



ANXIETY AND DEPRESSION ASSOCIATED WITH EPILEPSY (WEBINAR TRANSCRIPT)

- Laura Lubbers: [00:05](#) Welcome everyone to today's webinar. My name is Laura Lubbers, and I'm the Chief Scientific Officer of CURE. And I want to thank you all for joining us today. CURE is pleased to present our Leader's in Epilepsy Research webinar series which consists of webinars that highlight some of the key research that's being done in epilepsy. Today's webinar, which is being sponsored by our friends at Sunovion, will focus on two of the most common types of psychiatric disorders, anxiety and depression, that affect one-third of those diagnosed with epilepsy. This webinar will be presented by Dr. Andres Kanner. CURE's mission is to find a cure for epilepsy by promoting and funding patient-focused research. This year we're celebrating 20 years of impact in the field of epilepsy research. CURE's been instrumental in advancing research in many areas, including infantile spasms, posttraumatic epilepsy, Sudden Unexpected Death in Epilepsy, or SUDEP, and genetics, just to name a few.
- Laura Lubbers: [01:10](#) Today's webinar is entitled Anxiety and Depression Associated with Epilepsy. And will discuss how to identify and treat episodes of depression and anxiety in people with epilepsy. In addition, we'll review how those conditions have a negative impact on quality of life, tolerance of antiepileptic medications, and even increase the risk of suicidal thoughts, which is why it's so important to work with your health care providers on developing the best treatment plan that includes consideration of these mood disorders.
- Laura Lubbers: [01:42](#) Dr. Kanner is the chief of the epilepsy division in the Department of Neurology and the director of the International Comprehensive Epilepsy Center at the University of Miami Miller School of Medicine. Dr. Kanner is considered one of the leading authorities on the behavioral aspects of epilepsy. Before Dr. Kanner begins, I'd like to encourage everyone to ask questions. You may submit your questions any time during the presentation by typing them into the questions tab of the GoToWebinar control panel and clicking send. My colleague from CURE, Brandon Laughlin, will read them aloud during the Q&A portion of the webinar. We do want this webinar to be as

interactive and informative as possible. However, to respect everyone's privacy, we ask that you make the questions general and not specific to a loved one's epilepsy. I also want to mention that today's webinar, as well as all previous and future webinars, will be recorded and are available on the CURE website. With that, I'd like to turn it over to Dr. Kanner.

Andres Kanner: [02:48](#)

Thank you, Dr. Lubbers. And first, I'd like to thank you for having invited me to participate in this series of webinars. We're going to be addressing what I think is a very important topic that all patients, and family who have patients with epilepsy, need to be familiarized with because psychiatric comorbidities, and in particular mood and anxiety disorders, are relatively frequent in people with epilepsy and are a big cause of poor quality of life in these patients. I hope you find this presentation useful. And as Dr. Lubbers said, I'd be happy to answer any questions you may have after my presentation. I have no disclosures for this presentation.

Andres Kanner: [03:43](#)

So as Dr. Lubbers said earlier, psychiatric comorbidities are relatively frequent in people with epilepsy. And of the different type of psychiatric disorders, depression and anxiety are the most frequent conditions. And these are seen in approximately one-third of people with epilepsy in the course of their life. This slide represents data from a population-based study done in Canada where investigators compared the frequency of the different types of psychiatric disorders in the course of the lives of people with epilepsy to that of a controlled group of people in the Canadian population. And as you can see, those people with epilepsy had a significantly higher prevalence of depression and anxiety disorders with a combination of mood and anxiety disorders occurring in one out of every three people with epilepsy. Notice that one out of every four people with epilepsy at some point in their life experience suicidal ideation. And any kind of psychiatric disorder was identified in one out of every three people with epilepsy at some point.

Andres Kanner: [05:07](#)

Now it's very important that patients and families recognize what is the type of depressive and/or anxiety episode that the person is experiencing. What

does it represent? So this is a summary of how it should be thought of. So the first and most frequently recognized type of depressive and/or anxiety disorder is what we call the interictal depressive or anxiety episode. Interictal just means that these are episodes that occur independently of the occurrence of an epileptic seizures. They can occur at any time whether the patient has been seizure-free or has had recurring seizures, and are not related in time with the occurrence of the seizures.

