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EC EMERGENCY MEDICINE AND CRITICAL CARE
Case Series

Electroclinical Study of Neonate, Infant and Young Epileptic Patients

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Received: October 06, 2022; **Published:** December 26, 2022

Abstract

We have electroclinical examined 59 patients from three months old neonate patients to nineteen years old young patients. The following types of non ictal EEGs were observed, such as generalized slow waves, acute generalized waves, outbreak of paroxysmal median voltage spikes, spikes and large amplitude medium waves, and multifocal epileptogenic paroxysmal activity. Seven cases showed normal EEG.

We diagnosed the following epileptic types: One traumatic epilepsy, two epileptic absence types, fifteen cases of Lennox-Gastaut syndrome, ten cases of Rolandic Epilepsy, twenty seven cases of Landau-Kleffner syndrome. In addition, we have found 15 idiopathic generalized epilepsy, two tonic epilepsy type, one metabolic epilepsy, one epilepsy post Chikungunya viral infection, three myoclonic epilepsies, and one infant spasm. NMR images showed the extent and damage of epileptic network: enlargement of frontal horns, prominent cisterns and grooves, bilateral frontal meningitis thickening with right frontal subdural collection, periventricular gliosis, brain atrophy, deep cortical grooves, ventricular enlargement of posterior horns, hyperintense periventricular and supraventricular areas in relationship with leukomalacia foci.

Keywords: *Neonate; Infant; Young; Electroclinical Study; EEG; Lennox-Gastaut Syndrome*

Introduction

In each case of a patient suffering with epilepsy three diagnoses have to be made: the diagnosis of the seizure-type, the diagnosis of the epilepsy-type, the diagnosis of the etiology [1]. In clinical practice, the diagnosis of focal vs generalized epilepsy dictates the management of the patient. The distinction is at times imperfect and some epilepsies have features that fall in between these two extremes. An overlap of focal and generalized epileptiform abnormalities may support a continuum between focal and generalized epilepsy [2]. An International League Against Epilepsy task force proposed that the seizure type is typically determined by the predominant clinical feature and is classified into motor or non-motor presentations. Neonatal seizures are exclusively of focal onset (Okumura, 2020).

Neonatal seizures occur in their majority in close temporal relation to an acute brain injury or systemic insult and are accordingly defined as acute symptomatic or provoked seizures. However less frequently, unprovoked seizures may also present in the neonatal period as secondary to structural brain abnormalities, thus corresponding to structural epilepsies, or to genetic conditions [3].

In the present study we have examined 59 neonates, infant and young patients with focal and generalized epilepsy by means of conventional interictal EEG and NMR images in order to establish the identification of epileptic syndromes, the seizure type, and the damage of epileptic networks.

Material and Methods

59 neonate, infant and young patients ranging from three months old to seventeen years old were clinically studied at the Outpatient Clinical Unit of Biological Research Institute at the San Rafael Clinical Home in Maracaibo. Venezuela. This study was carried out according to the Principles of Helsinki Declaration for Research in Human Beings, The American Academy of Pediatrics (AAP) and the European expert opinion, 2007 [4].

Results and Case Reports

Case 1: YG. 14 years old. M. Three tonic generalized convulsions, loss of consciousness and epigastric pain, ovarian cyst and renal lithiasis. Mother with high blood pressure. EEG showed diffuse slow waves. NMR images showed isolated focus in left semioval center of doubtful pathological significance and NMR images showed hypertrophic adenoids. Diagnosed as idiopathic generalized epilepsy. Patient treated with carbamazepine.

Case 2: JM. Fifteen years old. F. Generalized febrile epilepsy and loss of consciousness. Family history of epilepsy. Genetic epilepsy. EEG showed generalized slow waves. Landau-Kleffner syndrome. Patient treated with valproic acid.

Case 3: MC, Seven years old. F. Generalized epilepsy, perinatal hypoxia, language disorders, cognitive deficit, attention and learning deficit. EEG showed generalized slow waves. Electroclinical data suggest Landau-Kleffner syndrome. Patient treated with valproic acid.

Case 4: YE. Sixteen years old. F. Generalized epilepsy. Convulsive syndrome since three years old, and hypoglycemia. First normal EEG in 2016. In EEG 2019 generalized slow waves projected to all cerebral regions. In December 2005 presented status epilepticus and viral infection. Metabolic epilepsy. Patient treated with valproic acid.

