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Dissertação I Artigo Original

# Psychiatric Comorbidities in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

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2020

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INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

# Psychatric Comorbidities in Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis

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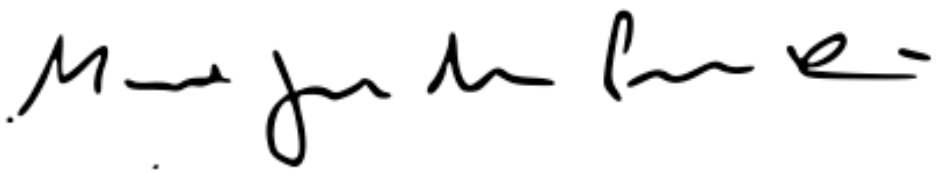
**Julho, 2020**

**Assinatura do Estudante**

**Assinatura do Orientador**

**Assinatura do Coorientador**



*Mestre, são plácidas*
*todas as horas*
*que nós perdemos.*
*Se no perdê-las,*
*qual numa jarra,*
*nós pomos flores.*

Ricardo Reis

## Acknowledgements

Ao meu orientador, Doutor João Chaves, pelo constante encorajamento.

À Professora Carolina Lemos, pela sua generosidade e paciência.

À Marta Cardoso, pelo inesgotável apoio.

Aos meus amigos e família, pela presença neste longo caminho.

A todos os professores que me guiaram até este ponto.

**Resumo**

**Introdução:** A epilepsia do lobo temporal mesial com esclerose do hipocampo é um tipo comum de epilepsia focal e associa-se a maior suscetibilidade e prevalência de doenças psiquiátricas. As comorbilidades psiquiátricas mais frequentemente encontradas nesta população são as perturbações afetivas e perturbações de ansiedade. Algumas perturbações psiquiátricas, como a depressão, podem dificultar o controlo das crises epiléticas e ter mais impacto na qualidade de vida do que as próprias crises. A associação da comorbilidade psiquiátrica com a lateralidade da esclerose é ainda alvo de controvérsia, com a maioria dos estudos a associar a lateralidade esquerda com as perturbações psiquiátricas mais comuns.

**Objetivos:** Identificar a prevalência de comorbilidades psiquiátricas nos doentes com epilepsia do lobo temporal mesial associada a esclerose do hipocampo e estudar as possíveis associações e influência da lateralidade.

**Metodologia:** Foi feita uma análise retrospetiva institucional dos dados demográficos e clínicos de todos os doentes com esta patologia (*n*=228) e com idade superior a 18 anos. O diagnóstico psiquiátrico foi feito por um médico psiquiatra, na sua maioria na Consulta de Psiquiatria de Ligação que faz parte da consulta multidisciplinar de epilepsia da nossa instituição, e cuja classificação teve por base a quarta edição do Diagnostic and Statistical Manual of Mental Disorders.

**Resultados:** Cento e trinta doentes (57,0%) tiveram o diagnóstico de perturbação psiquiátrica ao longo da vida. Setenta e nove (34,6%) apresentaram perturbações afetivas e sessenta e sete (29,4%) perturbações de ansiedade. As perturbações afetivas foram associadas ao sexo feminino (*p*=0,045). As perturbações psiquiátricas foram associadas a uma maior duração de epilepsia (*p*=0,025). Tendo em conta a lateralidade da esclerose do hipocampo, a esquerda foi a mais comum (52,2%), seguida da direita (40,8%) e da bilateral (7,0%). A esclerose do hipocampo esquerdo foi associada a uma maior duração de epilepsia (*p*=0,019) e a uma maior prevalência de história de convulsões febris (*p*=0,027). Não foram encontradas associações entre a lateralidade da lesão e os tipos de perturbação psiquiátrica, exceto entre as perturbações de ansiedade e a lateralidade direita (*p*=0,042). Não foi encontrada associação entre lateralidade e sexo.

**Conclusões:** Foi identificada uma alta prevalência de comorbilidades psiquiátricas ao longo da vida nesta amostra, com ênfase nas perturbações depressivas e perturbações de ansiedade. A probabilidade de um doente sofrer de perturbações de ansiedade tendo esclerose do hipocampo direito foi cerca do dobro da lateralidade esquerda.

