Disorders

Mission Statement

To lead the fight to overcome the challenges of living with epilepsy and to accelerate therapies to stop seizures, find cures, and save lives.

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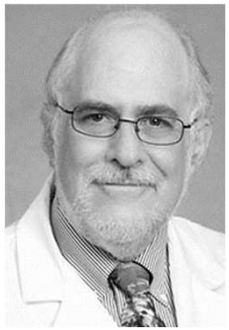

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Its contents are solely the responsibility of the authors and do not necessarily represent the views of the CDC.

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Objectives

- Review the epidemiology of psychiatric comorbidities in people with epilepsy
- Describe the bidirectional relationship between epilepsy and common psychiatric disorders
- Describe the temporal relationship between psychiatric symptoms and seizures
- Describe treatment options in patients with comorbid disease

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Seizures & Epilepsy

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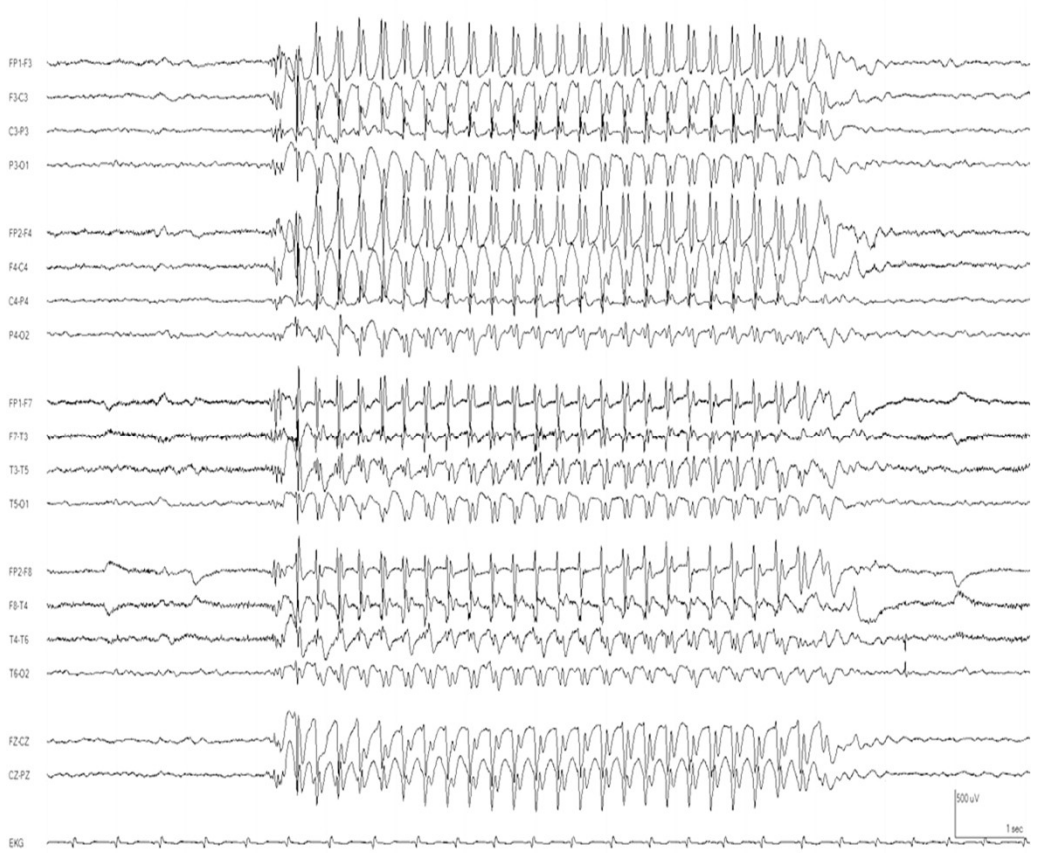
Seizures

- Electrical activity in the brain is usually carefully balanced
- A seizure occurs *when abnormal and excessive* electrical activity temporarily interrupts normal brain function
- **EVERY** brain has the potential to seize

The way a seizure appears depends on type of seizure a person is experiencing, and the area of brain involved.



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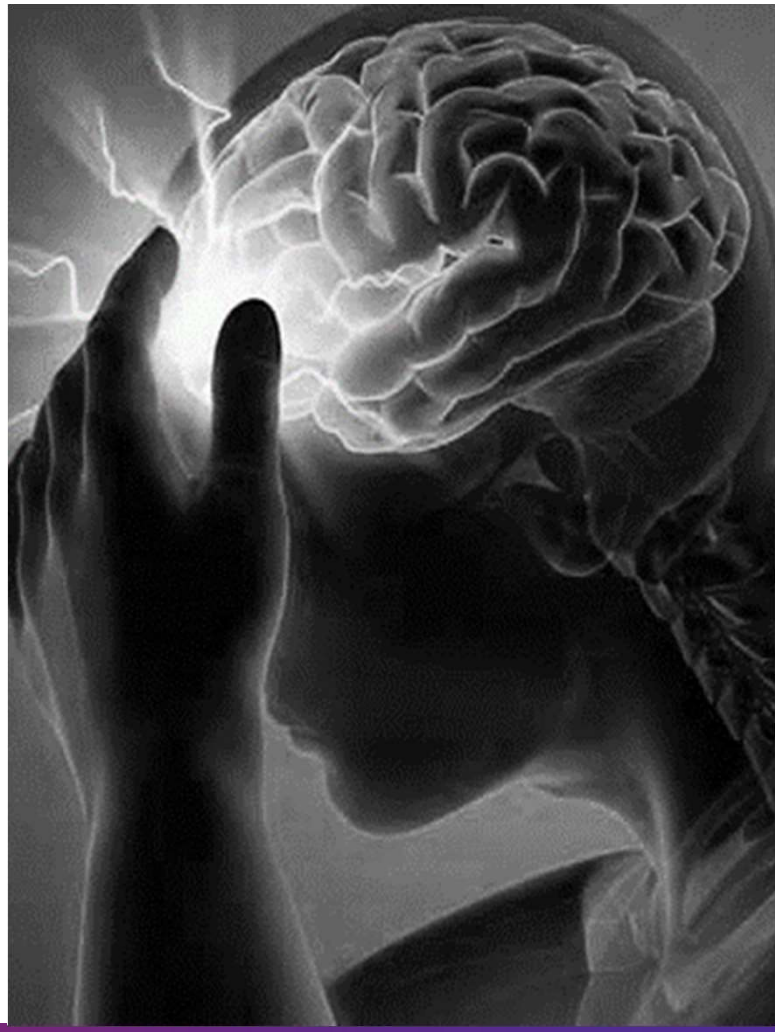
Epilepsy

The diagnosis of epilepsy indicates that a person is at risk for recurrent seizures.

- It does not indicate the cause
- It does not indicate prognosis
- There are many different “types” of epilepsies



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Epilepsy and Psychiatric Disorders

- 3.5 million people in the United States live with epilepsy
- Between 25 and 50 % of people living with epilepsy will be diagnosed with a psychiatric comorbidity
- **Complex** problem
- **Common** problem

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Patient Vignettes

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"I drove 2 hours to come to this support group tonight. It is the closest one to where we live. It is my first one. I just needed to speak with other moms. My son is 11 and has been suspended from school 5 times in two years. Yesterday was number 5. He has behavioral outbursts for no reason. We have seen behaviors at home too but not as bad as at school. Yesterday he threw his chair across the classroom. Thankfully no one was seriously injured. We can't figure out what is happening with him. He can't tell us. We feel lost. He hasn't had a seizure for 2 months. I don't know if we can go through another medication change. He is on a waiting list for cognitive behavioral therapy."

