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Drug Resistant Focal Epilepsy: Correlation between Ictal and Inter-ictal EEG Monitoring

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ABSTRACT

Background: Video EEG is the gold-standard investigation to assess Ictal and Inter-ictal epileptiform brain activity

Objective: To assess the concordance between ictal vs. inter-ictal Video-EEG during their pre-surgical evaluation.

Methodology: In this observational cohort study, we involved Thirty children and adolescents with focal drug-resistant epilepsy who presented to the neuro-pediatric Cairo University children hospital clinics. All of them were submitted to history taking, full examination and 6–24-h long-term Video EEG recording (including ictal and inter-ictal recordings).

Results: Analysis of long-term video EEG recordings showed that the ictal onset zone (IOZ) was right-sided in 50% of patients, left-sided in 43.3%, and bilateral in 6.7%. The IOZ was localized to the frontal lobe in 33.3%, temporal lobe in 30%, parietal lobe in 6.7%, and was multifocal in 30% of cases. Comparison between ictal and interictal EEG revealed no statistically significant differences in either lateralization ($p = 0.964$) or lobar localization ($p = 0.126$), indicating strong concordance between the two.

Conclusion: In patients with focal drug-resistant epilepsy (DRE), long-term video-EEG data showed strong concordance between the ictal onset zone (IOZ) and interictal focal paroxysmal discharges. This suggests that ictal EEG contributes limited additional value to presurgical evaluation. Clinically, this could reduce the need for inpatient IOZ localization, thereby decreasing the costs, time, and resources associated with long-term video-EEG monitoring.

Keywords: *Focal epilepsy, Drug-resistant epilepsy, Presurgical evaluation, Video-EEG*

1. INTRODUCTION

Drug-resistant epilepsy (DRE) is defined as failure of adequate trials of two appropriately chosen anti-seizure medications (ASM) with acceptable side effects 1.

Children and adolescents diagnosed with drug-resistant epilepsy are at increased risk for poor long-term intellectual and psychosocial outcomes, along with a poor health-related quality of life. In this form of resistant epilepsy, appropriate surgical management is often undertaken with the goal of reducing or stopping seizures, but there is limited evidence from trials showing the benefit in this age group 2.

The region of the cerebrum that is subjected to surgery depends on the localization of the origin of seizures in the cerebral

cortex and the functional importance of the surrounding brain tissue. These factors are determined on pre-surgical evaluation, including simultaneously acquired video electroencephalographic (video EEG) recordings and structural and functional imaging of the brain 3.

Video-EEG monitoring; the synchronous display of the ictal EEG pattern and the paroxysmal behavior, may be used to confirm the diagnosis of a seizure disorder, classify seizure type(s), assess seizure frequency and precipitating factors, and

for surgical localization. Although VEEG is the gold standard, it has some disadvantages including the inherent cost of the study and the need for special resources, personnel, and hospitalization4.

The aim of this work is to assess the concordance between long term VEEG ictal and inter-ictal focal findings, in order to assess their diagnostic usefulness in the presurgical evaluation of patient with focal DRE.

2. METHODOLOGY

This is a prospective observational analytical cohort study, that was carried out in Cairo University Children Hospital.

***Study Population*:** Thirty patients below 18 years of age who presented to the neurology outpatient clinic and suffer from focal epilepsy evident by seizure semiology & diagnosed with DRE were enrolled in this study from November 2021 till May 2023.

Patients who were found to be older than 18 years of age or presenting with generalized onset epilepsy or non-complaint to treatment were excluded from this study.

Ethical permission to carry out the study was sought from the hospital's Health Research Ethics Committee before the commencement of the study (Code: MD-87-2022). Informed written consent was taken from the parents.

***Methods*:** All cases enrolled were subjected to history taking and full general and neurological examination to exclude any generalized systemic illness and identify any associated neurological disorders.

Further evaluation with long-term video EEG monitoring to assess (Inter-ictal and Ictal epileptiform discharge) and to localize Ictal onset zones. Patients were subjected to 6–24-h long-term EEG video recording using multiple EEG systems according to the guidelines of the American Clinical Neurophysiology Society 5 . This was done by the use of scalp electrodes in the standard 10–20 system of electrode placement during wakefulness and sleep. Bipolar longitudinal, transverse montages and unipolar montages were used. Simultaneous ECG monitoring was done.

Statistical analysis:

Data were analyzed using Statistical Program for Social Science (SPSS) version 24. Quantitative data were expressed as mean ±SD. Qualitative data were expressed as frequency and percentage. Mean (average): the central value of a discrete set of numbers, specifically the sum of values divided by the number of values. Standard deviation (SD): is the measure of dispersion of a set of values. A low SD indicates that the values tend to be close to the mean of the set, while a high SD indicate that the values are spread out over a wider range.