**Palavras-Chave:** Epilepsia do Lobo Temporal; Esclerose Mesial Temporal; Esclerose do Hipocampo; Perturbações Psiquiátricas; Lateralidade;

**Abstract**

**Introduction:** Mesial temporal lobe epilepsy with hippocampal sclerosis is a common type of focal epilepsy and it is associated with a high prevalence and susceptibility to psychiatric disorders. Affective disorders and anxiety disorders are the most common psychiatric comorbidities found in these patients. Some psychiatric disorders, like depression, might hinder seizure control and might have a bigger impact on the quality of life than the seizures alone. Associating psychiatric disorders with the laterality of the hippocampal sclerosis remains a controversial subject, with most studies associating the main psychiatric disorders with the left hippocampal sclerosis.

**Objective:** To evaluate the lifetime prevalence of psychiatric comorbidities in patients with a diagnosis of mesial temporal lobe epilepsy with hippocampal sclerosis and to analyse a potential association between various variables and influence of laterality.

**Methods:** A retrospective institutional study was designed so that the demographic and clinical data from patients over the age of eighteen with this condition ($n$=228) were reviewed. The psychiatric diagnosis was made by a psychiatrist, often in the Consultation-Liaison Psychiatry, as a part of the multidisciplinary consultation for epilepsy in our institution. Its classification was based on the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders.

**Results:** One hundred and thirty patients (57,0%) had a lifetime diagnosis of psychiatric disorder, the most common being affective disorders, affecting seventy-nine patients (34,6%), and anxiety disorders, affecting sixty-seven patients (29,4%). Affective disorders were found to be associated with the female sex ($p$=0,045). Psychiatric disorders were associated with a lengthier duration of epilepsy ($p$=0,025). Concerning the laterality of the hippocampal sclerosis, we found that the left hippocampus was more affected (52,2%), followed by the right hippocampus (40,8%) and both hippocampi (7,0%). Left hippocampal sclerosis was associated with a lengthier duration of epilepsy ($p$=0,019) and a higher prevalence of febrile seizure history ($p$=0,027). There was no association between laterality of the sclerosis and type of psychiatric disorder except between anxiety disorders and right hippocampal sclerosis ($p$=0,042). There was no association between sex and laterality.

**Conclusions:** The high lifetime prevalence of psychiatric disorders in this study was notorious, especially affective disorders and anxiety disorders. The odds of a patient suffering from an anxiety disorder if there is right hippocampal sclerosis were two times the odds of the left laterality.

**Keywords:** Temporal Lobe Epilepsy; Mesial Temporal Sclerosis; Hippocampal Sclerosis; Psychiatric Disorders; Laterality;

# List of Abbreviations

| | |
|---|---|
| **AED** | Antiepileptic Drug |
| **CHUP** | Centro Hospitalar e Universitário do Porto |
| **DSM-IV** | Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition |
| **EEG** | Electroencephalography |
| **ICBAS** | Instituto de Ciências Biomédicas Abel Salazar |
| **MRI** | Magnetic Resonance Imaging |
| **MTLE-HS** | Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis |

# Table of Contents

# List of Tables

## Introduction

Temporal lobe epilepsy is one of the most common types of focal epilepsy in adults and it is usually associated with hippocampal sclerosis, or mesial temporal sclerosis.[1,2] This type of epilepsy is characterized by a poor response to antiepileptic drugs (AEDs).[3,4] Refractory epilepsy, or pharmacoresistant epilepsy, may be defined as a failure of two trials of appropriately chosen AEDs using maximum tolerated doses.[5] There is evidence that the hippocampal sclerosis progresses over time as both a cause and a consequence of seizures.[6-10]

Males and females are equally affected.[11] This condition is associated with initial precipitating injuries: febrile seizures in childhood are the most common.[12-15] Age of onset is usually in late childhood or early adolescence. [4,16]

