



Effects of surgical side and site on psychological symptoms following epilepsy surgery in adults



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ABSTRACT

This retrospective study examined the potential role of side and site of surgery in psychological symptom change after epilepsy surgery and determined the base rate of psychological change at the individual level. Two-hundred twenty-eight adults completed the Personality Assessment Inventory (PAI) before and after temporal (TLR; $n = 190$) or frontal lobe resection (FLR; $n = 38$). Repeated measures ANOVAs with bootstrapping examined differences in psychological outcome as a function of surgical site separately in patients who underwent left- versus right-sided resections. Individual's PAI score changes were then used to determine the prevalence of clinically meaningful postoperative symptom change. Following *left-sided resections*, there were significant group-by-time interactions on Somatic Complaints, Anxiety, and Anxiety Related Disorders. There was also a trend in this direction on the Depression scale. TLR patients endorsed greater preoperative symptoms than FLR patients on all of these scales, except the Somatic Complaints scale. After surgery, TLR patients reported symptom improvement on all four scales, while scores of FLR patients remained relatively stable over time. Endorsement of Mania-related symptoms increased in both TLR and FLR groups from pre- to post-surgical testing. Following *right-sided resections*, both groups endorsed symptom improvements on Somatic Complaints, Anxiety, and Depression scales following surgery. In addition, the TLR group endorsed more Mania-related symptoms than the FLR group regardless of time. Patterns of meaningful change in individual patients were generally consistent with group findings, with the most frequent improvements observed following TLR. However, there were a small subset of patients who reported symptom exacerbation after surgery. Our results suggest that surgical lateralization and localization are important factors in postoperative psychological outcome and highlight the importance of considering psychological change at the individual patient level. Further research is needed to identify potential risk factors for symptom exacerbation to aid in preoperative counseling and identify those patients most in need of postoperative psychological surveillance.

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1. Introduction

Psychopathology occurs at higher rates in patients with epilepsy than in the general population. An estimated 20–40% of patients with epilepsy are diagnosed with psychiatric disturbances, while rates as high as 70% can be seen in patients with pharmacoresistant seizures

[1–4]. Mood disorders are the most frequently observed psychiatric diagnoses in patients with epilepsy; the prevalence of depression ranges from 20 to 55% in this population [5]. Many studies suggest that depression is more frequent in patients whose seizures arise from left anterior (i.e., temporal, frontal) regions [6–8]. This finding is consistent with literature in other neurological populations and cognitive neuroscience theories regarding the neuroanatomy of emotion [9]. Many studies investigate other psychiatric symptomatology in patients with epilepsy [3,10–14]; however, research examining psychiatric outcome following epilepsy surgery is limited.

In clinical practice, there is often concern regarding risk for de novo psychiatric symptoms or exacerbation of pre-existing psychiatric symptoms following epilepsy surgery [15–18]. Research results are unclear; some studies purport that surgery leads to a reduction in psychiatric

Abbreviations: PAI, Personality Assessment Inventory; TLR, temporal lobe resection; FLR, frontal lobe resection.

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symptoms [19,20], while others have found postoperative symptom exacerbation [21,22]. Factors such as presurgical psychological adjustment, postoperative seizure-freedom, and time to follow-up have been shown to be related to psychological outcome [23–25], although these findings have not been universal [26,27]. To complicate matters, most existing studies on this topic have involved small sample sizes and the grouping of frontal, parietal, and occipital cases to have a robust enough sample to make comparisons to a frequently larger sample of temporal lobe cases [3,22,28]. As such, very few studies have examined the potential role of *both* anterior surgical site *and* side in postoperative psychiatric outcome simultaneously. Further, most existing studies have limited their examination of psychiatric symptom change to group data, which may obscure important findings in individual patients.

This study sought to extend the current literature by further examining mood and psychological outcome following epilepsy surgery in a large group of adults with pharmacoresistant seizures. The primary aims were two-fold: 1) to explore the potential role of both side *and* site of surgery in self-reported postoperative psychological symptoms, and 2) to determine the prevalence of postsurgical change in self-reported psychological symptoms at the individual level.

2. Materials and methods

2.1. Participants

This retrospective study acquired data from an Institutional Review Board-approved data registry containing pre- and postoperative neuropsychological data for patients who underwent epilepsy surgery at Cleveland Clinic between 1993 and 2014. Participants were selected for the study if they met the following inclusion criteria: 1) were at least 18 years of age; 2) completed both pre- and postoperative neuropsychological evaluations that included the Personality Assessment Inventory (PAI [29]); 3) had a standard score of 70 or higher on the Wechsler Adult Intelligence Scale – Third Edition (WAIS-III [30]) or on the Reading subscale of the Wide Range Achievement Test – Third or Fourth Edition (WRAT3 [31] or WRAT4 [32]); and 4) had a history of either frontal or temporal lobe resective surgery. Patients who had undergone other focal surgeries in posterior regions of the brain were not included due to small sample sizes that precluded the examination of side and site of surgery. Patients were also excluded from this study if they demonstrated right-hemispheric language dominance on fMRI or Wada testing, had an elevated score on more than one of the PAI validity scales, or if the evaluating neuropsychologist had concerns about patient effort during the evaluation. Patients who were excluded from the study (for reasons other than age or IQ/reading level; $n = 490$) were not significantly different in age, sex, education, age at seizure onset, or duration of epilepsy from patients included in the study. However, there was a significant difference in race, with fewer non-White patients in the final study sample.