- Allana, mom to Aiden, age 11

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"I can't sleep, so yeah, I drink a bottle of wine every night. I come home from work wound up. I have a plumbing business and I can't drive myself to jobs. I have to hire a kid to drive me around. It's making the finances tight. I can't keep buying pills that don't work so I take one instead of two in the morning. My wife is telling me she's going to leave. She can't handle the seizures, the money stress, and now the drinking."

- Paul, age 46, whose wife called in to neurologist to report her husband had been rationing his medication to save money, drinking nightly and having frequent generalized tonic clonic seizures

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“It wasn’t on our radar. We were focused on the seizures and the tests for surgery and getting him through the surgery. He didn’t tell us. He never wanted us to worry about him. He would be in the hospital having seizures recorded and wake up from a big seizure and say, “Mom, are you ok?”

We spent the past year thinking he’ll have the brain surgery and the seizures will stop. No one promised us that would happen. But it was what we all were desperate for as a family.”

- Esme, mom to Henry, who took his own life at age 24, seven months post epilepsy surgery

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The Intersection of Epilepsy and Psychiatric Disorders

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How big of a problem is it?

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Lifetime Prevalence of Psychiatric Disorders

Psychiatric Disorder	Controls (%)	Epilepsy (%)
Major Depressive Disorder	10.7 (10.2–11.2)	17.4 (10.0–24.9)
Anxiety Disorder	11.2 (10.8–11.7)	22.8 (14.8–30.9)
Mood/Anxiety Disorders	19.6 (19.0–20.2)	34.2 (25.0–43.3)
Suicidal Ideation	13.3 (12.8–13.8)	25.0 (17.4–32.5)
Any Psychiatric Disorder	20.7 (19.5–20.7)	35.5 (25.9–44.0)

Tellez-Zenteno, JF et al., Epilepsia, 2007; 48:2336-2344

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Lifetime Prevalence Mental Health Disorders

Prevalence of any mental health disorder in past 12 months:

23.5% - with epilepsy

10.9% - without epilepsy

Lifetime prevalence suicidal ideation:

25% - with epilepsy

13.3% - without epilepsy

Tellez -Zenteno, JF, et al, Epilepsia, 2007, 48:2336-2344

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Prevalence Rates of Psychiatric Disorders in Epilepsy

Psychiatric Disorder	In Epilepsy (range)	General Population (range)
Depression	11%-60%	12%-15%[1]
Anxiety	19%-45%	2.5%-6.5%[2]
Psychosis	2%-8%	0.5%-0.7%[3]
ADHD	25%-30%?	2%-10%[4,5]

[1]Anthony, et al. 1995; [2]Weissman and Merikangas. 1986;[3]Kessler, et al. 1994; [4]Costello.1989; [5]Rutter. 1970.

LaFrance & Kanner. 2006. Epilepsy. In Psy Asp. Of Epilepsy.

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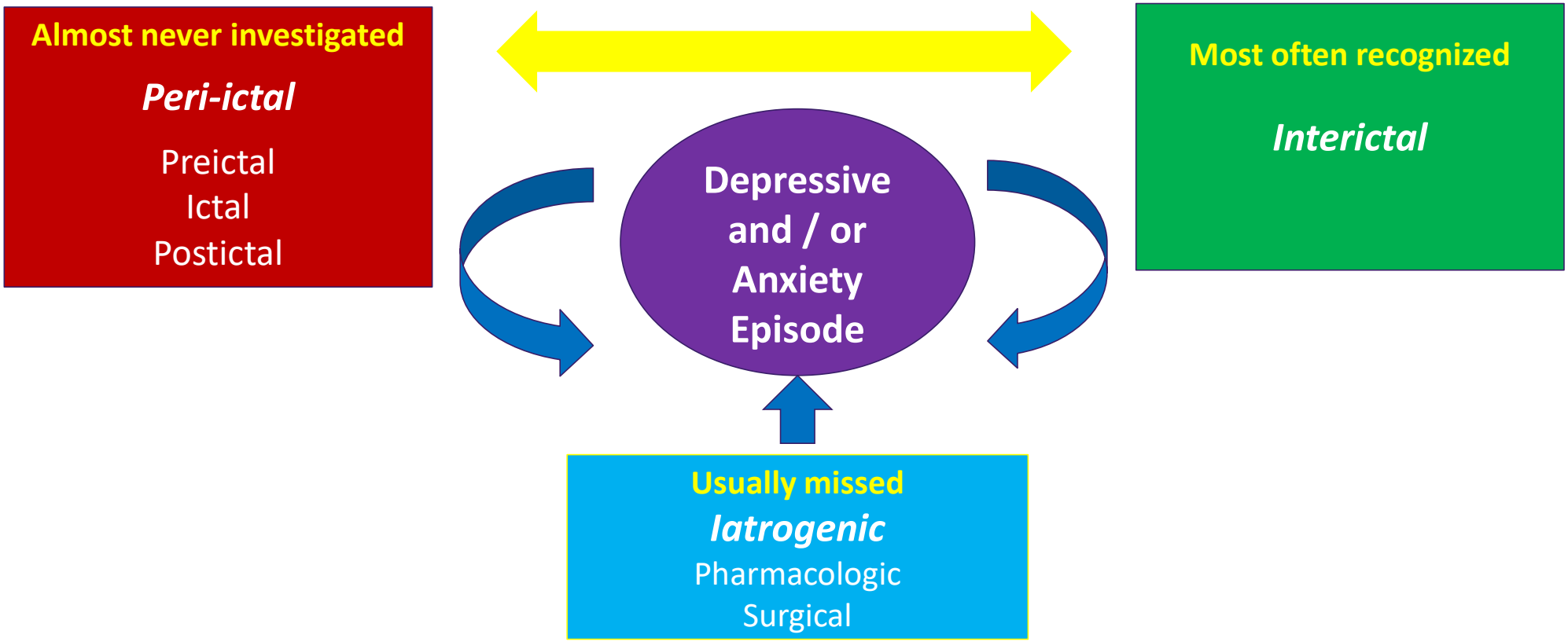
What type of psychiatric symptom is it?