Andres Kanner: [06:00](#)

On the other hand, there are symptoms or episodes of depression and anxiety that are temporally related to the occurrence of seizures, and those are known as peri-ictal. Pre-ictal because they either can precede the occurrence of the seizure. Postictal, they actually follow the occurrence of the seizure. And typically, the postictal symptoms occur about one or two days after the seizure. Or ictal, because they can be the expression of the actual seizure. And we're going to describe in greater detail how these manifestations of peri-ictal depressive and anxiety episodes present.

Andres Kanner: [06:48](#)

And then there is the important recognition that people who have interictal depressive and anxiety disorders can also experience peri-ictal symptoms of depression and anxiety. Finally, episodes of depression and anxiety can be the expression of what we call iatrogenic adverse events. That is, side effects caused by medication used to treat the seizure disorder or it can be a side effect of a surgical treatment. About one-third or 20% of people who undergo a temporal lobectomy may often develop symptoms of depression and anxiety in the first three to six months, and then these symptoms go away.

Andres Kanner: [07:51](#)

Obviously, it is important for patients and family and physician to recognize the type of depressive and/or anxiety episode because the treatment will be very different. If it is an interictal episode, then the treatment will have to require medication to abolish the symptoms, or a form of therapy. If it is peri-ictal, then the treatment will require the achievement of a seizure-free state to get rid of the seizures. And if it is caused by the medication that I use to treat the epilepsy, the treatment will require a switch to

another antiepileptic medication that is not associated with those side effects.

Andres Kanner: [08:37](#)

Now among the interictal episodes, it's important for patients and families to recognize when a patient is experiencing these types of symptoms. And this can be done easily in an outpatient epilepsy clinic with the use of certain questionnaires. And this is a questionnaire that was developed for the use of epileptologists and neurologists in epilepsy clinics specifically. It's call the Neurological Disorders Depression Inventory in Epilepsy. And I'm just showing this so that you can recognize the cardinal symptoms of depression so you can know whether you or your loved one is experiencing episodes of depression.

Andres Kanner: [09:25](#)

The most important symptom is difficulty finding pleasure. That's a cardinal symptom of depression. Other symptom obviously is a feeling of sadness. And then you can have the other associated symptoms such as feeling that everything that I'm doing is a struggle, feeling of frustration, poor tolerance to other people, irritability, the feeling that nothing that I do is right, sensation of guilt even though I haven't done anything bad. And the most serious one, suicidal ideation, where I have the feeling that I'd be better off dead.

Andres Kanner: [10:03](#)

And we give these instruments to patients when they come to our clinics and, as you can see, depending on their frequency, a score is given. And when a total score is greater than 15, that helps clinicians to suspect that this person may be suffering from a major depressive episode.

Andres Kanner: [10:22](#)

Likewise, there are instruments like this one for the detection of anxiety disorders where the cardinal symptoms are feeling of nervousness, anxiety, not being able to stop or control worrying, worrying too much about different things, trouble relaxing, being so restless that it is hard to sit still, being easily annoyed or irritable, and feeling afraid as if something awful might happen. Again, with this instrument, the scoring of the severity and frequency of the symptom generates a total score. And if it's greater than 10, it is a red flag to the clinician that the person may be suffering from an anxiety disorder. And

it's important to screen for both depression and anxiety because more often than not the two conditions tend to occur together.

Andres Kanner: [11:19](#) Now, there are different expressions that depressive disorders have in different patients. Some patients may just have a major depressive disorder, which is a more severe form of depression where the patient, for two weeks, is experiencing a variety of symptoms including marked difficulty experiencing any pleasure, feelings of sadness, crying constantly, feeling like nothing of what they do is right, feeling of hopelessness, helplessness, difficulty sleeping and waking up in the middle of the night, loss of appetite, loss of sexual drive. And suicidal ideation can also occur. And these episodes can last at least two weeks but can go on for months, and in some people even longer. And it's the most frequent form of severe depression that we see in people with epilepsy.

Andres Kanner: [12:21](#) Another form that is very typical of people with epilepsy is known as interictal dysphoric disorder, where in addition to the symptoms of depression the person can experience marked irritability as well as symptoms of anxiety. And those symptoms may come and go. They don't need to be present continuously for a period of at least two weeks. But what's very characteristic is the high association with symptoms of irritability, poor frustration tolerance and anxiety with the symptoms of depression.

Andres Kanner: [12:58](#) Then there is a less severe form of depression known as dysthymia. And this condition, while less intense, can go on for long periods of time, including two years or longer.