A total of 228 participants met inclusion criteria. Of these, 38 (16 left, 22 right) had undergone frontal lobe resections (FLR), and 190 (92 left, 98 right) had undergone temporal lobe resections (TLR). Participants ranged in age from 18 to 73 years ($M = 36.47$, $SD = 11.70$) and in education from 8 to 20 years ($M = 13.37$, $SD = 2.15$). Mean age at seizure onset was 17.57 years ($SD = 12.65$), and mean duration of epilepsy was 18.90 years ($SD = 12.25$). Participants were taking an average of 2.06 ($SD = 0.72$) anti-epileptic drugs (AEDs) at the time of their preoperative evaluation and an average of 1.90 ($SD = 0.81$) AEDs at their postoperative evaluation. Fifty-six percent of participants were female and 98% characterized themselves as Caucasian (Table 1). Patients completed postoperative neuropsychological testing a median of 6 months following surgery and 9 months following their preoperative assessment. The modes for these follow-up time points were also 6 and 9 months, respectively. There was no difference in time to follow-up between patients who underwent TLR versus FLR, regardless of side of surgery

[right side: $t(118) = -0.48$, $p = 0.61$; left side: $t(106) = 0.32$, $p = 0.75$], and time to follow-up was not significantly related to psychological change following surgery (r range = -0.12 to 0.11 , p range = 0.20 to 0.77).

Most of the patients in the study (58%) remained on the same number of AEDs postoperatively as they had been taking prior to surgery. Approximately 28% of patients had a reduction in the number of AEDs between their pre- and postoperative neuropsychological assessments. Only a small proportion of patients (14%) had one or more AEDs added to their medication regimen during this time period. There was no significant difference in the proportion of FLR and TLR patients whose number of AEDs changed or remained stable following surgery. Similarly, the vast majority of patients (83%) remained on the same number of psychotropic medications as they were taking prior to surgery. Several patients (5%) had a reduction in psychotropic medications following surgery, and a small subset (12%) had a psychotropic drug (most often an antidepressant) added to their regimen. There was no significant difference in the proportion of FLR and TLR patients whose psychotropic medications changed or remained stable following surgery.

Psychiatric history was available for 215 patients (94%) in the study sample. Based on medical record review, 32% of these participants had been previously diagnosed with a mood and/or anxiety disorder and 10% had been diagnosed with an adjustment disorder prior to surgery. One patient had a history of atypical psychosis, and one patient with a history of anxiety disorder experienced occasional post-ictal psychosis. A summary of patient psychiatric diagnoses and psychotropic medications is provided in Table 1.

2.2. Measures

The Personality Assessment Inventory (PAI [29]), a standardized, self-report measure of adult personality, was used to evaluate psychological functioning. This measure produces four validity scales (Inconsistency, Infrequency, Negative Impression Management, and Positive Impression Management) that were used to determine profile validity as described in the Participants section above. The PAI also produces 11 clinical scales, 5 of which were selected for examination in the present study: Somatic Complaints, Anxiety, Anxiety-Related Disorders, Depression, and Mania. The PAI has been well-validated and is commonly employed in clinical settings to assist in assessing psychopathology [29].

2.3. Statistical analyses

Given prior findings of greater depressive symptomatology in patients with left-sided seizure foci [6–8], all analyses described below were conducted separately by surgical side (left, right). Participants were further categorized based on surgical resection site (temporal, frontal) before analyses were conducted.

Potential group differences on relevant demographic and seizure variables were examined with chi-squares, Fisher's exact tests, and one-way ANOVAs. Next, analyses examined the role of both side and site of surgery on psychological symptoms. Exact tests were performed to determine if there were group differences in the proportion of individuals who had clinically significant scale elevations (t -score ≥ 70) on the PAI before or after surgery. A series of repeated measures ANOVAs was conducted on each of the five PAI clinical scales of interest to examine potential group differences in psychological outcome following surgery. Bootstrapping (1000 replications) was used to adjust for influential cases. Post-hoc t -tests were used to facilitate interpretation of significant interactions. As this was an exploratory study designed to identify any potential differences in psychiatric outcome following epilepsy surgery as a function of surgical site and side, p -values were not adjusted for multiple comparisons.

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