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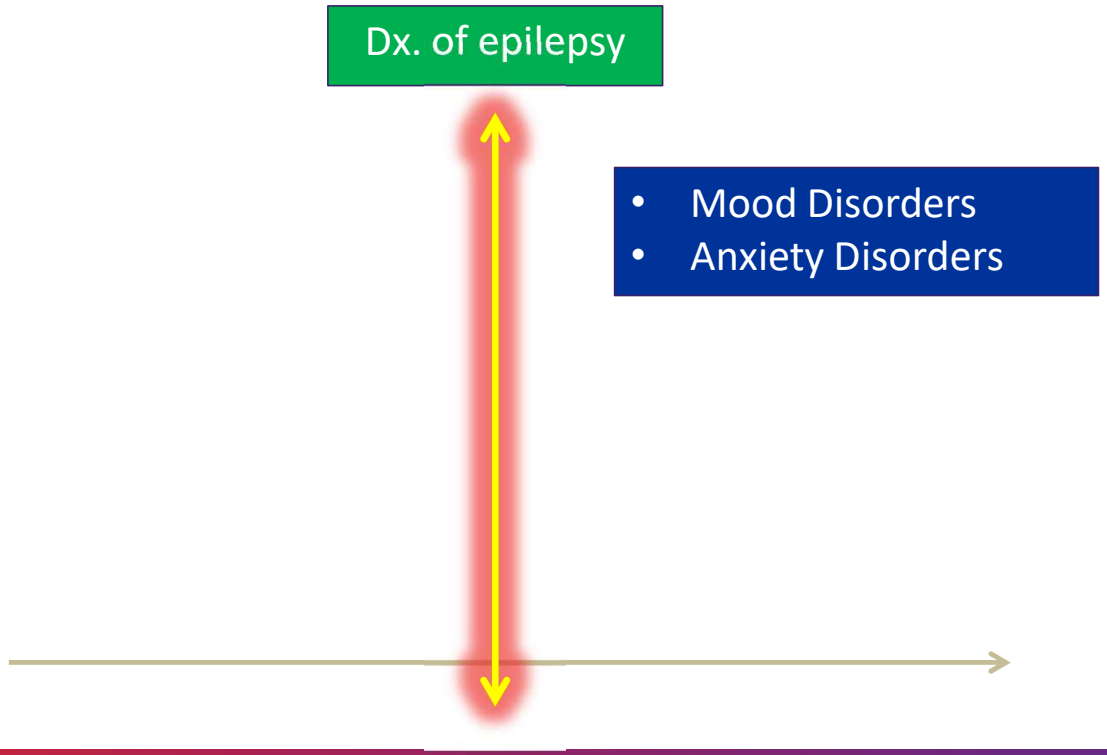
Onset psychiatric comorbidities relative to onset of epilepsy



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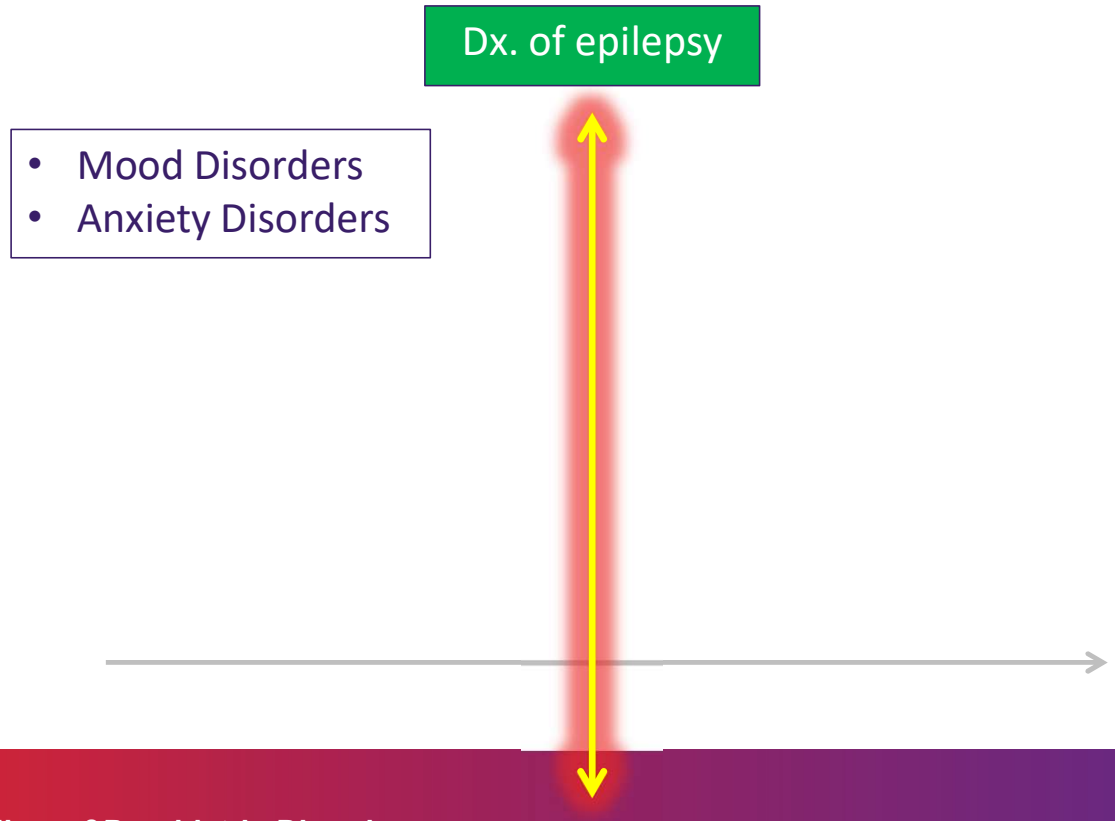

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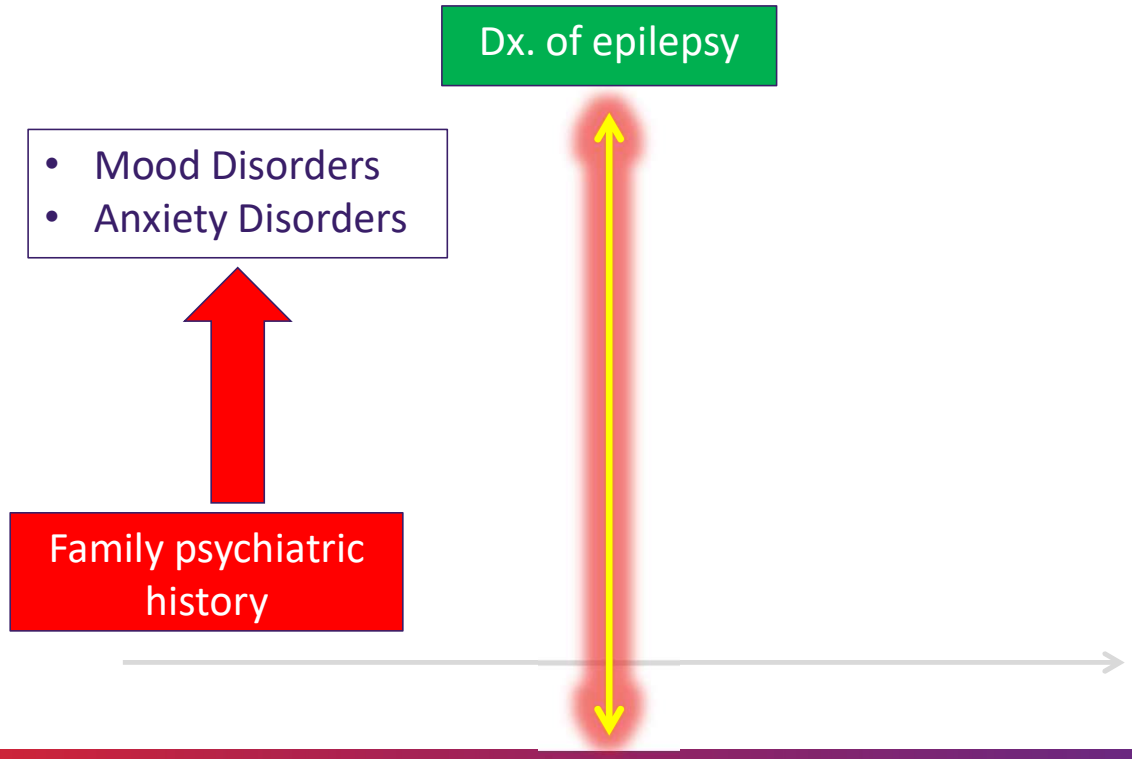

