

Interictal Electroencephalography (EEG) Findings in Children with Epilepsy and Bilateral Brain Lesions on Magnetic Resonance Imaging (MRI)

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ABSTRACT

Introduction: Neuroimaging procedures and electroencephalography (EEG) are basic parts of investigation of patients with epilepsies. **Aim:** The aim is to try to assess relationship between bilaterally localized brain lesions found in routine management of children with newly diagnosed epilepsy and their interictal EEG findings. **Patients and methods:** Total amount of 68 patients filled criteria for inclusion in the study that was performed at Neuropediatrics Department, Pediatric Hospital, University Clinical Center Sarajevo, or its outpatient clinic. There were 33 girls (48,5%) and 35 boys (51,5%). Average age at diagnosis of epilepsy was 3,5 years. **Results:** Both neurological and neuropsychological examination in the moment of making diagnosis of epilepsy was normal in 27 (39,7%) patients, and showed some kind of delay or other neurological finding in 41 (60,3%). Brain MRI showed lesions that can be related to antenatal or perinatal events in most of the patients (ventricular dilation in 30,9%, delayed myelination and post-hypoxic changes in 27,9%). More than half of patients (55,9%) showed bilateral interictal epileptiform discharges on their EEGs, and further 14,7% had other kinds of bilateral abnormalities. Frequency of bilateral epileptic discharges showed statistically significant predominance on level of $p < 0,05$. Cross tabulation between specific types of bilateral brain MRI lesions and EEG finding did not reveal significant type of EEG for assessed brain lesions. **Conclusion:** We conclude that there exists relationship between bilaterally localized brain MRI lesions and interictal bilateral epileptiform or nonspecific EEG findings in children with newly diagnosed epilepsies. These data are suggesting that in cases when they do not correlate there is a need for further investigation of seizure etiology.

Key words: interictal EEG, bilateral lesions, brain MRI, children.

1. INTRODUCTION

Electroencephalography (EEG) is important supplementary examination method in the investigation of neurological disorders, primarily epilepsies. Abnormal EEG findings include ictal patterns (observed during an epileptic ictal event), interictal epileptiform activity (observed in-between seizures) and non-epileptiform abnormalities (1). In management of children with epilepsies ictal EEG would be preferable, since it can provide various data about localization and spreading of epileptic discharges, but in real life routine diagnostics and follow up of these patients it is usually difficult to obtain. That is why we rely mainly on interictal EEGs. Interictal epileptiform activities, characterized by the presence of spikes and sharp waves, in combination or not with slow waves are strongly associated with epilepsy. The interictal EEG

serves several purposes that can aid in diagnosing epilepsy and can be examined for a specific epileptiform abnormality, the interictal spike or sharp wave. These discharges may be either generalized or focal in distribution and interictal EEG helps classify whether a focal or generalized seizure disorder is present (2). EEG does not provide sufficient specificity to determine the etiology of the brain dysfunction, so our best tool for that is magnetic resonance imaging (MRI).

Bilateral brain lesions, as interpreted by MRI, are common finding in children. Etiology of these changes is different, probably most of these findings, especially if found in thalamus and basal ganglia, are result of perinatal events, such as birth asphyxia, but can be also part of prenatal infections, and hereditary degenerative neurometabolic disorders etc. Antepartum

events have been associated with fetal brain injury and may contribute to later neurological sequelae (3) such as seizures. Acute and progressive brain disorders can result in bilateral symmetrical brain lesions, as seen on MRI. Primary acute causes include hypoxic-ischemic injury, infection, autoimmune disorders and toxic encephalopathy. Subacute or progressive pathologies are usually neurodegenerative and/or metabolic in nature (4).

Those lesions are often periventricular, which can be result of periventricular leukomalacia, especially in preterm children (5), with consequent dilatation of lateral ventricles as seen in older children. Bilateral periventricular white matter changes are often finding (6). The typical MRI pattern in such lesions is distribution of hyperintensity in the ventrolateral thalamus and the posterior part of nucleus lentiformis.

