

Temporal lobe epilepsy with mesial hippocampal sclerosis

Epilepsia do lobo temporal com esclerose hipocampal mesial

Epilepsia del lóbulo temporal con esclerosis del hipocampo mesial

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How to cite: Horta WG, Bezerra BN, Horta MS, Bernardino AO, Lima-Filho CA, Silva MVB. Temporal lobe epilepsy with mesial hippocampal sclerosis. *REVISA*. 2024; 13(1): 102-13. Doi: <https://doi.org/10.36239/revisa.v13.n1.p102a113>

REVISA

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Received: 12/10/2023
Approved: 15/12/2023

RESUMO

Objetivo: Compreender o cenário atual da ELT-HS, caracterizado por sua fisiopatologia, manifestações clínicas, métodos diagnósticos e tratamentos. **Método:** Trata-se de uma revisão integrativa da literatura, com caráter descritivo, de artigos indexados no Sistema de Análise e Recuperação da Literatura Médica Online MEDLINE/Pubmed, Literatura Latino-Americana e do Caribe em Ciências da Saúde LILACS, e nas bases de dados Científicas Electronic Library Online (SciELO), pesquisados no período compreendido entre outubro de 2022 e março de 2023. Foram incluídos artigos em português e inglês que contemplassem os objetivos da revisão, publicados nos últimos dez anos (2011-2021). **Resultados:** Inicialmente foram encontrados 144 artigos nas bases de dados, que após a leitura, foram selecionados na pesquisa 40 artigos que correspondiam ao objetivo proposto. Os artigos analisados correspondem aos anos de 2011 a 2021. **Conclusão:** O tratamento cirúrgico da ELT-HS tem se mostrado eficaz para resolução completa das crises na maioria dos pacientes. O conhecimento sobre sua fisiopatologia, manifestações clínicas, diagnóstico e tratamentos são de fundamental importância para os médicos que atendem pacientes com epilepsia.

Descritores: Epilepsia do Lobo Temporal; Esclerose Hipocampal; Epilepsia.

ABSTRACT

Objective: To understand the current scenario of TLE-HS, characterized by its pathophysiology, clinical manifestations, diagnostic methods and treatments. **Method:** This is an integrative literature review with descriptive character, of articles indexed in the Medical Literature Analysis And Retrieval System Online MEDLINE/Pubmed, Latin American and Caribbean Literature in Health Sciences LILACS, and Scientific databases Electronic Library Online (SciELO), researched in the period between October 2022 and March 2023. Articles in Portuguese and English that contemplated the objectives of the review, published in the last ten years (2011-2021), were included. **Results:** Initially, 144 articles were found in the databases, which after reading, 40 articles were selected in the research that corresponded to the proposed objective. The articles analyzed are equivalent to the years 2011 to 2021. **Conclusion:** The surgical treatment of TLE-HS has been shown to be effective for the complete resolution of crises in most patients. Knowledge about its pathophysiology, clinical manifestations, diagnosis and treatments are of fundamental importance for physicians who treat patients with epilepsy.

Descriptors: Temporal lobe epilepsy; Hippocampal Sclerosis; Epilepsy.

RESUMEN

Objetivo: Comprender el escenario actual de la TLE-HS, caracterizado por su fisiopatología, manifestaciones clínicas, métodos diagnósticos y tratamientos. **Método:** Se trata de una revisión bibliográfica integradora con carácter descriptivo, de artículos indexados en el Sistema de Análisis y Recuperación de Literatura Médica en Línea MEDLINE/Pubmed, Literatura Latinoamericana y del Caribe en Ciencias de la Salud LILACS, y bases de datos Scientific Electronic Library Online (SciELO), investigados en el período comprendido entre octubre de 2022 y marzo de 2023. Se incluyeron artículos en portugués e inglés que contemplaran los objetivos de la revisión, publicados en los últimos diez años (2011-2021). **Resultados:** Inicialmente se encontraron 144 artículos en las bases de datos, de los cuales luego de la lectura se seleccionaron 40 artículos en la investigación que correspondía al objetivo propuesto. Los artículos analizados corresponden a los años 2011 a 2021. **Conclusión:** El tratamiento quirúrgico del ELT-HS se ha mostrado eficaz para la resolución completa de las crisis en la mayoría de los pacientes. El conocimiento sobre su fisiopatología, manifestaciones clínicas, diagnóstico y tratamientos es de fundamental importancia para los médicos que tratan pacientes con epilepsia.

