



Published in final edited form as:

J Clin Neurophysiol. 2010 April ; 27(2): 87–92. doi:10.1097/WNP.0b013e3181d64b1e.

The relationship of interictal epileptiform discharges to clinical epilepsy severity: A study of routine EEGs and review of the literature

Megan F. Selvitelli, MD¹, Linsey M. Walker, BA¹, Donald L. Schomer, MD¹, and Bernard S. Chang, MD¹

¹Comprehensive Epilepsy Center, Department of Neurology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, Massachusetts

Abstract

Purpose—EEGs are widely used to detect interictal epileptiform discharges (IEDs) in patients with a known history of seizures. However, prior studies have not found a consistent association between the presence or frequency of IEDs and clinical epilepsy severity, possibly because of differences in subject characteristics and recording techniques. We sought to investigate this relationship in a population and setting reflective of the most common clinical usage.

Methods—We analyzed EEGs and clinical records of all consenting patients with a history of at least two presumed focal-onset seizures who presented for routine EEG recording over one year's time in an academic neurophysiology laboratory (n = 129).

Results—Despite adequate statistical power, we did not find an association between the presence or absence of IEDs or IED frequency and the most recently determined seizure frequency (median 4 per year). A higher IED incidence was seen in subjects with longer epilepsy duration (p = 0.04). Neither IED incidence nor frequency (median 10.0 per hour) correlated with age or antiepileptic drug use.

Conclusions—Our results differ from those of some prior studies, most of which focused on more narrow subject populations, suggesting that the patient's clinical circumstances must be taken into account before assuming the utility of IEDs on routine EEG in predicting epilepsy severity.

Keywords

Electroencephalography (EEG); interictal spikes; seizure frequency

Introduction

The use of EEG to detect interictal epileptiform discharges (IEDs) in patients with a history of seizures is routine. The presence of IEDs can help to confirm a clinical diagnosis of epilepsy, and their location and characteristics can help to identify the epileptogenic zone or suggest a particular epilepsy syndrome (Chabolla and Cascino, 2006). While clinicians may also use the

Contact author: Bernard S. Chang, MD, Comprehensive Epilepsy Center, E/KS-457, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, Boston, MA 02215, phone 617-667-2889, fax 617-667-7919, bchang@bidmc.harvard.edu.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

presence or frequency of IEDs to help predict clinical epilepsy severity, much of the evidence on this subject is limited to specific subpopulations or is quite dated. With regard to the most common clinical setting in which IEDs are sought, that of routine EEG recording in patients with a history of recurrent seizures, our understanding of the ability of IEDs to predict measures of epilepsy severity such as seizure frequency is remarkably limited.

Prior studies have demonstrated an increased incidence of IEDs in patients who have had a seizure within the previous two or seven days (Ajmone Marsan and Zivin, 1970; Sundaram et al., 1990), but not beyond that period. While multiple studies have reported an association between a higher clinical seizure frequency and a greater likelihood of detecting IEDs, or a higher IED frequency, the degree of association is unclear (Desai et al., 1988; Sundaram et al., 1990; Drury and Beydoun, 1998; Janszky et al., 2005; Krendl et al., 2008). This may stem from significant differences in techniques among the published studies, including the EEG recording method by which IEDs were detected and quantified (single routine EEG, multiple serial EEGs, or long-term inpatient EEG monitoring) and the characteristics of the subject cohorts (all epilepsy patients, only those with chronic or medically refractory epilepsy, or elderly patients with epilepsy). Some studies have also reported that increased duration of epilepsy may be associated with an increased likelihood of detecting IEDs or an increased IED frequency (Desai et al., 1988; Drury and Beydoun, 1998; Janszky et al., 2005).

Because of the clinical importance of these issues, and the lack of recent data addressing some of these central questions, we sought to investigate the relationship between IEDs and reported seizure frequency in a population and setting reflective of common clinical usage, namely that of all patients with a history of at least two presumed focal-onset seizures presenting for routine EEG at a general academic neurophysiology laboratory.

