

## Prevalence of Psychiatric Disorders in Patients with Mesial Temporal Sclerosis

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### ABSTRACT

**Objective:** Behavioral changes in patients with epilepsy can range from depression, anxiety to psychosis and personality traits. We evaluated the frequency of psychiatric disorders (PD) in a homogenous series of patients with refractory temporal lobe epilepsy (TLE) related to mesial temporal sclerosis (MTS) aiming at determining the frequency of PD and possible correlations to clinical variables and to laterality of MTS. **Methods:** Data from 106 refractory TLE patients were reviewed. Psychiatric evaluation was based on DSM-IV criteria. Statistical analysis was performed through the chi-square ( $\chi^2$ ), Student's t test and Fisher's exact test. P value considered significant was  $< 0.05$ . **Results:** PD were found in 65 patients (61.3%). Among them, mood disorders were the most frequent (32 patients; 30%), followed by interictal (15 patients; 14%) and postictal (10 patients; 9.4%) psychosis. Postictal and interictal psychosis were significantly associated with left side MTS ( $p < 0.05$ ), while PD in general and mood disorders were not associated to any side. **Conclusion:** There was a high prevalence of PD in patients with refractory TLE associated to MTS. The most common were mood and psychotic disorders. Psychosis was significantly associated to left side. These findings are concordant with data in literature, confirming the existence of anatomic alterations, and also a possible left laterality effect in the mesial temporal lobe structures in patients with epileptic psychosis.

**Key words:** temporal lobe epilepsy, mesial temporal sclerosis, psychiatric disorders.

### RESUMO

#### *Prevalência de transtornos psiquiátricos em pacientes com esclerose mesial temporal*

**Objetivos:** Foi avaliada a frequência de transtornos psiquiátricos (TP) em uma série homogênea de pacientes com epilepsia do lobo temporal (ELT) associada à esclerose mesial temporal (EMT), com o objetivo de verificar a prevalência e os tipos de TP nessa população e de correlacionar tais transtornos a aspectos clínicos e à lateralidade da EMT. **Metodologia:** Dados de 106 pacientes com ELT refratária associada a EMT foram revisados. A avaliação psiquiátrica foi baseada nos critérios diagnósticos do DSM-IV. A análise estatística foi realizada através do teste do qui-quadrado ( $\chi^2$ ), do teste t de Student e do teste exato de Fisher. O valor de P considerado significativo foi  $< 0,05$ . **Resultados:** TP foram diagnosticados em 65 pacientes (61,3%). Transtornos do humor foram os mais frequentemente encontrados (32 pacientes; 30%), seguidos por psicose interictal (15 pacientes; 14%) e por psicose pós-ictal (10 pacientes; 9,4%). Tanto a psicose interictal como a psicose pós-ictal foram associadas a EMT à esquerda ( $p < 0,05$ ), enquanto TP em geral e transtornos do humor não foram correlacionados a nenhum lado. **Conclusão:** Houve uma elevada prevalência de TP em pacientes com ELT refratária associada a EMT. Os mais frequentemente encontrados foram transtornos do humor e psicóticos. Quadros psicóticos foram associados a EMT à esquerda. Tais achados são concordantes com dados da literatura atual em relação à prevalência de TP na ELT, confirmando a existência de alterações anômicas e uma possível associação da EMT à esquerda com quadros psicóticos na ELT.

