

## Postoperative EEG association with seizure recurrence: Analysis of the NIH epilepsy surgery database

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### SUMMARY

The epilepsy surgery database from 1984 to 2012 at the National Institutes of Health (NIH) was reviewed to determine the association of postoperative electroencephalography (EEG) with seizure recurrence. Eighty-three patients were analyzed, with 41 having at least 5 years of follow-up. The relationship between epileptiform postoperative EEG findings and seizure recurrence at 1, 2, and 5 years was not significant, despite a significant decrease in abnormal EEG recordings after surgery. Clinicians use a variety of tools to predict seizure recurrence following epilepsy surgery to guide medication management and to modulate patient expectations. EEG is but one tool for assessing the likelihood of seizure recurrence following epilepsy surgery.

**KEY WORDS:** Surgery, Epilepsy, EEG, Outcome prediction.

Approximately 30% of patients with epilepsy have seizures that remain uncontrolled by medications. Surgery can be an effective option, leading to long-term seizure freedom in 47% of patients.<sup>1</sup> The largest prospective randomized study identified a cumulative 58% of patients with temporal lobe epilepsy achieving 1-year postoperative Engel class 1, versus 8% in the medical therapy group.<sup>2</sup> There is wide

variability in how clinicians decide when, or if, to taper antiepileptic drugs (AEDs) following epilepsy surgery, usually based at least to some degree on the perceived risk of seizure recurrence. There are conflicting data in the literature regarding the relative benefits of various predictive factors of seizure outcome, including postoperative electroencephalography (EEG), antiseizure drug levels, and extent of resection on magnetic resonance imaging (MRI). The aim of our study was to share the experience at our center in order to further the knowledge regarding this question: does postoperative EEG predict seizure outcome following epilepsy surgery?

### METHODS

A retrospective review was performed of the 151 consecutive, resective epilepsy surgical cases at the National Institutes of Health (NIH) Clinical Center between January 1, 1984, and January 1, 2012. All subjects were enrolled in NIH institutional review board–approved research

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protocols. We included patients who underwent their first surgical resection, had seizure outcomes available for at least 1 year postoperatively, and had at least one postoperative EEG within 5 years of surgery. Surgical planning included at a minimum the following: detailed history and physical examination, MRI, neuropsychological testing, and long-term video-EEG monitoring. Postoperative AED management was not reviewed, as the referring physician generally managed this. For the cases in which the subject's AED management was directed by the NIH, the general policy has been to continue medications unchanged for 2 years postoperatively.

All EEG recordings were performed with electrode placement according to the 10–20 system and reviewed using longitudinal bipolar, transverse, and referential montages. During these 30-minute recordings, standard provocation maneuvers were performed unless otherwise contraindicated. Patients were encouraged to sleep but were not sleep deprived prior to the study. Only definite spikes or sharp waves were considered as interictal epileptiform discharges (IEDs). Focal slowing was not considered for our analysis. EEG studies performed <2 months after surgery were not included, as IEDs found during this period may be attributable to temporary effects of surgery and may be less indicative of long-term outcome. In the case of multiple postoperative EEG studies, the presence of IEDs on even one recording designated that subject's placement into the "IED" group. EEG recordings were interpreted by an attending epileptologist (WT, SI, SS). One author (SS) was the head of the EEG laboratory for nearly 30 years, thus providing consistency in EEG interpretation. Seizure freedom was defined as freedom from disabling clinical seizures, including any events impairing consciousness, and those with overt motor phenomena. This outcome information was gathered by the NIH Clinical Epilepsy Section through outpatient clinic visits and telephone encounters.

Fisher's exact tests were used to compare the patients with favorable and unfavorable seizure outcomes at 1, 2, and 5 years postoperatively with respect to the presence of IEDs on EEG in the postoperative period. These analyses were performed using GraphPad (GraphPad Software, Inc., La Jolla, CA). Median seizure-free survival durations were calculated based on Kaplan-Meier analysis, and differences were assessed with the log-rank test using the R statistical package (v.3.2.3). A *P*-value of < 0.05 was considered significant.