Case 5: NW. Fourteen years old. M. Generalized epilepsy. Patient with viral meningoencephalitis and status epilepticus, mental retardation, and language disorders. Surgically intervened at frontal region. He has presented absence episodes by two or three seconds, facial tic and sleep disorders. Restless patient with involuntary arm and leg movements. More recently neurobehavioral disorders. The EEG showed slow diffuse waves delta and theta. Betha frequency of medium voltage, medium- and high-voltage spike-wave discharges in right brain hemisphere. Electroclinical findings suggest Landau Kleffner syndrome. TAC images showed enlargement of frontal horns, prominence of cisterns and grooves, bilateral meningofrontal thickening with right frontal subdural collection. Patient treated with valproic acid, piracetam, lamotrigine and phenobarbital.

Case 6: DP.M. Eleven years old. Patient with two generalized convulsive episodes, EEG 2016 showed acute generalized waves. Hyperactivity and attention and learning deficits. EEG 2019 generalized paroxysmal activity and slow waves in left frontal, parietal center and superior frontal region. The electroclinical data suggested Lennox-Gastaut syndrome. Patient treated with lamotrigine.

Case 7: BFR. M. Twelve years old. M. Patient with hypoxic ischemic encephalopathy. Presented three convulsive generalized episodes in December 2019, and in January 13th and 23rd. EEG showed slow delta and theta waves. The electroclinical data suggest Lennox-Gastaut syndrome. Patient treated with valproic acid and carbamazepine.

Case 8: EO. F. Ten years old. Patient with two generalized convulsive episodes, cognitive and learning deficits, and epigastric pain. EEG showed outbreak of generalized acute waves. The electroclinical date suggest Landau-Kleffner syndrome. Normal NMR images. Patient treated with carbamazepine.

Case 9: EM. F. Fourteen years old. Patient onset seizures at 5 years old. Received carbamazepine, in a second convulsive episode received oxicodal and clonac. The patient did not presented convulsive episodes for six years. EEG-2009 showed outbreak of paroxysmal median voltage spikes in medial and anterior regions of both hemispheres. EEG 2011: Paroxysmal activity in right parietal center. EEG 2016 diffuse slow alpha waves. Without medication during four month. Patient seizure free and epilepsy process apparently stabilized. Patient classified as Landau-Kleffner epilepsy. Patient treated with valproic acid and carbamazepine.

Case 10: EA. F. Fifteen years old. Patients with focal convulsive crisis, occipital headache, precordial pain. EEG 2016 showed paroxysmal activity in temporal region. Electroclinical details suggested Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 11: YV. F. Patient seventeen years old with perinatal hypoxia. Mother with twin pregnancy. First generalized febrile seizure at three years old and normal EEG. At ten year old convulsive episode without fever. Received trileptal. A third generalized convulsive tonic episode and EEG with spikes and large amplitude medium waves seizure in October 2019. The electroclinical data suggested Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 12: SL. M, Sixteen years old. F. Patient with generalized epilepsy, perinatal hypoxia, aggressiveness, language disorders, cognitive deficit, headache and sexual arousal. EEG 2013 showed left temporal paroxysmal activity and asymmetric pattern lateralized to right cerebral hemisphere. Electroclinical data suggest Rolandic epilepsy. MNR image showed gliosis focal temporal. Patient treated with valproic acid, carbamazepine and pregabaline.

Case 13: JC. Sixteen years old. F. Patient with focal epilepsy, mental retardation, language disorders. EEG 2018 showed focal moderate paroxysmal activity. Family history of neurobehavioral disorders. Electroclinical data suggest Landau-Kleffner syndrome. Patient treated with valproic acid.

Case 14: SB. Thirteen years old. M. Patient with generalized epilepsy, perinatal hypoxia, hyperactivity and aggressiveness. EEG showed generalized paroxysmal activity. Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 15: SV. F. Thirteen years old. Patient with focal febrile seizure at one year old. Received phenobarbital and valproic acid. Second focal convulsive episode with transitory loss of consciousness at seven years old. Received kopodex. A third convulsive episode without antiepileptic treatment. In 2017 the patient improved from the clinical point of view with the treatment. Normal EEG and normal NMR images. Idiopathic epileptic syndrome. Patient treated with carbamazepine and valproic acid.

Case 16: EA. Fifteen years old. F. Patient with generalized convulsive syndrome, loss of consciousness, brain trauma with fall to the ground and blow to occipital region. Lately frequent nocturnal convulsions and loss of memory. Normal EEG 2017. NMR image showed periventricular gliosis. Patient diagnosed as traumatic epilepsy. Received carbamazepine and valproic acid.

Case 17: JSV. Seventeen years old. M. Patient with history of two focal convulsive episodes at 4 and 7 years old. Normal EEG. Idiopathic generalized epilepsy. Patient did not received antiepileptic treatment.

Case 18: SC. Fourteen years old. M. Patient with history of fourteen generalized convulsive episodes, language disorders, inversion of the sleep-wake cycle and excessive use of TV and cell phone. EEG showed paroxysmal generalized activity to all brain regions. Family history of epilepsy and neurobehavioral disorders. Landau-Kleffner syndrome. Genetic epilepsy. Patient treated with carbamazepine and valproic acid.