Andres Kanner: [13:11](#) And then on the other end of the spectrum is bipolar disorder or manic depressive illness. Now what is typical of all of these forms of depression is their close association with anxiety disorders. And that's why I mentioned previously the need to always investigate symptoms of anxiety in the presence of depressive episodes, and vice versa.

Andres Kanner: [13:36](#) Now the peri-ictal episodes are the episodes that are temporally associated with the occurrence of seizures. Preictal, for which I don't have a slide, means

that it precedes the onset of a seizure. And usually patients notice a change in their mood about two to three days before a seizure is to happen. The intensity of their symptoms increases as the seizure gets closer. And then, once the seizure occurs, these symptoms go away. It's interesting that very often parents can tell when a child is going to have a seizure or a spouse can tell when a husband or wife can have a seizure because they notice these changes in their mood or level of irritability that they're displaying.

Andres Kanner: [14:24](#)

Ictal psychiatric symptoms, which is an aura or the expression of a psychiatric symptom as a seizure, have been studied. And this is just an interesting study, over 100 patients who reported these auras of a psychological nature of which 21 presented as symptoms of depression, 61 as symptoms of fear or panic, and 18 pleasurable or displeasurable emotions. What's characteristic and what patients should be aware of is that these symptoms are very short in duration, usually less than 30 seconds, 45 seconds. They're very stereotypic, that is they are identical in between episodes. And they often precede the loss of awareness of surroundings that occurs with the focal seizures with loss of consciousness. These are important to recognize because the treatment of these episodes of depression does not include the same treatment that we use for the depressive episodes occurring when the patient is not having seizures, or during the interictal period.

Andres Kanner: [15:45](#)

And then we have the postictal symptoms. And postictal symptoms are symptoms that, as I said before, occur between 12 hours and up to five days after the patient has had a seizure, typically within 24 to 48 hours. So often people do not connect the temporal relationship between the occurrence of this psychiatric symptom and the occurrence of the seizure. And they are rather frequent in people who don't respond to medication for their seizure disorder. This is in a study of 100 consecutive patients who had poorly controlled focal epilepsy. And we investigated the occurrence of psychiatric symptoms during the postictal period that we defined as the first 72 hours after a seizure. The symptoms had to occur after more than 50% of seizures and the patients had to

recognize them as being different when they're not having seizures. As you can see, about 43 patients endure symptoms of depression. And of those, 13 experience suicidal ideation during the postictal period. They had to identify these symptoms as occurring, as I said, in more than 50% of their seizures during the previous three months. So these were habitual psychiatric symptoms. And then anxiety symptoms were endured by 45 of the 100 patients.

Andres Kanner: [17:23](#)

Now what's important is that when we look at the duration of these symptoms, the median duration is about 24 hours. And it can range from one hour to up to 150 hours. So you have to think, for example, that a seizure lasts between 90 seconds and two minutes. But when patients experience these symptoms of depression or anxiety, because this also happens in anxiety, these symptoms may last up to 24 hours. So you can clearly understand how the occurrence of these psychiatric symptoms have a worse impact on the quality of life of patients than the actual seizures. If a person is having suicidal ideation after having a seizure, that has a terrible impact on the quality of life of this patient. What's important to understand is that these symptoms of depression and anxiety that occur in the postictal period do not respond to antidepressant medication and have a different mechanism of development than the symptoms that occur in the interictal period.

Andres Kanner: [18:40](#)

So why should patients and family care about recognizing and treating these episodes of depression and anxiety? The impact of the depression and anxiety episodes affects the life of people with epilepsy at several levels. The first one and most severe is increased mortality risk. Unfortunately, people with epilepsy have an increased mortality risk than people in the general population. And of these suicidal ideation and suicidal behavior is one of the causes of premature mortality risk. In a study done in Denmark by Christensen and collaborators, people with epilepsy without any psychiatric disorders were twofold more likely to commit suicide than the general population. In the presence of a depressive disorder, the risk increased 42-fold. And in the presence of an anxiety disorder, the risk increased 12-fold. So this illustrates how important it is to recognize

and treat these depressive and anxiety disorders, because they can lead to the patient attempting or completing suicide.