***The following tests were done: Chi-square test*:** was used when comparing between non-parametric data. Probability (P-value) P-value < 0.05 was considered significant. P-value < 0.001 was considered as highly significant. P-value > 0.05 was considered insignificant.

***Post-Hoc test*:** was used for multiple comparisons.

3. RESULTS

Table (1) shows the demographic data of our study group. The mean age of patients was 8.2 ± 3.6 years with minimum age of 2 years and maximum age of 17 years. There were 14 males (46.7%) and 16 females (53.3%) in the studied patients. Twenty-nine patients (96.7%) were full terms and 1 patient (3.3%) was pre-term. Eight patients (26.7%) were admitted to NICU and 22 patients (73.3%) were not. Twenty-four patients (80 %) had negative consanguinity and 6 patients (20%) had positive consanguinity. There were 5 patients (16.7%) with relevant family history (one family member or more affected with epilepsy) while the rest 25 patients (83%) had irrelevant family history.

There were 8 patients (26.7%) with delayed mental development and 6 patients (20%) with delayed motor development. There were 3 patients (10%) with past history of trauma, 2 patients (6.7%) with past history of CNS infection, 1 patient (3.3%) with past history of kernicterus and 1 patient (3.3%) with past history of ADHD while the remaining 23 patients (76.7%) had no relevant past history.

Table (2) describes inter-ictal EEG findings in the form of focal paroxysmal discharges as recorded during the long-term

video-EEG monitoring in all studied patients. There were 14 patients (46.7%) of right side, 14 patients (46.7%) of left side and 2 patients (6.7%) bilateral. Frontal lobe was affected in 6 patients (20%), temporal lobe was affected in 7 patients (23.3%) while it was multi-focal in 17 patients (56.7%).

Table (3) describes the ictal onset zone as recorded by long term video-EEG monitoring in all studied patients. There were 15 patients (50%) with ictal onset zone on the right side, 13 patients (43.3%) on the left side and 2 patients (6.7%) bilateral. Frontal lobe was affected in 10 patients (33.3%), temporal lobe was affected in 9 patients (30%) and parietal lobe was affected in 2 patients (6.7%) while it was multi-focal in 9 patients (30%).

Table (4) shows:

No statistically significant difference (p-value = 0.964) between Ictal EEG findings in the form of Ictal onset zone and Inter-ictal EEG findings in the form of focal paroxysmal discharges as regard the affected side as follows: Right side was affected in 15 patients (50%) by ictal EEG versus 14 patients (46.7%) by inter-ictal EEG. Left side was affected in 13 patients (43.4%) by ictal EEG versus 14 patients (46.7%) by inter-ictal EEG. Bilateral affection was present in 2 patients (6.7%) by ictal EEG versus 2 patients (6.7%) by inter-ictal EEG. These findings confirm the concordance between Ictal EEG and Inter-ictal EEG regarding the affected side. No statistically significant difference (p-value = 0.126) between Ictal EEG findings in the form of Ictal onset zone and Inter-ictal EEG findings in the form of focal paroxysmal discharges regard the affected lobe as follows: Frontal lobe was affected in 10 patients (33.3%) by ictal EEG versus 6 patients (20%) by inter-ictal EEG. Temporal lobe was affected in 9 patients (30%) by ictal EEG versus 7 patients (23.3%) by inter-ictal EEG. Parietal lobe was affected in 2 patients (6.7%) by ictal EEG versus 0 patients (0%) by inter-ictal EEG. Multi-focal affection was present in 9 patients (30%) by ictal versus 17 patients (56.7%) by inter-ictal EEG.

These findings confirm the concordance between Ictal EEF and Inter-ictal EEG regarding the affected lobe (Figures 1&2).

Table (1): Demographic data of all studied patients

			Studied patients (N = 30)	
Age (years)		**Mean ±SD**	**8.2 ± 3.6**	
		Min - Max	**2 – 17**	
Sex		**Male**	14	**46.7%**
		Female	16	**53.3%**
Mode of delivery		**NVD**	10	**33.3%**
		CS	20	**66.7%**
Gestational age		**Pre-term**	1	**3.3%**
		Full term	29	**96.7%**
NICU admission		**No**	22	**73.3%**
		Yes	8	**26.7%**
Consanguinity		**Negative**	24	**80%**
		Positive	6	**20%**
Family history		**Relevant**	5	**16.7%**
		Irrelevant	25	**83.3%**
GDD	**Mental**	**Normal**	22	**73.3%**
		Delayed	8	**26.7%**
	Motor	**Normal**	24	**80%**
		Delayed	6	**20%**
		None	23	**76.7%**

Past history	**Trauma**	3	**10%**
	CNS infection	2	**6.7%**
	kernicterus	1	**3.3%**
	ADHD	**1**	**3.3%**

Table (2): Inter-ictal EEG findings in all studied patients

		Studied patients (N = 30)	
Side	**Right**	14	46.7%
	Left	14	46.7%
	Bilateral	2	6.7%
Affected lobe	**Frontal**	6	20%
	Temporal	7	23.3%
	Multi-focal	17	56.7%

Table (3): Ictal EEG findings in all studied patients.