Case 19: FZ. Four months old. M. Neonate with frequent generalized convulsive syndrome since one month old. Mother with smoke and alcoholic habits. Distocic delivery. Severe perinatal hypoxia, microphthalmia bilateral and iris coloboma. Atonic cervical muscle and lateral head deviation. Dysmetria lower limbs. EEG showed outbreak of generalized slow waves. Patient diagnosed as Lennox-Gastaut syndrome. Patient treated with carbamazepine and valproic acid.

Case 20: GG. Four years old. M. Patient with generalized convulsive syndrome since 15 days ago. Severe perinatal hypoxia, persistent headache day and night, dizziness, hyperactivity and attention deficit, and psychomotor retardation. EEG showed diffused and slow alpha rhythm 5 - 6 HZ considered as minor brain dysfunction. Idiopathic generalized epilepsy. Patient treated with valproic acid.

Case 21: MN. Three years old. M. Patient with hyperactivity and attention deficit. Sleep disorders and nocturnal body jerks. EEG showed generalized outbreak of slow waves. Patient classified as Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 22: SS. Four years old. F. Patient with sclerosis tuberous, hypochromic skin spots and cardiac myxoma, infant spasms and drowsiness. Hospitalized during 15 day. EEG showed focal slow wave activity in left temporal region. Landau-Kleffner syndrome. Patient treated with valproic acid and lamotrigine.

Case 23: JS. Four years old. M. Patient with absence type epilepsy, sleep disorders, hyperactivity and attention deficit, EEG showed outbreak of generalized slow waves. Patient treated with valproic acid.

Case 24: ED. 5 years old. F. Patient with repetitive absence type epileptic episodes. EEG showed outbreak of slow waves projected to all brain regions. Patient classified as Lennox-Gastaut syndrome. Family history of epilepsy. Genetic epilepsy. Mother with toxoplasmosis during first trimester pregnancy. Patient treated with valproic acid.

Case 25: IB. Four years old. F. Patient with repetitive absence type epileptic episodes, sleep disorders and hyperactivity and attention deficit. EEG showed outbreak of slow waves projected to all brain regions. Landau-Kleffner syndrome. Patient treated with valproic acid.

Case 26: SC. Twelve years old. M. Patient with generalized myoclonic convulsive syndrome during three years. EEG showed paroxysmal and slow waves generalized activity. Patient treated with valproic acid.

Case 27: LC. Five years old. F. Patient with traumatic epilepsy after fall, loss of consciousness during one hour. EEG showed generalized outbreak of slow waves. NMR normal brain images. Traumatic epilepsy. Patient treated with valproic acid.

Case 28: MD. Three years old. F. Patient with generalized tonic convulsive syndrome, and loss of consciousness since four months ago. Normal EEG. Patient treated with valproic acid. Idiopathic generalized epilepsy.

Case 29: SD. Eight years old. M. Patient with four partial convulsive syndrome at night since 6 months old. Mother with partial placental abruption. Perinatal hypoxia, psychomotor retardation. EEG 2012 showed frontal, parietal and occipital center paroxysmal activity in both hemispheres. Myoclonic epilepsy. NMR images showed brain atrophy, deep cortical grooves, ventricular enlargement of posterior horns. Patient treated with valproic acid and clonazepam.

Case 30: AC. Five years old. F. Premature patient, perinatal hypoxia. Spastic paresis of lower limbs. Generalized convulsive syndrome since 18 months old. EEG showed multifocal epileptogenic paroxysmal activity. Myoclonic epilepsy. Patient treated with valproic acid.

Case 31: SSP. Three years old. F. Patient with generalized convulsive syndrome. Mother with renal lithiasis and urinary infection. EEG showed outbreak of generalized slow waves in all brain regions. Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 32: RL Three months old. M. Patient with severe perinatal hypoxia hospitalized during 27 days. Three generalized atonic convulsive syndromes, cervical atonic muscles and head deviation, and abnormal sleep. EEG showed asynchronous sigma activity in parietal region, hypnic activity sketch and vertex central waves. Landau-Kleffner syndrome. Patient treated with phenobarbital and valproic acid. Idiopathic generalized epilepsy.

Case 33: AR. Nine months old. F. Patient with generalized convulsive syndrome since 5 months old. Hospitalized during 15 days by bacterial meningitis, and acute febrile diarrhea. EEG showed outbreak of generalized slow waves. NMR images showed small periventricular intensities. Mother with preeclampsia and high blood pressure. Patient treated with carbamazepine and valproic acid. Postmeningitic epilepsy.

