Temporal lobe epilepsy
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ABSTRACT
In this paper we present a brief review of temporal lobe epilepsy from clinical aspects, neuroimaging, pathological and diagnosis that have led us to understand and identify more accurately this disease, as interesting as disturbing and as old as the humanity.

Key words: temporal lobe, epilepsy, neuroimaging, clinical aspects.

Epilepsia del lóbulo temporal
RESUMEN
En este artículo realizamos una pequeña revisión de la epilepsia del lóbulo temporal desde los aspectos clínicos, de neuroimagen, diagnóstico y patológico que nos han llevado a comprender e identificar con mayor exactitud esta enfermedad tan interesante como inquietante, así como tan antigua como la propia humanidad.

Palabras clave: lóbulo temporal, epilepsia, neuroimagen, aspectos clínicos.

Temporal lobe epilepsy (TLE) is the most common form of localization-related epilepsy (LRE) in adults accounting for approximately 60-80% of all patients with epilepsy\(^1,2\). Medial temporal lobe epilepsy (mTLE) is far more common than neocortical TLE, and represents a heterogeneous spectrum of focal seizures that are clinically expressed by structures of the medial temporal lobe, is also referred to as mesial temporal lobe epilepsy\(^3,4\).

Nevertheless, mTLE is a syndrome due the several pathologies and manifestations that have been classified based upon the site of suspected neuroanatomic origin by the International Classification of Epilepsies and Epileptic Syndromes in 1985\(^5\).

The terms used previously for the focal seizures of temporal lobe origin have included psychomotor seizures, limbic seizures and temporal lobe seizures, among others, and its use has changed over the years with most recent classification proposals that have included a change of complex partial seizures of temporal lobe origin to focal seizures with dyscognitive (or different) characteristic semiological characteristics, even though the definition is undergoing an evolution\(^6\).

It is important to note that mTLE is not only the epileptic syndrome most commonly diagnosed in adults, but is also the most frequent refractory treatment and strongly associated with hippocampal sclerosis (HS)\(^2\), doing it a frequent medical challenge.

While this is a fairly well-characterized clinical syndrome and relatively homogeneous, we also have a differential diagnosis and the interrelationship between psychiatric and behavioral homologues have been identified and defined mainly by the clinical information was obtained from surgical series consisting of patients requiring temporal lobectomy\(^7\).

The overall prognosis for patients with mTLE drug resistance is often associated with a higher rate of...
morbidity and deterioration of health-related quality of life (HRQOL). Added to this, often there is a higher mortality rate among the most severely affected patients, who often have in progress seizures and failed epilepsy surgery.

**Functional neuroanatomy of the temporal lobe**

The temporal lobe is the most epileptogenic area of the brain. The medial temporal lobe is a part of the limbic system concerned in emotional issues of behavior. Focal seizures may come from one or both medial temporal lobes, including the amygdala, hippocampus and parahippocampal gyrus.

The amygdala in humans, when activated during an aura, often produces a feeling of fear or creates a feeling of impending doom. The amygdala could also be involved in the defensive behavior consisting of pupillary dilation, aggressive stance and autonomic effects like piloerection, tachycardia, tachypnea, and seldom, a feeling of anger. It may be present, hypersexuality hyperactivity, and hyperorality after bilateral lesions in the amygdala. The medial temporal lobe is also very heavily involved with episodic memory (information which is linked to the time and location of occurrence) and declarative (the explicit memory of facts that can be verbalized) involving new memories for experienced events. The hippocampal formation (HF) comprises of the dentate gyrus (DG), hippocampus and subiculum. It is a three-layer allocortex of pyramidal cells in the hippocampus, subiculum and has the potential for neuronal plasticity through the long-term potentiation.