Aim of this study is to assess relationship between interictal EEG findings in children with newly diagnosed epilepsy and bilateral brain MRI lesions as seen on MRI.

2. MATERIALS AND METHODS

This survey assessed the population of patients aged from 1 month to 18 years of age, who were diagnosed as epilepsy or some of the epileptic syndromes according to International Classification of Diseases (ICD-10) code G40 (7), using criteria set by International League Against Epilepsy–ILAE (8,9), in four year period 2011–2014. The diagnosis was made at Neuropediatric Department, Pediatric Hospital, University Clinical Center Sarajevo, or its outpatient clinic. Out of investigated patients with epilepsy, 68 fulfilled criteria for inclusion in the study, age, newly diagnosed epilepsy, bilaterally localized lesion on MRI that was done within 6 months of diagnosis of epilepsy.

Each child had physical and neurological examination, done according to age of a child; we assessed mental status, motor function and balance, sensorium, newborn and infant reflexes in children less than 1 year, muscle stretch reflexes and cranial nerves examination according to age of a child. Examinations were done by child neurologists with special expertise in epilepsy.

Each child had a standard MRI scan with at least T1 and T2, sequences performed at the time of establishing diagnosis of epilepsy, or within the period of 6 months. MRI scans was done by 1.5 or 3.0 Tesla units scanner. Trained neuroradiologists interpreted results of brain MRI by visual analysis.

EEGs were done interically with electrodes positioned on scalp according to international 10.20 system, on Deymed TrueScan, and Schwarzer neurology systems, using 21 channel system, and reformatting to standard montages. EEG registrations were done as awake routine (20–30 minutes of registration), sleep routine (30–45 minutes), and sleep deprivation (30–45 minutes after at least 6 hours of night sleep deprivation). Children with normal finding on initial EEG registration had repeated registrations; those who had persistent normal findings had serial EEG registrations. The EEG was interpreted by three consultant child neurologist that are authors, trained and experienced in electrophysiological studies.

For statistical purposes interictal scalp EEG findings were classified as normal, non specifically changed (non-specific slowing), bilateral, unilateral epileptic discharges, or hypsar-

rhythmia. Bilateral epileptic discharges on EEG with clear predomination on one side were classified as unilateral, as well as clear focal discharges, while generalized, semi generalized and synchronous bilateral discharges without clear predomination on one side were classified as bilateral discharges.

Upon completion of survey, data were analyzed with standard statistical methods using MS Excel (Microsoft Office Excel 2010) and SPSS for statistical analysis (Statistical Package for Social Sciences, SPSS Inc., Chicago, Illinois, USA), version 22.0. Descriptive statistics and chi-square test were used as a measure of relationship, and data were found to be statistically significant at the level of $p < 0.05$. The results are presented in tables and graphs.

3. RESULTS

Our investigated sample consisted of 68 patients. There were 33 (48,5%) female children and 35 (51,5%) male. Average age at diagnosis of epilepsy was 3,56 years (std. dev. 3.941, age range 3 months to 17 years, median 2 years). Age distribution at diagnosis of epilepsy is shown on Figure 1.

Both neurological and neuropsychological examination in the moment of making diagnosis of epilepsy was normal in 27 (39,7%) patients, and showed some kind of delay or other neurological finding in 41 (60,3%).

EEG findings at diagnosis of epilepsy in selected group of patients with bilateral brain MRI lesions are shown on Figure 2.