Descritores: Epilepsia del lóbulo temporal; Esclerosis del Hipocampo; Epilepsia..

Introduction

Epilepsy is a brain disease characterized by at least two unprovoked (or reflex) epileptic seizures with an interval of 24 hours, one unprovoked (or reflex) seizure and a chance of recurrence within ten years of at least 60% or a diagnosis of one, epileptic syndrome.¹⁻³⁴ The pooled incidence rate of epilepsy was 61,4 per 100.000 person-years (95% CI 50,7-74,4), the incidence was higher in low/middle-income countries than in high-income countries, 139 (95% CI 69,4-278,2) vs 48,9 (95% CI 39,0-61,1)³⁵.

According to the classification of the International League Against Epilepsy (ILAE) in 2017, there are six etiological groups for epilepsies: genetic, structural, infectious, metabolic, immune and unknown^{2, 34}. Among temporal lobe epilepsies in drug-resistant patients, a concept that encompasses those undergoing two therapeutic regimens at maximum tolerated dose without seizure control, 70% have the condition called Mesial Temporal Sclerosis (MTS), which is also known as hippocampal sclerosis³.

Temporal Lobe Epilepsy (TLE) associated with Hippocampal Sclerosis (HS) is one of the most common types of focal epilepsies⁴. Temporal lobe epilepsy is the most common epileptic syndrome in adults, accounting for about 40% of cases epilepsy in general and 60% of cases of focal-onset epilepsy^{5, 6}. This is an epileptic syndrome commonly associated with drug-resistant epilepsies, and represents one of the most frequent indications for surgery for epilepsy⁴.

Epilepsy is considered refractory when there is no sustained decrease in the frequency of epileptic seizures after the use of at least two medications (monotherapy or in combination) indicated for the type of epilepsy^{38, 39}. The present work to understand the current scenario of TLE-HS, characterized by its pathophysiology, clinical manifestations, diagnostic methods and treatments.

Method

This is an integrative literature review study with a qualitative and descriptive character. The research brought together international studies on updating temporal lobe epilepsy associated with hippocampal sclerosis, published in previously selected electronic databases and books on neurology and epilepsy.

The bibliographic survey was developed through the electronic databases Scientific Electronic Library Online (SCIELO), Medical Literature Analysis and Retrieval System Online (MEDLINE) and Caribbean Literature in Health Sciences (LILACS). The search terms used during the survey were: "Temporal Lobe Epilepsy"; "Mesial Hippocampal Sclerosis". The combination of terms was performed using the Boolean connector "AND".

In this line, all articles dealing with temporal lobe epilepsy with hippocampal sclerosis together with other comorbidities were excluded, as were studies carried out in organisms other than *Homo sapiens* and *Rattus norvegicus* and articles which did not have free legal access.

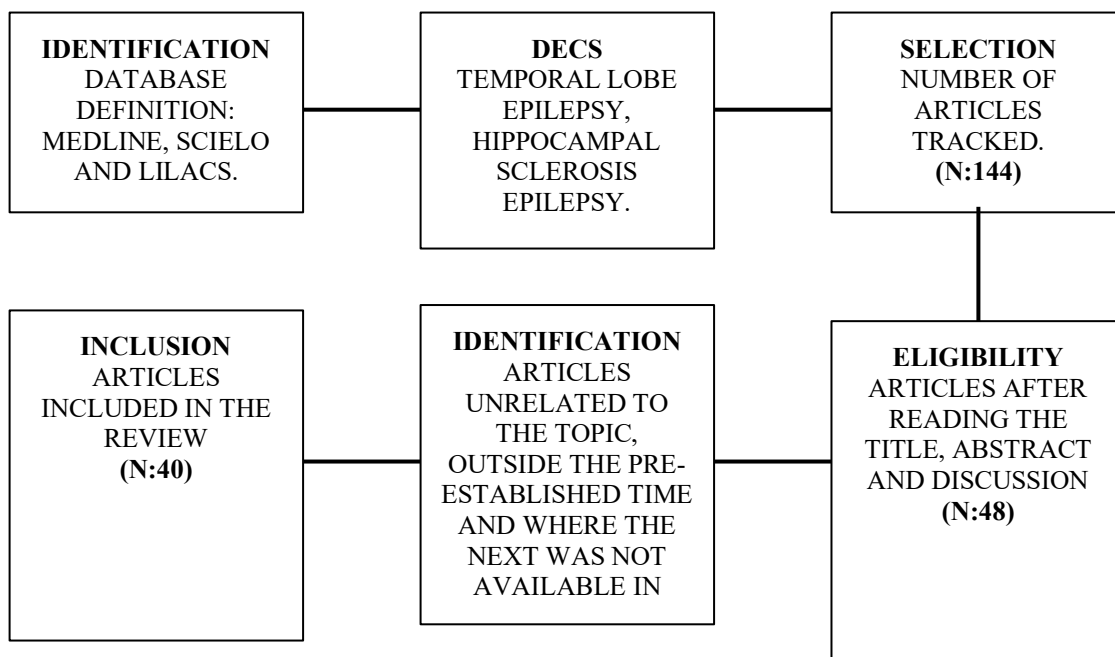
The articles selected by reading the abstracts met the inclusion criteria, namely: studies carried out as the central theme of temporal lobe epilepsy