Methods

Subject recruitment

All patients presenting to the EEG laboratory at Beth Israel Deaconess Medical Center, Boston, for a routine EEG study between January and December 2008, inclusive, were eligible to participate in the study. Potential subjects were approached by study staff while waiting for their routine EEG study to begin, and presented with a study information sheet and questionnaire. As approved by our institutional review board, subjects (or companions) who completed the questionnaire were considered to have consented to participation; those who did not complete the questionnaire were not further questioned or investigated.

Self-reporting of seizure history

The structured questionnaire contained the following questions and possible responses:

1. Have you ever had a seizure?
 - No (If you checked no, please stop here. You do not need to answer the remaining questions).
 - Yes, just once in my life (Please go on to answer question 2, then stop).
 - Yes, more than once in my life (Please answer all remaining questions).
2. When was your most recent seizure? Please be as precise as possible
 Month: _____ Date: _____ Year: _____
3. How often do you have seizures? Please fill in the two blanks below.
 I typically have _____ seizures in one month's time.

I typically have _____ seizures in one year's time.

EEG recording

All EEG studies were recorded digitally and reviewed remotely according to standard clinical practices in place at the clinical neurophysiology laboratory of Beth Israel Deaconess Medical Center. Recordings were obtained using silver-chloride, gold-plated electrodes placed according to the 10–20 International system, with measured impedances of less than 5 kOhms at all electrodes. All studies utilized both bipolar and average referential montages. Initial analog signal conditioning included a 0.3–1 Hz high pass filter, a 35–70 Hz low pass filter and a 60 Hz notch filter. The digital sampling rate was 200–500 per second. EEG recordings varied from 20–60 minutes, with the majority of recordings lasting 60 minutes. Activating techniques, including hyperventilation and intermittent photic stimulation, were used unless medically contraindicated. A small minority of studies were performed after sleep deprivation, but not all studies could be classified according to sleep deprivation status, so a subgroup analysis could not be performed.

IED analysis

Clinical EEG interpretations were reviewed for patients who reported a history of at least two seizures. Routine EEGs were categorized by whether IEDs were identified during the recording. All EEGs with findings potentially suggestive of IEDs were then independently reviewed in their entirety by an experienced electroencephalographer who remained unaware of the subjects' seizure frequencies or clinical EEG interpretations. IEDs were defined as spike or sharp wave discharges that clearly stood out from the background rhythms, with or without an aftergoing slow wave. Subjects demonstrating IEDs consistent with a diagnosis of primary (idiopathic) generalized epilepsy were excluded from further analysis. IED frequency was calculated by manually counting the total number of IEDs seen in the entire routine study and dividing by study duration.

Medical record analysis of seizure history

Medical records were reviewed for all subjects who reported a history of at least two seizures in their life. Those with records suggesting a diagnosis of primary (idiopathic) generalized epilepsy (as indicated by terms such as idiopathic generalized epilepsy, primary generalized epilepsy, juvenile myoclonic epilepsy, absence epilepsy or generalized tonic-clonic seizures upon awakening) were excluded from further analysis, as were subjects with records clearly documenting a non-seizure diagnosis by a neurological specialist (e.g. migraines, psychogenic nonepileptic seizures). Subjects who had seizures that were exclusively acute symptomatic ("provoked") were not included. When information regarding seizure frequency and the elapsed time since most recent seizure was available both from the subject questionnaire and from medical records, the more precise data were always used, unless the questionnaire reported seizures that had occurred since the last available documentation in the medical record, in which case the questionnaire data were used. Additional clinical information obtained from medical records included age at seizure onset, duration of epilepsy, and use of antiepileptic drugs (AEDs).