The hippocampus is divided into head, body and tail, has an approximate length of 4-4.5 cm and is important for functions such as memory and spatial navigation. It is divided into sub-areas of the cornu Ammonis (CA): CA1-CAN are surrounded by the DG, which is extremely important for the transmission of short-term memory to long-term storage in association areas. The parahippocampal gyrus has two-way connections between the hippocampus and in all major cortical association areas and primary olfactory (figure 1).

Patients with severe damage to the medial temporal lobes might become amnesiac with incapacity to form and retain new memories. The neuropsychological tests and intracarotid amobarbital test have allowed us to evaluate the functions of the hippocampal memory and other cognitive functions in epileptic patients.

The memory dysfunction has been shown by HM, a man who underwent bilateral resection of the mesial temporal structures for refractory epilepsy resulting in severe anterograde and retrograde amnesia.

The left temporal lobe normally functions as the dominant lobe for verbal memory rule. In a longitudinal study was performed a resective surgery for mTLE being observed a decrease of 30% after right temporal resection and 51% after left temporal resection, however, if the successful surgery was able to carry out then cease or reversal of decreased memory function was observed.

The dominant lateral temporal neocortex is implicated in the listening, comprehension and can get involved with medial temporal dysfunction. The role of language in the dominant temporal lobe is implicated both in understanding and naming. Confrontational naming and delayed memory has been shown to be decreased by up to 40% in patients with temporal lobe epilepsy compared with <5% of controls.

Temporal lobe structures nondominant are more involved in visual memory. The basal aspect of the temporal lobes seem to be more involved in the visual process of faces and scenes that reflect the activity in the fusiform gyrus and parahippocampal gyrus. Cognitive impairment commonly associated to mTLE and could be an effect of progressive hippocampal formation atrophy.
have been used to identify different cell populations in mTLE. Cell counts and immunohistochemical stains may appear absent using the current techniques of neuroimaging for its diagnosis. A very specific physiological mechanism could be the basis of drug-resistance even more confusing the identification of the cause-effect relationship between the HFA and mTLE.

Furthermore the levels of glutamate and the changes in neuronal glutamate transporters are involved and they are another mechanism that is out of order.

It has also been possible to identify genetic influences, which have been important in mTLE. A familiar and particularly temporal lobe epilepsy type has been reported with autosomal dominant although relatively uncommon and generally not associated with HFA. Different additional family forms have been identified and reported where mTLE was observed in some families but not associated with autosomal dominant transmission. Added to this, the HFA may be present in first-degree relatives without clinically evident seizures, making it even more confusing the identification of the cause-effect relationship between the HFA and mTLE.

Kauffman et al showed that the ApoE 4 allele is associated with an earlier onset of mTLE, in turn; the HFA has been associated with the ApoE4 allele. Patients with the 4 allele had an onset of epilepsy 5 years earlier, on average, than patients without the 4 allele. TLE phenotypes may be associated with SCN1B (the gene encoding the sodium channel α 1 subunit) mutations as a subtype of cryptogenic generalized epilepsies with febrile seizures. The role of pharmacogenetics in patients with drug-resistant epilepsy has most closely examined the genotype at ABCB1.

We can observe also other pathological findings such as the loss of the internal architecture of the HF, atrophy of the amygdala, mammillary bodies and even changes in the white matter. The hippocampus has several functional and DG subfields, CA 1-3 and of course the subiculum. The initial identification of hippocampal atrophy in TLE showed ipsilateral alteration and neuronal loss in the DG and CA1.

Wyler AR et al, have described four different patterns of atrophy in the hippocampus on mTLE because of HS: global atrophy, end folium sclerosis (DG atrophy) CA1 atrophy, and atrophy of the CA1 + DG.

The postoperative pathological series seem to show a wider participation, either global atrophy or only atrophy at CA1, CA3 and DG in patients with successful seizures results after temporal lobe surgery.