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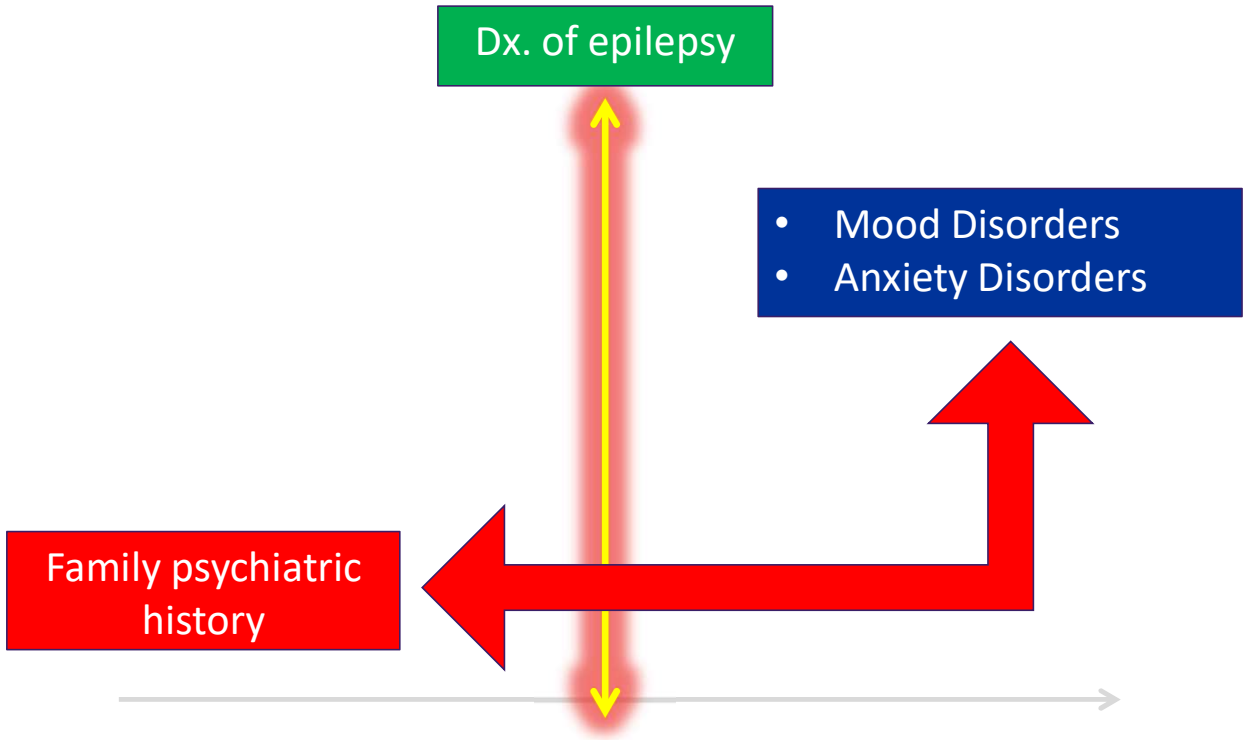

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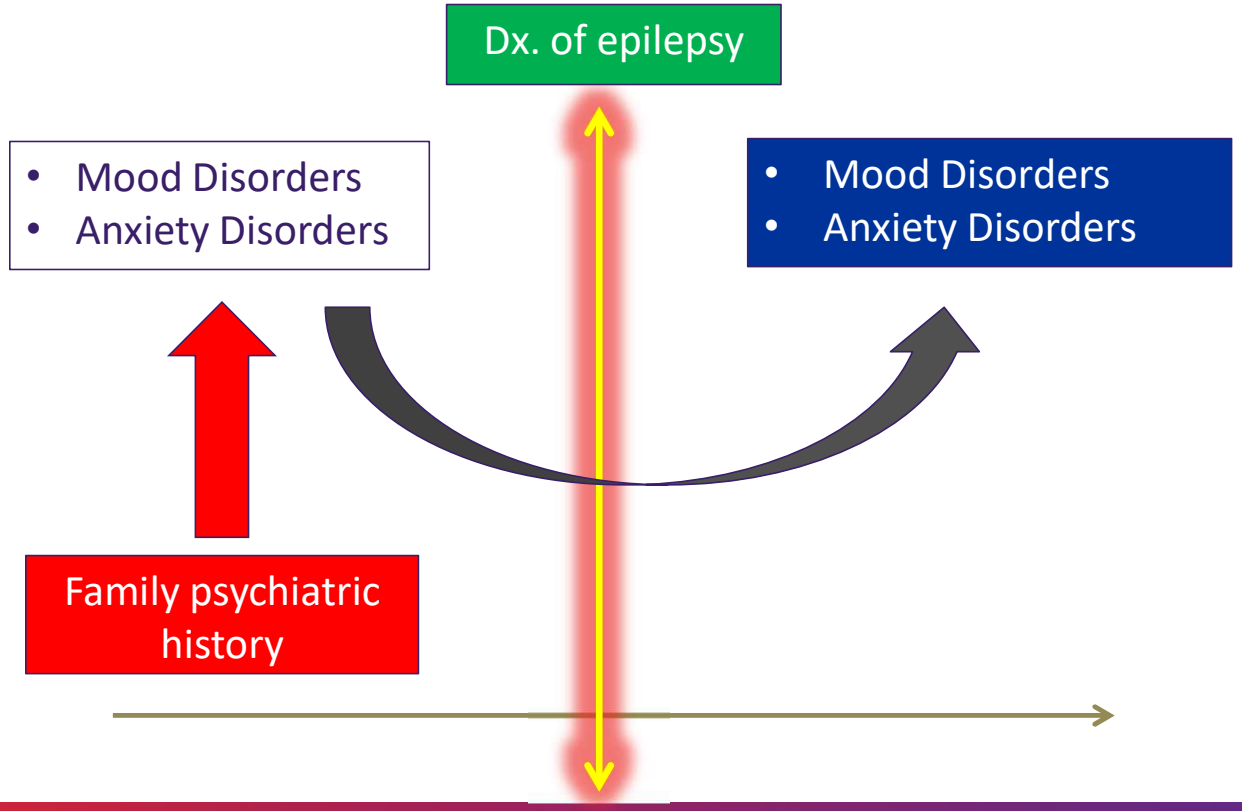