Statistical analysis

Seizure frequency and the elapsed time since most recent seizure were calculated for all subjects. The Mann-Whitney U test was used to compare those subjects with IEDs on routine EEG to those without IEDs on the following variables: seizure frequency, days since last seizure, age at time of EEG, and epilepsy duration. A significance level of $\alpha = 0.05$ was used for all analyses. For subjects with EEGs positive for IEDs, Spearman's correlation analyses were performed to detect any significant relationships among IED frequency, days since last

seizure, seizure frequency, age at time of EEG, and epilepsy duration. A Bonferroni correction for multiple comparisons was applied. The IED frequency of subjects on AEDs at the time of EEG recording was compared to that of subjects not taking AEDs using the Mann-Whitney U test, since the data were not normally distributed. Subjects with high IED frequency (at the median or higher) were compared to those with low IED frequency (lower than the median) on the following variables using two-sample Student t-tests: days since last seizure, seizure frequency, age at time of EEG, and epilepsy duration.

Ethics

This study was conducted in accordance with a protocol approved by the Committee on Clinical Investigations at Beth Israel Deaconess Medical Center, Boston.

Results

Subject characteristics

Of 1369 total patients presenting to the Beth Israel Deaconess Medical Center clinical neurophysiology laboratory for a routine EEG study between January and December 2008, inclusive, 392 agreed to participate by completing the study questionnaire. Of these, 129 subjects reported a history of at least two seizures and met all other criteria for inclusion in the study (Figure 1). Mean subject age was 40.33 years (range 16 to 80). Median seizure frequency was four per year (mean 12.66, range 0.3 to 365). Eighteen percent of routine EEGs demonstrated focal IEDs, with a median IED frequency of 10.0 per hour (mean 22, range 1 to 107). Drowsiness was achieved on EEG in 95% of the subjects, while 71% reached stage II sleep. Subjects who reached drowsiness were not more likely to demonstrate focal IEDs than those who did not (18% vs. 33%, $p = 0.31$), nor were subjects who reached stage II sleep compared to those who did not (16% vs. 24%, $p = 0.32$).

IED presence on routine EEG and clinical epilepsy characteristics

There was no significant difference between subjects with IEDs on routine EEG and those without IEDs on the following variables: days since last seizure, seizure frequency, or age at time of EEG (Table 1). However, those with IEDs had a significantly longer epilepsy duration than those who did not (Mann-Whitney U statistic = 708.0, $p = 0.04$).

IED frequency and clinical epilepsy characteristics

For the subjects with IEDs on routine EEG, a correlation matrix was used to assess for any significant relationships among the variables of IED frequency, days since last seizure, seizure frequency, epilepsy duration and age at time of EEG (Table 2). With $n = 24$ for most analyses, we had 80% power to detect a correlation of at least $r > 0.54$ strength and 90% power to detect a correlation of at least $r > 0.60$ strength. After a Bonferroni correction for multiple comparisons, no significant correlations were seen, although a positive trend was seen between age and epilepsy duration, ($r = 0.57$, corrected p value = 0.06). Notably, no correlation was noted between IED frequency and days since last seizure, seizure frequency per year, epilepsy duration or age at time of EEG.

There was no significant difference between the subjects with high IED frequency (those at or above the median) and those with low IED frequency (those below the median) with regard to days since last seizure, seizure frequency, epilepsy duration, or age at time of EEG (Table 3). Similarly, there was no difference in IED frequency between subjects who were taking AEDs at the time of the study and those who were not (Mann-Whitney U = 56.0, $p = 0.65$).

Discussion

Here we demonstrate that in a general population of patients who have experienced at least two presumed focal-onset seizures in life, the presence of IEDs as noted on a single routine EEG study is associated with longer epilepsy duration. However, neither the presence nor frequency of IEDs shows a relationship with any of several other measures of clinical epilepsy severity, including seizure frequency, elapsed days since most recent seizure, and AED usage.

