ORIGINAL ARTICLE

Electroencephalography, Magnetic Resonance Imaging and Response to Treatment in Children with Focal Seizures
A Prospective Cohort Study

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Abstract

Objectives

This study aimed to evaluate patients with focal seizures, their clinical manifestations, and their response to treatment, then compared the accuracy of electroencephalography and Magnetic Resonance Imaging (MRI) to assess the cost-effectiveness of the latter.

Materials & Methods

After selecting the appropriate individuals, the authors obtained the data by clinically evaluating the cases and interviewing them or their caretaker(s) on admission and the six-month follow-up visit. The researchers then analyzed the obtained data.

Results

Most cases (88.4%) had idiopathic seizures. A positive family history of seizures was observed in eight cases (5.4%). Respectively, the occipital, frontal, and temporal lobes showed the highest frequency of abnormalities on electroencephalography, while periventricular leukomalacia was the highest abnormal MRI finding (4.1%). However, in 87.8% of cases, this modality's results were normal. No recurrence of seizures was observed in 116 cases (78.9%) on the six-month follow-up visit, pointing towards an appropriate response to treatment.

Conclusion

While this study revealed that most had normal MRI, reporting an abnormality in electroencephalography was a more prevalent occurrence. This finding undermines the cost-effectiveness of the former modality, even though its importance in diagnosing the

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underlying abnormalities necessitates further studies regarding the subject at hand. Furthermore, the study of age groups showed that treatment response is less desirable in children under two years of age, suggesting more intense workups.

Keywords: Partial Seizure; Epilepsy; Magnetic Resonance Imaging; Electroencephalography; Neuroimaging; Children; Treatment.
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Introduction

Seizures are defined as abnormal and spontaneous activities of cortical neurons[1]. This activity made up of wave patterns, is intermittent and self-limited, lasting from a few seconds to several minutes (1). The wave patterns may start from one brain area and end while limited in the same area (i.e., focal seizures). However, they also can continue or even start diffusely, involving all areas of the brain (i.e., generalized/bilateral seizures)(1).

Based on clinical manifestations, seizures are mainly categorized into two groups, generalized and focal-onset, with the latter divided into three subtypes: those with impaired and retained awareness and those that are focal-to-bilateral tonic-clonic[2]. For a definite determination, clinical manifestations and electroencephalography would demonstrate whether the incident has started from a specific brain area or has diffusely involved all the structures (1,3). Furthermore, as far as the prevalence goes, studies have demonstrated that focal seizures are slightly more common than generalized ones (4).

Epilepsy, even though refined to the point that it cannot be stated in a sentence, comprises an enduring tendency to suffer from seizures[4]. The International League Against Epilepsy (ILAE) Epidemiology Commission[5] defined the condition as two or more seizures with at least 24 hours between episodes. Although the onset of a seizure without a stimulus (e.g., High fever) would usually point towards a start of a chronic seizure disorder or epilepsy, less than half of children who have suffered from a seizure would experience another episode[6]. The biologic base regarding seizure recurrence is probably multifactorial and can include severe underlying syndromes, neuropathological disorders, abnormal neuron organizations, receptor overstimulation via neurotransmitters, ion channel disorders, reactive autoimmune disorders, and inappropriate use of anticonvulsants (7,8).

Estimating the number of cases suffering

from this disorder worldwide is not feasible. Acute symptomatic seizures (i.e., seizures as manifestations of central nervous system insults) also occur in about 29 to 39 individuals in 100000 of the population, with the oldest and the youngest (under the age of one year) age groups being most commonly affected (9). The male sex is also more likely to report experiencing seizures than females. However, this difference might be due to the tendency of the female sex to hide the condition due to the devastating effects of this stigma (10).

It is estimated that about 1% of cases suffering from seizures will not experience another episode in their life[10]. Nevertheless, one study has estimated the lifetime prevalence of epilepsy/seizure disorder to be around 10.2 per 1000 of the population and the lifetime prevalence of currently ongoing epilepsy to be around 6.3 per 1000 (11).