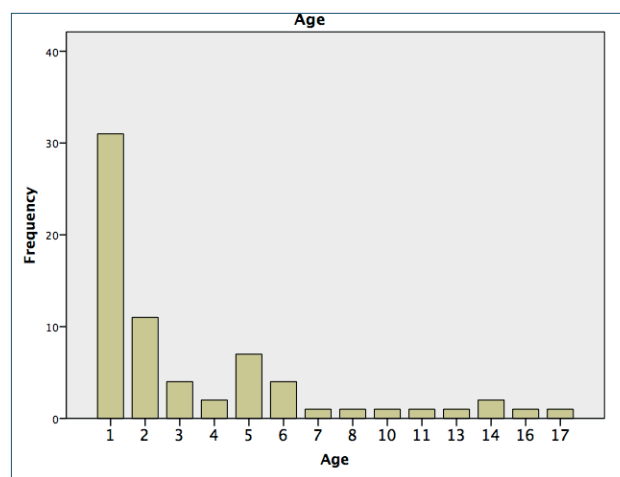


Figure 1. Age distribution at diagnosis of epilepsy

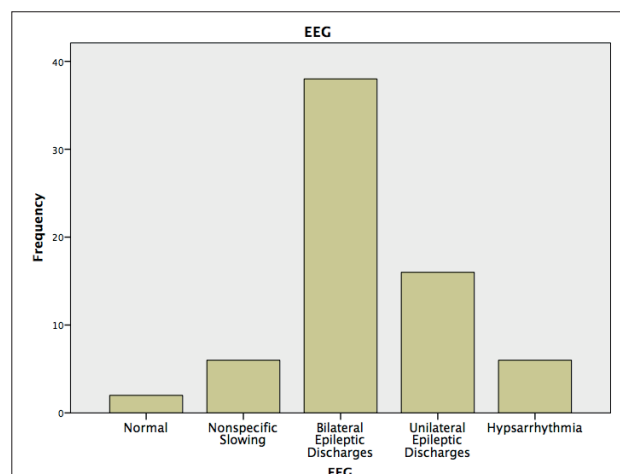


Figure 2. EEG findings in a selected group of patients with bilateral brain MRI lesions

Type of Lesion	No.	%
Bilateral Posttraumatic Lesions	2	2.9
Leucomalacia	4	5.9
Delayed Myelination & Post-hypoxic Changes	19	27.9
Bilateral Atrophy	8	11.8
Tuberous Sclerosis	2	2.9
Ventricular Dilatation	21	30.9
Bilateral Congenital Anomalies	3	4.4
Diffuse white matter abnormalities	5	7.4
Leukodystrophy	3	4.4
Megalencephaly	1	1.5
Total	68	100.0

Table 1. Type of bilateral MRI lesions in selected group of patients

	EEG					Total
	Normal	Nonspecific Slowing	Bilateral Epileptic Discharges	Unilateral Epileptic Discharges	Hypsarrhythmia	
Bilateral Posttraumatic Lesions	0	0	1	1	0	2
Leucomalacia	0	0	2	2	0	4
Delayed Myelination & Post-hypoxic Changes	0	2	13	4	0	19
Bilateral Atrophy	2	0	3	3	0	8
Tuberous Sclerosis	0	0	0	2	0	2
Ventricular Dilatation	0	4	14	1	2	21
Bilateral Congenital Anomalies	0	0	1	1	1	3
Diffuse white matter abnormalities	0	0	2	1	2	5
Leukodystrophy	0	0	1	1	1	3
Megalencephaly	0	0	1	0	0	1
Total	2	6	38	16	6	68

Table 2. MRI results versus EEG findings, cross tabulation

Frequency of bilateral epileptic discharges showed statistically significant predominance over other types on level of $p < 0.05$.

Neuroradiologists described several types of bilateral MRI lesions in patients with newly diagnosed epilepsies, and their frequencies are shown on Table 1.

When we compared results of EEG findings with type of brain MRI bilateral lesions we got data that are shown on Table 2.

There was no significant correlation between above values ($p = 0.09$).

4. DISCUSSION

Epileptic seizures are the most frequent manifestation of neurological impairment in the pediatric population. Diagnosis of epilepsy is based on them, and is supplemented with EEG recording, which can help us in seizure classification and establishing epilepsy syndrome, since each antiepileptic drug has relative specificity for clinical and EEG seizure patterns. Brain MRI can help us in establishing etiological diagnosis of epilepsy, as well as providing prognostic information, and directing treatment in children with recently diagnosed epilepsy. In our study we wanted to assess relationship between interictal EEG findings in children with newly diagnosed epilepsy and bilateral brain MRI lesions as seen on MRI.