associated with hippocampal sclerosis, definitions, classifications, diagnoses and treatments of epilepsy, published from 2011 to 2021. For the search results, the titles of the studies found were read and those that were not related to the topic or pre-established time period were excluded, as well as those that the full text was not available.

Results

The titles identified by searching the SCIELO, MEDLINE, and LILACS databases corresponded to 144 articles. After excluding duplicates, 48 articles returned, of which, after reading the texts and abstracts applying the inclusion criteria, 40 articles remained for reading the entire text in full, as shown in Figure 1.

Figure 1. Flowchart for selection of articles



Discussion

Pathophysiology

Studies have shown that structural and/or functional changes not only involve the temporal lobes, but also extend beyond these regions, and these structural and/or functional abnormalities have asymmetric characteristics⁷. Histologically, the hippocampus can be divided into four sectors of layers: CA1, CA2, CA3 and CA4 that vary in size and number of nerve cells⁸.

On histological examination, hippocampal sclerosis is characterized by degeneration and selective loss of pyramidal neurons, pathological proliferation of interneuron networks and marked gliosis⁸. In recent decades, several attempts have been made to classify specific patterns of neuronal loss in the hippocampus, however there was no consensus on definitions and terminology until a task force

was created by the ILAE to review previous classifications and propose a system based on semi-quantitative patterns. loss of hippocampal cells⁹.

This task force classified HS by histopathological examination into three types: Type 1 - It is the most common type of HE, about 60-80% of TLE-HS cases. The CA1 segment is the most affected >80% cell loss, but other segments also show significant neuronal loss, affecting 30-50% of pyramidal neurons in CA2, 30-90% in CA3 and 40-90% in CA4. The dentate gyrus is affected by 50-60% loss of granular cells; Type 2 - This type presents histologically with predominant neuronal loss in CA1, affecting about 80% of pyramidal cells. All other sectors show mild cell loss, visible only by microscopy, where CA2 has less than 20% cell loss, CA3 less than 20% and CA4 less than 25%. This pattern is uncommon, being seen in about 5-10% of cases; and Type 3 - Loss occurs predominantly in CA4, with approximately 50% cell loss and in the dentate gyrus with 35% cell loss, whereas the other regions are moderately affected with CA3 < 30%, CA2 < 25% and CA1 < 20 % cell loss. It is also a rare pattern of HE, occurring in around 4-7% of cases.

Other histological types found in TLE are gliosis without hippocampal sclerosis, where about 20% of TLE cases do not present significant neuronal loss, only gliosis occurring in a more accentuated form and granular cell dispersion, which occur in 50% of TLE cases⁹. Neuronal loss and gliosis occur mainly in Sommer's sector cells and hilar region neurons. In addition, an axonal reorganization is noticed, characterized by budding of axon collaterals of the granular cells (the mossy fibers) in the region of the inner molecular layer of the dentate gyrus¹⁰.

Thus, it is believed that pathophysiological changes involving the subiculum and dentate gyrus may be responsible for epileptogenesis in patients with mesial temporal lobe epilepsy¹¹. Involvement of other mesial structures, entorhinal cortex, and white matter and neocortex abnormalities can also be found^{13, 8}. The clinical expression of these alterations is revealing of the Epileptogenic Zone (EZ), this area of the cortex that is necessary and sufficient to initiate epileptic seizures and whose removal or disconnection is necessary for the cessation of epileptic seizures. The EZ consists of 5 distinct zones: irritative zone, ictal onset zone, symptomatogenic zone, lesional zone and deficit zone⁴⁰.

