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Morpho-functional and radiological approach of poststroke seizures

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Abstract

Epilepsy is characterized by recurrent seizures that cannot be associated with other specific causes. The presence of a single convulsive or tonic seizure after a stroke does not necessarily mean that a person develops a form of epilepsy unless the convulsions become chronic and recurrent poststroke epilepsy. The purpose of our study is to highlight the existence of a connection between the type and the topography of a vascular stroke on the one hand, and on the other hand, the type of seizures that have occurred and how long they have occurred after the stroke. The study was conducted in a total of 165 patients at the Prof. Dr. Nicolae Oblu Emergency Clinical Hospital, Iaşi, Romania, diagnosed with stroke and spastic seizures after stroke and who survived for at least one year. In this study, the ideal patient should be the patient diagnosed for the first time with temporal lobe epilepsy, followed longitudinally by high-resolution imaging techniques. Studying topography and morphopathology of poststroke sequelae can lead to an increase in accuracy prediction of epilepsy after it.

Keywords: seizures, ischemic stroke, cerebral stroke topography.

Introduction

Specialty literature presents the particular situation of patients developing seizures after a stroke. These seizures are a sign of irritative brain injuries that cause a sudden, disorganized electrical activity in the brain. Seizures are tonic or convulsive and occur especially in the elderly [1].

Approximately 5% of patients may develop a seizure after a stroke. There are no criteria to predict them, except a number of risk factors, such as serious stroke, a hemorrhagic stroke [2] or a stroke that affects the cerebral cortex.

More than 40 different types of seizures are described, from tingling sensations to agitation and loss of consciousness. The most severe form is the generalized seizures that are caused by electrical impulses from both brain hemispheres.

On the other hand, focal seizures occur only in one cerebral hemisphere with clinical expression within the controlateral half of the body.

Most of the patients who suffered from stroke and had convulsions did not develop epilepsy.

Epilepsy is characterized by recurrent seizures that cannot be associated with other specific causes [3–5]. The presence of a single convulsive or tonic seizure after a stroke does not necessarily mean that a person develops a form of epilepsy unless the convulsions become chronic and recurrent poststroke epilepsy (PSE).

At the same time, when the clinical signs of a stroke are not conclusive, such a seizure may be the pathognomonic sign, especially in children and infants [6, 7].

Etiopathogenesis of PSE is not yet fully understood. Other studies indicate the ischemic event as one of the most common causes of epilepsy in adults [8].

The impact of epilepsy on those who suffer from this disease extends far beyond the injuries brought about by the epileptic seizure itself [9–12]. The unpredictability of crises imposes severe restrictions on lifestyle and extensively inhibits the patient's social interactions. Medical and surgical treatments are associated with numerous side effects. The quality of life is impaired at the biological, psychological, social and economic level.

The most obvious impact of epilepsy is the result of the epileptic seizure itself. Seizures can lead to multiple injuries or traumas because of interactions with the environment at the time of the crisis. The most feared complication remains *status epilepticus*, followed by aspiration pneumonia and cardiac arrhythmias. Annually, 0.2% of sick epileptics die suddenly (SUDEP – sudden unexpected death in epilepsy).

Aim

All these aspects of PSE compel us to a precise knowledge of the subject in order to establish an appropriate prophylaxis and/or diagnosis and early treatment. The purpose of our study is to highlight the existence of a connection between the type and the topography of a vascular stroke on the one hand, and on the other hand, the type of seizures that have occurred and how long they have occurred after the stroke.

Patients, Materials and Methods

The study was conducted in a total of 165 hospitalized patients at the Clinic of Neurology I, Prof. Dr. Nicolae Oblu

Emergency Clinical Hospital, Iaşi, Romania, during April 1, 2016–April 1, 2018, diagnosed with stroke and spastic seizures after stroke and who survived for at least one year. This group represents about 7% of the total of 2357 patients diagnosed with stroke during this period and supervised for one year.

The diagnosis of stroke was done in admission, based on clinical, paraclinical and native computed tomography (CT) procedures. We used a Toshiba Aquilion CT scanner, which has the advantage that the examination is done in a very short time with a radiation reduced by almost half. The imaging exploration protocol included the sequences specific to T1, T2, fluid-attenuated inversion recovery (FLAIR), diffusion. Arteriography images were obtained with a SIEMENS Axiom Artis dFA angiography system. The administration of a contrast agent into the arterial or venous system may reveal a malformative pathology, aneurysm or stenosis caused by atheromatous plaques. At the same time, this method can be used in the embolization or stent endoprosthesis of the above-mentioned pathology.

