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Preoperative Prediction of Temporal Lobe Epilepsy Surgery Outcome

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Abstract

PURPOSE—There is controversy about relative contributions of ictal scalp video EEG recording (vEEG), routine scalp outpatient interictal EEG (rEEG), intracranial EEG (iEEG) and MRI for predicting seizure-free outcomes after temporal lobectomy. We reviewed NIH experience to determine contributions at specific time points as well as long-term predictive value of standard pre-surgical investigations.

METHODS—Raw data was obtained via retrospective chart review of 151 patients. After exclusions, 118 remained (median 5 years follow-up). MRI-proven mesial temporal sclerosis (MTSr) was considered a separate category for analysis. Logistic regression estimated odds ratios at 6-months, 1-year, and 2 years; proportional hazard models estimated long-term comparisons. Subset analysis of the proportional hazard model was performed including only patients with commonly encountered situations in each of the modalities, to maximize statistical inference.

RESULTS—Any MRI finding, MRI proven MTS, rEEG, vEEG and iEEG did not predict two-year seizure-free outcome. MTSr was predictive at six months (OR=2.894, p=0.0466), as were MRI and MTSr at one year (OR=10.4231, p=0.0144 and OR=3.576, p=0.0091). Correcting for rEEG and MRI, vEEG failed to predict outcome at 6 months, 1 year and 2 years. Proportional hazard analysis including all available follow-up failed to achieve significance for any modality. In the subset analysis of 83 patients with commonly encountered results, vEEG modestly predicted long-term seizure-free outcomes with a proportional hazard ratio of 1.936 (p=0.0304).

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CONCLUSIONS—In this study, presurgical tools did not provide unambiguous long-term outcome predictions. Multicenter prospective studies are needed to determine optimal presurgical epilepsy evaluation.

Keywords

epilepsy; surgery; outcomes; MRI; video EEG; long term monitoring

1. INTRODUCTION

Approximately 30% of patients with epilepsy have seizures that remain uncontrolled by medications (Kwan and Brodie, 2000). Surgery can be an effective option, leading to long-term seizure-freedom in 38–85% of patients (De Tisi et al., 2011; Engel et al., 2012; Jeha et al., 2006; Kelley and Theodore, 2005; Wiebe et al., 2001). The largest prospective randomized study (Wiebe et al., 2001) found 38% of temporal lobe epilepsy patients achieving 1-year postoperative complete seizure-freedom, versus 3% in the medical therapy group. A more recent smaller randomized study (Engel et al., 2012) reported 85% versus 0% 2-year complete seizure-freedom in surgical and medical groups respectively. Due to methodological differences (such as the timing of randomization), these two studies may not be directly comparable. Several studies emphasize the importance of a seizure-free outcome in order for patients to report significant improvements in quality of life after surgery (Birbeck et al., 2002; Leidy et al., 1999; Modi et al., 2009). Although surgery is often the best option to achieve seizure-freedom, surgery does carry some degree of morbidity. This emphasizes the importance of seizure outcome prediction in presurgical decision-making.

It is widely recognized that video-EEG is the bedrock of epilepsy diagnosis (Ghougassian et al., 2004; Jin et al., 2014; Perry et al., 1983; Theodore et al., 1983). It is a test with rare but measurable risks. An international survey from 147 inpatient EEG monitoring centers reported 49 deaths over 3008 patient-years (Ryvlin et al., 2013). Additional risks include status epilepticus, cardiac complications, dislocations and vertebral fractures (Noe and Draskowski, 2009). Aside from its role in diagnosis, ictal scalp video-EEG (vEEG) has also been considered a useful predictor of surgical outcome (Armon et al., 1996; Holmes et al., 2000; Tatum et al., 2008; Uijl et al., 2008a). However, a recent study discriminated the lowest surgical success group (48% seizure-free) from the highest (72% seizure-free) without including the results of vEEG (Garcia Gracia et al., 2014). Perhaps modern imaging has outpaced vEEG in identifying markers of surgical success, given that many studies have found valuable prognostic value from imaging, while fewer consistently find prognostic value from vEEG (Zhang et al., 2013). Even in the case of MRI imaging, it has been difficult to show a consistent unequivocal predictive value, possibly due to the lack of objective analytic techniques (Bernhardt et al., 2015).