Case 34: MR. Nine years old. F. Generalized tonic convulsive syndrome, perinatal hypoxia by double circular of umbilical cord. EEG showed outbreak of generalized slow waves. Patient treated with valproic acid. Idiopathic generalized epilepsy.

Case 35: AS. One year and seven months old. F. Generalized convulsive syndrome. Hyperactivity, language disorders, and moderate involuntary movements. Normal EEG. Patient treated with diazepam and valproic acid. Idiopathic generalized epilepsy.

Case 36: VD. 10 years old. M. Patient with generalized convulsive syndrome. Perinatal hypoxia by double circular of umbilical cord. Hyperexcitability. EEG 2014 showed multiple hyperexcitable focus in frontal, parietal and temporal regions. Lennox–Gastaut Syndrome. Mother with diabetes and high blood pressure. Patient with normal EEG and stabilized epileptic syndrome after receiving valproic acid and neurontin.

Case 37: KM. Neonate 5 day old. F. Generalized convulsive syndrome. Left eye strabismus. EEG outbreak of acute waves in all brain regions. Patient treated with valproic acid. Idiopathic generalized epilepsy.

Case 38: MC. Two years old. F. Generalized convulsive syndrome. EEG showed paroxysmal activity in all brain regions. Idiopathic generalized epilepsy. Patient treated with valproic acid.

Case 39: SP. 11 years old. M. Generalized convulsive syndrome. Hypoglycemia. Patient pale and sweaty. EEG showed paroxysmal activity in left temporal region. NMR images showed diminished callosal region and enlargement of ventricular posterior horns. Metabolic epilepsy. Rolandic epilepsy. Patient treated with carbamazepine and valproic acid.

Case 40: TG. 10 years old. M. Four generalized convulsive syndromes. Chikungunya viral infection two years ago. EEG showed paroxysmal activity in left frontotemporal regions projected bilaterally to contralateral areas. Rolandic epilepsy. Patient treated with carbamazepine and valproic acid.

Case 41: JS. 9 years old. M. Partial convulsive syndrome since 6 years old. Hyperactivity and attention deficit, aggressiveness. EEG showed paroxysmal activity and outbreak of slow waves in frontal and left temporal regions. Family history of epilepsy. Congenital epilepsy. Rolandic type. Patient treated with carbamazepine, valproic acid and risperidone.

Case 42: JP. Three years old. M. Partial convulsive syndrome and loss of consciousness. Lip cyanosis and bronchial asthma. EEG showed generalized outbreak of acute and slow waves. Idiopathic generalized epilepsy. Patient treated with valproic acid and carbamazepine.

Case 43: KI. Three years old. M. Partial convulsive syndrome and sialorrhea. Tricuspid and pulmonary valve insufficiency. EEG showed generalized outbreak of slow waves. Lennox-Gastaut epilepsy. Patient treated with valproic acid.

Case 44: RY. Five years old. M. Partial convulsive syndrome, hyperactivity and attention deficit, aggressiveness. EEG showed outbreak of generalized acute and slow waves. Family history of epilepsy. Congenital epilepsy. Lennox-Gastaut type. Patient treated with valproic acid, risperidone and haloperidol.

Case 45: IC. Five years old. F. Partial convulsive syndrome. Hyperactivity and attention deficit, aggressiveness, and autistic features with involuntary arm movements. EEG showed sporadic paroxysmal discharges. Mother with family and labor stress and high blood pressure. Autism and epilepsy. Patient treated with valproic acid, risperidone and haloperidol.

Case 46: LQ. I8 months old. Patient with partial convulsive syndrome featured by repetitive head jerks. Gait disturbances, dysphagia. EEG showed generalized outbreak of slow waves. Lennox-Gastaut Syndrome. Patient treated with valproic acid.

Case 47: RF. 16 years old. F. Partial convulsive syndrome in the last three years. EEG showed moderate focal epileptiform activity. Mother with high blood pressure. Patient treated with carbamazepine. Idiopathic generalized epilepsy.

Case 48: MA. Nine years old. Patient with two partial convulsive syndromes, perinatal hypoxia, laughing crisis, hip deviation, body growth deficit. EEG showed outbreak of generalized acute and slow waves. Lennox-Gastaut syndrome. Patient treated with valproic acid.

Case 49: JZ. Ten years old. M. Patient with generalized convulsive syndrome. Perinatal hypoxia by double circular umbilical cord. Bronchial asthma. Chikungunya viral infection at six years old preceding convulsive crisis. Normal EEG and NMR. Post-Chikungunya epilepsy. Patient treated with valproic acid.

Case 50: IR. Four years old. F. Partial convulsive syndrome. Severe perinatal hypoxia hospitalized during 15 days. EEG hypsarrhythmia suggesting infantile spasm. NMR images showed hyperintense periventricular and supraventricular areas in relationship with leukomalacia foci. Enlargement of ventricular posterior horns and prominent cortical grooves. Infantile spasm. Patient treated with valproic acid.