Psychiatric disorders are very common in epilepsy and might even precede the onset of seizures.[17-19] There is also a high prevalence of epilepsy in patients with psychiatric disorders, suggesting an association between these two conditions.[17,18,20] It is implied that patients suffering from Mesial Temporal Lobe Epilepsy (MTLE) have a greater tendency to develop psychiatric disorders due to the lymbic system's role in regulating emotions, affection and behaviors.[21,22] The frequency of psychiatric disorders is not only greater than that of the average population but also among patients with other neurologic diseases or chronic non-neurologic diseases, [21,23,24] reaching prevalence values as high as 70%.[25,26]. Determining the frequency of psychiatric disorders in epilepsy is a challenging task, considering the complex interaction between neurophysiological modifications caused by the seizures, adverse effects of AEDs and subjective and individual susceptibility.[27-29]

Several studies have evaluated sociodemographic and clinical characteristics of patients suffering from Mesial Temporal Lobe Epilepsy with Hippocampal Sclerosis (MTLE-HS), often with conflicting results. Concerning psychiatric comorbidities, affective disorders are often the most frequent (24-74%), followed by anxiety disorders (10-25%), psychotic disorders (2-7%) and personality disorders (1-2%).[21,30,31] Among affective disorders, major depression is predominant, with a very high risk of suicide. Bipolar disorder is uncommon[19,24,32-34]. In patients with refractory epilepsy, the presence of a depressive disorder seems to be one of the most determinant factors for the quality of life, even more than the frequency and severity of the seizures.[25,35] Duration and severity of the epilepsy are associated with a higher frequency and magnitude of psychiatric and intellectual disorders.[36,37] Family history of psychiatric disorders is associated with a higher prevalence of psychiatric disorders in this condition, as well.[25,38]

Concerning laterality, left MTLE-HS seems to be the most common, followed by right MTLE-HS and bilateral MTLE-HS.[31,39] Some studies suggest a higher prevalence of depressive, anxiety and psychotic disorders in patients with left MTLE-HS.[19,40-44] On the other hand, a study has associated anxiety disorders with right MTLE-HS.[33] Other studies have failed to show association between laterality of the hippocampal sclerosis and psychiatric disorder.[45-48]

Untreated depressive symptoms may hinder seizure control, prompting that the diagnosis and treatment of depression is crucial in these patients.[20,43,49-53]
Numerous studies highlight the underdiagnosis and undertreatment of psychiatric disorders in epilepsy.[17,19,20,25]

The aim of this study is to evaluate the prevalence and type of psychiatric comorbidities in patients with MTLE-HS and also to analyse a potential influence of hippocampal sclerosis laterality in these comorbidities.

## Methods

Participants

The present study included every patient with the diagnosis of MTLE-HS followed in the Epilepsy Clinic of the Neurology Service, Centro Hospitalar e Universitário do Porto (CHUP), between December of 1999 and December of 2019. CHUP is a national reference center for refractory epilepsy treatment and includes an epilepsy surgery program. Patients with indication for surgery and/or with refractory epilepsy are referred throughout the country to CHUP, mainly from the north of Portugal.

This study was approved by the local institutional Ethics Committee and all of the Departments involved.

Materials and Procedure

Sociodemographic and clinical data were reviewed from the clinical records present in the computer program SClínico, the database for CHUP's clinical records.

Inclusion criteria were: age above 18 years old and diagnosis of MTLE-HS according to the International League Against Epilepsy (ILAE) criteria.[1,54-56] Most of these patients underwent through an extensive pre-surgical evaluation, including Magnetic Resonance Imaging (MRI), electroencephalography (EEG), neuropsychological tests and psychiatric evaluation. The diagnosis of MTLE-HS was based on the clinical semiology of the seizures, on electrophysiological tests ( interictal and ictal routine EEG and/or prolonged video-EEG monitoring) and on brain MRI (minimum 1,5 Tesla). The imaging criteria of hippocampal sclerosis in brain MRI comprehended hippocampal atrophy, increased T2 signal and abnormal morphology in one or both hippocampi. These criteria may be or may not be associated with minor criteria like atrophy of the ipsilateral fornix, atrophy of the ipsilateral mammillary body or abnormalities in the ipsilateral entorhinal cortex. Bilateral MTLE-HS was included in this study. Other possible etiologies for MTLE-HS, such as the presence of dual pathology or abnormalities in the neurological examination not predicted in this condition, were excluded. Patients that had missing clinical and follow-up information were also excluded.

