



Presurgical depression and anxiety are not associated with worse epilepsy surgery outcome five years postoperatively

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ABSTRACT

Purpose: Anxiety and depression have been associated with poor seizure control after epilepsy surgery. This study explored the effect of presurgical anxiety or depression on two- and five-year seizure control outcomes.

Methods: Adult subjects were enrolled between 1996 and 2001 in a multicenter prospective study to evaluate outcomes of resective epilepsy surgery. A Poisson regression was used to analyze the association of depression and anxiety with surgical outcome, while adjusting for gender, age, ethnicity, number of years with seizures, and presence of mesial temporal sclerosis.

Results: The relative risk (RR) of presurgical depression on two-year seizure-free outcome in this cohort is 1.12 (95% confidence interval (CI), 0.84–1.49) and 1.06 (CI, 0.73–1.55) on five-year seizure free outcome. The RR of presurgical anxiety on two-year seizure outcome is 0.73 (CI, 0.50–1.07) and 0.70 (CI, 0.43–1.17) on five-year seizure outcome. When including Engel classes I and II, the RRs of presurgical depression, anxiety, or both two years after surgery were 0.96 ($p = 0.59$), 0.73 ($p < 0.05$), and 0.97 ($p = 0.70$), respectively, and they were 0.97 ($p = 0.82$), 0.84 ($p = 0.32$), and 0.89 ($p = 0.15$), respectively, five years after surgery.

Only presurgical anxiety was associated with worse epilepsy surgery outcome two year after surgery but not at five years postsurgery. Depression was not a risk factor for poor epilepsy surgical outcome in the long term.

Conclusion: These findings from a prospective study that utilized a standardized protocol for psychiatric and seizure outcome assessment suggest that presurgical mood disorders have no substantial impact on postsurgical seizure outcome for up to five years after surgery.

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1. Introduction

While neuroimaging, electroencephalography, seizure semiology, and cognitive testing are central components in surgical evaluations and presurgical prognostication of seizure and quality-of-life outcome, the role of psychiatric assessment remains unclear. Some studies have demonstrated that mood and anxiety disorders in people with epilepsy

are associated with antiepileptic drug (AED) resistance [1] as well as worse seizure control after epilepsy surgery [2–8]. Disturbances in glutamate and serotonin neurochemistry, neuroinflammatory mechanisms, as well as structural changes to frontal-temporal circuits have been postulated to account for a biological mechanism that leans towards an increased risk of worse seizure control in people with psychiatric history [9,10]. However, a few studies suggest that presurgical psychopathology is not a risk factor for poor epilepsy surgical outcome [11–15]. Unfortunately, all studies to date exploring the role of psychiatric risk factors on postsurgical outcomes are unblinded, most are retrospective, and all qualify as class IV evidence [16] (Table 1). Determining the role of psychiatric risk factors in epilepsy surgical outcome is

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Table 1
Reported associations between premorbid psychiatric history and epilepsy surgical outcome.