If it is identified involvement only in a single subdivision in isolation, then the presence of total HFA may appear absent using the current techniques of neuroimaging for its diagnosis. A very specific physiological mechanism could be the basis of drug-resistance to mTLE. Cell counts and immunohistochemical stains have been used to identify different cell populations in the dentate in mTLE. The loss of neurons in the hippocampus has also been accompanied by selective loss of somatostatin and neuropeptide Y interneurons that in essence reconnect the connections of the hippocampus. Some molecular mechanisms have been associated with drug-resistant on mTLE such as low levels of GABA in the brain.

Pathology

The mTLE is more than anything an acquired form LRE and is highly correlated with the pathophysiology of HS, especially in patients with drug-resistant seizures.

The HS is the main etiology in different surgical series published, which can be easily identified through the use of brain MRI. It can also be identified but with a much lower frequency associated with gliomas, hemangiomas, traumatic or infectious, among others, besides that also might happen dual pathology in 5-30%. Whereas the lesional mTLE is associated with temporal lobe damage, the mTLE without injury or nonlesional mTLE is distinguished based on neuro-imagenological studies and no identifiable underlying pathology. An apparently normal hippocampi occurs in 30-40% with the remaining 60-70% of patients with HS on histopathology.

The HS consists of a mix of atrophy and astrogliaosis in the amygdala, hippocampus, entorhinal cortex, and parahippocampal gyrus. Thom, M., et al on postmortem studies have shown that synaptic reorganization in the hippocampus in patients with HS is frequently a bilateral finding that appears to be a permanent feature in these kind of patients with mTLE.

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at least one seizure in early childhood where the majority of patients experience febrile seizures (FS), although some other symptomatic causes such as traumatic brain injury, perinatal injuries, CNS infections and tumors of slow growth may also occur. The FS represent the most common risk factor that occurs during infancy and early childhood. Approximately two thirds of patients with temporal lobe epilepsy in a series with FS had no apparent infection directly affecting the CNS before the onset of complex partial seizures.

About 75% of these febrile seizures were complex with prolonged or focal features that can be distinguished from simple febrile seizures. The Complex FS are the type of seizures associated with fever for 15 minutes or longer, also include clinical symptoms during the seizure activity, or recur within 24 hours. A history of childhood prolonged FS is often present in patients with refractory mTLE suggests HS as the underlying pathophysiology of recurrent seizures.

However, as reported Scott et al, a history of FS not increase the risk of epilepsy in a significantly rate in the general population. But, when complex febrile seizures are prolonged, swelling of the hippocampus can be documented and can be seen HS in a progressive evolution with MRIs serially or periodically when performed prospectively.

It has been described that the beginning of the mTLE usually occurs during the first or second decade of life in the vast majority of patients after a latency period when brain injury or FS have already happened. The most common types of seizures have been reported in mTLE are: focal seizures (auras) and with (complex partial) impairment of consciousness. Villanueva et al, have reported that there is hormonal influences during menstruation and also during ovulation. Seizure auras (from the Latin for breeze, Greek for air) occur in many TLE patients and often exhibit features that are relatively specific for TLE but few are of lateralizing value.

French et al, reported that a large percentage of patients have at least one aura with experiential and viscerosensory symptoms in mTLE. The experiential symptoms of temporal lobe seizures are hallucinations, illusions or both, and are also described as mental, intellectual or psychic symptoms, or dreamy states. They may involve any faculty of the human mind: thinking, emotion, memory and recollection, chronological order, speed, sensation, reality and unreality, and their interactions with past, present and imaginary experiences. Events and experiences may be reproduced intact or disturbed: the present may be misplaced to the past, and the past to the present; real may be seen as unreal and vice versa; time may be speeded up or slowed down; and shape and other morphology may be natural or unnatural, and deformed or undistorted.