Given the safety concerns and conflicting data, we reviewed the experience of the National Institutes of Health over a 28-year period. Our objective was to examine the prognostic value of pre-operative localizing procedures for temporal lobectomy outcome.

2. METHODS

A retrospective review was performed of the 151 consecutive, resective epilepsy surgical cases at the National Institutes of Health between January 1, 1984 and January 1, 2012. All subjects were enrolled in research protocols in accordance with our institutional review board. Each underwent presurgical evaluation, including 1.5 T or 3.0 T magnetic resonance imaging (MRI), interictal routine scalp electroencephalography (rEEG), and vEEG. The available interictal video EEG data was included, however in many cases data was no longer available for review. Dr. Sato, Dr. Theodore or Dr. Inati performed all primary EEG interpretation at NIH during the study period. Data from FDG-PET scans were excluded because not all patients in the sample had the test. After surgery, patients were followed in clinic for a median of 5.0 years, (range 0–23.2 years). Seizure-freedom outcome data was obtained via in-person clinic follow-up at the NIH Clinical Epilepsy Section. Data were corroborated with EEG clinical histories and nursing notes when possible. Of note, because of the retrospective nature of this study, there was no standard clinic follow up interval – each patient was somewhat different. When less than 2 years of clinical follow-up outcome data was unavailable, telephone or mail contact was used to obtain more updated outcome information.

For this study, patients who had extratemporal operations, repeat surgeries, or no follow-up were excluded. Temporal lobectomies were mostly standard anterior temporal lobectomies with the exception of 6 that included temporal lesionectomies. All the surgeries (except 6 cases) were performed at NIH. The included 118 patients (Figure 1) had each of the presurgical modalities coded as either “fully concordant,” “partially concordant,” “discordant,” or “normal/diffuse/no data.” The coding reflects the seizure focus localization by the modality compared to the location of surgical resection. Specifically, intracranial EEG (iEEG) coding represented the operative interictal localization, vEEG represented the ictal localization, the rEEG represented the interictal localization based on the most clear focal finding (epileptiform discharges when present, focal slowing when discharges were absent), and the MRI coding represented the location of the lesion if present. In cases where a modality was employed more than once, the composite of all exams was coded. Thus, when multiple routine EEGs were obtained, for example, if all of them identified the same region that was ultimately resected, then rEEG was coded “concordant”. On the other hand, if 2 routine EEGs were “concordant” and 1 was “discordant,” then rEEG would be coded “partially concordant”. Furthermore, if at least 1 was “concordant,” and others were “normal,” this was coded as “concordant” as well. Of note, MRI codes accounted for the sum of the final impression from the radiology report and the consensus opinion of the multidisciplinary surgical review conference findings – any focal findings from either would be included when coding. If multiple localizations were present, all of them were accounted for when coding concordance with surgical resection. Additional codes for presence or absence of mesial temporal sclerosis (by consensus of radiologist and epileptologists) on the MRI scan (MTSr) were also included. When the localization included multiple areas (e.g. bitemporal spikes on rEEG, or multifocal hyperintensities on MRI etc.), then when the surgical resection included part of the localization, these were coded as “partially concordant”. When localization did not include the resection volume (such as contralateral

hippocampal changes) then “discordant” was coded. Original clinical imaging, EEG and pathological reports were used, and the studies were not reinterpreted.

To address the possibility that changing MRI technology played a role in MRI predictive capability, we also divided the MRIs into subcategories based on the year of the most recent presurgical MRI available, using ranges of 1984–1990, 1990–2000, and 2000–2011 as categories. Unfortunately, the actual magnet strength and full descriptions of pulse sequences were often not documented in the available reports, therefore we used year of scan as a surrogate for technological improvement.

Two additional subsets of patients were evaluated for the proportional hazard analysis in an effort to decrease the heterogeneity of the population and thereby improve the statistical inference. In both, only the most common codes encountered were retained. Subset A was composed of 99 patients that had vEEG and rEEG codes “fully concordant” or “partially concordant” for each modality independently. This group was used to specifically assess the MTSr designation. Subset B was composed of 83 patients for whom rEEG and vEEG codes “fully concordant” or “partially concordant” were present and for whom MRI codes “fully concordant” or “normal/diffuse/no data” were present. Subset B was used to evaluate the role of vEEG when accounting for the influence of MRI and rEEG.