Table 1- Epileptogenic zones.

Irritant zone	Corresponds to paroxysmal interictal discharges
Zone of ictal onset	Area of cortex where seizures begin
Symptotogenic zone	Area of cortex that, when active, produces initial ictal signs and symptoms
Lesion zone	Macroscopic lesion that causes epileptic seizures due to secondary hyperexcitability or because the lesion itself is epileptogenic
Deficit zone	Area of cortex that does not function normally in the interictal period

The exact mechanisms of the pathophysiology of hippocampal sclerosis in epileptic seizures have not yet been completely clarified. It is believed to be a chronic inflammatory process, associated with a previous history of brain injury, usually occurring in childhood, in genetically susceptible patients^{12, 13}.

Clinical manifestations

TLE-HS is clinically manifested by focal seizures, usually perceptive and that rarely evolve into bilateral tonic-clonic seizures³. Some patients with TLE-HS experience pre-ictal events, which can be useful in predicting an upcoming crisis, which can last for minutes, hours and occasionally days. Examples of these prodromes are headache, mood change, personality change and anxiety¹⁴.

The initial subjective signs and symptoms of the crisis, which can be described by the patient, constitute what was previously known as aura (which represents the beginning of the crisis)¹⁴. The occurrence of this subjective ictal phenomenon is more common in seizures originating in the temporal and parietal lobes. Subjective ictal phenomena announcing the crisis include a sensation of heat or epigastric discomfort, nausea, olfactory and gustatory hallucinations, and a feeling of familiarity (*déjà vu*) or unfamiliarity (*jamais vu*), followed by oral automatisms, stop reaction, and fixed and vacant gaze¹⁵.

Focal seizures without impaired consciousness are clinically characterized by autonomic and/or psychic symptoms, and certain phenomena, such as olfactory and auditory (including hallucinations)¹⁵.

Focal seizures with compromised consciousness are preceded or not by subjective ictal phenomenon, which can be described as "strange" epigastric sensation, feeling of fear, *déjà vu* or never *vu*-like phenomena, depression, anxiety, visual, auditory, olfactory or taste hallucinations, somesthetic auras, eroticism and feelings of well-being, being clinically characterized by motor symptoms, typically followed by oral-food automatism, and other types of automatism may follow. The duration is usually longer than one minute and post-ictal confusion is common. Crises are usually followed by amnesia and recovery is gradual¹⁵.

Approximately 24 to 30% of patients have loss of contact with the environment and interrupt what they were doing before the epileptic seizure itself, as if they were "frozen" or "frozen" (stop reaction or behavioral arrest), with their eyes open and fixed (staring). About 40 to 80% have typical automatisms, mainly of the hands and mouth (gestures and chewing or oral-food), or movements of the trunk and/or limbs repeatedly. There may be changes in heart rate, respiratory rate, pupillary diameter and pallor or redness, associated with other symptoms. In the immediate post-ictal period, mental confusion and changes in behavior ("automatic behavior"), such as standing, walking or running, may occur. Some patients progress to generalized tonic-clonic seizures¹⁴.

There are some early precipitating events, which tend to occur before the age of five and are classically related to MTS, such as febrile seizures, trauma, hypoxia, central nervous system infections. There is a difficulty, however, in tracing a direct causal relationship between them³.

Diagnosis

TLE-HS is responsible for a great negative impact on patients' lives, based on the history of seizures resistant to treatments with the use of antiseizure medications. Furthermore, recent studies demonstrate the relationship with several other complaints, such as the increase in psychiatric disorders, intense daytime sleepiness and cognitive deficits generated by alterations in memory, language, attention, motor functions and non-verbal processes, affecting the performance of daily activities¹⁶.

Accurate diagnosis is essential, especially in drug-resistant epilepsies such as TLE-HS¹⁷. One of the main difficulties in diagnosing epilepsy is distinguishing between true seizures and other comorbidities, such as syncope and pseudoseizures¹⁸. The diagnosis of temporal lobe epilepsy is based on the patient's clinical history, on complementary tests to locate the focus of the epilepsy and, if possible, its etiology¹⁹.