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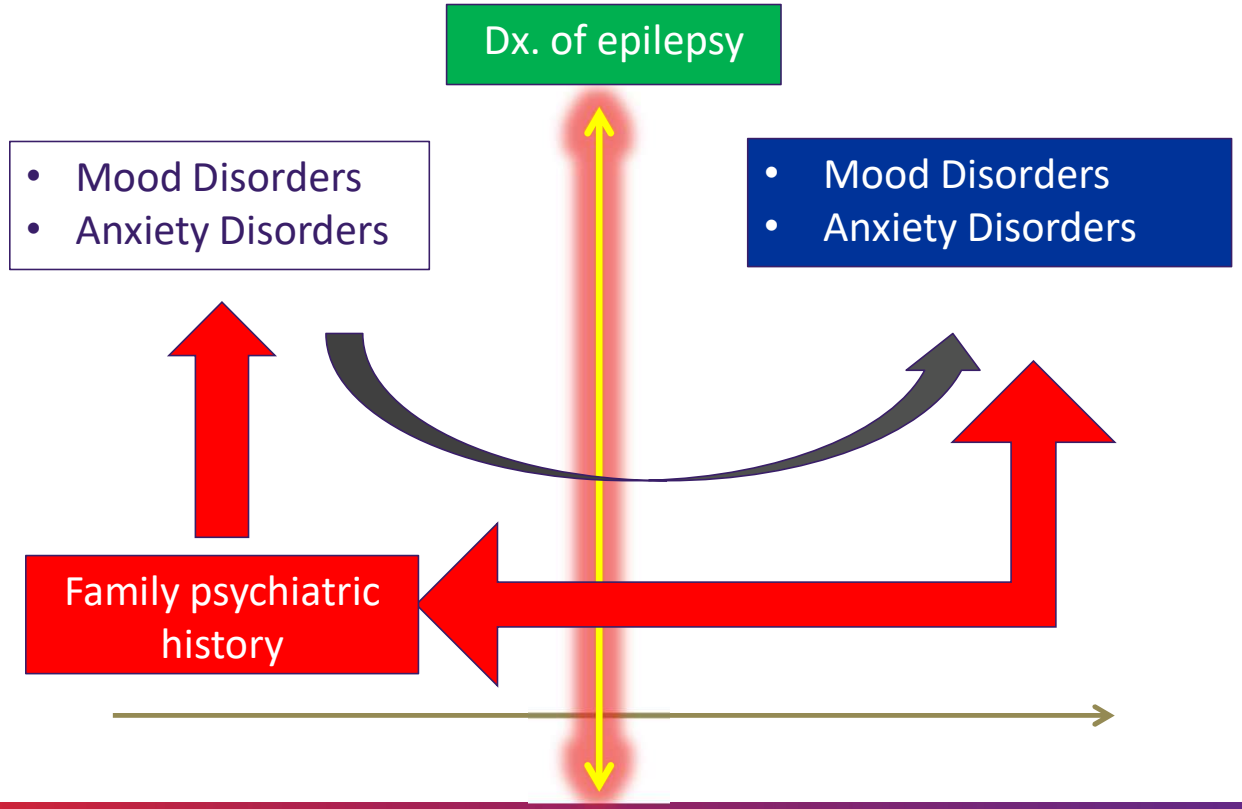

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Why should this be a priority?

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Impact of depression and anxiety episodes on the life of patients with epilepsy

Increased mortality risk
- *Christiansen et al., Lancet Neurol 2007*
- *Fazel et al., Lancet 2013*

Worse tolerance of antiepileptic drugs
- *Perucca et al., Neurology 2011*
- *Kanner et al., Epilepsia 2012*

Decreased quality of life
- *Guilliam et al., Neurology 2002*
- *Kanner et al., Epilepsia 2011*

Increased risk of psychiatric iatrogenic adverse events
- *Mula et al., Epilepsia 2003, 2007*

Worse seizure control with pharmacotherapy
- *Hitiris et al., Epilepsy Res, 2007*
- *Petrovsky et al., Neurology 2010*
- *Josephson et al., JAMA Neurol 2017*

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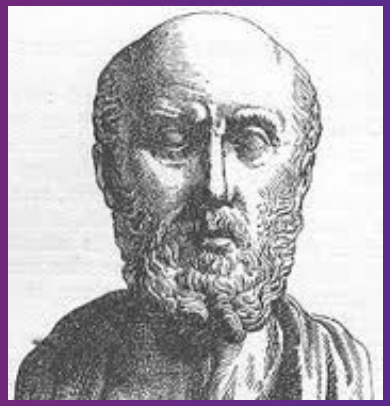
Hippocrates ' writings...



"...melancholics ordinarily become epileptics, and epileptics melancholics ....of these two states, what determines the preference is the direction the malady takes; if it bears upon the body, epilepsy, if upon the intelligence, melancholy "

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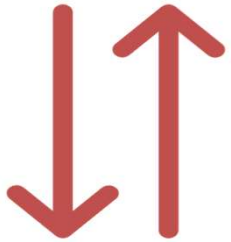
Bidirectional relation between epilepsy and psychiatric disorders

Patients with epilepsy have a 5 to 20-fold higher risk of developing depression



Patients with depression have a two-to five-fold higher risk of developing epilepsy

Hesdorffer et al., Ann Neurol 2012; Hesdorffer et al., Ann Neurol 2006

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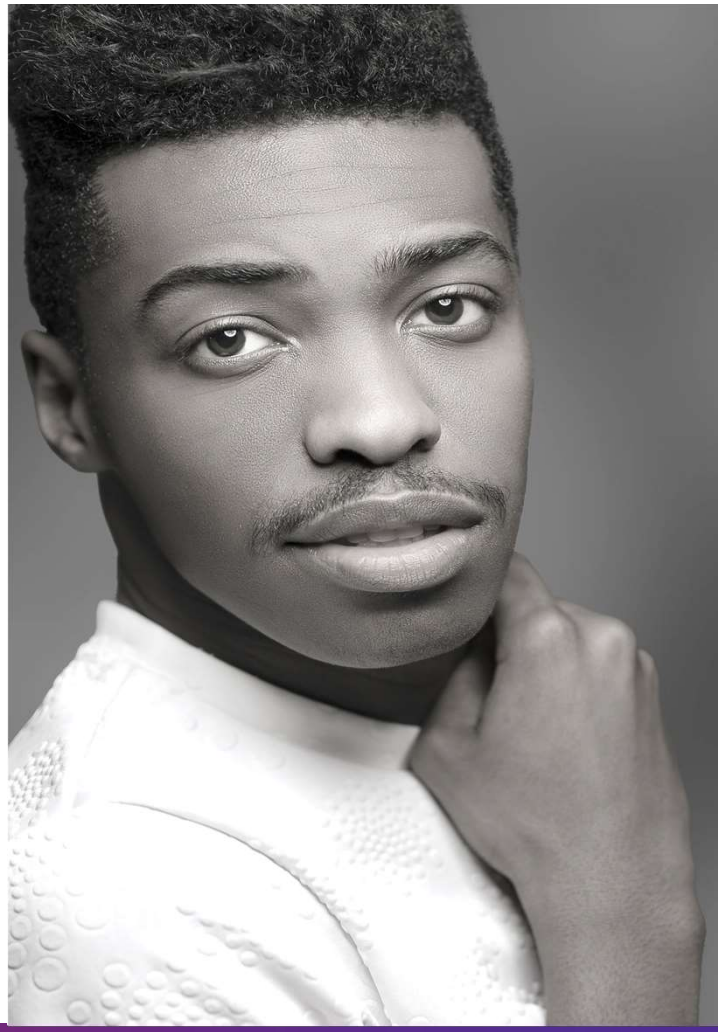
Risk of developing epilepsy associated with other psychiatric disorders