Fisher’s exact and Student’s t-tests were used to compare demographic data by outcome groups. For the time point analysis as well as for long-term analysis, the outcome variable was seizure-freedom at the specified time point, with the dependent variable the coding (as described above) for each modality. Conditional logistic regression tests with exact odds ratios were used to evaluate the significance of each modality at each of the three time points. Median unbiased estimates were recorded for tests that achieved statistical significance. To assess the long-term predictive ability of the presurgical evaluations independently and with covariates, proportional hazard models were used on all available follow-up data. All proportional hazard models utilized type 3 tests with Wald chi-squared estimates. R (v3.2.3) was used to compute t-tests and Fisher’s exact tests. SAS 9.3 software (Cary, NC) was used for all conditional logistic regression tests and proportional hazard models. MATLAB (Natick, MA) was used to generate the Kaplan-Meier curves. All statistical tests were two-sided and used $\alpha = 0.05$ as the level of significance.

3. RESULTS

3.1. Baseline Characteristics

Baseline characteristics of all patients with at least 1 year of follow up (N=105) were assessed between the seizure-free and not seizure-free groups (Table 1). None of the differences were statistically significant. Of note, MRI data was unavailable in 2 patients, and rEEG data was unavailable in 1 patient, while vEEG was available for all patients. Numbers of patients with each code are provided in Supplemental table S1.

3.2. Time Point Analysis

For all patients, each of the modalities (rEEG, vEEG, iEEG, MRI, MTSr) had predictive ability evaluated at 6 months, 1 year, and 2 years with the conditional logistic regression test

(Table 2). MRIs were also subcategorized by year of most recent presurgical MRI scan. The number of patients with MRIs in each group were as follows: 1984–1990: 40 patients, 1990–2000: 28 patients, 2000–2011: 41 patients, unknown dates (or unavailable scan): 9 patients. Regression was performed in all available patients that had sufficient follow-up for the studied time-point. Significance was attained at 6 months with MTSr, as well as at 1 year with MRI and MTSr. Notably, none of these modalities demonstrated significance at 2 years.

3.3. Long-Term Analysis

A total of 53 (45%) of patients were seizure-free throughout follow-up. The Kaplan Meier survival curves (Figure 2) were analyzed for all available follow up (median 5 years, range 0.1–23.2 years). Results of proportional hazard models based on those survival curves for the “all patients” group, and the subset groups are summarized in Table 3. The models compare survival estimates with single or multiple covariates. When all patients were included, neither the univariate nor the covariate correction achieved statistical significance for MRI, MTSr, rEEG, vEEG or iEEG. In subset A, MTSr and vEEG corrected for covariates did not achieve significance. In subset B, vEEG showed significant outcome prediction, both in the univariate analysis and when accounting for covariates of common MRI and rEEG codes.

Figure 2 shows survival estimates based on an independent univariate model of each of the presurgical tests in subset B (representing the case of commonly encountered codes in each of those modalities). Of these, only vEEG differed statistically significantly ($p=0.0304$, Table 3—Subset B), though this effect did not persist in the full population of patients ($p=0.4396$, Table 3—All Patients Included). Although the main estimates of the survival curves in each modality appear to separate, the 95% confidence intervals overlap considerably. This overlap is seen most strikingly with rEEG, for which outcomes appear indistinguishable regardless of rEEG designation of “concordant” or “partial concordance.”

As an internal validity check, MTSr localized by MRI was compared with hippocampal sclerosis found on pathologic examination of resected tissue (MTSp). The number of patients with MTSr – / MTSp –, MTSr – / MTSp+, MTSr+/MTSp–, MTSr+/MTSp+ are 60,13,6,25 respectively, with missing data in 2 cases from MRI and 12 cases from pathology. The MTSr and MTSp groups show a strong statistical association (Fisher’s exact test, $p < 0.0001$). This reaffirms a previously well-established association between the two (Junna et al., 2013).