IEDs and seizure frequency

Our findings differ from some of those reported in prior studies, several of which investigated different epilepsy subpopulations and utilized different EEG recording techniques (Table 4). In two reports, an association between IED frequency and seizure frequency was noted only when more than one seizure was reported per week in patients undergoing video-EEG monitoring for medically refractory temporal lobe epilepsy (Janszky et al., 2005; Krendl et al., 2008). Among patients older than 65 years at the time of EEG performance, Drury and Beydoun (1998) found an association between increased incidence of IED and a seizure frequency of more than one per month. Similarly, in the study most similar to ours, Sundaram et al. (1990) evaluated the results of a single routine EEG in adults with clinically definite epilepsy and found an association between increased incidence of IED and a seizure frequency of more than one per month.

The vast majority of our subjects had a seizure frequency of less than 10 per year, a lower figure than those noted above in prior studies that reported a correlation between IED frequency and seizure frequency. However, much of our cohort appears similar to that of Desai et al. (1988), who found no relationship between IED presence on routine EEG and clinical seizure frequency in patients with chronic epilepsy (43% of whom experienced no seizures and 25% of whom experienced fewer than 10 seizures in the six months prior to EEG recording). Our study included a much more heterogeneous, and also more clinically representative, population of patients than most prior series, since we enrolled subjects with a history of only two seizures (as well as those with medically refractory epilepsy), those with focal-onset seizures of any origin, not just temporal lobe, and those across the entire age spectrum of adulthood. The fact that we included individuals who had experienced only two seizures may explain the lower incidence of IED detection on routine EEG in our series (18%) compared to prior reports [e.g., 33% in Desai et al. (1988), 30% in Drury and Beydoun (1998), and 46% in Sundaram et al. (1990)]. Finally, our determinations of IED frequency were arrived at rigorously after exhaustive manual counts of all IEDs on the EEG studies of interest, rather than a reliance on automated spike detection algorithms applied to long-term EEG monitoring data, as used in some prior studies.

IEDs and recency of seizures

Some investigators have reported an increased incidence of IED when an EEG study is performed within two days (Sundaram et al., 1990) or within seven days (Ajmone Marsan and Zivin, 1970) of a recent seizure. Gotman (1991) hypothesized that increased IED frequency is indicative of a recent seizure, as patients admitted for presurgical video-EEG monitoring of medically refractory seizures demonstrated an increased spiking frequency postictally, for hours to days (Gotman and Marciani, 1985). We had too few subjects whose studies occurred within this time frame to allow for separate statistical analysis; among those with IEDs on routine EEG, the median number of days elapsed since the most recent seizure was 128.5. Again, this suggests an important difference in subject population between our study and others: Our subjects were much less likely to have just had a recent seizure, and are likely more representative of the typical clinical situation in which routine EEGs are ordered.

IEDs and AED therapy

Consistent with prior reports, we found no difference in IED incidence or frequency based upon whether AEDs were being used at the time of the EEG (Sundaram et al., 1970; Gotman and Marciani, 1985; Rosati et al., 2003).

IEDs and age or epilepsy duration

There have been variable reports of an association between IED incidence or frequency and epilepsy duration and age at EEG performance. In patients older than 65 years, Drury et al. (1998) found no association between IED presence on EEG and age at time of EEG or duration of epilepsy. Similarly, Sundaram et al. (1990) found no association between age at time of routine EEG and presence of IEDs. In contrast, in reviewing serial EEGs in patients of all ages, Ajmone Marsan and Zivin (1970) reported a decreasing incidence of IED with increasing age at time of EEG and an increasing incidence of IED with younger age of epilepsy onset. Desai et al. (1988) also found an increased incidence of IED in patients with epilepsy duration of greater than 10 years and those with a younger age of epilepsy onset. Janszky et al. (2005) noted an increased rate of IED with longer epilepsy duration and no association with age at time of EEG. The significant differences in subject age ranges, epilepsy characteristics, and types of EEG recording among these published studies (Table 4) provide a likely explanation for the discrepancies in these findings. Our findings demonstrated a longer epilepsy duration in those with IEDs on routine EEG compared to those without, but we found no such relationship with age at time of EEG.