## RESULTS

During the study period, 151 patients underwent surgical resection for epilepsy. Sixty-eight patients were excluded from this review because of a history of multiple resections or inadequate data. Inadequate data was defined as <1 year of follow-up and/or absence of documented EEG within 5 years after surgery (Table 1). Five of the patients underwent extratemporal resection; they were not analyzed

**Table 1. Patient characteristics**

Total number of patients <sup>a</sup>	83
Number of women (%)	40 (48)
Number of left-handed patients (%)	9 (11)
Average age at surgery (range)	32.3 (12–56)
Average years from diagnosis to surgery (range)	19.1 (0–50)
Surgical hemisphere	
Left (%)	40 (48)
Right (%)	43 (52)
Lobe of surgery	
Temporal (%)	78 (94)
Extratemporal (%)	5 (6)
Median years postoperative follow-up (range)	4.87 (1–22.97)
Median months to 1st postoperative EEG (range)	12 (0.6–58)
Median months to 1st postoperative EEG within 1 year (range)	7.1 (0.6–12)

<sup>a</sup>One hundred fifty-one patients were evaluated and 68 were excluded prior to analysis: 49 had no EEG data within 5 years of surgery, 13 had <1 year of postoperative follow-up, and 6 had prior epilepsy surgery.

separately given the small sub-sample size. The majority of cases were standard temporal lobectomies (70/83), with the remainder including lesionectomy, multiple subpial transections, and multilobar resection. For 34/83 cases, no pathologic diagnosis was available, in most cases because the data were not available. In 19/83 cases, the pathologic diagnosis was mesial temporal sclerosis, and in 16/83, the diagnosis was gliosis. The remaining cases were cavernous malformations, arteriovenous malformations (AVMs), postinfectious gliosis, and low-grade tumors. Of the included 83 patients, the median duration of follow-up for seizure outcome was 4.87 years (range 1–23 years). The median time to first postoperative EEG was just over 1 year (range 2 months–4.87 years), with 49 having an EEG within 1 year (average 7.1 months). Fifty-three patients had preoperative routine EEG data, postoperative EEG within 24 months, and at least 2 years of follow-up data available. Of these 53 patients, 42 (79%) had IEDs on preoperative routine EEG. This number declined significantly after surgery, to 12 (23%), *p* < 0.0001. (Table 2).

Of patients with EEG studies performed within 1 year postoperatively, 22/49 (45%) were seizure-free at 1 year, 19/45 (42%) at 2 years, and 6/22 (27%) at 5 years. In seizure-free patients, IEDs were observed in 8 (36%), 6 (32%), and 2 (33%) at 1, 2, and 5 years, respectively. In comparison, in patients with ongoing seizures, IEDs were present in 7/27 (26%), 7/26 (27%), and 3/16 (19%) at 1, 2, and 5 years, respectively. The presence of IEDs on postoperative EEG obtained within 1 year of surgery was not significantly predictive of seizure outcome at 1, 2, or 5 years.

Of patients with EEG studies performed within 2 years postoperatively, 31/66 (47%) were seizure-free at 2 years and 16/37 (43%) at 5 years. In seizure-free patients, IEDs were observed in 8 (26%) and 4 (25%) at 2 and 5 years, respectively. In comparison, in patients with ongoing

**Table 2. Presence of IEDs on preoperative versus postoperative EEG at 24 months**

24 Months			
	No IEDs	IEDs	Total
Preoperative	11	42	53
Postoperative	41	12	53
P	<0.0001		

seizures, IEDs were present in 10/35 (29%) and 6/21 (29%) at 2 and 5 years, respectively. The presence of IEDs on postoperative EEG obtained within 2 years of surgery was not significantly predictive of seizure outcome at 2 or 5 years.

Of patients with EEG studies performed within 5 years postoperatively, 18/41 (44%) were seizure-free at 5 years. In seizure-free patients, IEDs were observed in 5 (28%) at 5 years. In comparison, in patients with ongoing seizures, IEDs were present in 10/23 (43%). The presence of IEDs on postoperative EEG obtained within 5 years of surgery was not significantly predictive of seizure outcome at 5 years (Table S1).

The median seizure-free survival based on a normal first postoperative EEG compared to the abnormal first postoperative EEG showed no significant difference using a Kaplan-Meier analysis ( $p = 0.343$ ).