This study followed the principles outlined in the Declaration of Helsinki. Written informed consent was obtained from each participant who underwent medical procedures.

The histological specimens were collected during necropsy from six patients died one year after and were examined histologically. The technique consists of 10% neutral buffered formalin fixation, paraffin embedding and 3–5 μm thick-section cutting. We used the classical Hematoxylin–Eosin (HE) and Van Gieson trichrome histological staining techniques.

We distributed these patients according to age, gender and comorbidities.

Results

In the studied group, the largest percentage belongs to men and the age (75 years) is also a characteristic of its preponderance (Figure 1). One hundred five (63.64%) of the patients were diagnosed with hemorrhagic stroke and 60 (36.36%) with ischemic stroke.

Of the total of these patients who experienced convulsive seizures and/or tonic seizures, 132 (80%) became recurrent. All of our cases with recurrent post-stroke seizures presented convulsive seizures and lead to epilepsy within one year after stroke.

In a single patient, a hemorrhagic tumor lesion that triggered convulsive seizures (Figure 2) was objectively identified.

The highest incidence of PSE occurs in patients diagnosed with hemorrhagic stroke (60%). In this situation, the lesion that was most commonly associated with this pathology has as topography the middle cerebral artery (MCA) in the M2 (island of Reil lobe) and M4 (cortical) segments (Figure 3).

Only 11 of the patients in the study group started these seizures within the first 24 hours of admission (early seizures). Eight of these cases were diagnosed with ischemic stroke, with right occipital parietal ischemic edema without contrast intakes and without displacement of the median line or in the right posterior cerebral artery (PCA). The other three cases presented ischemic stroke in left frontal island area (Figure 4).

Most patients diagnosed with PSE present as the starting point of risk factors atherosclerotic disease localized to a large vessel (Figure 5).

Histological specimens showed cerebral infarct at three weeks from its onset as dead nervous tissue which was replaced by numerous newly formed capillaries surrounded by numerous lipid-laden macrophages (foam cells or gitter cells) (Figure 6). Also, higher magnification of the same histological section highlighted numerous lipid-laden macrophages (*i.e.*, previously microglia that became enlarged and laden with tissue breakdown products) that are rounded cells with distinct cytoplasmic border, small, darkly staining, and eccentric nuclei and a clear, granular cytoplasm that contain lipids resulted from myelin degradation and phagocytosis (Figure 7).

Other acute intracerebral hematoma aspect revealed red blood cells accumulation, which were embedded within nervous tissue (Figure 8). In other case of chronic intracerebral hematoma dead brain tissue was replaced by scattered lipid-laden macrophages with abundant finely granular cytoplasm (phagocyted lipids) and eccentric nuclei, along with numerous hemosiderin-laden macrophages and newly formed capillaries (Figure 9).

Discussions

The modern classification of different types of PSE is based on the characteristics of the seizures. In this respect, three criteria were considered regarding the topography of the lesion, the level of awareness during a seizure and the clinical aspects.

Regarding the first criteria, there were focal seizures which begin in an area or in a network of cells on one side of the brain. Also, we found a generalized type of seizures which involves networks on both sides of the brain at the debut. A tertiary type, with focal debut and bilateralization have been observed. It began in a part of the brain and spread on both sides.

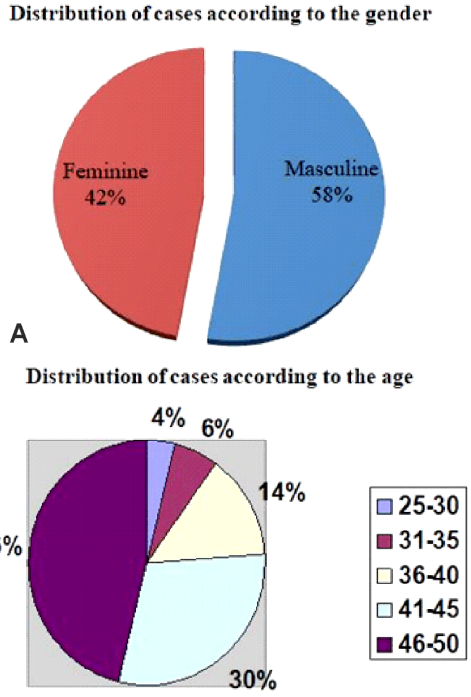

Figure 1 – ***Patients distribution by gender (A) and by age (B) within the study group.***

