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Research Article

Improving the Selection of Temporal Lobectomy Candidates Through the Use of Multiple Subdural Electroencephalographic Prognostic Parameters

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Abstract

Long-term subdural video-EEG monitoring was performed in a series of patients with medically intractable complex partial seizures to test the hypothesis that multiple subdural EEG parameters could be used to better predict seizure-free outcome after temporal lobectomy. The five subdural EEG parameters examined were the existence of evidence of ictal subdural EEG evidence of seizure activity before the onset of clinical seizure activity (ECOT), the time for interhemispheric propagation time of an electrocorticographic seizure (IHPT), unilateral seizure onset, evidence for fast spike trains (FST), and lack of frontal lobe desynchronization. In our series of 99 consecutive patients with refractory temporal lobe epilepsy, a significant correlation was found between these five factors and seizure freedom after surgery. This result provides the neurosurgeon and epileptologist with a quantitative tool capable of predicting seizure freedom after surgery based on quantifiable subdural-EEG parameters. The capability of these parameters to predict seizure freedom may allow the patient and epileptologist to anticipate results and the need for any future clinical intervention for seizure control.

Keywords: Temporal lobe epilepsy; Time factors; Subdural-EEG; Prognostic factors

Introduction

Drug-resistant epilepsy is defined by the International League against epilepsy as “a failure of adequate trials of two tolerated and appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom [8].” There have been multiple hypotheses as to the pathogenesis and etiology of this disorder [2,6,7,9]. Surgical methods have been developed to treat such patients [2,3,6,7]. Although surgical methods have advanced significantly in the past two decades, the selection of operative candidates has not been standardized.

Previous studies have shown that patients with medically-intractable seizures are candidates for temporal lobectomy, which is effective in decreasing the incidence of seizures; however, accurate localization is required. Approximately 70% of patients who require only noninvasive techniques for localization of seizures will enjoy full resolution of their seizures after temporal lobectomy [1,4,7].

On the other hand, there is a subset of patients whose seizures cannot be localized using traditional noninvasive monitoring methods alone. In these cases, invasive subdural electrode video-EEG monitoring can be performed to accurately localize an epileptogenic area that may be resected to treat the seizure disorder [2,5,10,11,14,15,20,21]. Subdural EEG provides electrocorticography data because leads are placed directly on the cerebral cortex. Patients that require this degree of invasive monitoring experience a quite poor 40% success rate with surgery. A recent study by Bulacio et al reported a probability of complete seizure freedom of 61% at one year postoperatively, which dropped down to 42% at 5 years and 33% at 10 years [2].

Certain electrocorticographic parameters have been identified with significant correlation with seizure frequency [11,14,15,20]. Our study aims to demonstrate that a higher number of these parameters that are concordance can be prognostic for seizure-free outcome following temporal lobectomy. The duration of time from the beginning of signs of electrical seizure activity to the clinical observable onset of seizures can be defined as the ECOT (electrical to clinical seizure onset time). This factor has been shown to have prognostic value for seizure-free outcome after temporal lobectomy [16]. As this delay between the time from electrical seizure activity to clinical seizure onset increases, the probability of a seizure free outcome after temporal lobectomy increases. The time delay from the electrical seizure onset in one temporal lobe to the first evidence of seizure activity in the opposite hemisphere is the interhemispheric propagation time (IHPT). As the IHPT increases, the likelihood of a patient remaining seizure-free following temporal lobectomy increases as well [17]. Evidence of frontal lobe desynchronization means that frontal lobe background activity changed at the time of electrical seizure onset. Patients who do not show evidence of frontal lobe desynchronization have a higher seizure free outcome after temporal lobectomy [18]. This may be due to a ruling out of a frontal lobe ictal focus. Fast spoke trains are an EEG finding where there are trains of rhythmic epileptiform spike or sharp waves. There are bursting discharges or continuous or almost continuous rhythmic spiking [13]. Positive spikes can be correlated with early

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seizure onset, and a less favorable outcome after temporal lobectomy. Lastly, unilateral seizure onset is defined as subdural-EEG evidence of epileptiform activity originating from one temporal lobe. We aimed to perform a quantitative mathematical analysis of the interrelationships between these five electrocorticographic time factors and seizure-free outcome after temporal lobectomy. This information may prove useful in not only improving outcomes through better patient selection, but also in providing patients with more information that may allay their anxiety and fears about surgery and increasing the number of qualified patients choosing to undergo the procedure [1].

Methods

Our study was designed as a clinical chart review of 99 patients evaluated and treated at a tertiary care epilepsy center who underwent invasive subdural-EEG preoperative monitoring and subsequent anterior temporal lobectomy. 52.5% were male and 47.5% were female. Patient age at the time of surgery ranged from 7 to 54 years with a mean age of 28.8 years. There was one patient below the age of 12, and nine patients below the age of 18. All patients subsequently underwent anterior temporal lobectomy with amygdalohippocampectomy for medically-intractable epilepsy. All subjects were required to have subdural-EEG monitoring for seizure focus localization and were followed for a minimum of twelve months postoperatively. Follow-up times ranged from 12 to 54 months with a mean follow up time of 22.6 months, the longest follow-up for any such epilepsy study. Five EEG parameters studied were assigned a binary value based on a numerical EEG cutoff or presence of certain EEG phenomenon. These factors were (1) subdural-EEG seizure onset before clinical seizure onset, (2) interhemispheric propagation time (IHPT) greater than eight seconds, (3) unilateral hemispheric seizure onset, (4) evidence of fast spike trains (FST), and (5) lack of frontal lobe desynchronization. The number of positive prognostic factors that each patient had was termed their "concordance." This degree of concordance refers to any of the parameters. Double concordance means that any two parameters are positive, not just the first two. Triple concordance means that any three parameters are positive. Patients were grouped by their concordance, and these groups were compared with regard to outcome after standard anterior temporal lobectomy. Chi-squared analyses were used to determine the statistical significance ($P < 0.05$) of the difference in seizure-free rates between groups.