IEDs and epilepsy outcome or etiology

Interestingly, Rosati et al. (2003) reported on the differences between patients with rare IEDs and those with frequent IEDs during prolonged video-EEG monitoring for medically refractory temporal lobe epilepsy. These investigators found that patients with fewer than one IED per hour, termed “oligospikers,” typically had a later onset of epilepsy, a shorter duration of epilepsy, a lower frequency of complex partial seizures, and a lower likelihood of having had status epilepticus compared to patients with frequent IEDs (not defined). However, there was no difference in AED therapy or in response to epilepsy surgery between oligospikers and frequent spikers.

Although not evaluated in our study, there have also been reports evaluating the presence or frequency of IEDs in relationship to epilepsy etiology. Both Ajmone Marsan and Zivin (1970) and Desai et al. (1988) demonstrated an increased IED incidence in patients with a history of head injuries compared to other etiologies. Rosenow et al. (1998) found increased electrocorticographic IEDs in patients with gangliogliomas compared to patients with cortical dysplasia or gliomas, although all demonstrated frequent IEDs. These limited data suggest that epilepsy of differing etiologies may be associated with varying tendencies to manifest IEDs.

Limitations

Our study has several important limitations. First, our questionnaire response rate was only 29%. While we may only speculate on the potential etiologies of this, since we could not further question or obtain data from those who chose not to complete the questionnaire, possible contributors to the low response rate might include cognitive impairment, a language barrier, or concern about allowing medical record review. However, we have no reason to expect a strong selection bias in voluntary participation that would be skewed across the two groups divided based on EEG result. Unfortunately, it is not possible to compare directly our participation rate with those of prior studies, which did not generally report this figure. Although only 24 patients with focal IEDs were enrolled during our year of study, this sample size provided adequate statistical power for us to detect even fairly weak linear correlations

between IED frequency and quantified measures of clinical epilepsy severity. Finally, patient self-reporting of seizure frequency can be highly inaccurate (Blum et al., 1996; Hoppe et al., 2007); however, we chose to combine self-reporting with a review of medical record documentation in an attempt to determine the most accurate estimate of seizure frequency possible for each subject. Although this method may actually underestimate seizure frequency, it is most comparable to the situation faced by neurological clinicians in everyday practice when evaluating patients in the office.

Conclusions

The important differences between our results and those of prior reports in the literature, and the likely bases for these discrepancies, indicate that it is necessary to take into account the patient's individual clinical circumstances, and the type of EEG recording being used, before assuming that IEDs seen on EEG testing will be helpful in predicting aspects of epilepsy severity. Our findings, in fact, strongly suggest that the presence or frequency of IEDs on a routine EEG, obtained in a general population of patients who have had at least two presumed focal-onset seizures, does not provide meaningful information regarding clinical seizure control. Further research is needed to better understand the association between IED frequency and seizure frequency. In particular, targeted evaluations of specific patient populations, including patients with frequent seizures, new-onset seizures and well-controlled epilepsy, may be especially useful, as may investigations based on specific epilepsy etiologies.

Acknowledgments

We thank the EEG technologists at the Beth Israel Deaconess Medical Center clinical neurophysiology laboratory for their invaluable assistance in the execution of this study. B.S.C. was supported by the U.S. National Institutes of Health (K23 NS049159).