Case 51: TM. M. Partial convulsive syndrome feature by head shakings, autistic syndrome and stereotyped movements, languages disorders, hyperactivity and attention deficit, impulsiveness. Mother with epilepsy. EEG showed focal sporadic paroxysmal activity in right frontal and parietal superior areas. Lennox-Gastaut Syndrome. Infantile spasm. Patient treated with valproic acid, carbamazepine and risperidone.

Case 52: YP. Two years old. F. Premature patient with generalized convulsive syndrome during the night and sialorrhea. EEG showed acute waves of median voltage in anterior and superior frontal and temporal regions. Rolandic Epilepsy. Infantile spasm. Patient treated with valproic acid.

Case 53: JM. 5 years old. M. Generalized convulsive syndrome, transitory loss of consciousness and corporal coldness, hypoxia perinatal, hyperactivity and attention deficit. EEG showed paroxysmal activity in centrotemporal region featured by large amplitude sharp waves. Rolandic epilepsy. Patient treated with valproic acid.

Case 54: DM. Five years old. F. Generalized convulsive syndrome since one day old, and in 2 and 4 years old. Maternal stress. EEG showed paroxysmal activity and slow waves in parietal center region. NMR images showed hyperdensity areas in brain cortex. Landau-Kleffner syndrome. Patient treated with valproic acid, carbamazepine and lamotrigine.

Case 55: AL. Four years old. M. Neonate with generalized convulsive syndrome post cerebral hemorrhage at 19 days old. Right hemiparesis. EEG showed irritative focal activity in left frontal and temporal regions. Rolandic epilepsy. Patient treated with phenobarbital, valproic acid and carbamazepine.

Case 56: DC. 18 months old. F. Partial convulsive syndrome and atonic head. Hyperactivity. EEG showed outbreak of generalized slow waves. Idiopathic generalized epilepsy. Patient treated with diazepam and valproic acid.

Case 57: DS. Six years old. M. Generalized tonic convulsive syndrome and transitory loss of consciousness. Hyperactivity and attention deficit. impulsiveness. EEG showed outbreak of generalized slow waves. Idiopathic generalized epilepsy. Patient treated with valproic acid and risperidone.

Case 58: DA. Eight years old. M. Patient with three generalized convulsive syndromes with intervals of several hours. Attention and learning deficit. Normal EEG and NMR. Patient treated with diphenylhydantoin and carbamazepine. Idiopathic generalized epilepsy.

Case 59: AL. Nine years old. F. Patient with generalized convulsive syndrome. Atonic head. Language disorders. Hyperactivity and attention deficit, screaming and sexual excitation. Genetic study showed chromosome 14, Karyotype 46xy. EEG showed generalized paroxysmal discharges. Ring chromosome 14 epilepsy syndrome. Patient treated with valproic acid and risperidone.

Interpretation of results

Semiology of seizures

We have examined the following seizures types in the 59 patients herein examined: Diffuse slow waves, generalized slow waves, diffuse waves delta and theta. Beta frequency of medium voltage, medium- and high-voltage spike-wave discharges in right brain hemisphere, Generalized paroxysmal activity and slow waves in left fronto, parietal center and superior frontal region. slow delta and theta waves, generalized acute waves, outbreak of paroxysmal median voltage spikes in medial and anterior regions of both hemispheres, paroxysmal activity in temporal region, spikes and large amplitude medium waves, left temporal paroxysmal activity, diffused and slow Alpha Rhythm 5 - 6 HZ focal slow activity in left temporal region, paroxysmal activity frontal, parietal and occipital center regions of both hemispheres, multifocal epileptogenic paroxysmal activity, asynchronous sigma activity in parietal region, multiple hyperexcitable focus in frontal, parietal and temporal regions, paroxysmal activity in left frontotemporal regions projected bilaterally to contralateral areas. sporadic paroxysmal discharges, hypsarrhythmia suggesting infantile spasm, and paroxysmal activity in centrotemporal region featured by large amplitude sharp waves (Table 1).

Seizure Semiology	Cases
Generalized and diffuse slow waves	30
Generalized and focal paroxysmal activity	22
Normal EEG	7
Total	59

Table 1: *Shows the main semiology seizures.*

According to electroclinical study we have found the following epileptic types: One traumatic epilepsy, two epileptic absence types, seventeen cases of Lennox-Gastaut syndrome, eight cases of Rolandic Epilepsy, eleven cases of Landau-Kleffner syndrome. In addition, we have found twenty two idiopathic generalized epilepsy, two tonic epilepsy type, one metabolic epilepsy, one epilepsy post Chikungunya viral infection, three myoclonic epilepsies, and one infant spasm (Table 2).