Results

Table 1 delineates concordance data while Table 2 highlights statistically significant differences in rates of seizure freedom between groups. Degrees of seizure freedom increased as concordance increased in a linear and direct fashion from 20% for patients with single concordance to 52% for patients with double concordance to 75% for patients with triple concordance to 81% for patients with quadruple concordance to 90% for patients with quintuple concordance. This robust direct correlation underpins the rationale for the study and shows that subdural-EEG data can be used to make prognostic decisions regarding treatment. Table 2 shows results of an analysis of statistical significance of the degrees of seizure freedom between concordance groups. This data shows that there are definite differences between the different concordance cohorts in terms of their outcomes. This provides further proof that our paradigm of using such parameters is of practical use.

Table 1: Seizure-free outcomes

Concordance	Seizure-free	Not Seizure-free	Total	Probability of Seizure-free
0	2	1	3	0.66
1	2	8	10	0.2
2	12	11	23	0.52
3	24	8	32	0.75
4	17	4	21	0.81
5	9	1	10	0.9
Total	66	33	99	0.66

Table 2: Statistical analysis of concordance data

Concordances compared	Chi-squared	P value
Single vs triple	9.77	< 0.01
Single vs quadruple	10.61	< 0.01
Single vs quintuple	9.9	< 0.01
Double vs quadruple	4.05	< 0.05
Double vs quintuple	4.31	< 0.05

Discussion

Despite numerous advances in the epilepsy surgery and continued technological innovations that have made surgery safer and more effective, temporal lobe epilepsy continues to be a challenging condition to treat for the neurosurgeon. As techniques become more advanced, responsibility grows regarding the decision-making process of when and how to make choices regarding surgery. When is it safe and effective? Which patients are likely to do well? Mathematical models have been developed answering these questions with respect to data [19]. However, despite the network gating and electrical conduction models that have been used to model temporal lobe epileptogenicity, there has been no consensus in the literature on a modeling method to closely approximate and model electrocorticographic subdural EEG parameters with respect to outcomes from temporal lobectomy [12,20].

Previous studies have provided convincing evidence that seizures with unilateral onset, an onset pattern that begins with FST, a lack of ictal subdural EEG frontal lobe desynchronization, and IHPT of greater than eight seconds can predict a higher likelihood of seizure-free outcome after a temporal lobectomy [14,15,17]. In addition to these criteria, a longer duration of time between subdural EEG seizure onset and the onset of clinical seizure phenomenology has been shown to predict favorable seizure outcome after temporal lobectomy [16].

According to our results and analysis, a linear relationship is seen between increasing concordance levels and increasing rates of seizure freedom after surgery [Table 1]. Seizure freedom rates were significantly different between the different cohorts that had different concordance levels [Table 2]. This data can arm the clinician with evidence to better select surgical candidates and to more effectively counsel patients before surgery regarding the probability of seizure free outcome after surgery. There was an outlier in the analysis showing the patients with zero concordance had a 66% seizure free rate [Table 1]. This anomaly in the data is due to the small sample size in this cohort (only three patients).

Others have evaluated, using stepwise logistic regression, other factors that were predictive for good seizure control [3], which included (1) clear abnormality on MR images; (2) absence of status epilepticus; (3) MR imaging-confirmed ganglioglioma or development neuroectodermal tumor; (4) concordant lateralizing memory deficit; and (5) absence of dysplasia on MR images. These factors point to imaging, EEG, pathological, and neuropsychological factors that can predict seizure free outcome. We believe that our study complements this data by giving clinicians another set of factors that can be gleaned from subdural-EEG data. This analysis was performed as proof of concept that such a correlation does exist and may, in the future, be added to other non-subdural-EEG parameters to produce a more highly sensitive, specific and accurately predictive model for outcomes of candidates for this type of surgery.

In addition to providing clinicians with evidence that surgery may be of use, this data can also help to identify patients who may be poor candidates. Table 1 reveals that patients with single and double concordance are actually very poor candidates for temporal lobectomy. Surgery should not be recommended for these cases because seizure-free outcome probability is low (less than or around 50%) [Table 1].

Conclusion

A significant correlation was found between the five subdural-EEG electrocorticographic factors and seizure freedom after surgery. The correlation is quite robust with easily observable increasing rates of seizure freedom with a higher concordance of these factors. This result provides the neurosurgeon and the epileptologist with a quantitative tool capable of predicting seizure freedom with a high degree of accuracy after surgery based on quantifiable preoperative subdural-EEG parameters. The capability of ECOT and other time factors to predict seizure freedom may allow the patient and epileptologist to anticipate results and the need for any future clinical intervention for seizure control.

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