



EPILEPSY UPDATE: A CASE SERIES

A CME Activity

Depression and Epilepsy: A Problem for the Neurologist?

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Depression and Epilepsy: A Problem for the Neurologist?

Depression is the most common comorbid disorder in people with epilepsy, but the diagnosis can be complicated by the presence of other common factors, such as the interictal effects of seizures and antiepileptic drugs. Studies in patients at epilepsy clinics and in the community have found a prevalence of depression ranging from 20% to 50% in persons with epilepsy. This is 2 to 5 times greater than the general population. Depression is a major health consideration in epilepsy because of increased disability, health care utilization, and mortality. In fact, depression and medication side effects are the two strongest predictors of poor quality of life in medically uncontrolled epilepsy. Since neurologists often serve as the “primary care” providers for epilepsy-related health problems, they need to be comfortable managing uncomplicated affective disorders. The following adult cases illustrate situations that clinicians often confront in the process of accurately diagnosing depression, which may require specific treatment.

Case 1

N.P. is a 63-year-old woman with a history of several generalized tonic-clonic seizures per year since she was 17 years old. She experienced infrequent myoclonic jerks during early adulthood, and her EEG showed intermittent 4-6 Hz generalized poly-spike and slow wave activity. During the past 10 years she had experienced intermittent periods of depressed mood that led to decreased social activities, which has become quite frustrating for her husband.

The mood symptoms were initially attributed to psychomotor slowing due to valproate, which led to a decision to convert to lamotrigine. Her insomnia subsequently worsened, so she was converted to levetiracetam. After the insomnia improved, her mood symptoms worsened and she was administered a screening instrument for depression that revealed a high score, in the severely depressed range.

A more detailed psychiatric history identified that she had symptoms consistent with the diagnosis of major depressive disorder that preceded her receiving levetiracetam. Within 4 weeks of initiating a selective serotonin reuptake inhibitor (SSRI), she and her husband reported marked improvement in her symptoms, and she began increasing her social and domestic activities.

Case 2

H.O. is a 37-year-old man with a 30-year history of partial seizures each month. The seizures consist of a vague sense of anxiety for 15 seconds followed by an unusual sensation in his stomach and throat for another 20 seconds. His family reported that after the initial symptoms he appeared to lose awareness and the ability to respond. Following the events he would not remember any of the symptoms. They estimated that he had 1 or 2 seizures each week, but emphasized that he would not be able to identify the seizures if no one was with him. His interictal EEG showed right anterior temporal sharp waves and his MRI revealed atrophy and increased T2 signal in the right hippocampus. Four antiepileptic medication changes during the past 7 years never achieved complete seizure control. He had also been treated intermittently for major depression with minimal success during the prior 10 years. The primary symptoms were loss of interest in activities that he typically found enjoyable, and a sense of guilt and self-deprecation. The patient and family noted that these episodes of depression were as disabling as the seizures, if not worse. More detailed history found that these symptoms were very intense during the two to three days after a witnessed seizure. The family was suspicious that other episodes of mood dysfunction may have been due to unwitnessed seizures.

After video/EEG monitoring confirmed that the ictal EEG and seizure semiology were consistent with the MRI and interictal EEG findings, he underwent a selective resection of the right anterior/mesial temporal lobe. Postictal evaluation during video/EEG

monitoring had confirmed that he was not aware of his seizures, and that he experienced intense symptoms of depression for up to 2 days. No further seizures were observed during the two years following surgery and no episodes of depression have occurred.

DISCUSSION

These two cases present common aspects of psychiatric comorbidity that neurologists frequently encounter in the outpatient epilepsy clinic. The clinician must resolve the questions: Are the symptoms of depression due to medication side effects or a predictable reaction to recent psychosocial distress, for which antidepressant treatment may not be warranted? Are the periods of depression due to peri-ictal effects that occur in over 50% of complex partial seizures, which would exclude the diagnosis of major depression by DSM-IV criteria? Or does the patient have a mood disorder, such as a current major depressive episode, that requires appropriate treatment? These questions can usually be efficiently and effectively answered by screening for severity and duration of depression symptoms with a validated instrument, and determining the temporal relationship of the depression symptoms to seizures and recent stressful life events.