		Studied patients (N = 30)	
Side	**Right**	15	50%
	Left	13	43.3%
	Bilateral	2	6.7%
Affected lobe	**Frontal**	10	33.3%
	Temporal	9	30%
	Parietal	2	6.7%
	Multi-focal	9	30.0%

Table (4): Comparison between Ictal EEG and Inter-ictal EEG findings as regard the affected side and lobe

		Ictal EEG (N = 30)		**Inter-ictal EEG (N = 30)**		**Stat. test**	**P-value**
Side	**Right**	15	50%	14	46.7%	$X^2 = 0.07$	0.964 NS
	Left	13	43.3%	14	46.7%		
	Bilateral	2	6.7%	2	6.7%		
Lobe	**Frontal**	10	33.3%	6	20%	$X^2 = 5.7$	0.126 NS
	Temporal	9	30%	7	23.3%		
	Parietal	2	6.7%	0	0%		
	Multi-focal	9	30%	17	56.7%		

X2: Chi-square test. NS: p-value > 0.05 is considered non-significant.

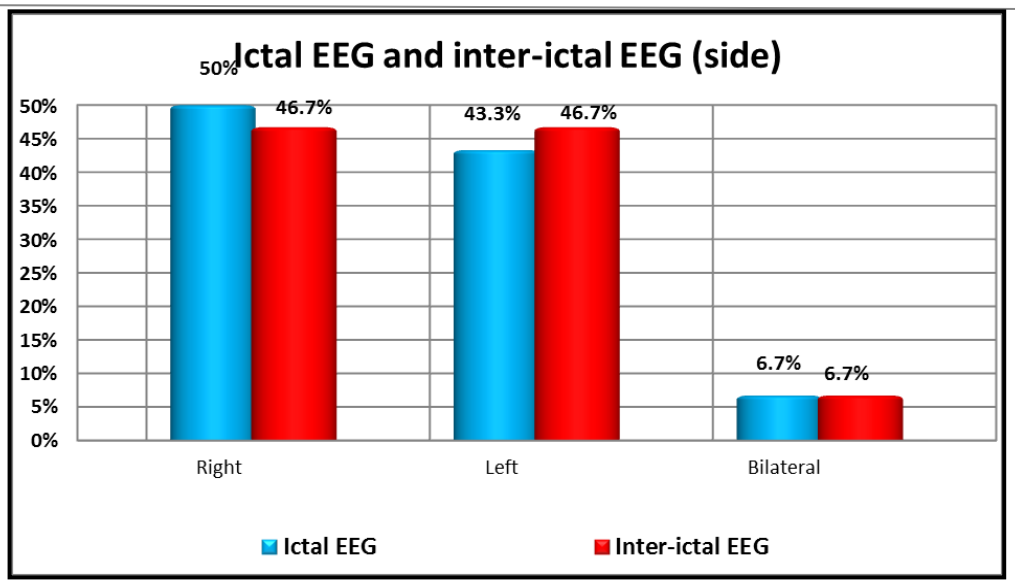

Figure (1): Comparison between ictal EEG and inter-ictal EEG as regard affected side