Psychic phenomenon including fear, anxiety, déjà vu (it is defined as any subjectively inappropriate impression of familiarity of a present experience with an undefined past), and autoscopic (patients may describe a sense of dissociation in which they report seeing their own body from outside), commonly occur with mTLE in addition to viscerosensory auras. Sensory and autonomic auras are characterized by changes in heart rate, piloerection, and sweating. Patients may experience nausea, "butterflies", or an epigastric "rising" sensation. Olfactory and gustatory illusions and hallucinations may occur; Acharya et al found that olfactory auras are more commonly associated with temporal lobe tumors whereas mesial temporal sclerosis was relatively uncommon.

Clinical features

Complex partial seizures (CPS) are a primary focal seizure type with impaired consciousness in mTLE and behavioral semiology reflecting their anatomical location of temporary structures with duration of 30 seconds to 1 to 2 minutes.

Both sexes are affected equally. However, it has been identified significant differences between clinical and semiologic manifestations in patients with TLE not only with respect to lateral and mesial distinction, but also to the evolution of semiology regarding the age of onset with increased motor manifestations which occur in <6 years.

Epilepsy occurs in all age groups, but the prevalence of seizures is highest early in life and peaks again after age 60. Complex partial seizures represent more than 50% of new seizure cases in the elderly. Complex partial seizures manifest some combination of altered awareness and amnesia during an attack. Recurrent partial seizures causing transient amnesia have also been reported. Tatum et al., suggest that memory dysfunction in the elderly may be caused by complex partial seizures and may present in two ways: discrete episodes of amnesia may occur or, alternatively, an insidious fluctuating course of memory dysfunction may simulate dementia.

The temporal lobes and the frontal lobes are the two most common sites where partial seizures originate. It is crucial to distinguish reliably these two types of seizures, because many epileptogenic lesions involve both temporal and frontal lobes.

Focal seizures with impaired consciousness (aka complex partial seizures) in mTLE usually occur with impaired consciousness, fixed stare, and automatisms.
The ipsilateral automatisms and contralateral dystonic posturing at the moment of the seizure are quite useful lateralizing signs that help us to identify the start of the crisis; however, they have a limited use.

Individuals with CPSs may be unaware that they had a seizure minutes earlier. They may also be unable to recall events which occurred before seizure onset. The degree of retrograde and anterograde amnesia is variable. Postictal amnesia likely results from bilateral impairment of hippocampal function. Stimulation of medial temporal lobe structures producing an afterdischarge affects the formation and retrieval of long-term memories. Automatisms represent coordinated involuntary motor activity that is stereotyped and virtually always accompanied by altered consciousness and subsequent amnesia. No uniform classification of this phenomenon has been developed. One system divides automatisms into de novo and preservative automatisms. De novo automatisms are said to occur spontaneously at or after seizure onset. They might be classified as “release” phenomena, which include actions normally socially inhibited or “reactive” phenomena when they appear to be reactions to external stimuli. For example, the patient may drink from a cup placed in his hand or chew gum placed in his mouth. Preservative automatisms might represent continuation of complex motor acts initiated prior to seizure onset, for example, opening and closing a door repeatedly. Automatisms occur in almost two thirds of CPSs of mesial temporal lobe onset. They often involve the hands (fumbling, picking, and fidgeting) or mouth (chewing, lip smacking, swallowing).

Blair R.D. has reported even less common behavioural, such as, crying (dacrystic), laughing (gelastic), and so-called “leaving behaviours,” for example, running out of the house or down the street during a seizure (cursive). A rare automatism, whistling, has also been recently reported to occur during temporal lobe seizures.

Seizure semiology does not appear to be clearly distinct with different pathologies though HS may be more characteristically associated with ipsilateral limb automatisms and contralateral dystonic posturing.

Temporal lobe seizures can be simple partial, complex partial, or secondarily generalized seizures, these latter are relatively infrequent and are usually controlled with AEDs and do not occur as the exclusive or predominant seizure type. Status epileptics and prolonged seizures are infrequent but may occur.

**Neuroimaging**

Brain MRI needed relatively short time to become the gold standard for neuroimaging at the time of evaluation and diagnosis of patients with focal, and/or structural anatomical lesions in patients with mTLE.