Demographic data (age and sex) and clinical data (age of onset, febrile seizure history, seizure frequency, laterality of the hippocampal sclerosis, lifetime history of psychiatric disorders and their type, lifetime history of psychiatric medication and its pharmacological

class, average lifetime number of AEDs, history of epilepsy surgery and family history of epilepsy) were collected from the digital records.

Bilateral MTLE-HS patients were not considered in hippocampal sclerosis laterality analysis.

Almost every psychiatric diagnosis was made by a psychiatrist on the muldisciplinary consultation of epilepsy from the CHUP's Consultation-Liaison Psychiatry. Patients that were followed by other Psychiatrist were also included. The Psychiatry consultation is part of the multidisciplinary consultation of epilepsy and follows patients with epilepsy that need psychiatric assessment or treatment. Psychiatric diagnosis was based on the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and on the 10th edition of the International Classification of Diseases (ICD-10). Medications prescribed by the psychiatrist were also reviewed.

Statistical Analysis

A descriptive analysis of the variables was made. Proportions were calculated for categorical variables and means and respective standard deviations were calculated for quantitative variables. For each type of variable an appropriate statistical test was employed (Pearson's Chi-Square Test or Fisher's Exact Test, Variance Analysis and Logistic Regression). A $p$-value $< 0,05$ was considered statistically significant. Every statistical operation was performed using the Statistical Package for the Social Sciences (SPSS), version 25.0 for Windows.

## Results

Clinical and Demographic Characteristics

Two hundred and twenty-eight patients with MTLE-HS were included in this study. Clinical and demographic characteristics of this sample are displayed in Table I.

Sex distribution revealed a slight predominance of females.

Patients had a mean age of 50,7 years, with a mean age of epilepsy onset of 14,3 years. The mean duration of epilepsy was 36,4 years.

One hundred and twenty-two patients (53,5%) had history of febrile seizures during childhood.

Most of the patients (70,6%) did not have family history of epilepsy.

The mean frequency of seizures was one per month.

Seventy-two patients (31,6%) had epilepsy surgery.

One hundred and seventy-one patients (70,6%) had refractory epilepsy.

Left MTLE-HS was the most prevalent, with 119 patients (52,2%), followed by right MTLE-HS, affecting 93 patients (40,8%). A minority of the patients (7,0%) had bilateral MTLE-HS.

The mean number in average lifetime of AEDs taken was 2,5. From the 228 patients, 116 (50,9%) used a mean of 3 or more AEDs.

A little over half of the patients (51,3%) had a lifetime history of psychiatric medication use: antidepressants, anxiolytics and antipsychotics. Between these three classes, antidepressants were the most prescribed (38,2%).

Psychiatric Comorbidity

The lifetime frequency of psychiatric disorders in these patients is displayed on Table II.

One hundred and thirty patients (57,0%) had a lifetime diagnosis of psychiatric comorbidity.

The most common psychiatric comorbidities diagnosed were affective disorders (34,6%), anxiety disorders (29,4%) and psychotic disorders (7,0%). Other psychiatric comorbidities were identified: sleep disorders (6,1%), substance use disorders (4,8%), personality disorders (3,9%), sexual dysfunction (2,2%), somatoform disorders (1,3%), neurodevelopmental disorders (1,3%) and unspecified mental disorders(3,1%).

Among affective disorders there were no other conditions besides depressive disorders.

Forty-four patients (19,3%) had both a diagnosis of affective disorder and anxiety disorder.

Patients with psychiatric comorbidity had a lengthier duration of epilepsy, with a mean of 38,2 years ($p$ = 0,025).

None of the sexes were associated with a higher prevalence of psychiatric comorbidity but the female sex was associated with affective disorders in this study ($p$ = 0,045).
Among the 50 patients that underwent epilepsy surgery and had a psychiatric comorbidity, 26 only had their diagnosis of psychiatric comorbidity after the surgical procedure.