The following NMR findings illustrates in few cases the damage of the brain parenchyma corresponding to the epileptic network:

Electroclinical Diagnosis	Cases
Traumatic epilepsy	2
Metabolic epilepsy	1
Epilepsy post Chikungunya viral infection	1
Postmeningitis epilepsy	1
Infant spasm	1
Autism and epilepsy	1
Ring chromosome 14 epilepsy	1
Absence types	2
Myoclonic epilepsies	3
Rolandic epilepsy	7
Lennox-Gastaut syndrome	17
Landau-Kleffner syndrome	9
Idiopathic generalized epilepsy	13
Total	59

Table 2: *Electroclinical diagnosis*

Source: Castejon (2022).

- Enlargement of frontal horns, prominence of cisterns and grooves, bilateral meningofrontal thickening with right frontal subdural collection (Case 5).
- Periventricular gliosis (Case 16).
- Brain atrophy, deep cortical grooves, ventricular enlargement of posterior horns (Case 29).
- Hyperintense periventricular and supraventricular areas in relationship with leukomalacia foci. Enlargement of ventricular posterior horns and prominent cortical grooves (Case 50).

Discussion

In the present study we have made a differentiation between focal and generalized epilepsy based mainly on clinical symptomatology and preictal electroencephalographic recordings. The differentiation between focal and generalized epilepsies based on clinical and electroencephalographic features is difficult and sometimes confusing, although both types of epilepsy can coexist [5]. Generalized epilepsy was associated to the following comorbidities perinatal hypoxia, language disorders, cognitive deficit, attention and learning deficit, mental retardation, aggressiveness, headache and sexual arousal. In focal epilepsy we found mental retardation, language disorders, impulsivity and hyperactivity.

Lennox-Gastaut syndrome (LGS)

Lennox-Gastaut syndrome (LGS) was observed in 17 cases featured by complex seizure semiology and patients with cognitive deficit and neurobehavioral disorder. Lennox-Gastaut syndrome (LGS) is considered an epileptic encephalopathy and is defined by a triad of multiple drug-resistant seizure types, a specific EEG pattern showing bursts of slow spike-wave complexes or generalized paroxysmal

fast activity, and intellectual disability. The etiology of LGS is often divided into two groups: identifiable (genetic-structural-metabolic) in 65 to 75% of the patients and LGS of unknown cause in others. The Lennox-Gastaut syndrome may be considered as secondary network epilepsy [6].

Landau-Kleffner syndrome

In the present study we have preliminarily classified nine cases of Landau-Kleffner syndrome according to Landau-Kleffner syndrome (LKS) is an epileptic encephalopathy characterized by acquired verbal auditory aphasia and seizures in most of the patients associated with continuous or almost continuous spike-and-wave discharges during slow wave sleep [7]. Landau-Kleffner syndrome (LKS) is a rare age-related epileptic encephalopathy, characterized by a developmental regression in the area of language and electroencephalogram (EEG) anomalies located mainly around the temporoparietal areas. When present, the seizures consist of absence seizures or tonic-clonic episodes and occur more frequently during sleep [8]. LKS is one of the childhood epileptic encephalopathy and acquired aphasia and epileptic seizures are two main clinical characteristics. Aphasia is characterized by verbal auditory agnosia. Psychological and behavioral abnormalities are very common in children with LKS [9]. Patients with temporal lobe epilepsy (TLE) commonly experience a broad range of language impairments. These deficits are thought to arise from repeated seizure activity that damages language regions. However, connectivity between the seizure onset region in the hippocampus and regions related to language processing has rarely been studied and could also have a strong impact on language function [10].

Rolandic epilepsy

We have herein diagnosed seven cases as Rolandic Epilepsy. All the studies agree with the fact that children with Rolandic epilepsy keep a normal global intellectual efficiency and a good long-term outcome. Nevertheless, some children may suffer transiently during the active phase of the epilepsy from oromotor dysfunction, neuropsychological deficits, or attention deficits with learning disorders. The analysis of cognitive and neurophysiological correlations evidenced a significant correlation between the epileptic focus localization and few specific dysfunctions [11].

Rolandic epilepsy (RE) affects children between 3 and 12 years of age, boys more often than girls (3:2). Focal sharp waves in the centrotemporal area define the electroencephalographic (EEG) trait for the syndrome, are a feature of several related childhood epilepsies and are frequently observed in common developmental disorders (eg, speech dyspraxia, attention deficit hyperactivity disorder and developmental coordination disorder [12]. These Authors reported the first genome-wide linkage scan in RE for the EEG trait, temporal center sharp waves (CTS), with genome-wide linkage of CTS to 11p13 (HLOD 4.30). The Authors hypothesize that a non-coding mutation in ELP4 impairs brain-specific Elongator-mediated interaction of genes implicated in brain development, resulting in susceptibility to seizures and neurodevelopmental disorders.