According to the DSM-IV, the diagnosis of a major depressive episode requires 2 weeks of persistent symptoms that are not explained by other factors, such as illness, medication effects, or bereavement, and that include at least 5 or more of the following:

1. Depressed mood
2. Diminished pleasure in daily activities
3. Significant weight loss or gain
4. Insomnia or hypersomnia
5. Psychomotor agitation or retardation
6. Fatigue
7. Feelings of worthlessness or excessive guilt
8. Diminished concentration or decisiveness, and
9. Recurrent thoughts of death or suicide.

The use of short screening instruments for rapid identification of at risk patients can accurately facilitate quantification of the severity of recent core symptoms of depression. The DSM-IV also emphasizes the need to exclude pharmacological or medical causes of

depression, which can be difficult in the settings of recurrent seizures with postictal depression symptoms or recent antiepileptic drug changes. Considering that depression symptoms may be worsened by some antiepileptic drugs, such as phenobarbital, levetiracetam, and topiramate, it is important to determine whether the symptoms increase after initiating or increasing the dose of a specific medication. In addition to the patient's description of the occurrence or exacerbation of depression symptoms after seizures, it is often necessary to confirm the history through interviews with family members or caregivers, and/or video/EEG monitoring of typical seizures.

Other psychiatric disorders, such as anxiety, are also common in persons with epilepsy. Although bipolar disorder and psychosis are also increased in prevalence, they are much less frequent than depression or anxiety. Anxiety typically co-occurs with depression, and is treated by SSRIs, so it may be relatively straightforward to handle in most clinical situations. It still remains important for the clinician to be aware of the possible diagnosis of anxiety and the significant impact on quality of life of people with epilepsy.

The neuroscience community is rapidly gaining information about the pathophysiology of depression in common forms of seizure disorders, such as temporal lobe epilepsy, which may modify our understanding of the etiology and treatment of depression. However, current guidelines support the systematic screening for depression at each patient encounter, and rapid initiation of appropriate treatment when depression is identified.

FAQs Frequently Asked Questions

Do selective serotonin reuptake inhibitors (SSRIs) make seizures worse?

The statements about risk of seizures in persons with epilepsy in most package inserts for most SSRIs are largely based on case reports. In contrast, a prospective study of 100 patients with epilepsy and depression treated with SSRIs found that only one patient had a significant worsening of seizure pattern. Also, a recent meta-analysis of placebo-controlled trials of SSRIs indicates that they may actually decrease the risk of seizures.

Continued on page 3 (Reverse side)

How can depression be quickly recognized?

Several national and international health organizations recommend the use of screening instruments for the identification of depression in the nonpsychiatric clinic setting. A brief 6-item instrument has been developed and validated for use in persons with epilepsy, and is shown in Table 1. A total score of >15 has a specificity of >90% and sensitivity of >80% for a major depressive episode. The diagnosis of a major depressive episode should be made by the clinician based on the DSM-IV criteria listed in the Discussion.

Table 1. Screening Instruments for Depression (Neurological Disorders Depression Inventory for Epilepsy—NDDIE). A score of >15 is considered high risk for a current major depressive episode.

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

For the statements in this table, patients are asked to circle the number that best describes them over the last 2 weeks, including the day of the assessment. (Source: *Lancet Neurol*. 2006;5:399-405.)

How common is postictal depression?

A systematic study of patients' mood status following seizures found that about 50% of patients experience a significant worsening of symptoms of depression or anxiety. The diagnosis of major depression should take into account the possibility that some symptoms may not be due to a mood disorder, but rather effects of seizures or antiepileptic drugs.

Should neurologists initiate treatment for major depression?

