

## The Role of Interictal Epileptiform Discharges in Epilepsy Surgery Outcome

### Abstract

**Background:** Epilepsy surgery is a fundamental treatment in refractory epilepsy. Video electroencephalographic (v-EEG) monitoring plays an essential role in presurgical evaluation of patients. However there are reports of favorable outcome based on interictal and magnetic resonance imaging (MRI) findings without any need for v-EEG monitoring in patients with temporal lobe epilepsy (TLE). This study aimed to investigate the prognostic effect of concordance between interictal findings and ictal and MRI data on postsurgical outcome of TLE and extratemporal lobe epilepsy (ETLE). **Methods:** A retrospective study was conducted on 199 patients with refractory focal epilepsy who were admitted for presurgical evaluation. The concordance between irritative zone (IZ) and seizure onset zone (SOZ) and also IZ and MRI lesion was registered, and subsequently the prognostic effect of relevancy on 1-year follow-up result based on Engel criteria was investigated. **Results:** In TLE and ETLE regarding relevancy between IZ and SOZ, 77.8% and 73.2% were concordant, 2.5% and 0% were discordant, and 19.6% and 26.8% had overlap, respectively. Concordance between IZ and MRI lesion was found in 76.6% and 51.2% of patients with TLE and ETLE while discordance was recorded in 2.5% and 12.2% and overlap registered in 20.9% and 36.6%, respectively. The concordance of interictal findings had no effect on postsurgical outcome of patients with TLE and ETLE. **Conclusions:** Our study showed that concordance of IZ with SOZ and MRI has no independent effect on postsurgical outcome of patients with TLE and ETLE. We suggest that excluding exceptional cases, v-EEG monitoring should be considered as the mainstay of presurgical evaluation.

**Keywords:** *Electroencephalography, epilepsy, neurosurgery, treatment outcome*

### Introduction

Epilepsy surgery is considered as a fundamental treatment in refractory epilepsy.<sup>[1]</sup> Presurgical evaluation often consists of detailed history taking and neurologic examination, determination of seizure semiology, video electroencephalographic (v-EEG) monitoring to define the irritative zone (IZ) and the seizure onset zone (SOZ), and also magnetic resonance imaging (MRI) and other imaging and EEG modalities as needed.<sup>[2]</sup> Concordance of these findings is very important and often affects the postsurgical outcome.<sup>[3]</sup>

Studies on temporal lobe epilepsy (TLE) have shown concordance between interictal and ictal EEG findings in presurgical evaluation.<sup>[4-7]</sup> In addition, relevancy of interictal EEG and MRI findings was correlated with favorable surgical outcome.<sup>[8]</sup> Due to this concordance

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between interictal findings and ictal EEG and MRI, few studies have emphasized the role of interictal EEG in presurgical evaluation and questioned the need for long-term v-EEG monitoring in patients with TLE.<sup>[9-11]</sup> However, we could not find any study with similar recommendation for patients with extratemporal lobe epilepsy (ETLE). To more exactly address this issue, we conducted this study to investigate the prognostic effect of concordance between IZ with SOZ and MRI lesion on postsurgical outcome of patients with TLE and ETLE.

### Methods

#### Patients

This retrospective study was conducted at the referral epilepsy surgery center of Isfahan medical school university hospital, Iran, based on database of patients admitted during 2010–2015. We enrolled adult patients with medically refractory focal epilepsy who were admitted for presurgical

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evaluation. All patients underwent noninvasive long-term v-EEG monitoring and subsequently underwent epilepsy surgery. The inclusion criteria were defined as follows: (a) age 18–60 years, (b) MRI evidence of lesion concordant to SOZ, and (c) 1-year follow-up. We excluded patients with prior epilepsy surgery, dual pathology on MRI, normal interictal EEG, no ictal event during v-EEG monitoring, and follow-up evidence of less than 1 year. In all, 214 patients were recruited. Eight patients were excluded because of dual pathology and seven had no ictal events or interictal epileptiform discharges (IEDs). Data for 199 patients fulfilled the inclusion criteria and were reviewed.