4. DISCUSSION

This study assessed the role of several modalities to predict seizure-freedom in temporal lobe epilepsy. In short-term assessments of 6 months and 1 year, presence of MTSr and any MRI lesion were able to significantly predict outcome in the univariate analysis (Table 2). With or without covariate correction, vEEG made no significant prediction at 6, 12 or 24 months. At 2 years, none of the tested modalities were able to significantly predict outcome, with or without covariate correction. In the proportional hazard analysis (Table 3), none of the modalities were able to predict long-term seizure-freedom when accounting for all patients. The iEEG was unable to predict outcome independently for 6,12 or 24 months, nor

was it able to predict long-term seizure freedom. The subset of patients with specific commonly encountered codes for MRI, vEEG and rEEG (subset B) was able to detect a modest effect of vEEG in predicting long-term outcomes, which persisted when correcting for covariates. We interpret the modest effect of vEEG in subset B as a reflection of a possible weak long-term predictive value of vEEG, but one that is overwhelmed by other factors when all patients are included. Consequently, one might be able to predict short-term outcome using these modalities, but these same modalities would fail to segregate long-term seizure-freedom from seizure-recurrence.

In our study, ictal video EEG did not show clear predictive advantages. Perhaps, therefore, presurgical ictal video EEG can be completed with fewer seizures captured (Garcia Gracia et al., 2014; Sainju et al., 2012; Struck et al., 2015). Indeed, in the logistical regression analysis (Table 2), vEEG did not predict outcome at the 3 time points. Previous studies have disagreed on this, suggesting that it may be time to re-assess the role of these procedures for presurgical prediction in a larger multicenter study.

4.1. Studies suggesting benefit from scalp ictal video EEG

One study found that using vEEG combined with MRI might be sufficient to predict outcome when the two were concordant, though the same study was unable to predict outcome in the discordant case (Uijl et al., 2008a). Another study used EEG to predict Engel class I outcome at 2 years, though that study consolidated intracranial EEG, vEEG and interictal scalp EEG (Armon et al., 1996).

In a series of 22 MRI-negative temporal lobectomy patients, ictal EEG onsets beginning at the basal-temporal region predicted better outcomes compared with those arising from the mid-posterior temporal region (Holmes et al., 2000).

A study of 39 patients found vEEG to be correlated with Engel Class I outcomes, but the correlation coefficient was only 0.29 (Tatum et al., 2008).

4.2. Studies suggesting no benefit from scalp ictal video EEG (vEEG)

One study found that vEEG discordant with MRI and surgical hemisphere in at least one recorded seizure did not affect outcome at >4 years follow-up (Castro et al., 2008). A prospective study of 43 patients found that vEEG correctly predicted outcome in only 32% of cases (Wheless et al., 1999). Several meta-analyses found either conflicting information or no association between vEEG and outcome (McIntosh et al., 2001; Zhang et al., 2013).

4.3. Studies suggesting benefit from prolonged interictal video EEG

Patients with normal MRIs may be further assessed with interictal video EEG. A study of 87 MRI-negative patients found that unilateral interictal video EEG epileptiform discharges was protective, with a relative risk of seizure remission of 0.31 (Burkholder et al., 2014). Similarly, a study of 23 MRI-negative patients found that the presence of unilateral interictal discharges improved seizure-freedom (79% vs. 29%) (Holmes et al., 2000).

Patients with lesions on MRI have been studied as well. In a series of 78 patients with mesial-basal temporal lobe epilepsy, interictal EEG concordance with an MRI lesion

predicted better surgical outcome (Gilliam et al., 1997). However, that study suffered from small numbers in each subgroup, and had no discordant ictal video EEG patients.

A study of 371 temporal lobectomy cases found that discordant interictal EEG portended a high risk of seizure recurrence at 1-year with an odds ratio of 4.92 (Jeha et al., 2006).

A meta-analysis of 97 studies from 1991–2000 found a positive association of interictal video EEG findings of either unilateral epileptiform abnormality or anterior temporal localization with good surgical outcomes (McIntosh et al., 2001).

4.4. Contribution of MRI

In this study, MRI and MTSr were significant predictors of early surgical outcome at 1 year, but not at 2 years (Table 2). Perhaps the effects of MRI lesions diminish prior to 2 years. Conversely, it may reflect heterogeneous underlying pathophysiology (Najm et al., 2013).