Several national and international health organizations have published recommendations for initial treatment of depression in primary care settings. These emphasize the necessity for primary care providers to begin treatment in order to minimize delays to remission and recovery of quality of life. A recent consensus panel of the Epilepsy Foundation suggested that treatment with an SSRI be considered immediately after a diagnosis of major depression, as summarized in Figure 1. Referral for psychotherapy is recommended for persons with clear social or psychological stressors. Some atypical antidepressants, such as bupropion, should be used cautiously because of seizure risk at high-range doses. Urgent referral for psychiatric evaluation should be considered if a patient under your care reports recent significant suicidal thoughts or behaviors, or has had prior mania episodes that could indicate bipolar disorder. If the symptoms of depression do not resolve adequately after achieving full doses of a first or second SSRI, then referral for management by a psychiatrist should also be recommended.

Are any other antidepressants besides SSRIs routinely used or recommended for epilepsy patients?

Older tricyclic antidepressant medications have more adverse side effects and pharmacokinetic interactions with antiepileptic drugs. They are subsequently reserved as second-line treatments. Antidepressants with effects on other neurotransmitters in addition to serotonin, such as venlafaxine or mirtazapine, can be useful in the treatment of moderate to severe depression. Most neurologists have more experience with SSRIs, and are therefore more comfortable prescribing them.

Do antiepileptic drugs increase suicidality?

A recent Alert issued by the FDA indicates that AEDs do increase the rate of suicidal ideation from 0.2% for placebo to 0.4% during the months following initiation of an AED. This report is based on the results of 199 placebo-controlled trials. However, it is important to recognize that the baseline rate of suicidal thoughts or behavior in the past 2 weeks is 13% in outpatient epilepsy clinics, and the strongest predictor of suicidality is major depression. All patients with epilepsy should be educated about the risks of suicidal ideation and behaviors, especially after initiating an AED or SSRI.



ABOUT THE AUTHOR

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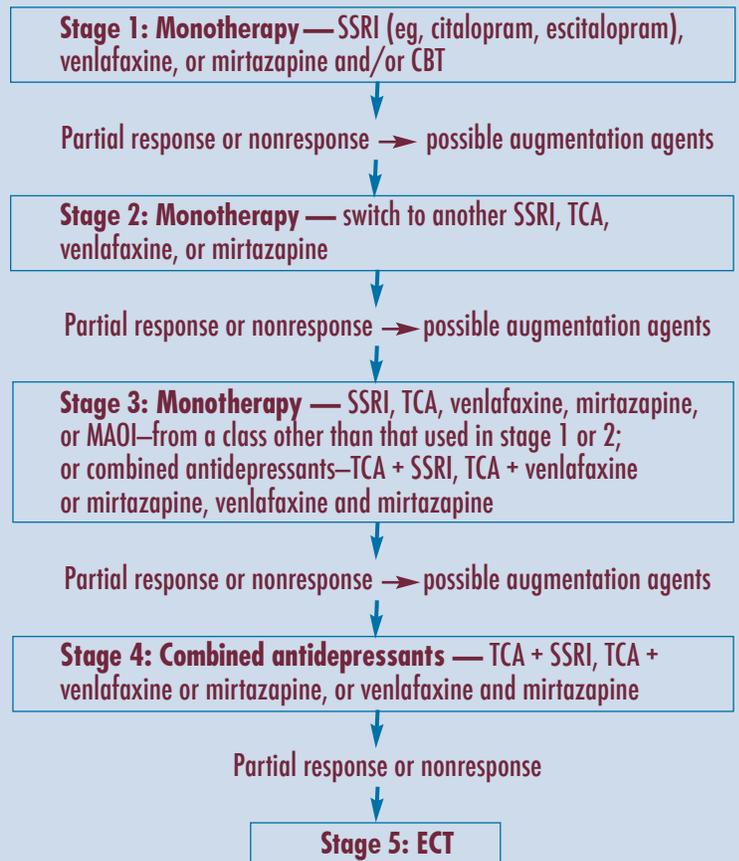
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Figure 1. Recent Epilepsy Foundation Consensus Panel Recommendations for Adult Antidepressant Therapy.