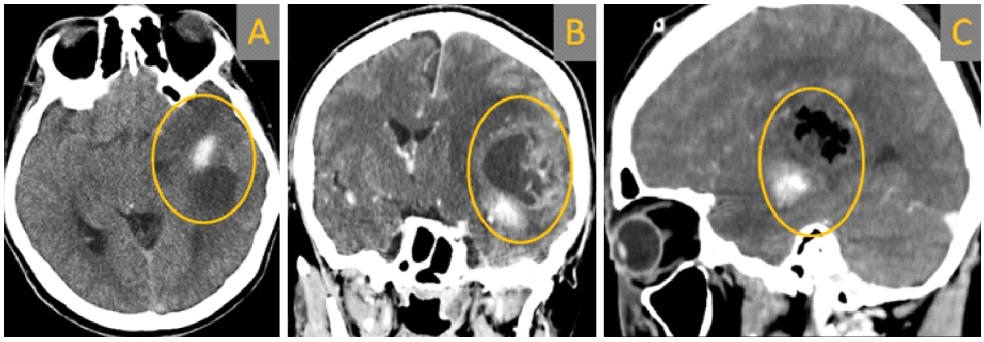

Figure 2 – ***Hemorrhagic glioblastoma: (A) Axial section in native CT examination that reveals a spontaneous hyperdensity lesion adjacent to a hypodense lesion in the left temporal lobe; (B) Coronary cross-section in cerebral CT with contrast showing a heterogeneous lesion in the left temporal lobe, with contrast and median line movement suggestive appearance for glioblastoma; (C) Sagittal section in native cerebral CT showing a heterogeneous lesion, hyperdense, with left temporal localization and with the movement of the median line. CT: Computed tomography.***

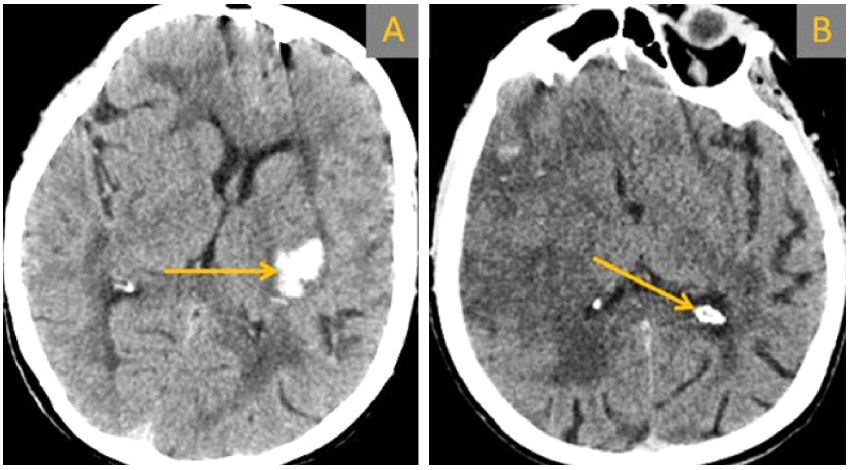

Figure 3 – ***Hemorrhagic stroke in M4 segment of the left MCA: (A) Native CT – hemorrhagic hyperdense lesion in the left internal capsule on the M2 segment of the left MCA; (B) Native cerebral CT – the hypodense area on the right MCA, with minimal hemorrhagic transformation on the M4 segment of the left MCA. CT: Computed tomography; MCA: Middle cerebral artery.***