- Andres Kanner: [20:05](#) Another important impact of poorly treated or not treated depression and anxiety is that patients have a worse tolerance of the antiepileptic medication. So people will complain more of adverse events of the antiepileptic medications, which will require patients having more laboratory tests to check levels or the need to change antiepileptic medications even if their seizures are well controlled.
- Andres Kanner: [20:36](#) The other is the fact that when you have an untreated depression or anxiety disorder, your quality of life is affected significantly. And it's been demonstrated that in people with poorly controlled epilepsy the variables that predict poor quality of life are the presence of depression and anxiety and not anymore the presence of the seizures. So it's important that depression and anxiety be identified and treated in order to improve the quality of life of people with epilepsy.
- Andres Kanner: [21:14](#) Then there is also the risk that patients with untreated or unrecognized previous psychiatric disorders or family history of depression and anxiety are at increased risk of developing psychiatric symptoms with certain antiepileptic medications. And I will touch up on that point in the next few slides.
- Andres Kanner: [21:39](#) And then, finally, people with a history of depression and anxiety disorders preceding the onset of epilepsy have been found to have a higher risk of developing treatment-resistant epilepsy. That is, are more likely. They have twofold a higher risk of developing [inaudible 00:21:59] to be well controlled with pharmacologic treatments.
- Andres Kanner: [22:05](#) As you can see, the impact of not recognizing or treating these psychiatric conditions is very serious and affects the life of people with epilepsy at various levels. Now we often think of depression and anxiety as a complication of the seizure disorder, but in fact it is a much more complex relationship. Patients with epilepsy have a five to 20-fold higher risk of developing depression. However, people with

depression who have never had epilepsy have a two to five-fold higher risk of developing epilepsy. So in fact there is a bidirectional relationship whereby if you have epilepsy you have a higher risk of developing depression and if you have depression you have a higher risk of developing epilepsy. And the same rule applies for anxiety disorders.

Andres Kanner: [23:09](#)

So one way of illustrating this is in this slide where you can see in the yellow arrow the time where the diagnosis of epilepsy was made. On the left-hand side is mood and anxiety disorders that preceded the onset of the epilepsy and which facilitate the development of the mood and anxiety disorders after the onset of epilepsy. And I want to highlight the role that family psychiatric history has in facilitating the development of mood and anxiety disorders after the onset of epilepsy. And this is also something that can have a direct impact on the development of iatrogenic symptoms of depression and anxiety as a consequence of the use of certain antiepileptic medications that are used to treat epilepsy or following epilepsy surgery, as we mentioned before. And here it's important for patients and family members to bring to the attention of the physician if they are experiencing any symptoms of depression or anxiety at a time when a pharmacologic regimen is to be started for the treatment of the epilepsy. Because the choice of the antiepileptic medication has to factor in the presence of a psychiatric disorder before the onset of epilepsy at the time that you're going to start the antiepileptic medication, as well as the family history of depression and anxiety disorders.

Andres Kanner: [25:07](#)

It's very important that the symptoms of depression and anxiety are not the expression of an iatrogenic effect. That is, that they are not caused by the antiepileptic medications. And this is an important concept that family members and patients need to keep in mind because certain antiepileptic medications have psychotropic properties, both positive and negative. And in people who are vulnerable for the development of psychiatric symptoms, those are patients where they've had a previous psychiatric history of depression and anxiety or who have a family history of depression and anxiety, those are people who when exposed to

certain antiepileptic medications are at risk of developing psychiatric symptoms of depression and anxiety.

Andres Kanner: [25:58](#)

The other aspect of the coin is that certain antiepileptic medications have positive psychotropic properties and are used, in fact, by psychiatrists to treat depression and anxiety disorders. If you have a patient with a previous history of depression and anxiety that had been under adequate control with the use of any of these antiepileptic medications with positive psychotropic properties and these medications are removed or discontinued, this can unmask a well-controlled depression and anxiety disorder and result in the recurrence of the symptoms of the depression and anxiety.

Andres Kanner: [26:40](#)

So this is a list of antiepileptic medications that, when they are added, in vulnerable patients, that being patients with a previous psychiatric history, current psychiatric history, or family psychiatric history, may result in the development of episodes of depression and anxiety. And those include the barbiturates, phenobarbital and primidone, benzodiazepines, levetiracetam, topiramate, zonisamide, vigabatrin, tiagabine and perampanel. Now in the next one are the antiepileptic medications that have positive psychotropic properties where the discontinuation of these drugs can unmask a well-controlled mood and anxiety disorder and result in the recurrence of the symptoms of depression and anxiety. And these include carbamazepine, valproic acid, oxcarbazepine, lamotrigine, gabapentin for anxiety symptoms and pregabalin, also for anxiety symptoms. So it's important that family members and patients communicate to their clinician the occurrence of psychiatric symptoms and family psychiatric disorders so that the clinician can factor that information in the choice of antiepileptic medications, both with respect to the start as well as the discontinuation of these medications.