- Anxiety disorder: 2.5
- Suicidality: 4.5
- ADHD: 3.5
- Psychosis: 4-6



Hesdorffer et al., Arch Gen Psych 2004 ; Hesdorffer et al., Ann Neurol 2012

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Interictal episodes…

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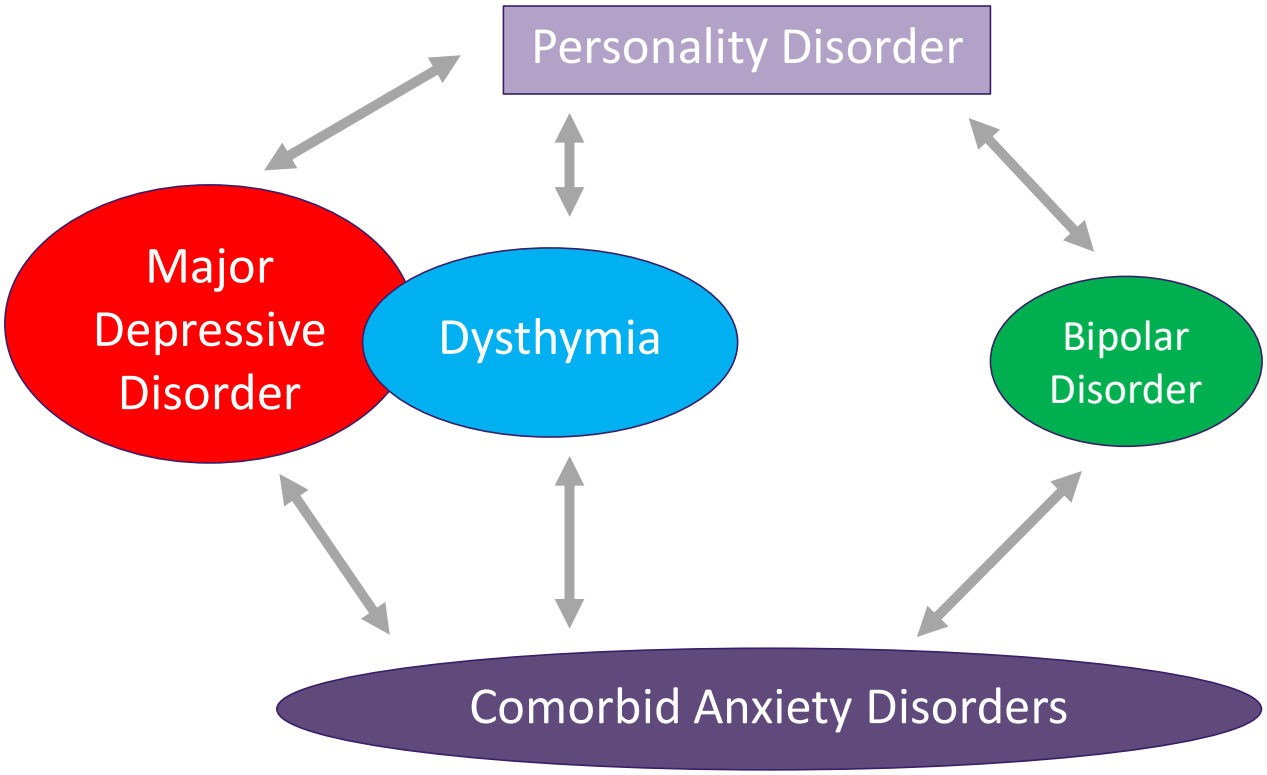
Interictal Depression in Epilepsy: Pleomorphic Presentation



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Iatrogenic Psychiatric Episodes

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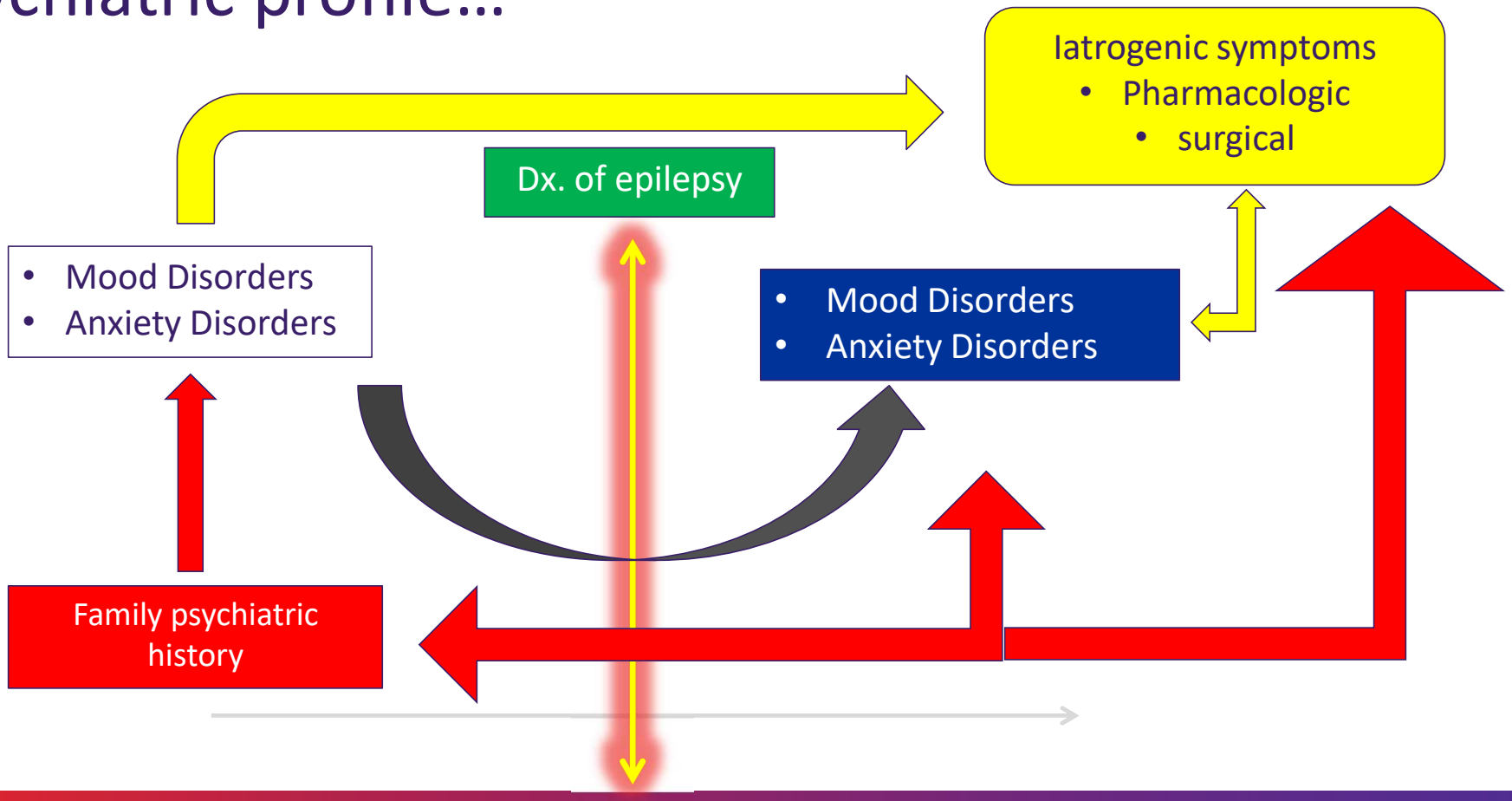
+ psychiatric profile…