Our sample consisted of 68 patients aged from 3 months to 17 years, with average age of diagnosis of epilepsy around 3,5 years, and almost equal gender distribution, which was something that we expected, but we must emphasize that mean age at diagnosis was much younger than in some other studies (10) which did not have selected sample of children with bilateral MRI lesions at time of diagnosis of epilepsy. We assume that this type of brain lesions that was inclusion

criterion in our study is probably manifested earlier in the life of children with seizures, since most of them had brain lesion prenatally.

In our sample some kind of neurodevelopmental delay or other neurological finding was present in 60% of patients which was quite high, and among those were children with mild, as well as severe clinical manifestations. Some studies have found that female gender, early onset, longer duration and abnormal interictal EEG have a negative effect on neuropsychological performance in children with temporal lobe epilepsy, and that children with early-onset epilepsy should be assessed carefully for neuropsychological impairment using sufficiently broad batteries of tests in order to detect even slight deficits (11).

Bilateral lesions seen on brain MRI often originate from prenatal period. They are associated with lower potential for functional plasticity and with worse outcome than unilateral brain lesions (12). Bilateral hemispheric lesions in early periods of development are commonly associated with epilepsy and represent one of the major neuropathologic conditions acquired in the pre- and perinatal periods (13). Most common types of lesions found in our study were delayed myelination, posthypoxic changes, ventricular dilatation and brain atrophy. They were probably in largest extent part of prenatal and perinatal events, and are supporting Volpe's notion. It is also well known that bilateral brain lesions may be induced by seizure activity, especially in cortical/subcortical regions, basal ganglia, white matter, corpus callosum, cerebellum and hippocampus (14) and are reversible in some cases, but we think that brain lesions in our group of patients, since they were newly diagnosed epilepsy could be part of this process only in small number of cases. This also has to be further investigated because some of recent studies are claiming that a single or a cluster of seizures cannot only induce transient, variably reversible MRI brain abnormalities, but also irreversible changes (15).

It would be expected that EEG changes in patients with such brain lesions should mainly be bilateral, and in our study 55,9% of patients had bilateral epileptiform discharges on interictal EEG recordings. That means that, together with 4 of 6 patients with nonspecific slowing on interictal EEG and six patients with hypsarrhythmia, about seventy percent of cases in our group were having bilateral interictal changes on EEG. Explanation for more than a quarter of patients in our group with clearly focal EEG abnormalities can be found in fact that certain patients diagnosed initially as having primary generalized tonic-clonic seizures with no clinical or EEG findings to indicate focal onset can develop to focal at a later time, fact that indicates need for periodic reassessment of seizure patients, especially if seizures remain frequent (16). Also, it must be emphasized that it would be hard to assume that all bilateral brain abnormalities seen on MRI have epileptogenic potentials, and probably some of MRI findings in our group are not really a cause of epilepsy in certain patient, but are coincidental. For instance, delayed myelination as a cause of epilepsy is often described in patients with metabolic diseases (17), and we had patients without signs of neurometabolic disease. Children younger than 2 years require special sequences at MRI, as immature myelination affects the ability to identify common causes of epilepsy (18), which

can also show variation in interictal EEG findings. For all of those cases we think that further investigation of etiology of epileptiform discharges is needed, especially in cases of resistance to antiepileptic drugs, and exploring possibilities of epilepsy surgery. In our study we were not able to establish statistically significant relationship between certain type of bilateral brain MRI changes and characteristic EEG finding.