Lennox-Gastaut epilepsy

We have herein classified seventeen cases with Lennox-Gastaut syndrome. This syndrome (LGS) is considered an epileptic encephalopathy and is defined by a triad of multiple drug-resistant seizure types, a specific EEG pattern showing bursts of slow spike-wave complexes or generalized paroxysmal fast activity, and intellectual disability. The etiology of LGS is often divided into two groups: identifiable (genetic-structural-metabolic) in 65 to 75% of the patients and LGS of unknown cause in others. The Lennox-Gastaut syndrome may be considered as secondary network epilepsy [6].

Brain structures involved in epileptic activity. The epileptic network

We have tried to localize the subsets of brain structures involved in both types of paroxysmal activity. We have herein reported two cases with focal temporal epilepsy. San-Juan., *et al*. (2013) reported hippocampal sclerosis in mesial temporal lobe epilepsy with a high

prevalence of psychiatric comorbidities, including major depression (50%), interictal psychosis (16%) and dementia (8%). Epileptogenic networks are defined by the brain regions involved in the production and propagation of epileptic activities. The concept of epileptogenic networks has been progressively introduced as a model better able to describe the complexity of seizure dynamics and realistically describe the distribution of epileptogenic anomalies in the brain The epileptogenic network concept is a key factor in identifying the anatomic distribution of the epileptogenic process, which is particularly important in the context of epilepsy [13]. There is a growing body of evidence suggesting that the epilepsies are network level disorders [14].

We have also reported frontal-parietal, frontal, parietal and temporal and frontal, parietal and occipital areas with epileptic activity showing the extent of epileptic network.

Barot (2020) [15] also reported frontal network epilepsy. According to this Author, epilepsy affects about 1% of the general population. Frontal lobe epilepsy is the second most common focal epilepsy accounting for nearly 25% of medically refractory epilepsies. This paper reviews frontal lobe epilepsy from a perspective of a network disease that may help us to understand epilepsy from the microscale of genes to local neuronal circuits, to the macrolevel of a whole-brain network.

We have characterized three parietal center epileptic types, one parietal-temporal epilepsy, one frontal-parietal-temporal and one frontal-parietal-occipital epilepsy. These epileptic types involving two or three different brain lobes indicate the existence of a large epileptic network and the presence of numerous comorbidities.

Temporal 'plus' epilepsies are characterized by seizures involving a complex epileptogenic network including the temporal lobe and the closed neighbors structures, such as the orbito-frontal cortex, the insula, the frontal and parietal operculum and the temporo-parieto-occipital junction [16].

Sensorimotor phenomenon and vestibular hallucinations suggest onset in the parietal lobe. Paresthesias, visual hallucinations, visual illusions, somatic illusions, vertiginous features can occur. Seizures arising from the dominant hemisphere can cause receptive language impairment. Parietal lobe complex partial seizures can have auras like epigastric sensations, visual hallucinations, panic attacks, and behavioral arrest. Often there is an involvement of other lobes as the seizure spreads. When focal seizures from the parietal lobe spread and involve the temporal lobe, loss of consciousness and automatisms may occur [17].

Temporal lobe epilepsies (TLE) represent the majority of the partial symptomatic/cryptogenic epilepsies. Seizure types in TLE include simple partial, complex partial and secondarily generalized seizures. Temporal lobe seizures most often arise in the amygdalo-hippocampal region. More than 90% of patients with mesial TLE report an aura, most commonly an epigastric sensation that often has a rising character. Other autonomic symptoms, psychic symptoms, and certain sensory phenomena (such as olfactory) also occur [18]. About one-quarter of patients with refractory focal epilepsies have frontal lobe epilepsy (FLE). The typical seizure semiology for FLE includes unilateral clonic, tonic asymmetric or hypermotor seizures. Interictal electroencephalograms (EEG) usually reveal interictal epileptiform discharges and rhythmical midline theta, which has localizing value [19].

Up to 30% of the patients with focal epilepsy have seizures arising from the frontal lobe. It is the most common extratemporal type. Seizures are accompanied by loss of consciousness in about half of the patients with frontal lobe epilepsy. Focal impaired awareness seizures can arise from various locations within the frontal lobe, except the rolandic strip. These seizures typically are brief, lasting about 30 seconds, occurring in clusters, multiple times a day, are often nocturnally occurring during sleep, and have minimal postictal confusion. Motor symptoms are predominant and range from hypermotor thrashing episodes like pelvic thrusting, bicycling movements to asymmetric tonic posturing. Sexual automatisms, bizarre behavior, and vocalizations are common. These seizures often have a stereotypical pattern for each patient. Epileptiform activity in frontal convexity can cause clonic seizures, and in the supplementary motor area can

cause tonic seizures. Unique semiology of the supplementary sensorimotor cortex includes deviation of head and eye to the side contralateral to seizure onset, the asymmetrical posturing of upper limbs with an extension of arm contralateral to the side of seizure onset, and flexion of ipsilateral arm [17].