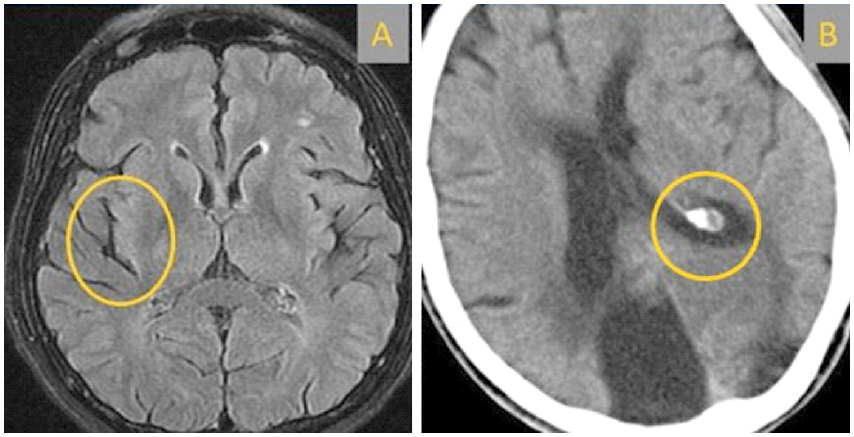

Figure 4 – ***Types of strokes in patients with early debut of poststroke seizures: (A) Ischemic right parietal occipital edema with no contrast intakes and without displacement of the median line, in the case of a patient with ischemic stroke in the right PCA; (B) Left frontal insular ischemic stroke with a discrete heterogeneous area in proximity. PCA: Posterior cerebral artery.***

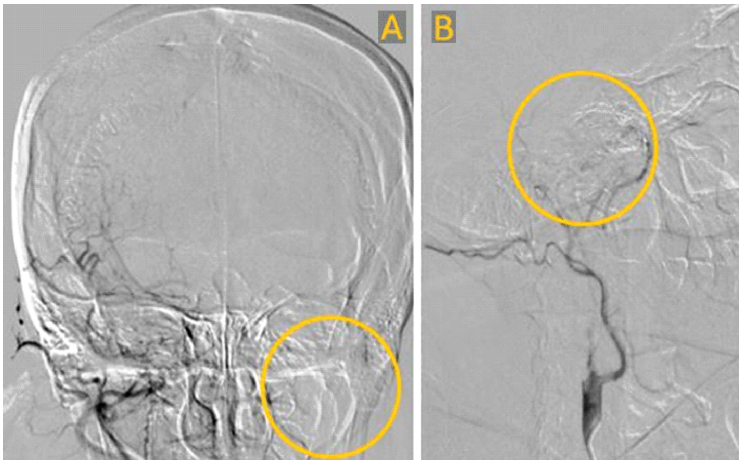

Figure 5 – ***Seldinger arteriography that highlights atherosclerotic disease at an advanced stage, at the level of the internal carotid arteries and total occlusion of the right internal carotid artery: (A) Seldinger arteriography, with the right internal carotid artery completely obstructed from its origin; (B) Seldinger arteriography, lateral view of the right internal carotid artery completely obstructed from the ophthalmic segment (supraclinoid).***

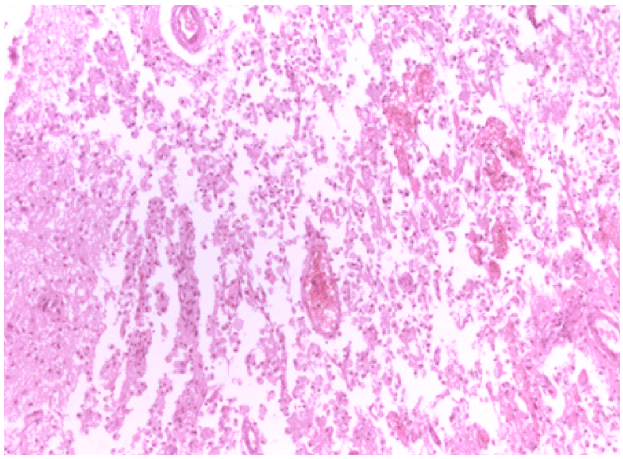

Figure 6 – ***Cerebral infarct at three weeks from its onset: dead nervous tissue was replaced by numerous newly-formed capillaries surrounded by numerous lipid-laden macrophages (foam cells or gitter cells) (HE staining, ×100).***