### Electroencephalogram analysis

Patients underwent long-term scalp EEG monitoring using Nihon Kohden system. Electrodes arranged in accordance with the International 10–20 system and also additional temporal electrodes (F9, F10, T9, T10, T1, T2) were used. The setting was organized at 200 Hz sampling rate, 0.1 s time constant, and 60 Hz notch filter.

### Data collection

Demographic data and clinical characteristics were obtained from patients' files. IZ, SOZ, preoperative 1.5 T dedicated MRI, and pathological findings were reviewed from database.

The concordance of IZ with SOZ and MRI lesion was investigated. Accordingly, we categorized patients into three groups. Group 1 included patients in whom more than 90% of IEDs occurred in the same area as SOZ or MRI lesion (Concordant group). Patients in whom their IEDs were recorded in a totally different area in comparison to SOZ or MRI lesion were assigned to group 2 (Discordant group). Group 3 consisted of those who showed <90% consistency between IZ and SOZ or MRI lesion (Overlap group).

### Surgery outcome

One-year follow-up results were obtained from registered postoperative outpatient visits. We classified them as favorable (Engel outcome scale<sup>[12]</sup> class I) and unfavorable (Engel outcome scale class II–IV).

### Statistical analysis

Statistical analysis was performed using SPSS version 22 software package (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as mean  $\pm$  standard deviation. Qualitative variables were reported as number (percent). Before the main analysis, Shapiro–Wilk testing for normality was performed. Independent sample *t*-test, Chi-square test, Mann–Whitney *U*-test, and one-way analysis of variance were used. All probability tests were two-tailed, and the level of significance was defined as *P* value  $\leq 0.05$ .

### Results

Patients' demographic data and clinical characteristics are summarized in Table 1. Investigating the concordance

**Table 1: Patients' characteristics**

Characteristics	Quantity
Gender; male/female (%)	60.3/39.7
Handedness; right/left (%)	90.5/9.5
Marital state; single/married (%)	59.8/40.2
Age at surgery (years)	27.1 $\pm$ 9.7
Age of onset (years)	11.2 $\pm$ 8.5
Epilepsy duration (years)	15.9 $\pm$ 10.2
Number of AEDs	2.7 $\pm$ 1
Family history; pos/neg (%)	7.5/92.5
TLE/ETLE	79.4/20.6
Pathological findings	
HS	101 (50.7)
Tumor	39 (19.6)
Gliosis	37 (18.6)
FCD	14 (7.1)
CA	8 (4)
Engel's surgical outcome	
Engel I (favorable)	163 (81.9)
Engel II, III, IV (unfavorable)	36 (18.1)

Data are presented as percent, *n* (%), and mean $\pm$ SD. AEDs=Antiepileptic drugs, TLE=Temporal lobe epilepsy, ETLE=Extratemporal lobe epilepsy, HS=Hippocampal sclerosis, FCD=Focal cortical dysplasia, CA=Cavernous angioma, SD=Standard deviation

between IZ and SOZ in patients with TLE, 123 patients (77.8%) were categorized in group 1, 4 (2.5%) in group 2, and 31 patients (19.6%) in group 3. In patients with ETLE, 30 (73.2%) were placed in concordant group and 11 patients (26.8%) classified as overlap. The amount of concordance between interictal and ictal findings was not significantly different in patients with TLE and ETLE (*P* = 0.38).

In patients with TLE, IZ was compatible with MRI lesion in 121 (76.6%) and had overlap in 33 (20.9%), but was totally different in 4 (2.5%). However in ETLE, concordance was found in 21 (51.2%), overlap in 15 (36.6%), and discord in 5 (12.2%). There was a significant difference between patients with TLE and ETLE regarding agreement rate between IZ and MRI lesion (*P* = 0.02).

Favorable outcome was detected in 82.6% of patients with TLE and 79.2% of ETLE without any significant difference (*P* = 0.58). Relevancy between IZ and SOZ showed no meaningful difference in TLE and ETLE and had no effect on outcome [Table 2]. As Table 3 indicates, in patients with favorable outcome, concordance between interictal findings and MRI lesion had a significantly higher level in TLE in comparison to ETLE (*P* < 0.001). However, when we classified patients with TLE based on pathology [with and without hippocampal sclerosis (HS)], concordance between IZ and SOZ or IZ and MRI had no difference and caused no significant effect on postsurgical outcome (*P* = 0.46 and 0.64, respectively).