Patients with parietal lobe epilepsy (PLE) exhibit an electroclinical epilepsy syndrome that is rarely seen even at large epilepsy centers. Clinically, most patients with PLE exhibit a somatosensory aura that may include painful dysesthesias, though vertigo, aphasia, disturbances of one's body image also occur, when ictal propagation occurs from the parietal lobe to the supplementary motor area, hypermotor manifestations are noted. When temporolimbic propagation occurs, complex visual or auditory hallucinations and automatisms may appear [20].

Seizures arising from the parietal lobe may be difficult to diagnose because of their subjective nature. Positive and/or negative sensory features are common. Sensorimotor phenomenon and vestibular hallucinations suggest onset in the parietal lobe. Paresthesias, visual hallucinations, visual illusions, somatic illusions, vertiginous features can occur. Seizures arising from the dominant hemisphere can cause receptive language impairment. Parietal lobe complex partial seizures can have auras like epigastric sensations, visual hallucinations, panic attacks, and behavioral arrest. Often there is an involvement of other lobes as the seizure spreads. When focal seizures from the parietal lobe spread and involve the temporal lobe, loss of consciousness and automatisms may occur [17].

Occipital lobe epilepsies (OLEs) manifest with occipital seizures from an epileptic focus within the occipital lobes. Ictal clinical symptoms are mainly visual and oculomotor. Elementary visual hallucinations are common and characteristic. Postictal headache occurs in more than half of patients (epilepsy-migraine sequence). Electroencephalography (EEG) is of significant diagnostic value, but certain limitations should be recognized. Occipital spikes and/or occipital paroxysms either spontaneous or photically induced are the main interictal EEG abnormalities in idiopathic OLE. However, occipital epileptiform abnormalities may also occur without clinical relationship to seizures particularly in children [21].

Seizures with ictal origin in the occipital lobe are characterized by a visual aura and are difficult to diagnose especially in young children. Visual auras, typically of elementary sensations, ictal blindness, versions of the head and eyes to the opposite side, rapid and forced blinking, oculoclonic activity are some features suggesting occipital lobe as an origin of focal seizure with impaired consciousness. Seizures from the primary visual cortex can cause bilateral loss of vision in the form of white-out or black-out [17]. Apparently commissural pathways play a contributory role in interhemispheric propagation in connectivity associated with seizure propagation patterns [22].

Neural correlates of experimental epilepsy

According to Avoli and Barbarosie (1999) [23] and Caolmonte., *et al*. (2000) [24] in rodent combined slices of hippocampus-entorhinal cortex continuous application of 4-aminopyridine induces: (i) interictal activity which initiates in CA3 and propagates via CA1 and subiculum to the entorhinal cortex, and return to the hippocampus through the dentate gyrus; and (ii) ictal discharges, which originate in the entorhinal cortex and propagate via the dentate gyrus to the hippocampus. Lesioning the Schaffer collaterals abolishes interictal discharges in CA1, entorhinal cortex and dentate gyrus and discloses entorhinal ictal discharges that propagate, via the dentate gyrus, to the CA3 subfield.

White matter contribution seems to be important in those case with paroxysmal activity in all brain regions (Cases 4, 6, and 22). White matter connectivity was previously studied by Campos., *et al*. [25].

Conclusion

According to electroclinical study we have found the following epileptic types: Two traumatic epilepsy, two epileptic absence types, seventeen cases of Lennox-Gastaut syndrome, seven cases of Rolandic Epilepsy, and nine cases of Landau-Kleffner syndrome. In addition,

we have found 13 idiopathic generalized epilepsy, two tonic epilepsy type, one metabolic epilepsy, one epilepsy post Chikungunya viral infection, three myoclonic epilepsies and one infant spasm. The following NMR findings illustrates the damage of the brain parenchyma corresponding to the epileptic network, such as prominence of cisterns and grooves, bilateral meningo-frontal thickening, right frontal subdural collection, periventricular gliosis, brain atrophy, ventricular enlargement of posterior horns, hyperintense periventricular and supraventricular areas in relationship with leukomalacia foci.

Acknowledgement

The present investigation has been carried out by the administrative support of Biological Research Institute, Faculty of Medicine. Zulia University, San Rafael Clinical Home of Maracaibo. Venezuela and Castejón Foundation.

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Volume 7 Issue 1 January 2023
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