Characteristics according to the Laterality of the Hippocampal Sclerosis

Clinical and demographic characteristics according to the laterality of the hippocampal sclerosis are displayed in Table lll. The frequency of psychiatric disorders according to the laterality of the hippocampal sclerosis is displayed in Table IV.
Left MTLE-HS was associated with a lengthier duration of epilepsy ($p$ = 0,019) and a higher prevalence of febrile seizure history ($p$ = 0,027).
There were no associations between any psychiatric comorbidity and laterality of the sclerosis except between anxiety disorders and right MTLE-HS ($p$ = 0,042).
A logistic regression was used to confirm the predictive value of the laterality in anxiety disorders. We found out that the odds of a patient suffering from anxiety disorders while having right MTLE-HS were 2,14 times greater than the odds relative to the left MTLE-HS.
There were no associations between laterality of the hippocampal sclerosis and: sex, any psychiatric medication and psychiatric disorder diagnosed after epilepsy surgery.

## Discussion

This study describes a cross-sectional observation of the neuropsychiatric profile of patients with MTLE-HS aiming to analyse several demographic and clinical charatecteristics and their association with laterality.

Clinical and Demographic Characteristics

The mean age of onset in this sample seems to be close to that displayed in the literature, that is, in early adolescence.[57-59] Epilepsy duration in this sample is also similar to other studies.[38,48,60]

Theoretically, considering that the male brain development and maturation is slower than its counterpart, and that this amplifies the period in which it's most susceptible to precipitating injuries, we could expect a higher prevalence of the male sex.[39] However, the distribution of sex was rather identical, as described in several studies.[11,39,60,61]

A little more than half of the patients had history of febrile seizures in childhood. Febrile seizures are one of the main risk factors for the development of MTLE-HS. Nonetheless, although it's the most common, it's only one of the many risk factors associated with this type of epilepsy, not approached in this study. If we had considered other risk factors, the prevalence of injuries with epileptogenic potential would be higher, which highlights the strong association of MTLE-HS with precipitating injuries.[2,59,62] Other risk factors, such as trauma, tumors or limbic encephalitis, could be the explanation for the late onset in some of these patients.[63-65] Most of these etiologies that may occur with MTLE-HS could be considered dual pathology and were excluded from this study.

The high prevalence of refractory epilepsy as well as the high percentage of patients that were on 3 or more AEDs emphasizes the evidence that this type of epilepsy has a difficult pharmacological management. Despite the high number of AEDs used, seizure frequency is still on average one per month, highlighting the characteristic pharmaco-resistance of MTLE-HS and the prompt necessity of other approaches to control seizures, such as epilepsy surgery.[3,4]

The laterality of the hippocampal sclerosis was distributed as described in other studies, with predominance in the left hemisphere.[19,31,39] This fact may be justified by the slower development of the dominant hemisphere compared to the non-dominant hemisphere,

extending the time period in which the hemisphere is susceptible to injuries with epileptogenic potential.[39]

The frequency of patients with a lifetime use of psychiatric medication was high (38,2% had used antidepressants) compared to other studies in which the frequency of antidepressant use, for example, is between 8% and 20%.[19,38,48]

The prevalence of family history of epilepsy in this study (29,4%) was not as frequent as expected.[11,38,48] Since this is a retrospective study, this result may be due to the lack of medical records concerning the patients' relatives, mainly first degree relatives.

Nearly one-third of the patients had already undergone epilepsy surgery, generally amygdalohippocampectomy, an important option for the treatment of this type of epilepsy, with satisfactory results.[66-69]

Psychiatric Comorbidity

This study confirms the high lifetime prevalence of psychiatric comorbidities in patients suffering from MTLE-HS.
The frequency of each type of psychiatric disorder in this study seems to match those described in literature, with affective disorders prevailing. Some types of psychiatric disorders were more frequent than expected, mainly anxiety disorders and personality disorders, which were expected to have a frequency between 10%- 25% and 1%- 2%, respectively.[21,30,31]

The fact that depressive disorders stand as the only affective disorders in this sample was not unexpected, since other affective disorders, like bipolar disorder, are rare in epilepsy.[33,34]

Nearly one-fifth of the patients had a lifetime diagnosis of depressive disorders and anxiety disorders. These two conditions usually occur concomitantly, supporting a common pathophysiology, the dysfunction of the lymbic structures.[20,70,71]