ComputedTomography(CT),Electroencephalography (EEG), and Magnetic Resonance Imaging (MRI) are currently the most beneficial diagnostic methods in the diagnosis of seizure type/epilepsy[12]. They are essential in differentiating nonepileptic events and symptomatic and unprovoked seizures from new-onset epilepsy (12). The ILAE's latest guidelines strongly recommend utilizing early MRI (with HARNESS-MRI protocol) in any individual with a first-time seizure to look for epileptogenic foci, especially in young children (13,14). Furthermore, the diagnostic accuracy of the conventional and epilepsy protocol-specific MRIs have been reported to be 30 and 60%, respectively[12]. The simultaneous performance of EEG and MRI is thought to provide further improved results (15).

The cost-effectiveness of obtaining MRIs from children with first-onset afebrile seizures (especially those between 1 and 12) has been relatively questioned. Two studies have demonstrated less than presumed effectiveness of MRI in detecting epileptogenic foci in the mentioned cases that necessitated a change in the nonsurgical management methods (1 and 17%, respectively) (16,17). The sedation of those younger than 12 years required during the MRI session further adds to the existing concerns (18).

A majority of the seizure disorders will be controlled by appropriate medical treatment. However, several studies show that if seizure episodes did not respond to the first anticonvulsant, the chances of responding to the drugs next in line would decrease significantly (8). Furthermore, about one-third of all cases would suffer from drug-refractory epilepsy (i.e., failure to respond to three antiepileptic drugs at maximum doses)(8). Based on available data from different studies, out of the available anticonvulsants, Carbamazepine (CBZ), Oxcarbazepine (OXC), and to a lesser extent, Clobazam (CLB) are the most promising options in the first-line treatment of focal-onset seizures (19).

Since detecting abnormal MRI and EEG findings in those with seizures is paramountThis research evaluated partial seizures via MRI and EEG results and compared their effectiveness and the cases' overall response to treatment.

Materials & Methods

This prospective study was conducted in a regional referral center for pediatric neurological disorders, evaluating all cases suffering from afebrile partial seizures from early-2020 until mid-2021. All eligible pediatric (under the age of 14 as implemented in the center) inpatient and outpatient cases suffering from symptoms of focal seizures with a definite diagnosis were included. Therefore, those without definite confirmation

of the disorder were excluded. The local ethics committee ethically approved this study. It was also performed following the ethical standards of the 1964 Declaration of Helsinki. Only those whose legally authorized representatives provided consent remained in the study. All the collected data remained confidential throughout the study and after its conclusion.

After selecting the appropriate cases and gaining informed consent, the data was collected on their first visit and then after six months, via interviewing the cases, if possible, and their caretakers, while also clinically and radiologically (via obtaining EEGs and MRIs) evaluating their condition.

The MRIs were obtained based on conventional protocols and the EEGs during a 30-minute session. The resultant data were then assessed.

Demographic data (age and sex), possible risk factors (including family history or a developmental disorder), presenting or initial clinical manifestations, possible etiology (idiopathic, cryptogenic, symptomatic), and the results of diagnostic and therapeutic interventions, including the EEG, Brain MRI, and the overall response to treatment, were assessed and documented.

Data were statistically analyzed using the 20th version of the IBM SPSS Statistics software via the frequency, standard deviation, mean, and chi-square tests. The P-value was set at <0.05 for statistical significance levels.

The cases were instructed to return for a follow-up visit after six months or earlier if they noted recurrence.

Results

This study evaluated 147 cases, out of whom sixty-two were male (42.2%) and eighty-five were female (57.8%). A positive history of seizures was found in the family in eight cases. However, in the overwhelming majority (88.4%), the seizure was idiopathic—73.5% suffered from focal-onset seizures with impaired awareness, and 26.5% from focal-to-bilateral tonic-clonic seizures. In the mentioned cases, twenty-nine (7.19%) also suffered from developmental delays. However, 116 cases (78.9%) did not experience further seizure episodes in the following six months, indicating a desirable therapeutic outcome (Table 1).