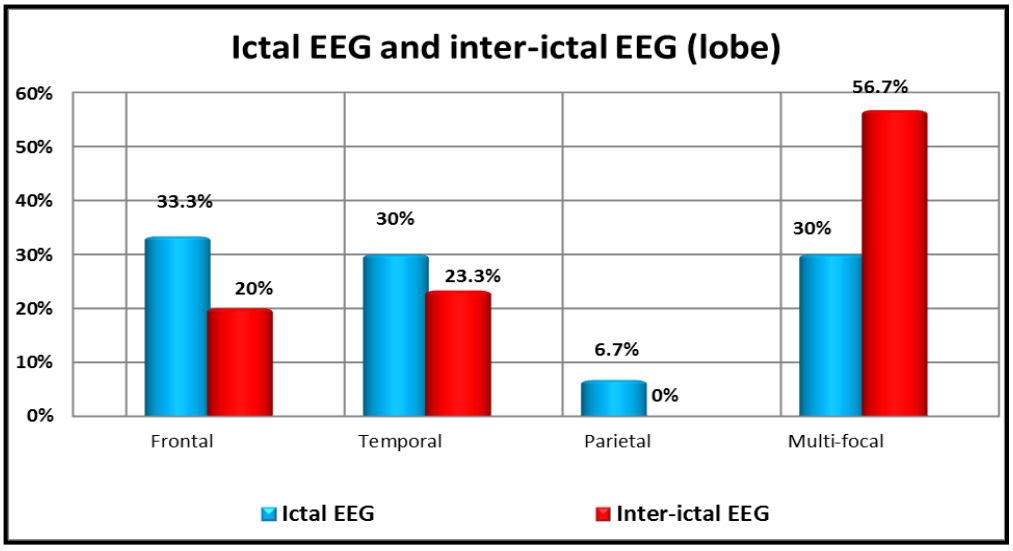

Figure (2): Comparison between ictal EEG and inter-ictal EEG as regard affected lobe

4. DISCUSSION

Children and adolescents diagnosed with drug-resistant epilepsy are at increased risk for poor long-term intellectual and psychosocial outcomes. Appropriate surgical management is often needed with the goal of reducing or stopping seizures 6.

Presurgical evaluation includes simultaneously acquired long-term video EEG recordings along with structural and functional imaging of the brain. Video-EEG monitoring; is the gold-standard investigation for DRE diagnosis 7.

The aim of this study is to conduct a prospective descriptive study involving children and adolescents younger than 18 years with focal DRE during their pre-surgical evaluation to find and describe possible correlations between ictal and inter-ictal long-term Video-EEG findings.

Thirty patients who fulfilled the inclusion criteria were enrolled in this study. All of them were submitted to history taking, full examination and 6–24-h long term video-EEG monitoring to delineate the ictal and inter-ictal EEG patterns of their seizures' electrical activity.

In patients whom long-term video EEG recording was successful in detecting both the inter-ictal epileptogenic activity as well as the ictal onset zone (IOZ), Analysis of the data collected revealed that as regard the IOZ side, there were 15 patients (50%) of right side, 13 patients (43.3%) of left side and 2 patients (6.7%) with bilateral affection in the study population. As

regard the IOZ lobe, frontal lobe was affected in 10 patients (33.3%), temporal lobe was affected in 9 patients (30%) and parietal lobe was affected in 2 patients (6.7%) while it was multi-focal in 9 patients (30%).

In comparison of Ictal and inter-ictal EEG, there was no statistically significant difference between the IOZ and the inter-ictal focal paroxysmal discharges localized by video-EEG as regard the affected side (p-value = 0.964) nor the affected lobe (p-value = 0.126) which confirms their concordance.

Those findings come in agreement with those of Cendes et al., as they found a strong correlation between ictal and interictal scalp EEG lateralization as well as between each of these 2 sets of EEG data and MRI lateralization in 184 consecutive patients with TLE. The current results are in agreement with their conclusion that a concordant outpatient EEG evaluation in patients with TLE and unilateral hippocampal atrophy would obviate the need for inpatient EEG monitoring 8.

The current results are also concordant with the findings of Van der Heide et al., where he assessed the Consistency and dominance of focal interictal epileptiform activity in 19 patients with a clinical definite diagnosis of TSC. The ictal onset zone was identified. Concordance between interictal and ictal findings was analyzed. They found dominant, consistently present, focal interictal epileptiform activity in 14 of the 19 patients 9.

5. Conclusion:

In patients with focal DRE, Data analyzed from long term video-EEG monitoring including ictal and inter-ictal recording revealed the concordance between ictal onset zone and inter-ictal focal paroxysmal discharges.

From these findings we can conclude that in our patient population, Ictal EEG added little value in the presurgical evaluation of patients with DRE. This would have important clinical implications in obviating the need for in-patient IOZ localization. Thus, reducing the costs, time and efforts spent in long term video EEG monitoring.

6. Ethics Approval and Consent to participate

Ethical permission to carry out the study was sought from the hospital's Health Research Ethics Committee (HREC) before the commencement of the study (Code: MD-87-2022).

Detailed information, explanation and nature of the study were offered to the parents of the selected subjects who were eligible for the study and an informed written consent was obtained for participation and publication of the study. Each participant was given the opportunity to ask questions about the study and appropriate answers were provided.

7. Funding for the study

The funding for the study was provided solely by the researcher. The researcher is the only funding body for the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

8. List of Abbreviations:

DRE	**Drug resistant epilepsy**
EEG	**Electroencephalogram**
TSC	**Tuberous sclerosis complex**
TLE	**Temporal lobe epilepsy**
IOZ	**Ictal onset zone**
MRI	**Magnetic Resonance Imaging**
ASM	**Anti-seizure medications**
ECG	**Electrocardiogram**
CNS	**Central nervous system**
ADHD	**Attention deficit hyperactive disorder**

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