Andres Kanner: [28:23](#)

Now antidepressant drugs are safe in patients with epilepsy, and this is an important concept that has been the source of much confusion because a lot of physicians and patients have the impression that antidepressant drugs can worsen seizures. And while

that is true, that is only true in the following circumstances. Antidepressants can result in the worsening of seizures in the case of overdoses. That's it. So if people take excessive doses of antidepressant medications, they can result in increased seizures. But when used at therapeutic doses, antidepressant medications are safe.

Andres Kanner: [29:14](#)

And this is an example of these phenomenon. This is a study where an investigator looked at the incidence of seizures between patients who were randomized to a selective serotonin reuptake inhibitor or a selective norepinephrine reuptake inhibitors, on the one hand, and placebo, in the course of regulatory studies. These are studies that are done to test the efficacy and safety of these antidepressant medications for the treatment of primary depression, so these people did not have any history of epilepsy. And the investigator wanted to know whether people who were given the antidepressants or those who were placebo had a different incidence of seizures in the course of the trials. And what they found is that people who were treated with the actual antidepressant had a significantly lower incidence of seizures than those that were treated with placebo. And that included all the antidepressants of the selective serotonin reuptake inhibitors and serotonin norepinephrine reuptake inhibitor family, which are the drugs that we use today as a first-line treatment for depression and anxiety disorders. So when used at therapeutic doses, these drugs clearly are safe.

Andres Kanner: [30:38](#)

And, in fact, those people who were placed on placebo, that is a sugar pill, they were found to have 19-fold higher incidence of seizures than expected in the general population. So this data nicely illustrates the safety of these medications in people with epilepsy.

Andres Kanner: [30:58](#)

So what do you do when you identify a patient who has depression or anxiety? One way of treating it is with pharmacotherapy, with antidepressant medications. The other one is with the use of cognitive behavior therapy. And in some instances you have to use both modalities.

Andres Kanner: [31:17](#) Now with the pharmacotherapy, the first choice antidepressants are the selective serotonin reuptake inhibitor family, such as citalopram, escitalopram or sertraline. If the patient does not become symptom-free with this medication, then they are treated with an antidepressant of the family of the serotonin norepinephrine reuptake inhibitors, such as venlafaxine or duloxetine. And if that doesn't result in complete remission of symptoms, then the clinician has the option of using another type of antidepressant, such as mirtazapine. Of note, if an individual patient has not become symptom-free after two trials of antidepressant medication, that patient needs to be treated by a psychiatrist that has expertise in mood disorders. And antidepressants have to be used very carefully in people where there is a family history or previous history of manic depressive illness. And those are patients who have had not only depressive episodes but episodes of hypomania where they experience, in addition to the episodes of depression, they experience symptoms of feeling a tremendous amount of energy, they start speaking very fast, they have a flight of idea, they start spending a lot of money, they become hypersexual, et cetera. And these can be suspected also in people where there have been family history bipolar illness or where the first major depressive episode occurred in adolescence.

Andres Kanner: [33:00](#) Of note is that the majority of the antidepressant medications that we use for depression are also effective for the treatment of anxiety disorders. So you can use one drug to treat both depression and anxiety with good results.

Andres Kanner: [33:17](#) So the points to take home is that in patients with epilepsy, mood and anxiety disorders are relatively frequency psychiatric comorbidities. They yield serious and negative impacts on the management of the seizure disorder and life at several levels, including worse seizure control, worse tolerance to antiepileptic medications, increased suicidal risk, worse quality of life. And they can be safely treated with antidepressant medication of the selective serotonin reuptake inhibitors or serotonin norepinephrine reuptake inhibitors.