Using actuarial methods, a group of 135 patients were separable into low (20%), medium (50%) and high (69%) 5-year seizure-free outcome groups based on MRI findings (Berkovic et al., 1995). A study of 400 patients found that presence of MTSr on MRI was a strong predictor of Engel class 1 outcome with a relative risk of 4.28 (Junna et al., 2013). Unfortunately, that study had <19% of their patients available for 3 years follow up, so longer term assessment was unavailable.

A meta-analysis of 40 prior studies found that the presence of either MRI or histology proven lesion increased the odds of seizure freedom by 2.5 (Téllez-Zenteno et al., 2010). Similarly, associations between MRI or MTSr with outcome have been found in several other meta-analyses (McIntosh et al., 2001; Tonini et al., 2004).

A large series of 371 patients found that MRI normal or concordant findings predicted better seizure outcomes than bilateral MRI findings (Jeha et al., 2006). One interpretation of this may be that unilateral or normal MRI findings may not be a long-term predictor at all, but rather bilateral findings may predict a poor outcome. Supporting this idea, a study of 21 patients found 62% of MRI-negative patients were Engel Class I at 8 years, using a 1.5T MRI machine (Smith et al., 2011).

Surgery prior to the advent of clinical MRI led to seizure-free outcomes in 55–66% of patients (Foldvary et al., 2000; Penfield and Steelman, 1947), comparable to some of the more modern estimates (De Tisi et al., 2011; Jeha et al., 2006; Wiebe et al., 2001). Fifty percent of temporal lobectomy cases between 1965–1974 were seizure-free 30 years postoperatively (Kelley and Theodore, 2005). Although these outcomes may have been affected by more conservative patient selection as well as the evolution of MRI over time, the relative contribution of MRI to surgical outcomes is difficult to assess.

4.5. Limitations of this Study

The definitions chosen in this study may restrict some our findings, such as our choice for coding of “concordant”, “discordant”, etc., as well using seizure-freedom rather than Engel Class (used by some authors), and classification of “failure” even in cases with a single

documented seizure. We studied Engel class 1 as an alternative to true seizure-freedom, but did not find significant differences in our results (not shown). Several studies have noted that as many as 30–40% of patients with 1–3 seizures postoperatively may not continue to have recurrent seizures (Jeha et al., 2006; Jehi et al., 2010; Kelley and Theodore, 2005). Accounting for overall follow-up with a single statistical model as we do here has its drawbacks – some argue (Jeha et al., 2006) that a multi-phase hazard model is more appropriate, because there appear to be at least two distinct phases in seizure recurrence which may reflect differing underlying pathophysiology (Najm et al., 2013), though this hypothesis is untested. Another consideration is that some significant percentage of surgical “failure” patients may go on to seizure-freedom after some years pass, representing a conversion from pharmacoresistant to pharmaco-sensitive due to the surgery (Elsharkawy et al., 2011). In addition, the degree of concordance of presurgical modalities to each other, rather than to the surgical site, is one that was not explored in this paper directly, though our subset analysis approached those relationships indirectly. Our experience with this dataset suggested that a much larger set of data would be required to properly address all possible combinations. Future studies with a more nuanced view of surgical success as well as modality concordance must account for additional issues.

The comparison of MTSr to MTSp showed strong concordance, though some MTSr patients were not identified as MTSp and vice versa. This is partially due to incomplete path specimen availability, partially due to changing MRI and pathological techniques over time, and partially due to the inherent differences in what each modality is capable of.

An inherent problem of any retrospective surgical outcome study in epilepsy is the selection bias. Epilepsy centers will tend to progress patients to surgery when they have clinical characteristics deemed “favorable” - the more the better. Those characteristics, in turn, were identified primarily by retrospective case series similar to this study. Potentially, some patients who would have had successful outcomes were excluded from surgery (and therefore series like this) due to this same selection bias.

Difficulty in predicting prognosis over more than one year may be due in part to natural fluctuations in the course of epilepsy, with remissions and exacerbations unrelated to specific therapy (Berg and Rychlik, 2015). A study of patients with drug-resistant epilepsy showed that a six-month seizure-free period occurred spontaneously as frequently as after a change in AED regimen (Callaghan et al., 2007).