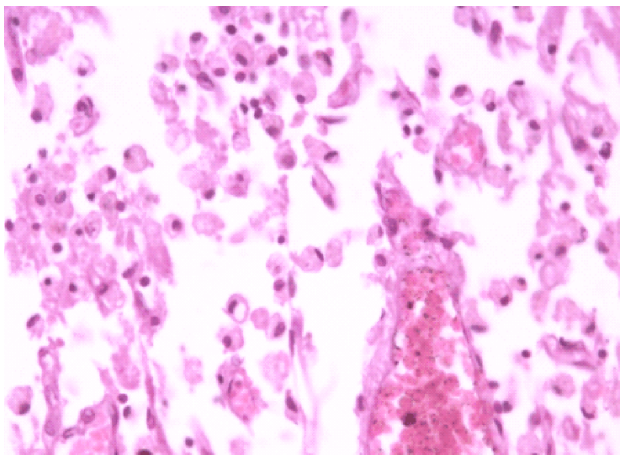

Figure 7 – ***Higher magnification of the same histological section: numerous lipid-laden macrophages (i.e., previously microglia that became enlarged and laden with tissue breakdown products) that are rounded cells with distinct cytoplasmic border, small, darkly staining, and eccentric nuclei and a clear, granular cytoplasm that contain lipids resulted from myelin degradation and phagocytosis (HE staining, ×400).***

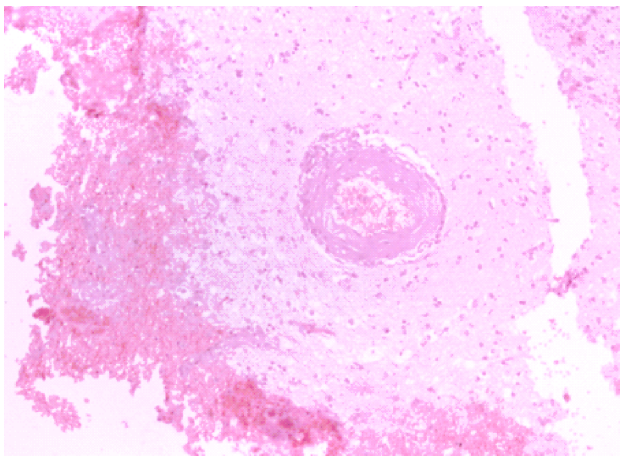

Figure 8 – ***Acute intracerebral hematoma: red blood cells accumulation, which is embedded within nervous tissue (HE staining, ×100).***

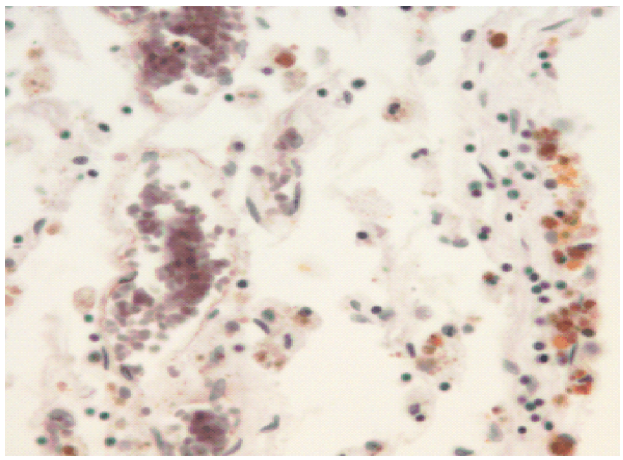

Figure 9 – ***Chronic intracerebral hematoma: dead brain tissue replaced by scattered lipid-laden macrophages with abundant finely granular cytoplasm (phagocyted lipids) and eccentric nuclei, along with numerous hemosiderin-laden macrophages and newly formed capillaries (Van Gieson trichrome staining, ×400).***

Regarding the level of awareness during a seizure, the focal ones showed maintained consciousness even if the person was unable to speak or respond. Deficiencies at exteroceptive and proprioceptive level, with alteration of the state of consciousness characterized the generalized type. These persons still had a vague idea about what happened. This category includes people who live alone or have seizures only at night.

Considering the associated type of motor symptoms, we noticed that motor focus means that during the seizures a certain type of movement occurs (stiffness, automatic movements such as tight lips, rubbing, walking or running). Another non-motoric type of focusing shows other onset symptoms, such as changes in sensation, emotions, thinking or experiences. It is also possible that a crisis of focal or depressive awareness to be subclassified as motor or non-motor debut.

After the symptoms (*aura*), a person may feel at the beginning of a crisis. These involve rapid changes in awareness and can be accompanied by automatic or repetitive movements [13].

Hemorrhagic lesion of MCA occurs primarily on the left (80%) of cases of hemorrhagic stroke. From the declarative data of these patients or their relatives, the right or left topography of the MCA's hemorrhagic lesions is correlated with the same type of hemisphere dominance.