**Table 2: Effect of concordance between interictal and ictal electroencephalographic findings on outcome**

Outcome	TLE	ETLE	P
Favorable			
Concordant	104 (79.4)	23 (71.9)	0.34
Discordant	3 (2.3)	0 (0)	
Overlap	24 (18.3)	9 (28.1)	
Unfavorable			
Concordant	19 (70.4)	7 (77.8)	0.81
Discordant	1 (3.7)	0 (0)	
Overlap	7 (25.9)	2 (22.2)	

Data are presented as *n* (%). TLE=Temporal lobe epilepsy, ETLE=Extratemporal lobe epilepsy

**Table 3: Effect of concordance between interictal and magnetic resonance imaging findings on outcome**

Outcome	TLE	ETLE	P
Favorable			
Concordant	102 (77.9)	15 (46.9)	<0.001
Discordant	3 (2.3)	5 (15.6)	
Overlap	26 (19.8)	12 (37.5)	
Unfavorable			
Concordant	19 (70.4)	6 (66.7)	0.78
Discordant	1 (3.7)	0 (0)	
Overlap	7 (25.9)	3 (33.3)	

Data are presented as *n* (%). TLE=Temporal lobe epilepsy, ETLE=Extratemporal lobe epilepsy

## Discussion

This study assessed the prognostic effect of interictal findings on postsurgical outcome of patients with focal refractory epilepsy based on the amount of concordance with ictal and MRI findings. The valuable role of long-term v-EEG monitoring has been demonstrated in several studies. However, it is a time-consuming and expensive procedure that might cause potential risks for patients during drug withdrawal. Cascino *et al.* in their study on the prognostic role of routine interictal EEG, video EEG, and MRI findings in the postoperative outcome of patients with TLE found that interictal EEG abnormalities were unilateral in most of them and there was a statistically significant relationship between MRI and interictal EEG findings.<sup>[6]</sup> There are few studies which suggested surgery based on IZ and MRI lesion under certain conditions. The study by Patariaia *et al.* has shown that concordant history, unilateral HS on MRI, and unilateral interictal EEG are highly sensitive for focus localization without any need for additional information from ictal recording.<sup>[4]</sup> Holmes *et al.* in their study on patients with TLE have shown that interictal EEGs demonstrate consistent unilateral IEDs in anterior-midtemporal area which is concordant with other findings and have the same postsurgical outcome as those with same characteristics who underwent v-EEG monitoring.<sup>[11]</sup> In a similar study, Cendes *et al.* demonstrated that almost all patients with

unilateral HS had concordant ictal and interictal EEG findings, and in only 3% of them interictal and ictal EEG were not concordant. They suggested that in this group of patients, serial routine interictal EEG would make v-EEG monitoring unnecessary.<sup>[5]</sup> In line with previous findings, Alvim *et al.* in their prospective study in patients with mesial TLE with HS (mTLE-HS) have shown that in patients with compatible semiology and ipsilateral IEDs, v-EEG monitoring is not necessary.<sup>[10]</sup> Similar to previous studies,<sup>[5,6]</sup> in our study discordance of IZ and SOZ occurred in 2.5% of patients with TLE but presence or absence of the concordance had no effect on postsurgical outcome. In comparison to patients with ETLE, the concordance between IZ and MRI was significantly higher in patients with TLE who experienced favorable outcome, but in contrast to previous reports it had no relevancy to underlying pathology. Studies which targeted postsurgical outcome in ETLE have reported that concordance between presurgical evaluations indicates a better surgical outcome, but no specific role for IEDs has been considered.<sup>[13,14]</sup> In addition, in our study neither concordance with SOZ nor MRI defined any role for interictal findings in postsurgical outcome of this group of patients.

## Conclusions

Although a high concordance has been reported between IZ and SOZ and MRI in mTLE-HS, it should be considered that this finding could not be extended to other types of epilepsy and still v-EEG monitoring has its fundamental role in localization of epileptogenic zone particularly in ETLE.

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## Conflicts of interest

There are no conflicts of interest.

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