This study was underpowered to assess more comprehensive combinations of modalities and their interactions. However a much larger study of 484 patients had difficulty achieving positive predictive values higher than 83%, and more importantly negative predictive values higher than 60%, thus limiting clinical practicality (Uijl et al., 2008b).

During the first 3 years, there were more dropouts in the MRI concordant group (12 patients, 24%) compared with the normal/diffuse group (3 patients, 10%). This raises the possibility that perhaps the seizure-free patients were less likely to continue follow-up, and therefore informed censoring would mask the difference between seizure-free and non-seizure-free

groups. Future studies, if sufficiently large, should consider modeling the censoring directly to address this question.

Our conclusions about MRI are complicated by the evolving nature of the technology. Over the course of the years studied, the MRI hardware has been upgraded from 0.5T to 1.5T to 3.0T. Additionally, the expertise of our radiologists has evolved over the years as more subtle findings became apparent with higher resolution scans and optimized pulse sequences. This limitation is difficult to control for given the number of patients available in our study, and is an often-unstated limitation in many other studies on MRI in epilepsy. We were unable to retrieve the original MRI scans from the earlier patients in the dataset, therefore our analysis was based entirely on the interpretation on record from the time when the scans were originally reviewed. Outcomes did not reach statistical significance in univariate analysis when accounting for the year of MRI scan (Tables 2 and 3). In spite of all these limitations, long-term outcomes have not significantly changed from the pre-MRI to the present (Callaghan et al., 2007; De Tisi et al., 2011; Jeha et al., 2006; Kelley and Theodore, 2005).

Our study does not address the diagnostic role of ictal and interictal video-EEG. In appropriate settings it could change the diagnosis in 60–84% of patients, including detection of non-epileptic events and distinguishing focal from generalized epilepsy (Ghougassian et al., 2004; Jin et al., 2014; Perry et al., 1983; Theodore et al., 1983). The interictal video-EEG data was no longer available for review in the case of older recordings; therefore no outcome prediction conclusions were possible for that modality. Almost all studies of preoperative testing for epilepsy surgery, including ours, suffer from design weaknesses limiting the level of evidence. One of the most serious, and most difficult to avoid, is contribution of the diagnostic data to be tested in the decision-making process (Gaillard et al., 2011).

5. Conclusions

In our study only MRI contributed modestly to predicting 6-month or 1-year outcomes, but had minimal overall predictive effect. The modalities evaluated were unable to predict 2-year or long-term surgical outcome. These findings, consistent with other centers' experience, suggest the need for a multi-center prospective study to determine definitively the contribution of presurgical evaluations to long-term outcome prediction. Although blinded randomized trials of presurgical evaluation modalities may not be possible due to ethical concerns, other approaches, such as "change in practice" models, may provide a reasonable approximation of more rigorous methods (Gaillard et al., 2011).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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ABBREVIATIONS

EEG	electroencephalogram
vEEG	inpatient scalp video-electroencephalogram
rEEG	routine scalp outpatient electroencephalogram
MRI	magnetic resonance imaging
MTS	mesial temporal sclerosis

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HIGHLIGHTS

- MTS predicted outcome at 6 months, as did MRI and MTS at 1 year.
- Routine EEG, MRI findings, ictal video EEG, and MRI proven MTS did not predict 2-year seizure outcome.
- Analysis of all available data failed to achieve significant long-term outcome prediction for any modality.

FIGURE 1.

Patient allocation. Patients were drawn from consecutive epilepsy resection surgeries from Jan 1, 1984 to Jan 1, 2012. Subset A refers to patients that have rEEG codes “concordant” or “partially concordant” as well as vEEG codes “concordant” or “partially concordant”. Subset B are patients in subset A that also have MRI codes of either “concordant” or “normal/diffuse/no data”. The subsets were chosen because they represent the most commonly encountered codings.

FIGURE 2.

Kaplan Meier survival curves, with 95% confidence intervals. Of note, the only modality in this set that demonstrated a statistically significant difference was vEEG. Also note that these are a subset of the full dataset. If all patients would have been included, none of the modalities show a difference statistically. The curves for rEEG, vEEG and MRI are produced from subset B, meaning common codes from each of these three modalities only. The curves for MTSr is produced from subset A, meaning common codes from rEEG and vEEG are included. Shown in this figure is the first 3 years, however all available follow up was included in the statistical comparisons.