Within this context, the importance of neuropsychological assessment is highlighted, especially in patients who will undergo surgery. This assessment selects candidates for surgical treatment, determines the risks and benefits associated with the procedure and the probability of post-surgery efficacy¹⁹.

The electroencephalogram (EEG) in TLE is able to provide information about the presence of epileptiform activity. Persistent or intermittent finding of 4-7Hz of theta activity or 1-3Hz of uni or bilateral delta activity in the temporal regions is a nonspecific finding in various conditions such as stroke, hippocampal sclerosis or may not have any pathological substrate, however the pattern persistent is more related to structural abnormality²⁰.

According to Javidan (2012), the typical epileptiform abnormality is characterized by a tip or wave with negative polarity and often followed by a slow wave, where the temporal peaks have the maximum negativity in the temporal basal electrodes F7, F8, T1, T2 and sphenoid electrodes. In cases where the interictal EEG does not reveal abnormalities and when there are doubts regarding the diagnosis, the patient may be submitted to prolonged monitoring by video-electroencephalography (video-EEG). The main objective of prolonged video-EEG monitoring is to study the nature of a behavioral change, through EEG and synchronized video recordings.

Neuroimaging tests are also used, especially cranial nuclear magnetic resonance (MRI), capable of identifying hippocampal atrophy. This is the main diagnostic tool to detect anatomical abnormalities and when combined with EEG, it can more precisely identify the agreement or not with the ictal onset zone (ZII)¹⁷.

Among imaging studies, high-resolution MRI is the main method used to assess disease progression and identify the lesion caused by epilepsy, its location and extension, in addition to being decisive for the diagnosis of mesial temporal lobe epilepsy with hippocampal sclerosis¹⁹.

Hippocampal sclerosis has a high signal on T2 and FLAIR sequences, and MTLE can be detected by comparing the two hippocampus; differences in volume measurements between both characterize the atrophy that usually occurs in MTLE²¹. This comparison obviously takes into account that there is normality in one of the hippocampus, which means that patients with bilateral MTLE could

go unnoticed, requiring the use of other diagnostic tools. The interpretation of the difference in hippocampal volume can also be confounded when observed in elderly individuals (due to the aging process itself) or in patients with brain damage resulting from infection or previous trauma²².

Voxel-based morphometry (VBM) based on magnetic resonance is also another quantitative analysis technique that estimates the regional change in gray matter in epilepsy, used to describe functional and structural image changes in patients with TLE-HS²³. In this context, it is evaluated that the abnormalities commonly found in patients are characterized by signal changes, loss of volume and loss of differentiation between white and gray matter. The accuracy of the findings of these structural changes, however, will depend on the experience of the operator²⁴.

The recent enhancement of neuroimaging resources has enabled a greater ability to analyze brain metabolism, structure and functional deficiencies found in patients with TLE-HS²⁵. In patients being considered for epilepsy surgery, functional neuroimaging tests such as ictal single photon emission computed tomography (SPECT) and ictal positron emission tomography (PET) can provide information related to alterations in regional cerebral blood flow and focal cerebral metabolism, respectively, if they are in agreement with ZII²⁶.

A promising resource within neuroimaging innovations is magnetic resonance fingerprinting (RMF), a new modality capable of analyzing several parameters at the same time, in a single image acquisition. This makes the RMF able to recognize subtle changes that would not be detected in the conventional magnetic resonance, which increases the sensitivity and accuracy in identifying lesions²⁴.

Treatments

Attention to the treatment of mesial temporal lobe epilepsy associated with hippocampal sclerosis remains of special interest due to its high prevalence and frequent resistance to antiseizure medications. The so-called "Clinically intractable epilepsy" is a term defined by the International League Against Epilepsy (ILAE) to define a group of patients who do not respond to treatment with antiseizure medications for a certain period of time²⁷. Thus, surgery should be considered in these patients²⁸.

Although the main focus of drug and surgical treatment is the control of crises, carrying out the neuropsychological assessment is important as it can detect risks and sequelae associated with the surgical procedure in cognitive functions, especially in the area of the visual, motor, speech and memory system, even in patients who no longer have seizures²⁸.

The preoperative evaluation is responsible for determining the brain area where the crises originate and the precaution of a safe resection without postoperative sequelae. It is a multidisciplinary process that involves the performance of structural tests (computed tomography and magnetic resonance), functional tests (neuropsychological assessment, sodium amytal test, SPECT and brain PET), video-EEG monitoring (non-invasive and possibly invasive) and psychosocial assessment. The main data to consider are magnetic resonance, interpreted in the context of clinical data and EEG²⁹.