- Andres Kanner: [33:54](#) And with that, I'm going to stop and I'd be happy to take any questions from the audience.
- Laura Lubbers: [34:03](#) Thank you, Dr. Kanner. We'll now begin the Q&A session. Again, if you have any questions, please submit them in the questions tab of the GoToWebinar control panel and click send. And Brandon will go ahead and read them out loud. Brandon, are there some questions that have come in?
- Brandon: [34:19](#) Absolutely. Thank you Dr. Kanner and thank you Laura. The first question for you, Dr. Kanner, is a very general question. How does the acceptance of an epilepsy diagnosis contribute to the development of both mood and anxiety disorders?
- Andres Kanner: [34:34](#) So that's a very important question. And this is a question that unfortunately we neurologist do not spend enough time discussing with patients. Because failure to accept the diagnosis of epilepsy is very frequent, a very important cause of the development of symptoms of depression and anxiety. One of the most difficult things about dealing with epilepsy, in addition to having seizures, is the loss of predictability of life. That is, when you have epilepsy you don't know when or if you're going to develop another seizure. And that loss of predictability is very difficult to come to terms with in the beginning. It causes tremendous anxiety in the patient. It causes tremendous uncertainty in parents of children with epilepsy. And it's not unusual that some patients may deal with that through denial and saying, "No, this was not epilepsy. This is not going to happen to me again."
- Andres Kanner: [35:43](#) And the emotional energy that patients and family use to deny the diagnosis of epilepsy results in the opposite effect. They become more anxious, more depressed. And what often happens, in my experience, is that when a child or adolescent experiences epilepsy and senses that the parent is having a very hard time accepting the diagnosis of epilepsy, the young man or the child will then react by denying the occurrence of the seizure disorder and will start acting out, will become noncompliant. And it's going to result in a vicious circle. One of the common mistakes is that family members don't want to upset the patients. And when they are talking

about the epilepsy, they say, "No, no. Don't worry about it. Everything is okay. We don't want to upset you." What needs to be done is the opposite. You need to talk openly about the diagnosis of the epilepsy, the fear of what can happen if you have epilepsy or an epileptic seizure.

Andres Kanner: [37:00](#)

And the big elephant in the room is, particularly for patients and parents, "Am I going to die if I have a convulsion?" And that fear needs to be openly discussed by the patient, the family and all family members. And by coming to terms with this loss of predictability, which takes time, it's equivalent to a mourning process, if you will, that somebody experiences with the loss of a loved one, over time people come to terms with accepting the diagnosis. And then one morning they wake up and they say, "You know what? I can live with this." But this is essential. This is a very essential part of accepting the diagnosis of epilepsy. And it prevents the development of unnecessary depression and anxiety that is a reactive process to this.

Brandon: [38:03](#)

Great. Thank you. We received a few questions about the idea of surgery. And so I'm going to turn into a two-part question for you, Dr. Kanner. What is the mechanism behind surgery resulting in anxiety and depression right away? And also, are there any studies going on on people pre and post-surgery and their levels of anxiety and depression?

Andres Kanner: [38:30](#)

Yes. That's a very important question. And it's a very interesting question, because it's not a very simple process. So what we see is that about 20 to 30% of people who undergo temporal lobectomy may experience episodes of depression and anxiety during the first three to six months. And after a period of 12 months, those symptoms remit completely in most of the patients. There's about 10% of patients that may continue to experience these symptoms. A majority of people who experience these episodes of depression and anxiety may have had depression and anxiety before their surgery. So what these episodes consist of are a reactivation of a presurgical depressive and anxiety disorder. And so those are episodes that need to be recognized before the patient goes to surgery. And the patient and family

need to be educated as to the possibility that these episodes may recur during the first three to six months. And they can be easily treated with low doses of antidepressant medication.

Andres Kanner: [39:50](#)

There is, however, about 15% of patients to 20% who may develop the normal... That is, they have never had episodes of depression and anxiety and they develop the normal episodes of depression and anxiety. And the explanation for that may lie in chemical changes that occur with a [inaudible 00:40:14] seizure disorder and the [inaudible 00:40:20] when that happens. And that's one of the hypotheses. We really don't know exactly how to explain [inaudible 00:40:29].

Andres Kanner: [40:29](#)

Another interesting observation is that about 50% of patients who had a history of depression and anxiety prior to their surgery, after their surgery those episodes go away. And so not only is the temporal lobectomy resulting in improvement or remission of the seizures, but it also results in the remission of the depression and anxiety disorder. So it's a complex occurrence of symptoms of depression that can get worse, and then they go away permanently, the normal development of these symptoms and they go away. And the most important thing is the complete remission of symptoms of depression and anxiety that were present before surgery that the surgical procedure results in their remission completely.

Andres Kanner: [41:26](#)

And what was the second part of the question?