The contrast between the frequency of psychotic disorders (7,0%) and antipsychotic use (22,8%) suggests that this pharmacological class was required in the treatment of other psychatric disorders. A possible justification is the widespread use of these drugs when psychotic symptoms occur, such as in depression; as a sedative and hypnotic in anxiety;

to control impulsivity in personality disorders; or in a postictal psychosis that doesn't fulfill criteria for a psychotic disorder.[72,73]

Some studies have shown an association between psychiatric comorbidity and a shorter duration of epilepsy. This could be justified by a shorter time to adapt to a new health condition.[74-76] Our study contradicts this result, displaying an association between psychiatric comorbidity and a lengthier duration of epilepsy. This result may be explained by the evidence that MTLE-HS is a progressive condition: neural networks are progressively damaged along its course, increasing the odds of suffering from a seizure or a psychiatric disorder.[6-8,10]

In agreement with the literature, the female sex was associated with a higher frequency of affective disorders.[77,78] This association has already been extensively studied and may be justified by hormonal fluctuations and differences in the development of the brain's neural circuits, among other reasons.[79] Although anxiety disorders are usually associated with depression, and anxiety is generally more prevalent in the female sex, we haven't found an association between the female sex and anxiety disorders.[80]

Patients subjected to amygdalohippocampectomy or other epilepsy surgery were not excluded from the sample since the relationship between epilepsy surgery and psychiatric comorbidity is still largely controversial. Some studies show an improvement or recovery of the psychiatric disorder after the surgical intervention [33,81,82], while others show the emergence of *de novo* psychiatric disorders or their exacerbation.[27,83,84] Since the aim of this study was not analysing the relationship between psychiatric comorbidity and epilepsy surgery we did not carry out a subanalysis of this group. Considering that this is a rather relevant ambiguity, we alert for the importance of more studies to clarify this issue.

Characteristics according to the Laterality of the Hippocampal Sclerosis

The association between left MTLE-HS and a lengthier duration of epilepsy, although previously described, does not seem to convey clinical significance. A lengthier duration of epilepsy is expected since the patients' ages are similiar between both lateralities and age of onset in left hippocampal sclerosis is lower that the right one. These differences weren't statistically significant in this study.[85]

The association between left MTLE-HS and a higher prevalence of febrile seizure history is not new in the literature. This association renders the evidence that the left hemisphere

is more susceptible to injuries with epileptogenic potential, especially in the first two years of life, the period in which most febrile seizures occur. [86,87]

The theory that the left MTLE-HS would be more prevalent in the male sex, also through a slower brain development [39], was not supported by our results.

Most studies show an association between higher prevalences of the main psychiatric comorbidities (affective, anxiety and psychotic disorders) and left MTLE-HS [19,40-44]. On the contrary, this study did not associate laterality with any psychiatric disorder except anxiety disorders. Furthermore, the laterality associated with anxiety disorders was the right one. Although it contradicts most of the published literature, there is one study reporting this association.[33] There is evidence that an abnormal and excessive activation of right lymbic structures, mainly the amygdala, has an important role in anxiety. Even in studies concerning non-epileptic neurological pathology, an association between anxiety and right hemispheric lesions has already been described.[88] However, further studies will be necessary to clarify this conflicting data.

There was no association between laterality of the hippocampal sclerosis and psychiatric disorder diagnosed after epilepsy surgery, in this study. This result has been reported before.[84]

All of these divergences from the literature, mainly the association between anxiety disorders and right MTLE-HS, may be explained by considerable differences in methodology: while in some studies the DSM-IV criteria were not used to diagnose psychiatric conditions, our study used them, since it may be considered valid for patients with epilepsy.[20,25,48,89] In this study we performed a retrospective analysis with the lifetime cumulative prevalence of psychiatric comorbidities. Other studies only analysed the prevalence at the moment of its attainment.[19,90,91] In specific cases, psychiatric diagnosis is not very linear, and will always depend and differ between psychiatrists. Sometimes the adverse effects of AEDs, vastly used by this population, might exacerbate or improve psychiatric disorders resulting in, respectively, an overdiagnosis or underdiagnosis of these disorders.[92,93] We did not study the relation between AEDs and psychiatric disorders beacuse most of the patients were taking more than one AED. As explained above, patients that had already been subjected to epilepsy surgery were included in this study, considering the ongoing debate about the effects of this surgical intervention in psychiatric disorders. In various other studies, these patients were excluded.[19,38,90]