Study	Patient characteristics	Diagnostic criteria	Design/classification of evidence	Findings	Comments
<i>Studies showing no association between presurgical psychiatric history and postsurgical outcome</i>					
Jensen et al. (1977)	N = 74 Temporal lobectomy	Unblinded Clinical psychological diagnosis	Retrospective Single center Median follow-up: 5 years Class IV	HxPsyDx was not related to seizure improvement	Evaluations conducted prior to the publication of the DSM-III and likely relied on psychodynamic conceptions of mental illness
Blumer et al. (1998)	N = 44 Temporal lobectomy With and without IDD	Unblinded Clinical diagnoses as well as use of a neurobehavioral inventory by a neuropsychiatrist experienced in epilepsy care with tailored evaluation	Prospective Single center Mean follow-up: 2 years Class IV	HxPsyDx (56.8%) did not predict surgical outcome; less favorable surgical outcome was found among those without HxPsyDx who developed de novo mental illness	All patients with dysphoria (57% of subjects) were treated with an antidepressant preoperatively
Guarnieri et al. (2009)	N = 186 Temporal lobectomy (hippocampal sclerosis)	Unblinded Clinical diagnoses by psychiatrists experienced in epilepsy care using DSM diagnoses and Blumer's criteria for IDD (20)	Prospective Single center Average follow-up: 6 years Class IV	Preop DSM axis I HxPsyDx, depression, dysphoric disorder, interictal psychosis, PIP did not predict surgical outcome; preop anxiety disorder (n = 10) and personality disorder (n = 23) significantly associated with less favorable surgical outcome	No association between psychiatric disorders and seizure outcome was significant after correcting for multiple comparisons
Adams et al. (2012)	N = 72 Temporal lobectomy (hippocampal sclerosis)	Unblinded Clinical diagnoses by a psychiatrist experienced in epilepsy care	Retrospective Single center Mean follow-up: 5 years. Good seizure outcome — grade I Class IV	Lack of preop HxPsyDx was not associated with surgical outcome; nonsignificant increase in HxPsyDx among those with good seizure outcome (OR, 1.8)	Of the patients with Engel class I outcome, 41.8% (23/55) had PPHx versus 23.5% (4/17) of patients with classes II–IV
Lackmayer et al. (2013)	N = 45 Temporal lobectomy (hippocampal sclerosis)	Unblinded BDI (>10 defined as depressed)	Retrospective Single center 3-year follow-up Class IV	Preoperative depression did not predict postoperative seizure outcome at year 2 or 3 (nonsignificant increase in seizure freedom with preop depression)	By the 3rd postoperative year, 17/19 patients with depressive symptoms were seizure-free; no data regarding psychiatric treatment
<i>Studies showing an association between presurgical psychiatric history and postsurgical outcome</i>					
Anhoury et al. (2000)	N = 109 Temporal lobectomy	Unblinded Clinical diagnoses by psychiatrists experienced in epilepsy care and review of prior psychiatric history	Retrospective Single center 1-year follow-up Class IV	HxPsyDx (44%) correlated with less favorable seizure control postop; 20% of the cohort had PPHx and de novo psychiatric postop symptoms — nonsignificant trend for less favorable surgical outcome; 100% of this group had bilateral temporal spikes which was an independent risk factor for poor surgical outcome	ICD and DSM criteria not used; no correction for multiple comparisons; finding was positive in correlational analysis but not in multivariate analysis; preoperative HxPsyDx correlated with bilateral interictal spikes, which was a significant predictor of unfavorable surgical outcome
Kanner et al. (2009)	N = 100 Temporal lobectomy	Unblinded Single psychiatrist by SCID interview	Retrospective Single center Surgical outcome after 2 years (mean, 8.3 years) Class IV	Lifetime HxPsyDx predicted 10.4-fold less favorable chance of class IA/B outcome (p < .0001); lifetime mood disorder was associated with 7.2 less favorable outcome	With multivariate analysis, HxPsyDx was more strongly associated with outcome than size of lesion, side of lesion, age at onset, and pathology
Metternich et al. (2009)	N = 115 97 temporal lobectomy, 18 frontal lobectomy	Unblinded BDI	Retrospective Single center 1-year outcome Class IV	Lower preop BDI score was associated with improved surgical outcome for overall (p = .01) and temporal lobectomy group (p = .03)	BDI results were treated as a continuous variable; only BDI results and not surgical location (frontal versus temporal) were significantly associated with seizure outcome
Cleary et al. (2012)		Unblinded Clinical diagnoses by psychiatrists experienced in epilepsy care using DSM-IVR diagnoses and nonepileptic seizures, and interictal and PIP	Retrospective Single center 2-year follow-up Class IV	Lack of preop HxPsyDx associated with better surgical outcome (OR, 0.53; p = .04); 29% had preop PsyDx	About 18% of the sample developed de novo psychopathology, but there was no association with de novo psychopathology and seizure outcome; history of secondarily generalized seizures was also associated with worse seizure outcome
Araujo Filho et al. (2012)	N = 115 Cortico-amygdalo-hippocampectomy	Unblinded Clinical diagnoses by a psychiatrist experienced in epilepsy care using DSM-IVR diagnoses and ILAE criteria for epilepsy-specific psychiatric disorders such as PIP and IDD	Retrospective Single center Good seizure outcome — grade IA Class IV	Lack of preoperative psychiatric treatment and lack of preop nondepressive disorder were not associated with surgical outcome; preoperative MDD was associated with less favorable surgical outcome (OR, 5.2; p = .003); 40.8% had preop PsyDx	The number of patients with PIP and IDD were too low to evaluate statistical significance; the only HxPsyDx that was significantly associated with outcome was MDD

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