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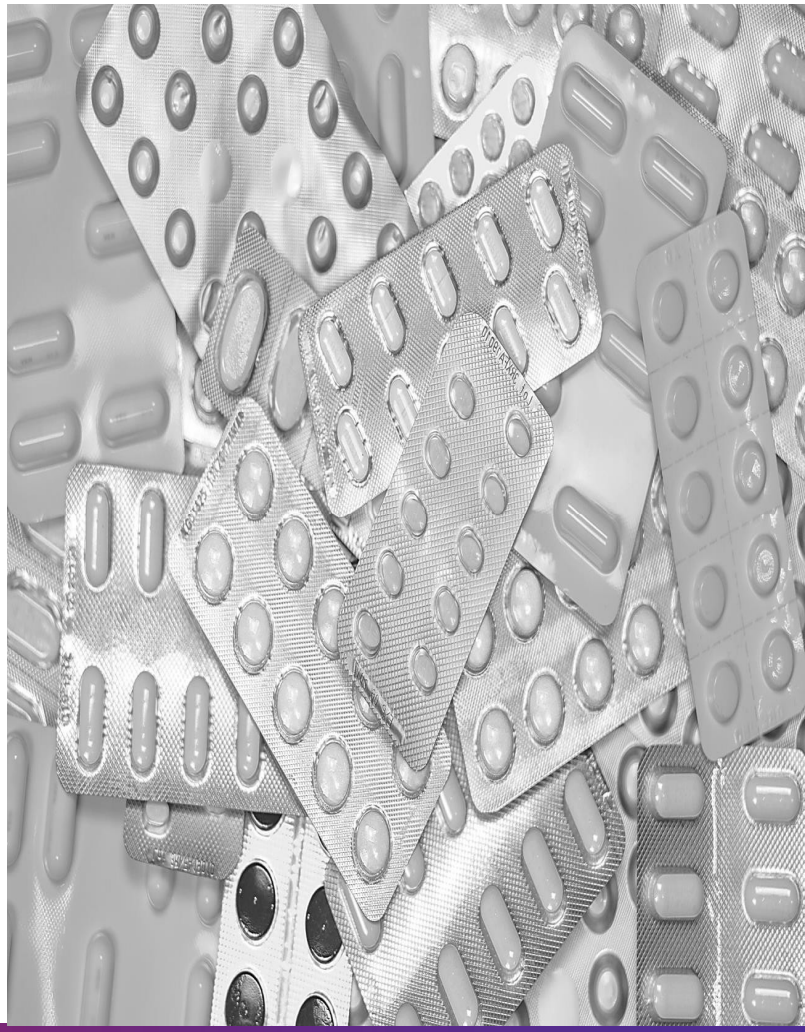
Mechanisms associated with the development of iatrogenic psychiatric episodes

1) Introduction of AED with negative psychotropic properties *in patients with + psychiatric history*

2) Withdrawal of AED with positive psychotropic properties *in patients with + psychiatric history*



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AEDs with psychotropic properties that can cause iatrogenic psychiatric episodes

Addition

Negative Properties

- Barbiturates
- Benzodiazepines
- Levetiracetam
- Topiramate
- Zonisamide
- Vigabatrine
- Tiagabine
- Perampanel

Discontinuation

Positive Properties

- Carbamazepine
- Valproic acid
- Oxcarbazepine
- Lamotrigine
- Gabapentin
- Pregabalin
- Benzodiazepines

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Peri-ictal Episodes

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Panic disorder… or is it ictal panic?

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Clinical Differentiation: Panic Disorder vs. Ictal Panic

	Panic Disorder	Ictal Panic
Symptom intensity	Feeling of impending doom	Less intense
Associated symptoms	Agoraphobia, GAD	Deja-vu, epigastric discomfort, excessive salivation
Duration of attack	>5 min	<30 seconds
Anticipatory anxiety	Common	Uncommon
Antidepressants	Helpful	No impact
Sleep-deprived interictal EEG	Normal	Often normal

Kanner AM, Nature Neurology 2016.

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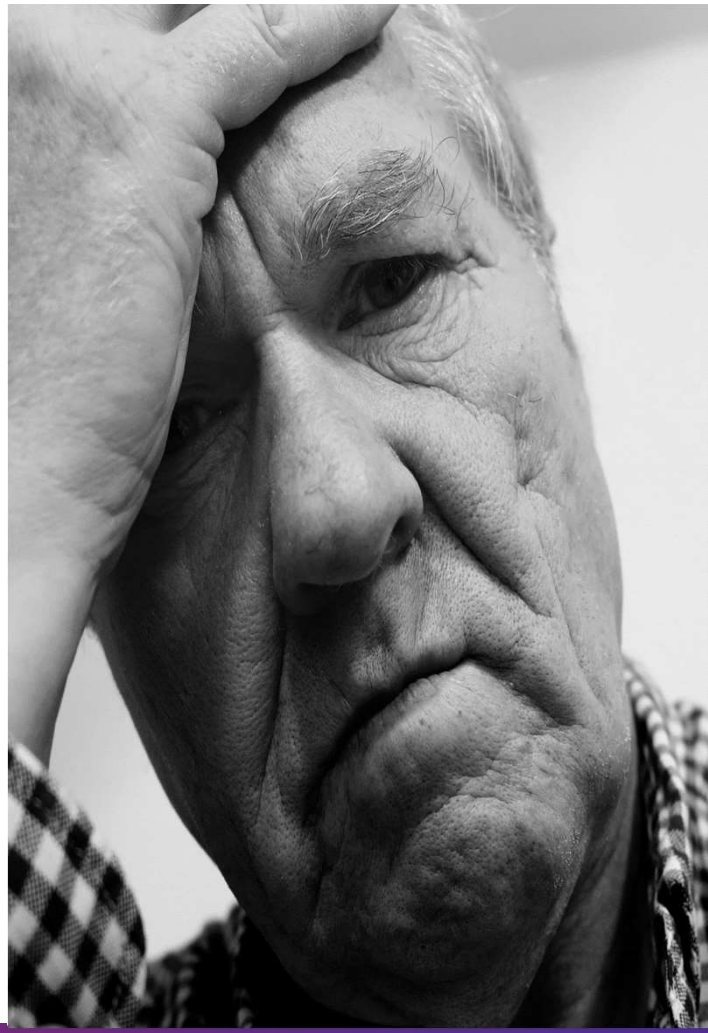
Postictal Psychiatric Symptoms Prevalence by Category

- N = 100
- Depression, n = 43
- ***Postictal suicidal ideation, n = 13***
- Anxiety, n = 45
- Psychosis, n = 7
- Neurovegetative, n = 62
- Cognitive, n = 82
- Cognitive without psychiatric, n = 14
- No symptoms, n = 12



Kanner et al, Neurology, 2004

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Postictal Symptoms of Depression

Any postictal symptom of depression, n = 43
Median number of symptoms 5 (range: 2-9)

Postictal symptom	Frequency (N = 100)	Duration (range, hrs)
Poor Frustration	36	24 (0.5-108)
Anhedonia	33	24(0.1-148)
Hopelessness	25	24(1.0-108)
Helplessness	31	24(1.0-108)
Crying Bouts	26	6(0.1-108)
Suicidal Ideation	*13*	*24(1.0-240)*
Irritability	30	24(0.5-108)
Guilt	23	24(0.1-240)
Self deprecation	27	24(1.0-120)

Kanner et al., Neurology 2004

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Postictal symptoms of anxiety

Symptoms of anxiety, total	N = 45	Median duration (range in hours)
Constant worrying	33	24 (0.5 – 108)
Panicky feelings	10	6 (0.1 – 148)
Agoraphobic symptoms	29	24 (0.5 – 296)
Due to fear of seizure recurrence	20	-
Compulsions	10	15 (0.1 – 72)
Self-consciousness	26	6 (0.05 – 108)

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Are antidepressant drugs safe in patients with epilepsy?