Technological advances now allow neurophysiological monitoring and minimally invasive surgical interventions, thus avoiding major craniotomies and associated morbidities³⁶. Surgical treatment for drug-resistant mesial temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) is the most effective alternative, although the literature reports seizure recurrence in 30% of patients treated surgically¹⁹. In these patients who are refractory to surgical treatment, third-generation anti-seizure drugs can be used, in an attempt to better control the seizures after the procedure, since these medications provide improvements in terms of safety, tolerability and pharmacokinetics³³.

Among the standard techniques for patients refractory to clinical treatment, the anterior temporal lobectomy (ATL) stands out. The analyzed studies demonstrate to be the most effective treatment for the control of crises³⁰. This technique consists of removing the anterior portion of the temporal lobe, removing structures such as the amygdala, hippocampus and temporal neocortex. The ATL surgical technique is a consolidated and effective procedure, with minimal mortality after the surgical procedure. However, ATL presents complications such as psychiatric disorders, visual field defects and cognitive disorders.

Another technique established as a surgical alternative for mesial temporal lobe epilepsy associated with hippocampal sclerosis (TLE-HS) is selective tonsilhippocampectomy (SAH), which from advances in neuroimaging allowed the emergence of improved techniques that spare healthy brain tissue³¹. The technique consists of selective resection of mesial structures through various types of access, including the transcortical, transsylvian, transinsular and subtemporal access.^{31,37}

No statistically relevant differences were found that show the superiority of any of the analyzed techniques over the other in the surgical treatment of MTLE, when considering the control of convulsive crises and memory alterations in the postoperative period³¹.

Among the techniques developed for the surgical treatment of TLE-HS, magnetic resonance-guided interstitial thermal therapy (LiTT) is a minimally invasive technique that has shown promise and an alternative to open surgery³². Reports favorable to the safety and efficacy of the technique were found in the literature, however, this new surgical technique is not universally available and the indications, safety and efficacy need further evaluation.^{30,32}

Another technique that has emerged as an alternative to open surgery (ATL and SAH), which has been adopted, is stereoelectroencephalography (SEEG). The SEEG electrode coverage allows for a very accurate three-dimensional exploration of the epileptic network, but also provides the chance to generate thermocoagulation lesions of the epileptogenic zone using a radio frequency (RF) generator connected to the electrode contacts³².

It is a minimally invasive technique that, compared to open surgical techniques, has superiority in terms of patient discomfort, which is less, better preserved brain function, reduced surgical complications and shorter hospital stay³². This technique has been indicated for patients with focal lesions such as hypothalamic hamartomas. However, SEEG-guided RF-TC is not the first-line therapeutic option for the treatment of TLE-HS, due to its lower and more

durable efficacy than ATL³². Literature reports that this technique may be a promising option for the treatment of TLE-HS³².

Prospective randomized studies have demonstrated significantly higher seizure-free rates in patients treated surgically compared to those who received the best drug therapy³². Thus, surgical treatment has been shown to be effective for the complete resolution of crises in the vast majority of cases, given the advances in the surgical area and the number of patients refractory to clinical treatment. However, treatment flows need to be further explored. The success of the process is related to a good preoperative evaluation, a well-performed surgical procedure and an appropriate post-surgical follow-up. possible sequelae.

Conclusion

TLE-HS has peculiarities that must be well understood, mainly because it is a type of epilepsy that is highly prevalent in the population and difficult to control with medication.

Knowledge about its pathophysiology, clinical manifestations, diagnosis and treatments are of fundamental importance for physicians who treat patients with epilepsy.

It is necessary to institute further research, which aim to elucidate the mechanisms involved in the development and perpetuation of TLE-HS, thus providing a more effective treatment.

Aknowledgment

This study was financially supported for authors themselves.