References

- Ajmone Marsan C, Zivin LS. Factors related to the occurrence of typical paroxysmal abnormalities in the EEG records of epileptic patients. *Epilepsia* 1970;11:361–81. [PubMed: 5278205]
- Blum DE, Eskola J, Bortz JJ, Fisher RS. Patient awareness of seizures. *Neurology* 1996;47:260–4. [PubMed: 8710091]
- Chabolla, DR.; Cascino, GD. Application of electroencephalography in the diagnosis of epilepsy. In: Wyllie, E.; Gupta, A.; Lachhwani, DK., editors. *The treatment of epilepsy*. Lippincott Williams & Wilkins; Philadelphia: 2006. p. 169-82.
- Desai B, Whitman S, Bouffard DA. The role of the EEG in epilepsy of long duration. *Epilepsia* 1988;29:601–6. [PubMed: 3409846]
- Drury I, Beydoun A. Interictal epileptiform activity in elderly patients with epilepsy. *Electroencephalogr Clin Neurophysiol* 1998;106:369–73. [PubMed: 9741765]
- Gotman J. Relationships between interictal spiking and seizures: Human and experimental evidence. *Can J Neurol Sci* 1991;18:573–6. [PubMed: 1777872]
- Gotman J, Marciani MG. Electroencephalographic spiking activity, drug levels, and seizure occurrence in epileptic patients. *Ann Neurol* 1985;17:597–603. [PubMed: 3927818]
- Hoppe C, Poepel A, Elger CE. Epilepsy: Accuracy of patient seizure counts. *Arch Neurol* 2007;64:1595–9. [PubMed: 17998441]
- Janszky J, Hoppe M, Clemens Z, et al. Spike frequency is dependent on epilepsy duration and seizure frequency in temporal lobe epilepsy. *Epileptic Disorders* 2005;7:355–9. [PubMed: 16338679]
- Krendl R, Lurjer S, Baumgartner C. Absolute spike frequency predicts surgical outcome in TLE with unilateral hippocampal atrophy. *Neurology* 2008;71:4138.
- Rosati A, Aghakhani Y, Bernasconi A, et al. Intractable temporal lobe epilepsy with rare spikes is less severe than with frequent spikes. *Neurology* 2003;60:1290–5. [PubMed: 12707431]

- Rosenow F, Lüders Ho, Dinner DS, et al. Histopathological correlates of epileptogenicity as expressed by electrocorticographic spiking and seizure frequency. *Epilepsia* 1998;39:850–6. [PubMed: 9701375]
- Sundaram M, Hogan T, Hiscock M, Pillay N. Factors affecting interictal spike discharges in adults with epilepsy. *Electroencephalogr Clin Neurophysiol* 1990;75:358–60. [PubMed: 1691085]