Brandon: [41:31](#)

The second part of the question was about any studies that are going on, that have been conducted, that analyze the pre and postsurgery and their levels of anxiety and depression.

Andres Kanner: [41:43](#)

Yeah. Unfortunately, there is very little in the way of formal studies that have been conducted. There are some studies that were done in Australia where they actually identified that people with a previous history of depression and anxiety were more likely to experience those depressive episodes after surgery. And, hence, you could actually identify those people who are at increased risk of developing postsurgical episodes of depression by just taking a very careful

history of their psychiatric disorders before surgery. Now what we don't have studies is on whether the mechanisms that facilitate the development of the normal episodes of depression and anxiety. But hopefully, with new neuroimaging techniques and higher-resolution MRI studies, we will be able to have some answers in the future.

Brandon: [43:00](#) Great. Thank you. As you might imagine, we received many questions about obviously treatment and treatment options available. The first question actually we received from a few different people about the level of effectiveness of yoga and meditation and other homeopathic options that might help reduce mood issues before trying additional medications, and wanted to know your thoughts behind that.

Andres Kanner: [43:30](#) Yes. So that's a very important question. And I actually advocate the use of yoga and relaxation techniques in people who report that they notice a worsening of their seizures or an increase in seizure frequency when they are going through very stressful situations. So in these patients, the use of these relaxation techniques, and yoga in particular, can be very effective in teaching the patient to do self-relaxations. And, in turn, it results in a decrease in seizure frequency. With respect to the use of yoga and relaxation techniques for the actual treatment of depression or anxiety disorder, it can be beneficial of course. But if there is a long history of depression and anxiety disorder, sometimes it may be necessary to use additional treatment strategies. If medication is something that patients are not interested in considering, cognitive behavior therapy is a very effective form of treatment for depression and anxiety.

Andres Kanner: [44:47](#) Cognitive behavior therapy is a form of therapy that is provided by psychologists. It consists of 12 sessions. That's it. One session a week. And what the psychologist does is he teaches patients how to counteract the symptoms of depression and anxiety. So you learn strategies of how to overcome the symptoms of depression and anxiety. And the effect of this therapy is extremely impressive. And sometimes the effects are as good, or even better, than the results seen with medications. And we use it all the time. We refer our patients for cognitive behavior

therapy to the school of psychology of the University of Miami, or to other neuro-psychologists in the community, with very good results.

Brandon: [45:40](#) Great. Thank you. The next question, sticking with that theme of treatment options, is is there any research being done on the ability of cannabidiol to help obviously not only control seizures but also some of the mood disorders associated with it?

Andres Kanner: [45:58](#) So there is no data on the use of cannabidiol on the treatment of mood and anxiety disorders that I'm aware of. I know that there is very extensive use of marijuana, that patients smoke marijuana as a way of self-management of anxiety and depressive symptoms. The literature, the psychiatric literature on the impact of marijuana on a mood and anxiety disorder is indicative that in the long term it has a negative effect. Now we're talking about marijuana that has the THC component. We're not just talking about the cannabidiol extraction that is being considered for the treatment of epilepsy. And people with a history of mood and anxiety disorders have to be careful with the use, and particularly excessive use, of marijuana as a self-treatment, because in the long term it can worsen these conditions. We don't know what is the effect of cannabidiol in the treatment of depression and anxiety. And this is something that I'm sure will be investigated in the future, but today we don't know.

Brandon: [47:21](#) Great. Thank you. The next question actually references the questionnaires that you discussed earlier in your presentation. Would a patient request for these questionnaires to be completed or are they just a normal part of the diagnosis and treatment?

Andres Kanner: [47:39](#) So many clinics today in the United States are using those questionnaires when the patients come into the epilepsy clinic. The clinic will have the patient fill out these questionnaires in the waiting room. And when patients go to see the physician, they're giving the questionnaires to the physician, and this is a nice way for the physician to screen for the presence of mood and anxiety disorders and to follow from visit to visit as to the presence of these symptoms. If the clinician that the patient is seeing is not using those screening

instruments, patients can suggest it to the clinicians. These are instruments that can be downloaded for free from the webpages of the American Epilepsy Society or the Epilepsy Foundation. Or they can email me and I'll be happy to give them the reference of where they can obtain these instruments. And I think that, in the case of physicians who have started to use it, they have found it to be extremely effective. The NDDIE now has become the screening instrument for depression adopted by the International League Against Epilepsy and has been translated into close to 17 languages, and so it's widely used across the world.