TABLE 1**BASELINE CHARACTERISTICS.**

	Seizure-free N=60	Not seizure-free N=45	P value
Age (years at time of surgery)	32 +/- 10	31 +/- 8	0.718
Female (%)	47	62	0.695
Febrile Seizures (%)	30	29	1.000
Prior Insults (%)			
TBI	17	31	0.102
Infection	18	11	0.413
Perinatal	15	20	0.603
Time from Habitual Seizure Onset to Surgery (years)	20 +/- 10	20 +/- 10	0.720
Side of Surgery: Left (%)	48	44	0.843
Pathology: HS (%)	39	32	0.522

P values calculated using t-tests for continuous variables and Fisher's exact test for categorical variables.

Note: for pathology, N = 54 for "Seizure-Free" and N = 41 for "Not Seizure-Free" because 10 patients did not have their pathologies recorded. HS = hippocampal sclerosis.

TABLE 2

CONDITIONAL LOGISTIC REGRESSION TESTS.

	6 months	1 year	2 years
MRI	p = 0.0902 —	p = 0.0144, * OR = 10.4231	p = 0.2831 —
MRI (Year 1984–1990)	p = 0.4055 —	p = 0.3390 —	p = 0.3943 —
MRI (Year 1990–2000)	p = 0.2581 —	p = 0.1433 —	p = 0.2809 —
MRI (Year 2000–2011)	p = 1.0000 —	p = 0.4812 —	p = 1.0000 —
MTSr	p = 0.0466, * OR = 2.894	p = 0.0091, * OR = 3.576	p = 0.0709 —
rEEG	p = 0.8021 —	p = 0.9816 —	p = 0.4664 —
vEEG	p = 0.5426, —	p = 0.400 —	p = 0.1773 —
iEEG	p = 0.1508 —	p = 0.7515 —	p = 0.9422 —
vEEG given MRI and rEEG	p = 0.7443 —	p = 0.5548 —	p = 0.2322 —
vEEG given MTSr and rEEG	p = 0.2749 —	p = 0.2749 —	p = 0.1544 —
vEEG given MRI	p = 0.6479 —	p = 0.5415 —	p = 0.2470 —
vEEG given MTSr	p = 0.6144 —	p = 0.2748 —	p = 0.1586 —

*
- statistically significant.

OR = odds ratio, listed for each item that achieved statistical significance. When a variable lists A “given” B, C, that indicates correcting A for the covariates B and C. Thus for example, the row with “vEEG given MRI and rEEG” describes the result of regression with vEEG after correcting for the effect of MRI and rEEG first. When such a correction is performed for the 3 time points listed, vEEG does not achieve a statistically significant prediction of outcome. When years are listed, these indicate the year of the most recent MRI scan performed. iEEG = intracranial EEG.

TABLE 3**PROPORTIONAL HAZARD MODELS.**

	P-Value	Estimate
ALL PATIENTS INCLUDED		
MRI	0.1939	—
MRI (years 1984–1990)	0.2191	—
MRI (years 1990–2000)	0.2504	—
MRI (years 2000–2011)	0.5982	—
MTS	0.1560	—
rEEG	0.9859	—
vEEG	0.4396	—
iEEG	0.5094	—
vEEG given (MRI, rEEG)	0.4936	—
vEEG given (MTSr, rEEG)	0.7530	—
SUBSET A: (vEEG and rEEG common codes)		
MTSr	0.2641	—
vEEG given (MTSr, rEEG)	0.1084	—
SUBSET B: (Subset A and MRI common codes)		
MRI	0.1161	—
rEEG	0.6716	—
vEEG	0.0304 *	1.936
vEEG given (MRI, rEEG)	0.0463 *	1.940

* = Statistically Significant.

Common codes in rEEG = “concordant” or “partially concordant”. Common codes in vEEG = “concordant” or “partially concordant”. Common codes in MRI = “concordant” or “normal/diffuse/no data”. When a variable lists A “given” B, C, that indicates correcting A for the covariates B and C.