References

1. Fisher, R.S. et al. The practical clinical definition of epilepsy. *Epilepsy*, v. 55, no. 4, p. 475-482, 2014.
2. Fisher RS, Cross JH, French JA, Higurashi N, Hirsch E, Jansen FE, et al. Operational classification of seizure types by the International League Against Epilepsy: Position Paper of the ILAE Commission for Classification and Terminology. *Epilepsy*. 2017;58(4):522-530. doi:10.1111/epi.13670.
3. Spengler L.F.M., Enock A., Lin K. Mesial Temporal Sclerosis: Prevalence Study in a Reference Outpatient Clinic at University Hospital Professor Polydoro Ernani de São Thiago. *Architect. Med.* Oct-Dec; 49(4):55-68, 2020.
4. Bianchin, M.M. et al. Understanding the association of neurocysticercosis and mesial temporal lobe epilepsy and its impact on surgical treatment of patients with drug-resistant epilepsy. *Epilepsy & Behavior*, [s. l.], v. 76, p. 168-177, 2017.

5. Chiang S. & Haneef Z. Graph Theory findings in the pathophysiology of temporal lobe epilepsy. *Clinical Neurophysiology*, S1388-2457 (14) 00192-8, 2014.
6. Telles Zentano, J.F., Hernandez Ronquillo, L.. A review of the epidemiology of temporal lobe epilepsy. *Epilepsy Research and Treatment*, 2012.
7. Zhao, Xu et al. Reduced interhemispheric white matter asymmetries in medial temporal lobe epilepsy with hippocampal sclerosis. *Frontiers in Neurology*, v. 10, p. 394, 2019.
8. Sendrowski K., Sobaniec W. Hippocampus, hippocampal sclerosis and epilepsy. *Pharmacological Reports*, 65, 555565, 2013.
9. Blumcke, I.; Thom, M.; Aronica, E.; Armstrong, D.D.; Bartolomei, F.; Bernasconi, A.; Bien, C.G.; Cendes, F.; Coras, R.; Cross, H.; et al. International consensus classification of hippocampal sclerosis in temporal lobe epilepsy: A Task Force report from the ILAE Commission on Diagnostic Methods. *Epilepsy*, [S.l.], v. 54, no. 7, p. 1315-29, 2013.
10. Elkommos, Samia et al. Hippocampal internal architecture and postoperative seizure in temporal lobe epilepsy due to hippocampal sclerosis. *Seizure*, v. 35, p. 65-71, 2016.
11. Elkommos, Samia et al. Hippocampal internal architecture and postoperative seizure in temporal lobe epilepsy due to hippocampal sclerosis. *Seizure*, v. 35, p. 65-71, 2016.
12. Horta, Wagner G. et al. Genetic association study of the HLA class II alleles DRB1, DQA1, and DQB1 in patients with pharmaco-resistant temporal lobe epilepsy associated with mesial hippocampal sclerosis. *Seizure*, v. 31, p. 7-11, 2015.
13. Thom M. Hippocampal sclerosis in epilepsy: a neuropathology review. *Neuropathology and Applied Neurobiology* 40, 420–543. 2014.
14. Blair, R.D.G. Temporal lobe epilepsy semiology. *Epilepsy Research and Treatment* 2012.
15. Miguens-Blanco, I.; Rodriguez-Acevedo, B. Temporal lobe epilepsy: déjà vu in primary attention. *Semergen*, [S.l.], v. 39, no. 7, p. 57-59, 2013.
16. Vascounto, Helena Dresch et al. Is self-report sleepiness associated with cognitive performance in temporal lobe epilepsy?. *Arch Neuropsychiatr*, v. 76; n. 9, p. 575-581, 2018.
17. Memarian, N.; Thompson, M.P.; Engel, J. Jr.; Staba, R. Quantitative analysis of structural neuroimaging of mesial temporal lobe epilepsy. *Imaging Med*, [S.l.], v. 5, no. 3, 2013.