Brandon: [49:11](#) Great. Thank you. The next question actually came through in a couple of topics. But a few people wanted to know if many of the studies that you referenced earlier in the presentation take into account gender differences, meaning like hormones and catamenial epilepsy.

Andres Kanner: [49:28](#) Yes, that's a very important question. We know that in non-epileptic patients with depression, that is in patients who suffer from primary depression, women have a higher incidence of depression than men. In people with epilepsy, we're not seeing that gender difference. The risk of depression is as high in men and in women. And so that is not something that we are seeing that much of difference. And that's an important difference that one sees in people with and without epilepsy.

Andres Kanner: [50:14](#) Now, catamenial epilepsy, which consists of seizures occurring around the time of menstrual periods, had an equivalent of change in mood during the menstrual period that women may experience. There are some women who are on the time of their menstrual period, they notice that they can become more easily depressed. They have to push themselves to do things. They become more tearful for little things. They become irritable, cranky. And they notice that their concentration is affected. So it's as if they were experiencing mini-depressive episodes that last a few days or a couple of days.

Andres Kanner: [51:02](#) Very often, women with these conditions have had a previous history of depression or have a family

psychiatric history of mood and depression disorders. And mood and depression disorders are genetically mediated. So when somebody has a family history, the next generation or first-degree relatives have an increased risk of experiencing these psychiatric disorders because they are mediated by several genes. And, depending on how many genes and the expression of the genes, a given member of the family will or will not experience these mood disorders. But the occurrence of changes in mood around the time of menstrual periods should alert the person to identify any risk factors. And they will often find out that, "Oh, my mother used to suffer from severe depression or anxiety," or my grandmother or whatever. And the fact is that the sexual hormones that have the same impact on seizures also have a similar impact on the development of symptoms of depression.

Brandon: [52:29](#)

Good. Thank you. And one more question we have time for. And it's a good wrap-up question. Can you summarize the main causes of mood disorders that affect epilepsy patients?

Andres Kanner: [52:43](#)

So the main causes... What people have to be aware of is that mood and anxiety disorders have multiple causes. As I said earlier, in response to your first question, one cause can be a reaction to the diagnosis of epilepsy and it can be the reaction to the impact that having a seizure disorder has on dealing with the limitations of not being able to drive, not being independent, et cetera. Then there are the risk factors associated with family history of mood and anxiety disorders. And these include whether there's a first or a second-degree relative who has suffered from these kind of psychiatric disorders. The third one are the chemical changes associated in the brain by the seizure disorder itself. And one of the things that we have identified is that the neurochemical changes that occur in brains with people with epilepsy are similar to those of people who have seizure disorders. And then there is the effect of the treatment of the seizure disorders, both pharmacologic treatment and surgical treatment, that can contribute in people who have a predisposition to psychiatric disorder to development of these psychiatric symptoms. So it's multiple causes.

- Andres Kanner: [54:30](#) And then you have the peri-ictal psychiatric symptoms, which is a development of these symptoms of depression and anxiety, that are temporally related to the occurrence of the seizure and that have to be recognized, because obviously those symptoms have a different mechanism of development and are not responsive to pharmacologic treatment with antidepressant medications.
- Brandon: [54:59](#) Great. Thank you so much for those informative responses. Go ahead. Laura, I'll turn it back over to you.
- Laura Lubbers: [55:09](#) Great. Well this concludes our webinar about the mood disorders associated with epilepsy. A special thank you to you, Dr. Kanner, for a very insightful presentation, and one that gives people, hopefully, really great guidance and ideas to talk about with their physicians. And we also appreciate the support from our sponsor Sunovion for today's webinar. I'd also like to thank our audience for being so engaged and asking great questions that hopefully have helped other people learn as well. If you do have questions about this topic or CURE's research programs, please visit our website which is seen on the screen, www.CUREepilepsy.org. If you do have questions, please feel free to reach out through our email address, info@cureepilepsy.org, also seen at the bottom of our screen.
- Laura Lubbers: [55:58](#) Please do join us for our next webinar which will discuss the new approaches to defining and classifying the epilepsies. This has been an interesting and confusing topic, and we're trying to find ways to simplify how we describe seizures. This webinar will be presented by Dr. Fisher from Stanford University, and it'll take place on Wednesday, September 26th, at 1:00 PM Eastern time. So thank you all. Have a wonderful day.