



**UW PACC**

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

# SEIZURES AND DEPRESSION

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# GENERAL DISCLOSURES

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# SPEAKER DISCLOSURES

- ✓ Honorarium from Academy of Psychosomatic Medicine - 2016
- ✓ No other conflicts to report

# OBJECTIVES

1. Described the relationship between seizures and depression
2. Describe the relationship between SI and seizure patient with co-morbid depression
3. Discuss the risks/benefits of treating comorbid depression in patient with seizure

# SEIZURES

- Seizure disorder = Epilepsy
- Involuntary activity in the brain
- 5/1000 people to 10/1000 people with 50/100,000 new diagnoses of epilepsy each year.  
Sander JW. The epidemiology of epilepsy revisited. CurrentOpinion in Neurology 2003;16(2):165–70.
- Multiple medical problems can present with seizure

# QUESTION 1

- Seizures protect against depression?

True

False

# QUESTION 1

- Seizures protect against depression?

True

False

# PSYCHIATRIC COMORBIDITY & SEIZURES

- Seizures and neuropsychiatric comorbidities are not a new observation
  - Hippocrates 1st commented on melancholy and depression Lewis.A Melancholia: a historical review J Ment Sci, 80 (1934), pp. 1–42
  - Noted that depression and seizure disorders can occur together
- Depression and anxiety have a bidirectional relationship with seizure disorders Kanner AM. Depression and epilepsy: a bidirectional

relation? Epilepsia2011;52(Suppl. 1):21–7. <http://dx.doi.org/10.1111/j.1528-1167.2010.02907.x>.



# PSYCHIATRIC COMORBIDITY & SEIZURES

[O' Rourke G1](#), [O' Brien JJ2](#). Seizure. 2017 Feb;45:160-168.  
doi: 10.1016/j.seizure.2016.12.006. Epub 2016 Dec 23.

- Systematic Review assessing barriers to AED adherence
  - Anxiety and depression common causes
  - Others include: beliefs about medication
  - Poor memory and self medication management
  - Multiple medications

# PSYCHIATRIC COMORBIDITY & SEIZURES

- Life time prevalence of depression in seizure disorders 20 - 60%

Grabowska-Grzyb A, Jedrzejczak J, Nagańska E, Fiszler U. Risk factors for depression in patients with epilepsy.

Epilepsy Behav 2006;8(2):411-7.

- Maybe more likely to develop depression if foci is front or temporal

# SPECIFIC DIAGNOSTIC CONSIDERATIONS

- Often helpful to describe symptoms as occurring
  - Preictal
  - Postictal
  - Interictal
- Unlike anxiety/aggression/confusion, depression is most commonly interictal phenomenon.
- Monitor for loss on interest in activities

# ICTAL VS NONICTAL

Appearance of symptoms	Length of symptoms	Associated symptoms	Consciousness	Recall	Episode EEG
Ictal	short < 3 min	stereotyped motor	Maybe altered	Limited	Abnormal
Nonictal	>20 min	None	Generally intact	Intact	Normal

Stern, Theodore A. (2010-06-25). Massachusetts General Hospital Handbook of General Hospital Psychiatry (Expert Consult Title: Online + Print) (Kindle Locations 15082-15085). Elsevier Health. Kindle Edition.

# QUESTION 2

- Suicide rates are highest prior to a diagnosis of a seizure disorder?

True

False

# QUESTION 2

- Suicide rates are highest prior to a diagnosis of a seizure disorder?

True

False

# SUICIDE & SEIZURE DISORDERS

- Suicidal ideation and suicide risk are 2x higher than general population
- Suicide is associated with up to 5% of all epilepsy deaths
- Highest risk periods are within 6 months of diagnosis and within a year of gaining good seizure control
- Never be afraid to screen and safety plan with these patients

Kanner AM. Depression in epilepsy: a complex relation with unexpected consequences. *Curr Opin Neurol* 2008; 21(2):190Y194.  
doi:10.1097/WCO. 0b013e3282f4e978.

# TREATMENT OF DEPRESSION IN SEIZURE DISORDERS

- Yoga
  - Cocrane reivew. Panebianco M1, Sridharan K, Ramaratnam S. Cochrane Database Syst Rev. 2015 May 2;(5):CD001524. doi: 10.1002/14651858.CD001524.pub2.
    - Limited data, but maybe better then no movement threrapy
    - No evidence for uncontrolled seizures



# TREATMENT OF DEPRESSION IN SEIZURE DISORDERS

Jackson CF, Makin SM, Baker GA. Neuropsychological and psychological interventions for people with newly diagnosed epilepsy. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD011311. DOI 10.1002/14651858.CD011311.pub2.