Strenghts and Limitations

Several studies approached the underdiagnosis and lack of treatment of psychiatric disorders in epilepsy.[17,19,20,94] As we could observe in this study, the majority had already or were currently having psychiatric follow-up and treatment. The size of the sample and the psychiatrist's experience were other positive aspects in this study.

This study had various limitations and the most important come from the retrospective nature of this study. Another limitation was the lack of a control group. Since this study was performed in a tertiary center for epilepsy treatment which receives patients with refractory epilepsy to be surgically treated, there might be a selection bias and consequently, a greater prevalence of psychiatric disorders. Including patients that had already been surgically treated may be a confounding factor in our results. Diagnosis of psychiatric disorders in patients with MTLE-HS will always be a limitation, since there are no definitive criteria for the neuropsychiatric diagnosis in epilepsy, for now.
The lack of data concerning family history of psychiatric disorders prevented us from studying this factor, which may be an important predictor for psychiatric comorbidity and seizure control in patients with MTLE-HS.[38,95]

## Conclusion

MTLE-HS is the most frequent cause of focal epilepsy in adults and commonly refractory to various AEDs. Many of these patients are referenced to Reference Centers for epilepsy surgery, a procedure that carries a great cost for the patient and the society.

In this study, left MTLE-HS was associated with a lengthier duration of epilepsy and a higher prevalence of febrile seizure history.

Furthermore, patients with MTLE-HS have a high prevalence of psychiatric comorbidities, mainly depression and anxiety disorders. Right MTLE-HS was associated with anxiety disorders in this study and the odds of a patient suffering from anxiety disorders while having right MTLE-HS were double the odds relative to the left MTLE-HS.

The physician must be alert to make an early diagnosis of psychiatric conditions associated with MTLE-HS and be able to predict the comorbidities related to each laterality of the hippocampal sclerosis, in order to start treatment as soon as possible.

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**Table I** - Clinical and Demographic Characteristics in patients with MTLE-HS

| | Patients (*n*=228) | |
|---|---|---|
| | ***n* or mean** (SD) | **Proportion** (%) **or median** (range) |
| **Sex** | | |
| Male | 103 | 45.2% |
| Female | 125 | 54.8% |
| **Age** (years) | 50.66 (12.24) | 50.50 (19 - 83) |
| **Age of Onset** (years) | 14.28 (11.62) | 12.00 (0 - 65) |
| **Epilepsy Duration** (years) | 36.38 (14.45) | 38.00 (1 - 76) |
| **Febrile Seizure History** | 122 | 53.5% |
| **Refractory Epilepsy** | 161 | 70.6% |
| **Laterality on MRI** | | |
| Left | 119 | 52.2% |
| Right | 93 | 40.8% |
| Bilateral | 16 | 7.0% |
| **Psychiatric Medication** | 117 | 51.3% |
| Antidepressants | 87 | 38.2% |
| Anxiolytics | 70 | 30.7% |
| Antipsychotics | 52 | 22.8% |
| **Family History of Epilepsy** | 67 | 29.4% |
| **AEDs** (number) | 2.54 (0.99) | 3.00 (1 - 6) |
| <3 AEDs | 112 | 49.1% |
| ≥3 AEDs | 116 | 50.9% |
| **Epilepsy Surgery** | 72 | 31.6% |

AEDs, antiepileptic drugs; MRI, magnetic resonance imaging; MTLE-HS, mesial temporal lobe epilepsy with hippocampal sclerosis; SD, standard deviation