The mean age of evaluated cases was 7.27±3.50 years. The minimum and maximum ages were 2 and 14 years, respectively. Furthermore, the mean age of onset in those evaluated was 5.49±3.48 years.

The most frequent EEG findings were occipital, frontal, and temporal changes. Furthermore, the most frequent abnormal finding on their MRIs was periventricular leukomalacia (4.1%). However, 87.8% of cases had normal MRIs (Table 2).

The authors also noticed that the mean age of onset for seizures was significantly different based on sex (P-value=0.009), family history (P-value=0.001), etiology (P-value=0.001), and developmental disorders (P-value=0.001) of each of the individuals. However, the differences were not statistically significant regarding the response to treatment (Table 3).

Comparing the response to treatment and EEG and MRI findings in those with ongoing seizure episodes and those with no further episodes in the following six months revealed statistical significance in favor of those with only an isolated seizure episode. Furthermore, those with occipital and frontal lobe seizures had the best and worst responses to treatment, respectively (P-value=0.022). However, based on their MRI, the difference regarding abnormal findings was not statistically significant

(P-value 0.837) (Table 4).

The differences between EEG and MRI findings in those with focal-onset and impaired awareness seizures and those with focal-to-bilateral tonic-clonic seizures were also not statistically significant (P-value=0.772 and 0.317, respectively). The difference in EEG and MRI findings was also not statistically significant based on sex (P-values of 0.431 and 0.399, respectively). The difference in EEG findings in those with positive and negative family histories was also insignificant (P-value=0.718). However, the difference regarding abnormal MRI findings was statistically significant in the two groups (P-value=0.022) (Table 4).

No statistical significance was noted in the differences between the frequency of EEG findings of those with and those without developmental disorders (P-value=0.587). However, the MRI results revealed a statistical significance in those with developmental disorders (P-value=0.001) (Table 4).

The authors also divided the included cases into three age subgroups: below two years of age, between 2 and 12 years, and over 12. The difference in MRI findings in these subgroups was insignificant (P-value=0.246)(Table 5). However, evaluating the response to treatment based on the incidence of seizure episodes in the following six months revealed a significantly more inadequate response to treatment in those aged two years and below (P-value=0.001) (Table 6).

Table 1. Summary of Demographic and Clinical Data

Variable		Number of cases	Percent
Sex	Male	62	42.2
	Female	85	57.8
Family History	Positive	8	5.4
	Negative	139	94.6
Response to treatment	A positive incident of seizure in the following six months	31	21.1
	No incident of seizure in the following six months	116	78.9
Etiology	Idiopathic	130	88.4
	Symptomatic	12	8.2
	Cryptogenic	5	3.4
Type	Focal-onset with impaired awareness	108	73.5
	Focal-to-bilateral tonic-clonic	39	26.5

Variable		Number of cases	Percent
Anticonvulsant Used	Sodium Valproate	112	76.2
	Primidone	10	6.8
	Levetiracetam	9	6.1
	Carbamazepine	8	5.4
	Primidone and Sodium Valproate	4	2.7
	Primidone and Levetiracetam	4	2.7
Developmental Disorders	Positive	29	19.7
	Negative	118	80.3

Table 2. EEG and MRI Findings

Modality	Findings	Number of cases	Percentage
EEG	Occipital	73	49.7
	Frontal	56	38.1
	Temporal	18	12.2
MRI	Normal MRI	129	87.8
	Periventricular leukomalacia	6	4.1
	Gliosis	5	3.4
	Stroke-like lesions	2	1.4
	Demyelinating lesions	2	1.4
	Structural disorder Dandy-Walker	1	0.7
	Astrocytoma	1	0.7
	Venus anomaly	1	0.7

