



# Psychiatric Residue of Epilepsy Surgery: De Novo or Not

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## Predicting De Novo Psychopathology After Epilepsy Surgery: A 3-Year Cohort Study

Novais F, Pestana LC, Loureiro S, Andrea M, Figueira ML, Pimentel J. *Epilepsy Behav.* 2019;90:204-208. doi:10.1016/j.yebeh.2018.11.037. PMID: 30573340.

**Objective:** The aim of this study was to determine the potential risk factors for de novo psychiatric syndromes after epilepsy surgery. **Methods:** Refractory epilepsy surgery candidates were recruited from our Refractory Epilepsy Reference Centre. Psychiatric evaluations were made before surgery and every year, during a 3-year follow-up period. Demographic, psychiatric, and neurological data were recorded. The types of surgeries considered were resective surgery (resection of the epileptogenic zone) and palliative surgery (deep brain stimulation of the anterior nuclei of the thalamus [ANT-DBS]). A survival analysis model was used to determine pre- and postsurgical predictors of de novo psychiatric events after surgery. **Results:** One hundred and six people with refractory epilepsy submitted to epilepsy surgery were included. Sixteen (15%) people developed psychiatric disorders that were never identified before surgery. Multilobar epileptogenic zone ( $P = .001$ ) and DBS of the ANT-DBS ( $P = .003$ ) were found to be significant predictors of these events. **Conclusion:** People with more generalized epileptogenic activity and those who undergo ANT-DBS seem to present an increased susceptibility for the development of mental disorders, after neurosurgical interventions, for the treatment of refractory epilepsy. People considered to be at higher risk should be submitted to more frequent routine psychiatric assessments.”

## Commentary

Does surgery for epilepsy disrupt some sort of equilibrium that could yield psychiatric illness? That is the argument put forth in part by Novais and colleagues. It is an intriguing consideration, though the subject is very difficult to study, mostly because heterogeneous sampling and timing challenge interpretations of results. Not surprisingly, such efforts have only been attempted intermittently through the years.<sup>1-3</sup>

The difficulties are not resolved in this study, but there are so many positive aspects of the report that one can tolerate the limitations inherent in the conclusions. The investigators created a database of psychiatric illness in patients with surgically-treated epilepsy, and assessments were performed prior to the procedure and every year for 3 years after the procedure. The psychiatric detail is high quality and includes data from broad-based questionnaire measures as well as psychiatric assessments at various stages of the surgical process. Involvement of a psychiatrist in the surgical process just by itself makes this a valuable report, and sends an important message about the validity and notability of this report.<sup>4</sup> Although the assessments are not gold standard—which would include structured diagnostic interviews by research-trained psychiatrists—the study still offers valuable information and is easily a model for future teams to follow.

The details themselves raise some questions. The surgical procedures are varied as are the underlying pathologies. The sample is large (106) and most of the patients (85%) had a temporal focus. That percentage would suggest high psychiatric comorbidity, and while a sizeable portion of the sample did have psychiatric illness at the outset (42%), that number may be higher with so many having a temporal focus.<sup>5-7</sup> It could also be expected that presence of psychiatric illness would differ between temporal lobe foci and extra-temporal lobe foci, but the sample did not allow reasonable numbers to compare. The vast majority (93%) received resective surgery; the remainder received deep brain stimulation of the anterior thalamic nucleus. Those receiving deep brain stimulation and those with multilobar foci were more likely to develop de novo psychiatric illness. Multilobar itself is not well-defined, and that group plus the group receiving deep brain stimulation are very few, 5 and 7 respectively. Thus the idea that those two circumstances led to de novo psychiatric illness more than other factors is also a bit suspect.

Still, the underlying point is that de novo psychiatric illness may emerge after surgery, and while the reasons may be speculative, to consider it impossible is simply unrealistic. The more important question is why it emerges. The fact that this



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report allows us to speculate in such a dimension is a worthwhile endeavor. To ask why necessitates considering 3 main theories, though not fully explained in the article, clinical scholars and researchers will see recurring themes in the literature.

The first theory has to do with failure to establish an adequate baseline. In this study, although baseline questionnaire measures were obtained, not every subject had a full psychiatric evaluation. Despite this, a reasonable baseline was still obtained, though with the caveat of potential underreporting. This may occur even using a psychiatric interview to determine the baseline, because patients may minimize symptoms for fear of jeopardizing surgical plans. Neurologists and neurosurgeons may unwittingly enable such denial as all are motivated for surgery to occur without untidy psychiatric illness rearing its presence. Thus the de novo psychiatric illness may simply be underreporting at baseline.

The second major theory has to do with surgery potentially eliminating seizures, which could be an endogenous psychiatric treatment. This idea is most plausible in the context of depression but is also possible for psychosis. A (medically monitored) generalized seizure is a particularly effective treatment for depression. Not having this type of “reset” may yield psychiatric symptoms that would otherwise be restrained by seizures. The theory of forced normalization is consistent with this idea and suggests that not all aspects of seizure occurrences are negative. Despite the counterintuitive notion, it still may be the case that surgically preventing a therapeutic generalized seizure may unmask previous depressive or other psychiatric symptoms.

However, what if neither of the two theories above is sufficiently correct? What if the surgery is simply incomplete, and neglects to extract “depressogenic” tissues? Extreme precision and care are taken to remove only epileptogenic portions of seizure foci, and to protect so called eloquent cortex. However, no effort is given to excise depressogenic networks or tissues. So surgery may simply be solving one problem but leaving the second problem untouched. It still could be that the psychiatric illness is minimized to some degree as in theory one, or unmasked as in theory two, but those explanations may be too simplistic.

Perhaps the psychiatric illness is an inherent and constituent part of the epilepsy, thus surgical excision to remove epileptogenic zones is only partially treating the disease. It may defy conventional wisdom to accept this theory, but it may in fact be the most accurate, and the idea is fully consistent with the findings of Novais and colleagues.

The psychiatric presurgical assessments and postsurgical follow-up are as solid as most other reports in the literature and cannot be ignored. If theory #1 was correct, then we would expect uniformly higher numbers of psychiatric illness post-surgery. If forced normalization (theory #2) explained the de novo findings, then why do the majority of patients get better psychiatrically after the seizures are cured surgically?

Unfortunately, today it is not possible to map psychiatric illness prior to surgery. However, the most optimistic part of the study is that even in those patients who had de novo psychiatric illness, all improved with medication treatment. This fact is the most interesting, as it suggests that in patients with medically refractory epilepsy, multiple objectives must be kept in mind, and regardless of etiology, the condition(s) can be well treated with a blend of psychiatric medicines and surgical treatment.

By Jay Salpekar

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