5. CONCLUSION

Our data are showing that there exists relationship between bilaterally localized brain MRI lesions and interictal bilateral epileptiform or nonspecific EEG findings in children with newly diagnosed epilepsies. These data are suggesting that in cases when they do not correlate there is a need for further investigation of seizure etiology, as well as possibilities for epilepsy surgery in patients with seizures refractory to antiepileptic drugs therapy.

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES

- Schaal N. The fundamental neural mechanisms of electroencephalography. *Electroencephalogr Clin Neurophysiol* 1998; 106: 101-107.
- Pillai J, Sperling MR. Interictal EEG and the diagnosis of epilepsy. *Epilepsia*. 2006; 47 Suppl 1: 14-22.
- Scher MS, Belfar H, Martin J, Painter MJ. Destructive brain lesions of presumed fetal onset: antepartum causes of cerebral palsy. *Pediatrics*. 1991; 88(5): 898-906.
- Zuccoli G, Yannes MP, Nardone R, Bailey A, Goldstein A. Bilateral symmetrical basal ganglia and thalamic lesions in children: an update (2015). *Neuroradiology* 2015; 57(10): 973-989.
- Krägeloh-Mann I, Toft P, Lunding J, Andresen J, Pryds O, Lou HC. Brain lesions in preterms: origin, consequences and compensation. *Acta Paediatr*. 1999 Aug; 88(8): 897-908.
- Krägeloh-Mann I, Helber A, Mader I, Staudt M, Wolff M, Groenendaal F, DeVries L. Bilateral lesions of thalamus and basal ganglia: origin and outcome. *Dev Med Child Neurol*. 2002 Jul; 44(7): 477-484.
- World Health organization . International Statistical Classification of Diseases and Related Health Problems 10th Revision. <http://apps.who.int/classifications/icd10/browse/2015/en>
- Commission on Classification International League Against Epilepsy. Proposed provisions of clinical and electroencephalographical classification of epileptic seizures. *Epilepsia*. 1981; 22: 489-501.
- Commission on Classification and Terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia*. 1989; 30(4): 389-399.
- Moffat C, Dorris L, Connor L, Espie CA. The impact of childhood epilepsy on quality of life: a qualitative investigation using focus group methods to obtain children's perspectives on living with epilepsy. *Epilepsy Behav* 2009; 14(1): 179-189.
- Mankinen K, Harila MJ, Rytty SI, Pokka TM, Rantala HM. Neuropsychological performance in children with temporal lobe epilepsy having normal MRI findings. *Eur J Paediatr Neurol*. 2014 Jan; 18(1): 60-65.
- Hadders-Algra M. Early diagnosis and early intervention in cerebral palsy. *Frontiers in Neurology*. 2014; 5: 9-21.
- Volpe JJ. *Neurology of the newborn*. Philadelphia: Saunders, 1995: 314-369.
- Cianfoni A, Caulo M, Cerase A, Della Marca G, Falcone C, Di Lella GM, Gaudino S, Edwards J, Colosimo C. Seizure-induced brain lesions: a wide spectrum of variably reversible MRI abnormalities. *Eur J Radiol*. 2013 Nov; 82(11): 1964-1972.
- Xiang T, Li G, Liang Y, Zhou J. A wide spectrum of variably periictal MRI abnormalities induced by a single or a cluster of seizures. *J Neurol Sci*. 2014; 343(1-2): 167-172.
- Weisberg LA, Garcia C, Strub R. *Essentials of Clinical Neurology: Seizures and Epilepsy*. www.psychoneuro.tulane.edu/neurolect/
- Thomas B, Al Dossary N, Widjaja E. MRI of childhood epilepsy due to inborn errors of metabolism. *AJR Am J Roentgenol*. 2010; 194(5): W367-374.
- Gaillard WD, Chiron C, Cross JH, Harvey AS, Kuzniecky R, Hertz-Pannier L, Vezina LG; ILAE, Committee for Neuroimaging, Subcommittee for Pediatric. Guidelines for imaging infants and children with recent-onset epilepsy. *Epilepsia*. 2009; 50(9): 2147-2153.