Table 3. Comparing the Mean Age of Onset for Seizures

Variables		Mean age of onset	p-value
Sex	Male	4.62±3.55	0.009
	Female	6.13±3.30	
Family History	Negative	5.70±3.45	0.001
	Positive	1.87±1.32	
Response to Treatment	Further Episodes of Seizure in the following six months	4.79±4.13	0.278
	No Episodes of Seizure in the following six months	5.68±3.28	
Etiology of Seizure	Idiopathic	5.96±3.39	0.001
	Symptomatic	1.87±1.52	
	Cryptogenic	1.88±1.49	
Type of Seizure	Focal-onset with impaired awareness	5.54±3.66	0.757
	Focal-to-bilateral tonic-clonic	5.34±2.95	
Developmental Disorders	Positive	1.83±1.27	0.001
	Negative	6.39±3.26	

Table 4. comparing the response to treatment and type of seizures based on MRI and EEG findings

Modality	Findings	Response to treatment			Type of Seizure	
		Further episodes of seizure in the following six months	No Further episodes of seizure in the following six months	p-value	Focal-onset with impaired awareness	Focal-to-bilateral tonic-clonic
EEG	Frontal	18 (58.1%)	38 (32.8%)	0.022	43 (39.8%)	13 (33.3%)
	Temporal	1 (3.2%)	17 (14.7%)		13 (12%)	5 (12.8%)
	Occipital	12 (38.7%)	61 (52.6%)		52 (48.1%)	21 (53.8%)
MRI	Normal	27 (87.1%)	102 (87.9%)	0.837	96 (88.9%)	33 (84.6%)
	Gliosis	2 (6.5%)	4 (3.4%)		5 (4.6%)	0
	Periventricular leukomalacia	0	2 (1.7%)		3 (2.8%)	3 (7.7%)
	Demyelinating lesions	0	1 (0.9%)		1 (0.9%)	1 (2.6%)
	Structural disorder Dandy-Walker	0	2 (1.7%)		1 (0.9%)	0
	Stroke-like lesions	0	1 (0.9%)		1 (0.9%)	1 (2.6%)
	Astrocytoma	0	1 (0.9%)		1 (0.9%)	0
	Venus anomaly	0	1 (0.9%)		0	1 (2.6%)

Table 5. Comparing the MRI Findings based on age group

Modality	**Finding**	**Age Group**			**p-value**
		Below two years	**2-12 years**	**Over 12 years**	
MRI	Normal MRI	7 (63.6%)	102 (87.9%)	20 (100%)	0.246
	Gliosis	2 (18.2%)	3 (2.6%)	0 (0)	
	Periventricular leukomalacia	1 (9.1%)	5 (4.3%)	0 (0)	
	Demyelinating lesions	0 (0)	2 (1.7%)	0(0)	
	Structural disorder Dandy-Walker	0 (0)	1 (9/0%)	0 (0)	
	Stroke-like lesions	1 (9.1%)	1 (0.9%)	0 (0)	
	Astrocytoma	0 (0)	1 (0.9%)	0 (0)	
	Venus anomaly	0 (0)	1 (0.9%)	0 (0)	

	Sex			Family History			Developmental Disorders		
p-value	Male	Female	p-value	Negative	Positive	p-value	Positive	Negative	p-value
0.772	20 (32.3%)	36 (42.4%)	0.431	54 (38.8%)	2 (25%)	0.587	11 (37.9%)	45 (38.1%)	0.587
	9 (14.5%)	9 (10.6%)		17 (12.2%)	1 (12.5%)		2 (6.9%)	16 (13.6%)	
	33 (53.2%)	40 (47.1%)		68 (48.9%)	5 (62.5%)		16 (55.2%)	57 (48.3%)	
0.371	52 (83.9%)	77 (90.6%)	0.399	123 (88.5%)	6 (75%)	0.022	18 (62.1%)	111 (94.1%)	0.001
	2 (3.2%)	3 (3.5%)		5 (3.6%)	0		5 (17.2%)	0	
	4 (6.5%)	2 (2.4%)		6 (4.3%)	0		5 (17.2%)	1 (0.8%)	
	2 (3.2%)	0		1 (0.7%)	1 (12.5%)		0	2 (7/1%)	
	0	1 (1.2%)		1 (0.7%)	0		1 (3.4%)	0	
	1 (1.6%)	1 (1.2%)		1 (0.7%)	1 (12.5%)		0	2 (1.7%)	
	1 (1.6%)	0		1 (0.7%)	0		0	1 (0.8%)	
	0	1 (1.2%)		1 (0.7%)	0		0	1 (0.8%)	