## DISCUSSION

In our patient population, the postoperative EEG result was not associated with seizure freedom at 1, 2, or 5 years following surgical resection for drug-resistant epilepsy. This implies that either postoperative EEG is not a helpful predictor or that the effect size is small and thus not significant in our cohort. In addition, we found that a significant number of patients had normal EEG results after surgery, compared to preoperative EEG, but this was not associated with seizure freedom. We postulate that surgery often decreased the seizure focus below a critical threshold for EEG detection. Although there is support in the literature for the predictive value of postoperative EEG, the results of our study are more supportive of the position that EEG results should not be a strong factor when determining postoperative seizure recurrence risk, and subsequently, decisions to taper AEDs and/or allow participation in potentially dangerous activities such as driving. Based on our results, postoperative EEG can be used as an *adjunctive* aide among the many factors used to estimate the probability of seizure freedom in patients who have undergone epilepsy surgery.

The published literature on this topic has largely provided supportive evidence for the use of postoperative EEG in seizure freedom prediction. A recent review looked at several prognostic tests and reviewed the evidence supporting their use. Three of the 7 studies examining postoperative EEG as

a predictor of seizure freedom found that interictal epileptiform activity significantly predicted seizure recurrence, including 2 rigorous, prospective trials with large cohorts.<sup>3</sup> One was a review of experience with 262 postoperative patients in whom EEG was done at 3 months, and 1, 2, and 3 years after surgery. Abnormal EEG increased the risk of recurrent seizures, and 4 abnormal EEG studies were 98% specific for seizure recurrence. Conversely, 4 normal EEG studies had a 90% specificity for seizure freedom. These patients all underwent AED withdrawal trials and were generally similar in baseline characteristics.<sup>4</sup> The remaining studies were retrospective and generally did not find that postoperative EEG was predictive of eventual seizure freedom. In another study, researchers performed EEG studies at 1 month and again at 1 year after surgery for temporal lobe epilepsy, and found that IEDs were predictive of seizure recurrence. However, 58.3% of patients with IEDs and seizures at 1 month became seizure-free with no IEDs at 1 year.<sup>5</sup> More recent work by that group reviewed 107 patients after surgery and performed longer EEG studies, including sleep, and at 12 and 24 months postoperatively. They found a significant relationship between IEDs and recurrence, but in 50% of the patients with IEDs, abnormalities were detected only during sleep.<sup>6</sup> In the 2016 study by Chen et al., 70 patients were evaluated for predictors of seizure recurrence at a mean of 48 months after either temporal (77%) or extratemporal (23%) resection, based on 12 variables. The only independent predictors of seizure recurrence over the long term were resection site and ictal EEG concordance. Patients with extratemporal resection sites and those patients who had ictal EEG discordant with resection area were more likely to have recurrence after surgery.<sup>7</sup>

There are several limitations to our study. First, this was a retrospective study with postoperative EEG procurement generally obtained at the time of follow-up visit. Although follow-up visits were generally sought out, they may have occurred more routinely in patients who did relatively poorly after surgery and thus had cause to return to the NIH. Our cohort was heterogeneous in terms of the timing of EEG after surgery, with wide variation, which we attempted to control by including only patients with EEG studies done within 5 years of surgery. These control parameters led to the exclusion of many patients, thereby reducing the power of our study. The data were collected over 28 years, during which time EEG technology changed dramatically from paper readouts to fully digitized computer displays. Prolonged EEG, including sleep, was not obtained in most cases. Finally, follow-up data were quite variable given the wide geographic catchment area of the NIH and the fact that most patients were followed clinically after surgery by their local referring providers. This does not allow us to control for the status of patient seizure medication maintenance and/or withdrawal.

The predictive value of postoperative EEG for seizure freedom remains unsettled despite numerous publications

from experts around the globe. The results of well-conducted trials, on homogenous populations, provide excellent data; however, these data may not be widely applicable to heterogenous populations. Our study suggests that postoperative EEG is but one variable the clinician can use to help determine long-term risk of seizure recurrence after surgery. Prospective studies with larger, more typical postoperative patient populations, with pre-defined time points and methods of evaluation, are much needed to better inform our clinical decision-making. Until those data become available, data from retrospective studies such as this one may allow for data sharing and meaningful aggregation of patient outcomes across centers and continents, in order to determine the preoperative, intraoperative, and postoperative variables that significantly influence long-term outcome.

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### DISCLOSURE

The authors have no significant conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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### SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

**Table S1.** Seizure freedom at 1, 2, and 5 years postoperatively, based on presence of IEDs during EEG within 1 year of surgery.