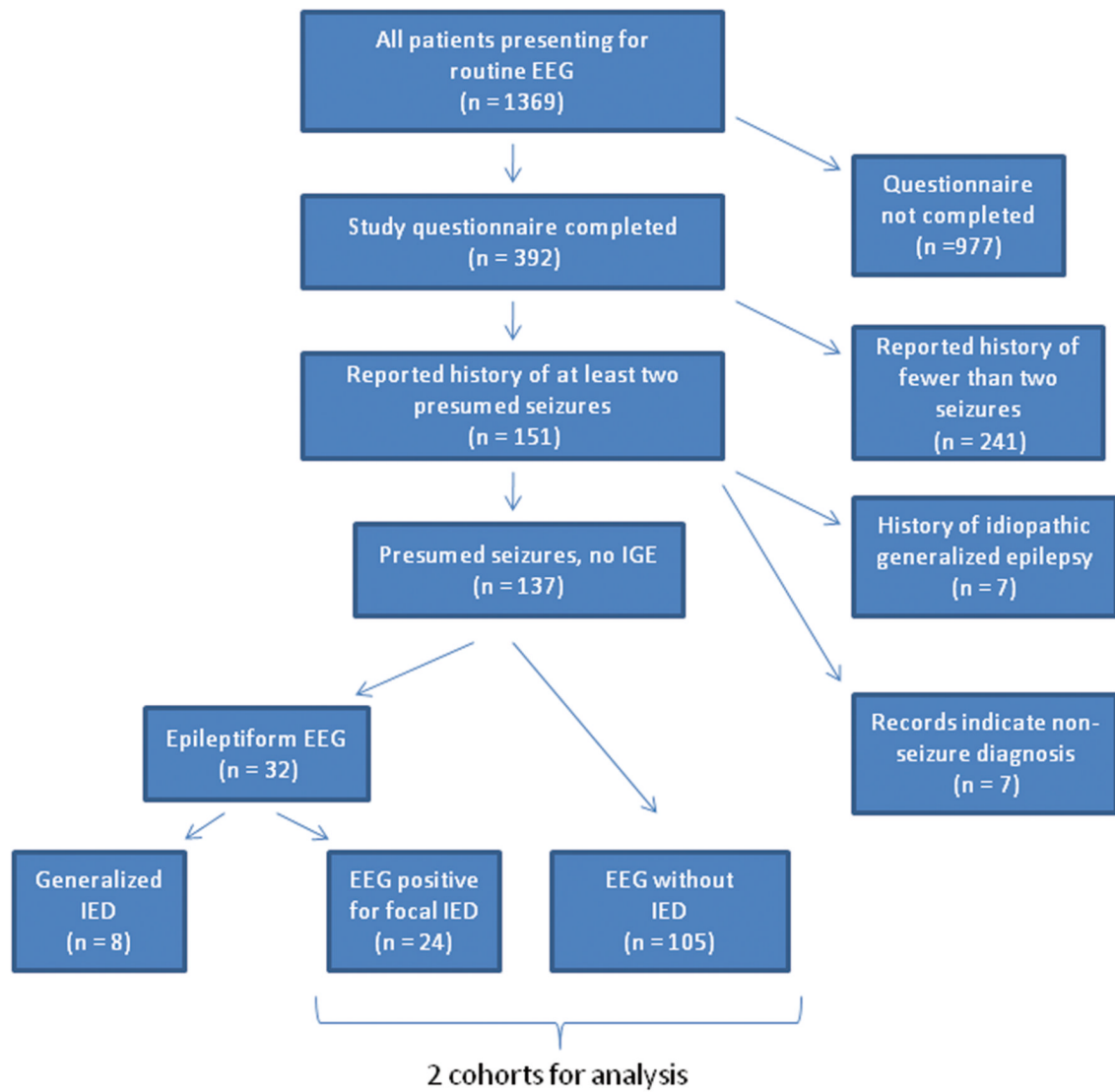


Figure 1. Subject recruitment, exclusions, and classification

The two subject cohorts for study (bottom middle) were those with focal interictal epileptiform discharges (IEDs) on routine EEG and those without IEDs. All subjects in these groups had at least two presumed seizures in life and no indication of a primary (idiopathic) generalized epilepsy syndrome. IGE = idiopathic generalized epilepsy.

Table 1
Clinical epilepsy characteristics of subjects with and without IEDs on routine EEG

	EEG positive for focal IED (n = 24)	EEG without IED (n = 105)	Statistical comparison
Median elapsed time since most recent seizure, in days (mean, range)	128.5 (829, 2 to 8063)	94 (1557, 0 to 17346)	MW = 1176.5, p = 0.91
Median seizure frequency, per year (mean, range)	2.5 (8.49, 0.3 to 36)	2.5 (25.53, 0.33 to 365)	MW = 592.0, p = 0.94
Median duration of epilepsy, in years (mean, range)	25 (22.78, 0.08 to 46)	11 (14.95, 0.01 to 57)	MW = 708.0, p = 0.04
Median age at time of EEG, in years (mean, range)	44 (44.58, 18 to 79)	37 (39.36, 16 to 80)	MW = 1054.5, p = 0.21

The statistical comparison in bold indicates a significant difference ($p < 0.05$). IED = interictal epileptiform discharge. MW = Mann-Whitney U statistic.