Table 6. Comparing the Response to Treatment Based on Age Groups

Response to treatment	**Age groups**			**p-value**
	Below two years	**2-12 years**	**Over 12 years**	
Positive History of repeats of episodes in the following 6 months	8 (72.7%)	19 (16.4%)	4 (20%)	0.001
No Repeat of Seizure episodes in the following 6 months	3 (27.3%)	97 (83.6%)	31 (21.1%)	

Discussion

Contrary to the current estimates and reports (10), the majority in this study were female. However, consistent with the mentioned estimates (10), Over 90% had no prior family history, and in over 80%, the seizures' etiology was idiopathic. The most common type of observed focal seizure was the focal onset with impaired awareness. The present study also found that the mean age of onset of the first seizure episode was significantly higher in female cases with no family history or developmental delays who suffered from idiopathic seizures. These findings were consistent with the mentioned estimates and prior studies (10, 20).

In Conclusion

This study demonstrated that the most abnormal EEG findings belonged to the occipital and frontal cortexes. However, only 12% of cases had abnormal MRIs. The latter contrasts with what has been reported, with previous data pointing towards higher accuracies (13, 21).

In addition, no statistical significance was noted regarding the response to treatment in many factors, bar age (younger than two years) among cases, demonstrating that timely diagnostic and therapeutic interventions and strict adherence to treatment regimens generally determine the outcome. As suggested by current guidelines[13], regarding the age subgroup differences, further diagnostic interventions (i.e., repeating MRIs, obtaining Prolonged EEG) must be undertaken in these age groups compared to others to detect possible underlying factors.

On EEG of those who suffered from further episodes in the following six months, frontal cortex changes were the most common finding, whereas, in those without any further episodes, the most common EEG changes belonged to the occipital cortex. The difference in the presence of these two findings compared to those without was statistically significant. However, no statistical significance could be noted when comparing the results based on the MRI findings, as most cases had normal MRIs. In addition, the differences between the groups regarding the findings in both modalities based on age, sex, family history, type of seizure, or the presence of developmental disorders revealed no statistical significance.

The current study showed that even though over 85% of patients had normal MRI results, abnormal EEGs were much more common, undermining the cost-effectiveness of obtaining an MRI. Furthermore, as those younger than two years of age less desirably respond to initial medical treatment, a more thorough workup to find the underlying lesion(s) at fault is recommended.

Ultimately, and with all the findings mentioned in mind, this study suffered from sample size limitations. In addition, the availability of more recent technological advances was left to be desired. Therefore, conducting studies with larger samples to evaluate and compare MRI and EEG results in those suffering from focal-onset seizures is suggested. Further evidence can optimistically presume that the results would greatly aid the scientific community regarding the suitability of each diagnostic modality and the criteria for further developing the guidelines. In addition, with the introduction of the HARNESS-MRI protocol in detecting epileptogenic foci (especially of the occipitofrontal origins), the authors still believe that seizures' etiologies, in general, must not be undermined. Therefore, future studies should investigate the subject further

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This study was approved by the Ethics Committee of Kerman University of Medical Sciences(Licensed under the code "IR.KMU.AH.REC.1398.001").

Author's contribution

Habibe Nejad Biglari: Data interpretation and critical revision of manuscript draft

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Conflicts of interest

The authors declare that no conflict of or competing interests existed or occurred in the conduction of this manuscript.