Cases diagnosed with hemorrhagic stroke had the following common clinical signs, depending on the lesion topography: in MCA M2, we found seizures with focal or generalized debut, characterized by motor debut with automatic, repetitive movements, with deterioration of conscious proprioceptive sensitivity; in MCA M4, we found generalized or bilateral seizures, stiffness, loss of

consciousness; in the area of anterior cerebral artery (ACA), we observed 19 cases that have focal seizures with facial hemiparesis, speech disorders and monocrural post-critical convulsions, while in the area of PCA we found 12 cases that have focal or generalized seizures, with loss of motor coordination and balance, consciousness disorders.

In the case of patients diagnosed with ischemic stroke, they present the following types of association between symptomatology and topography of stroke: faster debut in the vast majority of cases than in hemorrhagic stroke; correlates as a symptomatology/lesion topography ratio with hemorrhagic stroke only as clinical manifestation is more severe; over 35% of cases have in anamnesis atherosclerotic disease.

In order to prevent epilepsy in stroke patients, it can be considered a number of easy to measure and detect risk factors. These risk factors, as well as interactions between them, show a great variability, which makes seizure crises to be difficult or even impossible to predict. Recent attempts to customize the approach to assessing the risk of stroke have led to the development of a multivariate model called "SeLECT". This it is based on five risk factors: stroke severity, major artery affected by atherosclerosis, early seizures, cortical involvement, and the territory that involve MCA [14]. On the other hand, this model is still experimental and raises many question marks [15].

It has not been scientifically proven if poststroke convulsive seizures can cause brain damage. In animal studies, electrical stimuli below the limit of neuronal excitability but repeatedly applied to the limbic system led to the formation of a chronic triggering epileptic seizure. Histologically, this lesion source has a marked loss of neurons, located at the level of the hippocampal formations in the temporal lobe. This cellular loss is associated with the decline of the memory function [16].

In humans, based on a long-term study on individuals with seizures located primarily in the temporal lobe, the crises are associated with the same histological description from experienced animals, and also similarly associated with memory deficiency. Also, in this study, patients who did not undergo an epileptic surgical treatment and who continued to have seizures showed a decline in memory function over 10 years of control. Long-term studies that include not only epileptic patients with temporal lesions, but several etiologies and localizations have highlighted that the overall epileptic patient manifests a decline in mental function by measuring the intelligence quotient (IQ) [2].

Another effect of temporal recurrent chronic crises is a chronic change of personality, Geschwind's syndrome. This syndrome includes changes that include loss of spontaneity, hyposexuality, a tendency to obsessively focus on a single subject, or an inability to finish a conversation ("stickiness"), hypergraph, and an excessive concern over the moral implications that can be brought about by daily events. Alterations of religious beliefs with excessive tendencies along with the development of an idiosyncratic system may also accompany this syndrome. Most often, these patients isolate themselves socially [17, 18].

Most of the epileptic patients accuse secondary lesions after seizures by interacting with the environment during the crisis. This explains possible bone fractures or cranio-cerebral trauma [19]. Burns are also commonly found by the escape of objects or hot liquids, the convulsive passage of a limb by fire, contact with hot surfaces, radiators, or even cigarette burns on the forearm by automatisms (repetitive exhausting feelings) in some complex crises.

The patient also becomes vulnerable during activities such as driving, handling electric tools, even climbing stairs, if we are talking about a tonic-clonic crisis. More severe cases include drowning in the debut of a seizure, during swimming or even in the bath.

The highlighted histopathological (HP) aspects confirm and support the results of clinical and radiological studies. At the same time, they are consistent with the HP aspects found in other published clinical studies.

Conclusions

Ideally, a study that could highlight whether or not epileptic seizures are associated with hippocampal lesions would be high-resolution functional magnetic resonance imaging (fMRI) monitoring over a long period of time to assess whether and how these lesions appear. In this study, the ideal patient should be the patient diagnosed for the first time with temporal lobe epilepsy, followed longitudinally by high-resolution imaging techniques. Our results suggest that a HP examination is useful in high-lighting the morphological and functional features of the different forms of after strokes seizures brain areas and in the orientation towards a more efficient treatment. Studying topography and pathology of poststroke sequelae can lead to an increase in accuracy prediction of epilepsy after it.

Conflict of interests

The authors declare that they have no conflict of interests.

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