Table 2
Spearman's correlation matrix demonstrating relationships between IED frequency and clinical epilepsy characteristics

	IED Frequency	Days Since Last Seizure	Seizure Frequency	Epilepsy Duration	Age
IED Frequency	$r = 1$				
Days Since Last Seizure	$r = 0.16, p = 0.45$	$r = 1$			
Seizure Frequency	$r = 0.12, p = 0.63$	$r = -0.53, p = 0.04$	$r = 1$		
Epilepsy Duration	$r = -0.22, p = 0.29$	$r = 0.21, p = 0.33$	$r = 0.35, p = 0.16$	$r = 1$	
Age	$r = -0.23, p = 0.26$	$r = 0.12, p = 0.58$	$r = 0.24, p = 0.34$	$r = 0.57, p = 0.006$	$r = 1$

With $n = 24$ subjects with at least two presumed focal-onset seizures in life and at least one focal IED on routine EEG, there is 80% power to detect a correlation of strength at least $r > 0.54$ and 90% power to detect a correlation of strength at least $r > 0.60$, with $\alpha = 0.05$. Raw p values are presented here; after Bonferroni correction for multiple comparisons, no significant correlations were seen, although a positive trend is noted in bold (corrected p value = 0.06). IED = interictal epileptiform discharge.

Table 3
Clinical epilepsy characteristics of subjects with high and low IED frequencies on routine EEG

	Median elapsed time since last seizure, in days (mean, range)	Median seizure frequency, per year (mean, range)	Median epilepsy duration, in years (mean, range)	Median age at time of EEG, in years (mean, range)
High IED frequency, n=12	174 (545.36, 23 to 2486)	2.25 (6.19, 0.5 to 24)	21.5 (19.94, 0.08 to 45)	38.5 (40.33, 18 to 68)
Low IED frequency, n=12	25 (1089, 2 to 8063)	3.00 (10.79, 0.3 to 36)	27 (25.63, 4 to 46)	53.5 (48.83, 22 to 79)
Statistical comparison (Mann-Whitney U statistic, p value)	42.0, p = 0.15	25.0, p = 0.51	50.5, p = 0.23	t = 1.17, p = 0.25

The Mann-Whitney U test was used in all comparisons in which data were not normally distributed; Student's t-test was used for the analysis of age at time of EEG. IED = interictal epileptiform discharges. High IED frequency indicates those subjects with IED frequency at or above the median of 10 discharges per hour; low IED frequency indicates those below the median.

Table 4
Published studies on the association between IEDs and clinical epilepsy characteristics

Study	Type of EEG	Subject Population	Clinical Epilepsy Characteristics Associated With Presence of or Higher Frequency of IEDs				
			Epilepsy Duration	Age at time of EEG	Recent Seizure	Seizure Frequency	Use of AEDs
Selvitelli et al. (this paper)	Single routine EEG	Adults with history of ≥ 2 presumed focal-onset seizures	No association	No association	No association	No association	No association
Sundaram et al. (1990)	Single routine EEG	Adult epilepsy patients with focal or generalized seizures	N/A	No association	Within 2 days	>1 seizure/month	No association
Janszky et al. (2005)	LTM	Medically refractory temporal CPS	Increased epilepsy duration	No association	N/A	>1 seizure/week	N/A (off AEDs for LTM)
Krendl et al. (2008)	LTM	Medically refractory temporal CPS	N/A	N/A	N/A	>1 seizure/week	N/A
Ajmoné Mansan and Zivin (1970)	Serial routine EEGs	All ages with focal or generalized seizures	N/A	Younger age	Within 7 days	>1 seizure/day	Inverse association (fewer IEDs off AEDs)
Drury and Beydoun (1998)	Single routine EEG	Elderly patients with focal or generalized epilepsy	No association	No association	N/A	>1 seizure/month	No association
Desai et al. (1988)	Single routine EEG	Adult chronic epilepsy patients with focal or generalized seizures	>10 years of epilepsy	N/A	N/A	No association	Use of >1 AED

IED = interictal epileptiform discharge; AED = antiepileptic drug; IGE = idiopathic generalized epilepsy; CPS = complex partial seizure; LTM = long-term monitoring; N/A = not available (data not reported).