References

1. Nordli Jr DR, Pellock JM, Sankar R, Wheless JW. Pellock's Pediatric Epilepsy: Diagnosis and Therapy. Springer Publishing Company; 2016: 177-278..
2. Scheffer IE, Berkovic S, Capovilla G, et al. ILAE classification of the epilepsies: Position paper of the ILAE Commission for Classification and Terminology. Epilepsia. Apr 2017;58(4):512-521. doi:10.1111/epi.13709
3. Wirrell EC. Classification of Seizures and the Epilepsies. Epilepsy. 2021:11-22.
4. Camfield P, Camfield C. Incidence, prevalence and aetiology of seizures and epilepsy in children. Epileptic Disord. Jun 2015;17(2):117-23. doi:10.1684/epd.2015.0736
5. Thurman DJ, Beghi E, Begley CE, et al. Standards for epidemiologic studies and surveillance of epilepsy. Epilepsia. Sep 2011;52 Suppl 7:2-26. doi:10.1111/j.1528-1167.2011.03121.x
6. Nordli DR, Jr. Infantile seizures and epilepsy syndromes. Epilepsia. 2002;43 Suppl 3:11-6. doi:10.1046/j.1528-1157.43.s.3.4.x
7. Barkovich AJR, Charles. Pediatric Neuroimaging. 6th ed. Lippincott Williams & Wilkins (LWW); 2018.
8. Aneja S, Jain P. Refractory Epilepsy in Children. The Indian Journal of Pediatrics. 2014/10/01 2014;81(10):1063-1072. doi:10.1007/s12098-014-1533-1
9. Hauser WA, Beghi E. First seizure definitions and worldwide incidence and mortality. Epilepsia. 2008;49 Suppl 1:8-12. doi:10.1111/j.1528-1167.2008.01443.x
10. Beghi E. The Epidemiology of Epilepsy. Neuroepidemiology. 2020;54(2):185-191. doi:10.1159/000503831
11. Russ SA, Larson K, Halfon N. A national profile of childhood epilepsy and seizure disorder. Pediatrics. Feb 2012;129(2):256-64. doi:10.1542/peds.2010-1371
12. Gavvala JR, Schuele SU. New-Onset Seizure in Adults and Adolescents: A Review. Jama. Dec 27 2016;316(24):2657-2668. doi:10.1001/jama.2016.18625
13. Bernasconi A, Cendes F, Theodore WH, et al. Recommendations for the use of structural magnetic resonance imaging in the care of patients with epilepsy: A consensus report from the International League Against Epilepsy Neuroimaging Task Force. Epilepsia. Jun

2019;60(6):1054-1068. doi:10.1111/epi.15612
14. Hur YJ. Guideline for advanced neuroimaging in pediatric epilepsy. Clin Exp Pediatr. 2020;63(3):100-101. doi:10.3345/cep.2019.01403
15. Drenthen GS, Jansen JFA, Gommer E, et al. Predictive value of functional MRI and EEG in epilepsy diagnosis after a first seizure. Epilepsy Behav. Feb 2021;115:107651. doi:10.1016/j.yebeh.2020.107651
16. Shinnar S, O'Dell C, Mitnick R, Berg AT, Moshe SL. Neuroimaging abnormalities in children with an apparent first unprovoked seizure. Epilepsy research. 2001;43(3):261-269.
17. Rauch DA, Carr E, Harrington J. Inpatient brain MRI for new-onset seizures: utility and cost effectiveness. Clin Pediatr (Phila). Jun 2008;47(5):457-60. doi:10.1177/0009922807313766
18. Berg AT, Testa FM, Levy SR, Shinnar S. Neuroimaging in children with newly diagnosed epilepsy: a community-based study. Pediatrics. 2000;106(3):527-532.
19. Stevens CE, Stafstrom CE. Pharmacotherapy for Focal Seizures in Children and Adolescents. Drugs. 2018/09/01 2018;78(13):1321-1337. doi:10.1007/s40265-018-0959-6
20. Rizvi S, Ladino LD, Hernandez-Ronquillo L, Téllez-Zenteno JF. Epidemiology of early stages of epilepsy: Risk of seizure recurrence after a first seizure. Seizure. 2017/07/01/2017;49:46-53. doi:https://doi.org/10.1016/j.seizure.2017.02.006
21. Ho K, Lawn N, Bynevelt M, Lee J, Dunne J. Neuroimaging of first-ever seizure: contribution of MRI if CT is normal. Neurology: Clinical Practice. 2013;3(5):398-403.