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Impact of mood disorders and antidepressant drugs on the occurrence of spontaneous seizures

- Assessment of seizure incidence between patients randomized to SSRIs, SNRIs, TCAs and placebo in regulatory studies
- Antidepressant treatments associated with *lower seizure incidence* relative to placebo for all SSRIs and SNRIs
- Standardized seizure ratio: 0.48, 95% CI 0.36-0.61
- The incidence of seizures among patients randomized to placebo was ***19-fold higher*** than that of the general population.

Alper et al., Biol Psychiatry 2007.

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Identifying in patients with epilepsy the presence of depressive and/or anxiety disorders in the outpatient clinic…

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Neurological Disorders Depression Inventory in Epilepsy (NDDI-E)

For statements below, please circle number that best describes you over the last two weeks including today.

SYMPTOMS	Always or Often	Sometimes	Rarely	Never
Everything is a struggle	4	3	2	1
Frustrated	4	3	2	1
Nothing I do is right	4	3	2	1
Feel guilty	4	3	2	1
Difficulty finding pleasure	4	3	2	1
I'd be better off dead	4	3	2	1

A score of > 15 is suggestive of major depressive episode

Gilliam et al. Lancet Neurol. 2006;5(5):399-405.

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Generalized Anxiety Disorder-7 (GAD-7)

Please circle number that best describes you over the last 2 weeks, including today.

SYMPTOMS	Nearly every day	More than half the days	Several days	Not at all
Feeling nervous, anxious or on edge	3	2	1	0
Not being able to stop or control worrying	3	2	1	0
Worrying too much about different things	3	2	1	0
Trouble relaxing	3	2	1	0
Being so restless that it is hard to sit still	3	2	1	0
Being easily annoyed or irritable	3	2	1	0
Feeling afraid as if something awful might happen	3	2	1	0

A score of > 10 is suggestive of generalized anxiety disorder

Spitzer et al. Arch Int Med. 2006;166:1092-1097

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Treatment

- Pharmacotherapy
- Cognitive behavior therapy
- Both

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Aims of Pharmacotherapy…

1) Remission of all symptoms of depression and anxiety

2) Adjust dose of antidepressant drug in the presence of enzyme-inducing antiepileptic drugs

3) Adjust the dose of AEDs according to inhibitory effects of SSRIs

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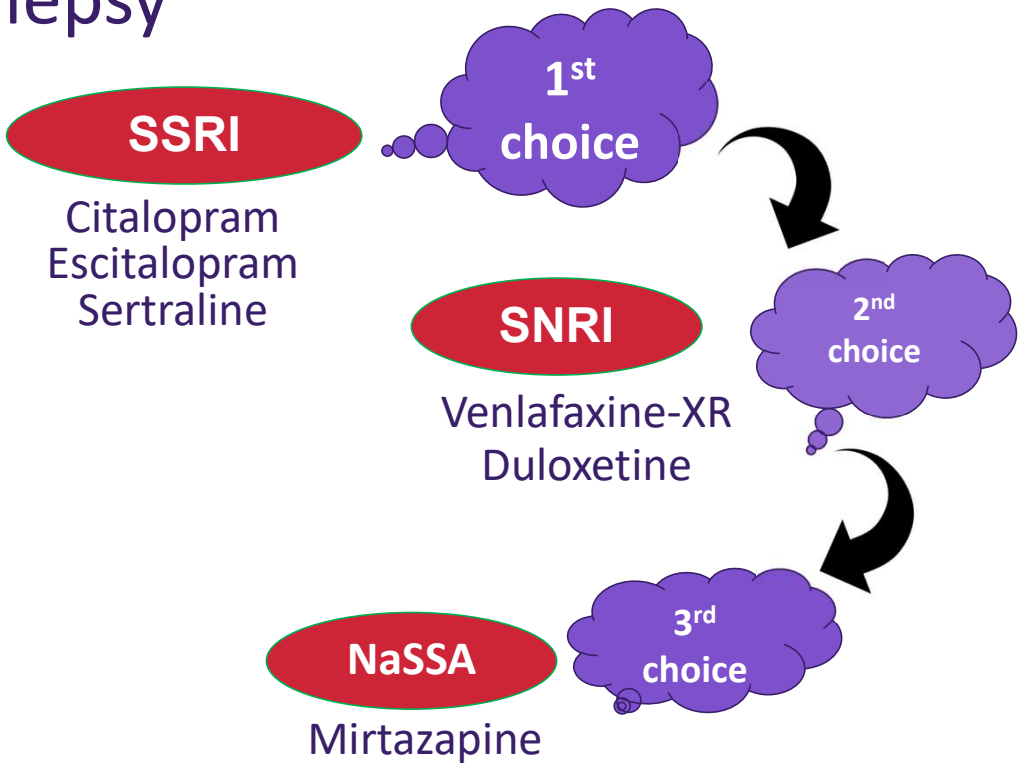
Pharmacotherapy of Depression and Anxiety Disorders in Epilepsy

In patients with bipolar disorder antidepressant medication should be used with great caution!



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Key Points …

In patients with epilepsy…

1) Mood and anxiety disorders are relatively frequent psychiatric comorbidities

2) Mood and anxiety disorders yield *serious and negative impacts* on the management of the seizure disorder and life of these patients at several levels including,

- decreased seizure control
- worse tolerance of AEDs
- increased suicidal risk
- decreased quality of life

3) Depression and anxiety can be safely treated with SSRIs and/or SNRIs

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Resources for Providers

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Epilepsy Foundation (EF) – Information for Professionals and Patients
www.epilepsy.com

Epilepsy Foundation 24/7 Helpline 1-800-332-1000

Centers for Disease Control and Prevention (CDC)
www.cdc.gov/epilepsy/index.html

American Epilepsy Society (AES)
www.aesnet.org

National Association of Epilepsy Centers
www.naec-epilepsy.org

American Academy of Neurology (AAN)
www.aan.com/Guidelines/home/ByTopic?topicId=23

American Academy of Pediatrics (AAP)
www.aap.org/en-us/Documents/Epilepsy%20Compendium%20Final.pdf

Veterans Affairs Epilepsy Centers of Excellence (VA-ECE)
www.epilepsy.va.org

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Managing Epilepsy Well (MEW) Newtwork

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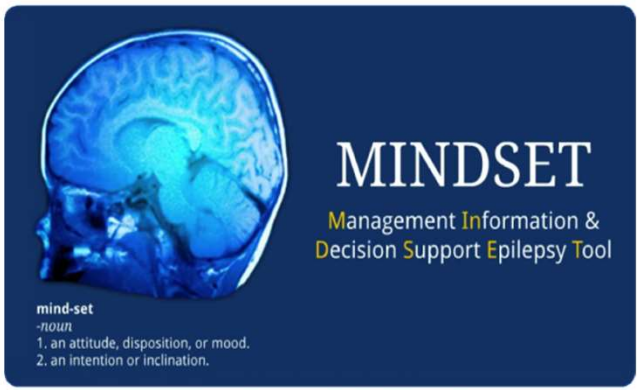

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- Epilepsy Basics
- Intersection of Epilepsy and Psychiatric Disorders
- Medical Therapy in Epilepsy
- Psychogenic Nonepileptic Seizures
- Cognitive Behavioral Therapy in Epilepsy
- Epilepsy Self-Management Programs

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Thank you

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