(Note: After one or two monotherapies have failed, a psychiatrist should guide subsequent stages of therapy. Source: *Epilepsy & Behavior* 2008,13:S1-S29)

Proposed Algorithm: Stages of Medical Therapy



CBT = cognitive behavioral therapy; ECT = electroconvulsive therapy; MAOI = monoamine oxidase inhibitor; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

Adapted from Crismon ML, et al. *J Clin Psychiatry*. 1999;60 (suppl 3): 16-20.

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KNOWLEDGE GAP ADDRESSED

Current practice recommendations in the general neurology community are limited and need to be supported. This activity will make the general neurologist more aware of the complex issues involved in treating patients with epilepsy and be able to apply the appropriate resources.

LEARNING OBJECTIVES

- Evaluate the importance of comorbid affective disorders in order to manage the patient with epilepsy more appropriately and to enhance his/her quality of life.
- Recognize that treatments may have consequences that impact a patient beyond seizure control, and how best to address these consequences.
- Given that patients with epilepsy can have a number of medical and psychological issues that require intervention, in addition to control of their seizures, determine the best ways to address these issues.
- Recognize the barriers that patients with epilepsy may encounter in an effort to sustain an optimal quality of life.

TARGET AUDIENCE

General neurologists, nurses, and other healthcare professionals involved in the care of patients with epilepsy.

ACCREDITATION STATEMENT

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A CME certificate will be sent to you within three weeks should you obtain a grade of 100%.

1. The most common condition comorbid with epilepsy is:

- a. Migraine
b. Schizophrenia
c. Depression
d. Cerebrovascular Disease

2. The diagnosis of a current major depressive episode requires:

- a. Loss of interest in enjoyable activities
b. Sleep dysfunction
c. Sad or depressed mood
d. Changes in appetite
e. Either a or c, or both.

3. Guidelines for treatment of depression in people with epilepsy recommended by the Epilepsy Foundation Consensus Statement include:

- a. Follow-up after treatment to confirm an adequate response
b. Delay treatment until evaluation by a psychiatrist
c. Initiation of a selective serotonin reuptake inhibitor or cognitive behavior therapy
d. Both a and c

Please circle the correct answers:

1. a b c d 2. a b c d e 3. a b c d

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SCALE: 5=Excellent 4=Very Good 3=Satisfactory 2=Fair 1=Poor

Evaluate the importance of comorbid affective disorders in order to manage the patient with epilepsy more appropriately and to enhance his/her quality of life.

5 4 3 2 1

Recognize that treatments may have consequences that impact a patient beyond seizure control, and how best to address these consequences.

5 4 3 2 1

Given that patients with epilepsy can have a number of medical and psychological issues that require intervention, in addition to control of their seizures, determine the best ways to address these issues.

5 4 3 2 1

Recognize the barriers that patients with epilepsy may encounter in an effort to sustain an optimal quality of life.

5 4 3 2 1

2. Questions Relating to Your Intent to Make Practice Changes

Based upon your participation in this CME activity, please answer the following:

Did the information in this activity increase your ability to judge whether to screen your patients who have epilepsy for depression?

- YES NO

Did the information in this activity increase your confidence in assessing and treating your patients for depression?

- YES NO

Will the information in this newsletter alter your prescribing patterns or influence the discussions that you have with patients when selecting an AED?

- YES NO

Can we contact you in a follow-up survey to measure the impact of this educational intervention?

- YES NO

3. Based on your participation in this CME activity, which of the following strategies do you now plan to use in your practice that you haven't used before? (Check all that apply)

- I will consider depression screening for my patients who report "feeling blue."
 I will consider prescribing antidepressants for my patients who score highly on my depression screener.
 I will consider that my patients are depressed only after checking that their seizures are well controlled and they consistently report symptoms of depression.
 I will consistently screen my epilepsy patients for depression periodically.

4. Are there any barriers to implementing these strategies? (Check all that apply)

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 Other: _____

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- 1.) _____
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