- Some evidence that CBT focusing on acceptance, coping skills, and depression management is effective
  - However, study quality are at risk of bias

# QUESTION 3

- With a few key exceptions, antidepressants do not clearly destabilize seizure control

True

False

# QUESTION 3

- With a few key exceptions, antidepressants do not clearly destabilize seizure control

True

False

# ANTIDEPRESSANTS & SEIZURE RISK

- Antidepressants are often described as inducing seizures
  - Most of this data comes from overdoses or overdoses in animal models
    - R. Ribot et al. / *Epilepsy & Behavior* 70 (2017) 5–9
    - S. Preskorn, G. Fast Tricyclic antidepressant induced seizures and plasma drug concentration *J Clin Psychiatry*, 53 (1992), pp. 160–162 - 300% the therapeutic dose range
    - W.S. Waring, J.A. Gray, A. Graham Predictive factors for generalized seizures after deliberate citalopram overdose *Br J Clin Pharmacol*, 66 (6) (2008), pp. 861–865 - 400% clinical dose
    - R. Clinckers, I. Smolders, A. Meurs, G. Ebinger, Y. Michotte Anticonvulsant action of hippocampal dopamine and serotonin is independently mediated by D2 and 5-HT<sub>1A</sub> receptors *J Neurochem*, 89 (2004), pp. 834–843 - 900% therapeutic level

# IMPACT OF ANTIDEPRESSANTS ON SEIZURES

- Ribot R, Ouyang B, & Kanner 2017
  - Retrospective 100 patient with epilepsy
  - $< 1$  seizure/month went on to have  $\geq 1$  seizure/month after initiating treatment with antidepressants
  - no seizure recurrence among patients that had been seizure-free
  - $\geq 1$ /month, 27.5% had a reduction in seizure frequency to  $< 1$ /month
  - $\geq 1$  seizure/month, 48% exhibited a  $> 50\%$  reduction in seizure frequency

# IMPACT OF ANTIDEPRESSANTS ON SEIZURES

- Maguire MJ, Weston J, Singh J, Marson AG. Antidepressants for people with epilepsy and depression. Cochrane Database of Systematic Reviews 2014
  - Unable to do a meta-analysis
  - No clear association between antidepressants and increased frequency of seizures

# ANTIDEPRESSANTS TO AVOID

- Bupropion
- Maprotiline
- Clomipramine
- Amoxapine

Kanner AM. Most antidepressant drugs are safe for patients with epilepsy at therapeutic doses: A review of the evidence *Epilepsy & Behavior* Volume 61, August 2016, Pages 282–286

Table 1. Efficacy and doses of SSRIs and SNRIs in primary depression and anxiety disorders.

+: used for the treatment of this condition. +: has FDA indication for this condition. a SSRI. b SNRI.

Antidepressant drug	Depression	Panic disorder	Generalized anxiety	Starting dose	Maximal dose	Inhibits some AEDs	Clearance increased by EIAED
Paroxetine <sup>a</sup>	+	+	+	10	60	Yes	Yes
Sertraline <sup>a</sup>	+	+	+	25	200	Mild	Yes
Fluoxetine <sup>a</sup>	+	+	–	10	80	Yes	?
Citalopram <sup>a</sup>	+	+	+	10	60	No	Yes
Escitalopram <sup>a</sup>	+	+	+	5	30	No	No
Fluvoxamine <sup>a</sup>	+	+	+	50	300	Yes	No
Venlafaxine <sup>b</sup>	+	+	+	37.5	300	No	No
Duloxetine <sup>b</sup>	+	+	+	20	120	No	No



# QUESTION 4

- Topiramate has been found to always improve concentration and memory in seizure disorders patients.

True

False

# QUESTION 4

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True

**False**

# AEDS AND MOOD SYMPTOMS

- Psychiatric SE occur with AEDs
  - Topiramate - memory problems
  - Phenobarbital - depression and associated with SI
  - Keppra - irritability
- Symptoms and medication timeline is important
  - When possible discuss switching to Depakote, Lamictal, Tegretol

Sirven JI. Management of Epilepsy Comorbidities. Continuum (Minneapolis Minn) 2016;22(1):191–203

# SUMMARY OF ASSESSMENT

- Safety
- Characterize the symptoms and seizure history well
- AEDS
- Psychotherapy
- Pharmacotherapy