



### MOOD DISORDERS AND EPILEPSY SURGERY: LIGHTENING THE BURDEN IN MORE WAYS THAN ONE?

#### Changes in Depression and Anxiety after Resective Surgery for Epilepsy

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**OBJECTIVE:** To determine changes in depression and anxiety after resective surgery.

**METHODS:** Data from subjects enrolled in a prospective multicenter study of resective epilepsy surgery were reviewed with the Beck Psychiatric Symptoms Scales (Beck depression inventory [BDI] and Beck anxiety inventory [BAI]) and Composite International Diagnostic Interview (CIDI) up to a 24-month period.  $\chi^2$  analyses were used to correlate proportions.

**RESULTS:** A total of 358 presurgical BDI and 360 BAI results were reviewed. Moderate and severe levels of depression were reported in 22.1% of patients, and similar levels of anxiety were reported by 24.7%. Postoperative rates of depression and anxiety declined at the 3-, 12-, and 24-month follow-up periods. At the 24-month follow-up, moderate to severe levels of depression symptoms

were reported in 17.6% and 14.7% of the patients who continued to have postoperative seizures. Moderate to severe depression and anxiety were found in 8.2% of those who were seizure-free. There was no relationship, prior to surgery, between the presence or absence of depression and anxiety and the laterality or location of the seizure onset. There were no significant relationships between depression or anxiety at 24-month follow-up and the laterality or location of the surgery.

**CONCLUSIONS:** Depression and anxiety in patients with refractory epilepsy significantly improve after epilepsy surgery, especially in those who are seizure-free. Neither the lateralization nor the localization of the seizure focus or surgery was associated with the risk of affective symptoms at baseline or after surgery.

#### COMMENTARY

Mood disorders have long been recognized as a complicating factor for patients with epilepsy. Hippocrates proposed a direct relationship between epilepsy and “melancholia” (1). While the relationship between mood disorders and epilepsy has been documented repeatedly, the factors responsible for the symptoms have been difficult to disentangle from one another. Potential contributing factors include situational influences, underlying neuropathology, neurotransmitter fluctuations related to seizures, and anticonvulsant effects. In patients with refractory epilepsy, the majority of these factors cannot be manipulated and thus theories as to which factors are most important remain largely conjecture. Patients under-

going epilepsy surgery present an opportunity to understand the issue more fully. Whereas new medications offer little hope for complete seizure control in patients with medically refractory epilepsy, resection of the seizure focus will often result in seizure control. Thus, following resection, it should be easier to distinguish and separate out the direct and indirect effects of seizures on mood disorders.

Devinsky and colleagues report on the psychiatric effects associated with epilepsy surgery for patients enrolled in a multicenter, prospective trial. The vast majority (83%) of patients studied before surgery were evaluated after surgery. Prior to surgery, nearly one quarter of the patients reported depression and a similar number reported anxiety. These numbers are lower than prior reports cited by the same authors (2,3)—perhaps, because for this study, the authors used a threshold designed to include only patients with moderate-to-severe depression and anxiety. After surgery, the percentage of patients

reporting mood disorders decreased dramatically; the previously affected patients improved, more than offsetting the small minority of patients who developed new symptoms of depression and anxiety.

Although improvement in the majority of depressed and anxious patients was clearly documented, Devinsky et al. were rightfully guarded in their interpretation of the results, acknowledging that surgery often yields a powerful placebo effect. The authors do not mention whether patients suffering from moderate-to-severe depression or anxiety before surgery were routinely receiving medications or counseling. It seems likely, however, that these patients received increased medical attention around the time of surgery—a factor that alone might have favorably affected mood status. While it is possible that resection of the seizure focus improved mood symptoms by altering aberrant cerebral circuitry, the fact that patients improved, regardless of seizure focus localization or lateralization, suggests that any such mechanism must not be terribly specific.

The fact that postoperative depression and anxiety were twice as likely to occur in patients who did not achieve seizure control indicates that seizure control also played an important role (either directly or indirectly) in ameliorating the mood disorders. Improved seizure control may have improved symptoms of depression and anxiety by generally improving the patient's life situation. As the authors note, however, the improvement in symptoms typically occurred shortly after surgery at a time when most seizure-related psychosocial morbidity (such as unemployment and driving restrictions) would not have changed. Nonetheless, optimism and hope resulting from newfound seizure control certainly cannot be discounted as factors that potentially could improve patients' mood disorders following surgery. Given the rapid improvement in anxiety and depression closely following surgery, it is doubtful that adjustments in the patients' anticonvulsant medications played a major role. However, it is possible that seizure control may have improved the mood disorders by normalizing neurotransmitter abnormalities associated with seizures. To this end, it would have been very helpful if the preoperative disorders had been classified according to the presence or absence of a temporal relationship to the seizures. It would be interesting to know whether patients with postictal depression are more likely to respond favorably to the seizure control conferred by surgery; however, this possibility will have to be addressed by future studies.

While not the focus of the report, the patients who developed new anxiety and depression after surgery comprise an interesting cohort, worthy of further examination. It is not possible from the data presented, to know whether mood symptoms in this group were related to seizures. The data only indicate that together with residual mood disorders de novo depression, and anxiety were less common in patients who became seizure-free. A potential mechanism for the occurrence of new

depression in the subset of patients whose epilepsy became well-controlled following surgery is *forced normalization*—a theory that seizures improve psychiatric symptoms for some patients in the same manner as does electroconvulsive therapy. This concept, originally taken from the observation that patients occasionally developed psychosis as their EEG normalized, sometimes has been used to explain the occurrence of mood-related adverse effects associated with anticonvulsant treatment (4). Although the potential contribution of forced normalization to de novo mood disorders in this study cannot be estimated precisely, the relatively low rate of new symptoms in this group of patients undergoing the most effective possible seizure treatment suggests that it must be a very rare cause of psychiatric symptoms in anticonvulsant studies.

The study by Devinsky et al. is most relevant, however, for physicians caring for patients who are similar to those of the study cohort. Despite the limitations mentioned, the report represents a comprehensive assessment of mood in a large series of patients undergoing surgery. On the basis of the authors' observations, the following recommendations can be made for treating patients with surgically amenable epilepsy and mood disorders:

1. Most patients with mood disorders improve after surgery, and potentially life-saving surgery should not be delayed.
2. New psychiatric symptoms are rare after surgery, and when they occur, they are typically amenable to medical treatment.
3. Approximately one third of patients with preoperative mood disorders will have their symptoms persist after surgery, so surgery should not be considered a primary treatment—appropriate psychiatric treatment is still indicated.
4. After surgery, mood status should be reassessed to determine the need for ongoing treatment of anxiety and depression.

by Paul A. Garcia, MD

## References

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