18. Alves-Leon, S.V.; Pinto, M.P.; Andraus, M.E.C.; Pereira, V.C.S.R.; Meira, I.D.; Oliveira, R.C.; Villas Boas, S.; Rego, C.C.S.; Souza, J.P.B.M.; Pedrosa, R.C. Syncope in patients with drug resistant epilepsy without apparent cardiovascular disease. *Arq Neuropsychiatr.*, São Paulo, v. 71, no. 12, p. 925-30, 2013.
19. Gaça, Larissa Botelho et al. Morphometric MRI features and surgical outcome in patients with epilepsy related to hippocampal sclerosis and low intellectual quotient. *Epilepsy & Behavior*, v. 82, p. 144-149, 2018.
20. Javidam, M. Electroencephalography in mesial temporal lobe epilepsy: the review. *Epilepsy Research and Treatment*, [S.l.], v. 12, 2012.
21. Liao Congyu et al. Detection of lesions in mesial temporal lobe epilepsy by using MR fingerprinting. *Radiology*, v. 288, no. 3, p. 804-812, 2018.
22. Mettenburg, J.M. et al. Improved detection of subtle mesial temporal sclerosis: validation of a commercially available software for automated segmentation of hippocampal volume. *American Journal of Neuroradiology*, vol. 40, no. 3, p. 440-445, 2019.
23. Wei, Wei et al. More severe extratemporal damages in mesial temporal lobe epilepsy with hippocampal sclerosis than with other lesions: a multimodality MRI study. *Medicine*, s. 95, no. 10, 2016.
24. Wang, Kang et al. Magnetic resonance fingerprinting of temporal lobe white matter in mesial temporal lobe epilepsy. *Annals of clinical and translational neurology*, v. 6, no. 9, p. 1639-1646, 2019.
25. Tang, Yingying et al. Short-term cerebral alterations after surgery in patients with unilateral temporal lobe epilepsy associated with hippocampal sclerosis: a longitudinal resting-state fMRI study. *Seizure*, v. 46, p. 43-49, 2017.
26. Malmgren, K.; Thom, M. Hippocampal sclerosis origins and imaging. *Epilepsy*, [S.l.], v. 53, no. 4, p. 19-33, 2012.
27. Burneo, Jorge G et al. "Disparities in surgery among patients with intractable epilepsy in a universal health system." *Neurology* v. 86.1: p 72-78, 2016.
28. Engel, Jerome Jr. "What can we do for people with drug-resistant epilepsy? The 2016 Wartenberg Lecture." *Neurology* v. 87.23: p. 2483-2489, 2016.
29. Behling, Jonny et al. "Temporal lobe epilepsy: is it possible to cure?". *Medical Minutes - Academic Leagues*. v. 39, p. 6, 2018.
30. Birth, Fabio. et al. Anterior temporal lobectomy versus selective amygdalohippocampectomy in patients with mesial temporal lobe epilepsy. *Arch Neuropsychiatrists* v. 74, p. 35-43, 2016.

31. Teixeira, Aquila. Barreiro, Leonardo. Comparison Between the Outcomes of Anterior Temporal Lobectomy and Selective Amygdalohippocampectomy in the Surgical Treatment of Temporal Lobe Epilepsy. *J Bras Neurosurgery* v. 29, p. 634 - 641, 2018.
32. Fan, Xiaotong, et al. Optimized SEEG-guided radiofrequency thermocoagulation for mesial temporal lobe epilepsy with hippocampal sclerosis. *European Journal of Epilepsy* v. 71, p. 304-311, 2019.
33. LaPenna, P, Tormoehlen, L.M. The Pharmacology and Toxicology of Third Generation Anticonvulsant Drugs. *Journal of Medical Toxicology*. 13, 329-342, 2017.
34. Alison, M. Epilepsy Overview and Revised Classification of Seizures and Epilepsies. *American Academy of Neurology*, 306-321, 2019.
35. Beghi, E. The Epidemiology of Epilepsy. *Neuroepidemiology*, 54, 185,191, 2020.
36. Seto, E.S. Epilepsy Surgery: Monitoring and Novel Surgical Techniques. *Neurologic Clinics*, 39, 723-742, 2021.
37. Santos, A.R., Conceição, P.O., Cruz, P.L., Cavalcanti,D.D., Filho, P.N. Surgical Treatment of Mesial Temporal Lobe Epilepsy: Selective Amygdalohippocampectomy Using Niemeyer's Approach. *Neurosurgery - Caes and Reviews*, 2018.
38. Chang, B.; Xu, J. Deep brain stimulation for refractory temporal lobe epilepsy: a systematic review and meta-analysis with an emphasis on alleviation of seizure frequency outcome. *Childs Nerv Syst*, v. 34, n. 2, p. 321-327, Feb 2018.
39. Steinhoff, B. J.; Staack, A. M. Is there a place for surgical treatment of nonpharmacoresistant epilepsy? *Epilepsy & Behavior*, v. 91, p. 4-8, 2019.
40. San Juan, D, Rodriguez Mendez, D.A. Epilepsia como uma enfermidade de redes neuronales. Un punto de vista neurofisiológico. *Neurologia*, 2020.

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