The MTS can be relatively easy visible and identified qualitatively in the high-resolution brain MRI with the typical characteristics of the HFA plus the increased signal on fluid attenuated inversion recovery (FLAIR) or T-1 in coronal/axial section best noted, and T-2 weighted sequences in coronal sections with particular protocols that include anatomical orientation, thin sections, and imaging sequences to augment visualization (figure 2).

Semiologies that suggest lateralizing or localizing value are shown on the table below.

<table>
<thead>
<tr>
<th>Feature Location</th>
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<tbody>
<tr>
<td>Unilateral limb automatism Ipsilateral focus</td>
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<tr>
<td>Oral automatism (m) Temporal lobe</td>
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<tr>
<td>Unilateral eye blinks Ipsilateral to focus</td>
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<tr>
<td>Postictal cough Temporal lobe</td>
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<tr>
<td>Postictal nose wiping Ipsilateral temporal lobe</td>
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<tr>
<td>Ictal spitting or drinking Temporal lobe focus (R)</td>
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<tr>
<td>Gelastic seizures (m) Temporal, hypothalamic, frontal (cingulate)</td>
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<tr>
<td>Dacrystic seizures (m) Temporal, hypothalamic</td>
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<tr>
<td>Unilateral limb automatisms Ipsilateral focus</td>
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<td>Whistling Temporal lobe</td>
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<tr>
<th>Motor Location</th>
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<tr>
<td>Early nonforced head turn Ipsilateral focus</td>
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<tr>
<td>Late version Contralateral focus</td>
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<tr>
<td>Eye deviation Contralateral focus</td>
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<tr>
<td>Focal clonic jerking Contralateral perirolandic focus</td>
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<tr>
<td>Asymmetrical clonic ending Ipsilateral focus</td>
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<tr>
<td>Fencing (MZE) Contralateral (supplementary motor)</td>
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<tr>
<td>Tonic limb posturing Contralateral focus</td>
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<tr>
<td>Dystonic limb posturing Contralateral focus</td>
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<tr>
<td>Unilateral ictal paresis Contralateral focus</td>
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<tr>
<td>Postictal Todd’s paresis Contralateral focus</td>
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<th>Autonomic Location</th>
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<tr>
<td>Ictal emeticus Temporal lobe focus (R)</td>
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<td>Ictal urinary urge Temporal lobe focus (R)</td>
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<tr>
<td>Piloerection Temporal lobe focus (L)</td>
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<tr>
<th>Speech Location</th>
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<tr>
<td>Ictal speech arrest Temporal lobe (usually dominant hemisphere)</td>
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<tr>
<td>Ictal speech preservation Temporal lobe (usually nondominant)</td>
</tr>
<tr>
<td>Postictal aphasia Temporal lobe (dominant hemisphere)</td>
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Berg reported that a volumetric analysis across different studies demonstrates normal hippocampal volumes as mean ranges from 2660 to 5180 mm3 with a standard deviation lower than 10% from normal volumes in young adults, and the determination of volumes depends greatly on experience, methods and age.
(SISCOM) may assist with localization, operative subtraction ictal SPECT coregistered with MRI photon emission computed tomography (SPECT) and compared with contralateral regions (43). Ictal single-photon emission computed tomography (SPECT) and subtraction ictal SPECT coregistered with MRI (SISCOM) may assist with localization, operative strategies, and even in predicting surgical outcome44.

CONCLUSIONS

mTLE is a well-known epilepsy syndrome, distinct, and often with a well-recognized clinic, neuroradiographic, electroencephalographic, and pathologic profile. Recent neuroimaging techniques are increasingly recognizing symptomatic “causes” of mTLE acquired through higher resolution of temporal neuroanatomy. Although not yet fully know the natural history of this disease, are impressive advances that have been achieved with these techniques to identify more quickly this disease as old as humanity itself.

REFERENCES

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