**Table II** - Lifetime Frequency of Psychiatric Disorders in patients with MTLE-HS

| **Psychiatric Disorder** | Patients (*n*=228) | |
|---|---|---|
| | ***n*** | **Proportion** (%) |
| **Any Disorder** | 130 | 57.0% |
| **Affective Disorders** | 79 | 34.6% |
| **Anxiety Disorders** | 67 | 29.4% |
| **Psychotic Disorders** | 16 | 7.0% |
| **Sleep Disorders** | 14 | 6.1% |
| **Substance Use Disorders** | 11 | 4.8% |
| **Personality Disorders** | 9 | 3.9% |
| **Sexual Dysfunction** | 5 | 2.2% |
| **Somatoform Disorders** | 3 | 1.3% |
| **Neurodevelopmental Disorders** | 3 | 1.3% |
| **Unspecified Mental Disorders** | 7 | 3.1% |

MTLE-HS, mesial temporal lobe epilepsy with hippocampal sclerosis

**Table III** - Clinical and Demographic Characteristics according to Laterality, excluding Bilateral HS

| | Patients (*n*=212) | | |
|---|---|---|---|
| | **Left** (*n*=119) | **Right** (*n*=93) | ***p - value*** n.s. if $p \geq 0,05$ |
| **Sex**; *n* (%) | | | n.s.* |
| Male | 54 (45%) | 39 (42%) | |
| Female | 65 (55%) | 54 (58%) | |
| **Age**; Mean (SD) | 51.34 (12.58) | 49.83 (11.82) | n.s.** |
| **Age of Onset**; Mean (SD) | 13.11 (10.70) | 16.33 (13.10) | n.s.** |
| **Epilepsy Duration**; Mean (SD) | 38.23 (14.76) | 33.49 (14.17) | $p = 0.019$** |
| **Febrile Seizure History**; *n* (%) | 71 (60%) | 41 (44%) | $p = 0.027$* |
| **Refractory Epilepsy**; *n* (%) | 87 (73%) | 61 (66%) | n.s.* |
| **Psychiatric Medication**; *n* (%) | 56 (47%) | 50 (54%) | n.s.* |
| Antidepressants | 45 (38%) | 34 (37%) | n.s.* |
| Anxiolytics | 29 (24%) | 34 (37%) | n.s.* |
| Antipsychotics | 24 (20%) | 21 (23%) | n.s.* |
| **Family History of Epilepsy**; *n* (%) | 38 (32%) | 25 (27%) | n.s.* |
| **AEDs**; Mean | 2.55 | 2.43 | n.s.*** |
| <3 AEDs; *n* (%) | 59 (50%) | 50 (54%) | n.s.* |
| ≥3 AEDs; *n* (%) | 60 (50%) | 43 (46%) | n.s.* |
| **Epilepsy Surgery**; *n* (%) | 43 (36%) | 28 (30%) | n.s.* |

AEDs, antiepileptics drugs; HS, hippocampal sclerosis; SD, standard deviation

* Fisher's Exact Test ** Variance Analysis *** Pearson's Chi-Square Test

**Table IV** - Lifetime Frequency of Psychiatric Disorders according to Laterality, excluding Bilateral HS

| | Patients (*n*=212) | | |
|---|---|---|---|
| | **Left** (*n*=119) | **Right** (*n*=93) | ***p - value*** n.s. if $p \geq 0,05$ |
| **Any Disorder**; *n* (%) | 65 (55%) | 55 (59%) | n.s.* |
| **Affective Disorders** | 41 (34%) | 33 (35%) | n.s.* |
| **Anxiety Disorders** | 28 (24%) | 34 (37%) | $p = 0.042$** |
| **Psychotic Disorders** | 11 (9%) | 4 (4%) | n.s.* |
| **Sleep Disorders** | 10 (8%) | 4 (4%) | n.s.* |
| **Substance Use Disorders** | 4 (3%) | 7 (8%) | n.s.* |
| **Personality Disorders** | 3 (3%) | 5 (5%) | n.s.* |
| **Sexual Dysfunction** | 2 (2%) | 2 (2%) | n.s.* |
| **Somatoform Disorders** | 2 (2%) | 1 (1%) | n.s.* |
| **Neurodevelopmental Disorders** | 1 (1%) | 1 (1%) | n.s.* |
| **Unspecified Mental Disorders** | 4 (3%) | 2 (2%) | n.s.* |

HS, hippocampal sclerosis

* Fisher's Exact Test ** Logistic Regression