**Unitermos:** epilepsia do lobo temporal, esclerose mesial temporal, transtornos psiquiátricos.

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## INTRODUCTION

The complex relationship between temporal lobe epilepsy (TLE) and psychiatric disorders (PD) has been matter of interest, and important studies have emphasized this association. It is already known that psychiatric comorbidity compromise patients' quality of life.<sup>(1-3)</sup> Behavioural changes in patients with epilepsy can range from depression and anxiety to psychosis, including also some specific personality traits that have variously been referred to as the interictal personality disorder of epilepsy and the Gastaut-Geschwind syndrome.<sup>(4)</sup> A specific association between these syndromes and TLE has been claimed. Studies highlighted TLE patients to be at increased risk for PD compared with extra-TLE or primary generalized epilepsies because of limbic system's involvement in the regulation of emotions and behavior, while others did not find such differences.<sup>(5-8)</sup> However, the frequency of PD in epilepsy and particularly in TLE has not been easy to establish, and psychopathology is likely also to reflect factors such as seizure severity, global cerebral damage, medication effects and adequacy of psychosocial supports.<sup>(4)</sup> Few studies in literature verified the frequency of PD in patients presenting the same etiology of TLE, particularly mesial temporal sclerosis (MTS). We evaluated the frequency of PD in a homogenous series of patients with refractory TLE related to MTS aiming at determining the frequency of PD and possible correlations to clinical variables, such as duration of epilepsy, neurologic and psychiatric family antecedents, previous psychiatric treatment, type and frequency of seizures, occurrence of status epilepticus and type and number of antiepileptic drugs (AED). The possible correlation of PD to the laterality of mesial temporal atrophy was also studied.

## PATIENTS AND METHODS

All patients were accompanied at the outpatient epilepsy clinic of Universidade Federal de São Paulo, Brazil, from March 2005 to May 2006.

Clinical and socio-demographic data from 106 patients with refractory TLE related to MTS were reviewed. The inclusion criteria were the presence of electroclinical diagnosis of refractory TLE related to MTS based on ILAE classification<sup>(9)</sup> and magnetic resonance image (MRI) findings, and having been treated in our unit for at least 6 months with stable doses of AED. We excluded patients with clinical illnesses besides epilepsy. Psychiatric evaluation was part of presurgical evaluation and was done based on axis I criteria of the Diagnostical and Statistical Manual of Mental Disorders, 4<sup>th</sup> edition (DSM-IV).<sup>(10)</sup> None of them had presented any seizures, antihistamine administration or alcohol consumption

within 12 hours prior to the evaluation. The temporality between epileptic seizures and psychotic symptomatology was considered the criteria to differentiate postictal from interictal psychosis. Statistical analysis was performed with SPSS 10.0 software. Some socio-demographic characteristics were presented as one-sample proportions and with confidence intervals. The chi-square ( $\chi^2$ ), Student's t test and Fisher's exact test were used to calculate the correlations. P value considered significant was  $< 0.05$ .

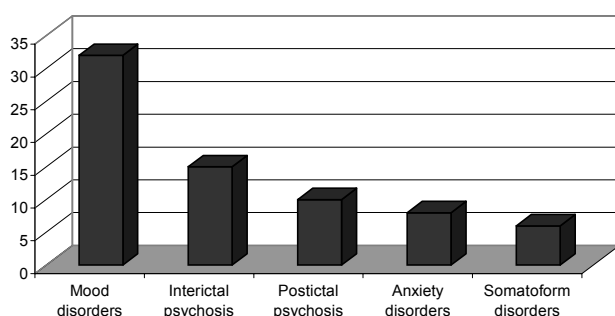
## RESULTS

We included psychiatric evaluation from 106 patients with refractory TLE related to MTS. Sixty-one females and 45 males were evaluated. MTS occurred more frequently on left side (72 cases; 68%), followed by right side (30 cases; 28.3%) and by four cases in which this lesion was seen bilaterally (3.7%). Most of the patients (88 cases; 83%) had been in use of two or more medications. Carbamazepine, alone or in association with other drugs was the most frequent AED, being used in 70 patients, followed by benzodiazepines, particularly clobazam, in 56 patients. Thirty-nine patients had a history of initial precipitant injury (IPI) being febrile seizures the most frequent (23 cases; 59%). There was also 12 cases of head trauma, three of meningoencephalitis and one of perinatal hypoxia. The majority of patients (76 cases; 71.7%) had had TLE for more than 20 years. The demographic data are summarized in Table 1.

**Table 1.** Clinical and sociodemographic data of 106 patients with refractory temporal lobe epilepsy related to mesial temporal sclerosis

Variables	Frequency (%)
Number of patients	106
Gender (% females)	57.5
Age in years (mean $\pm$ SD)	15 to 62 (39.5 $\pm$ 13.4)
Age at epilepsy onset in years (mean $\pm$ SD)	1 to 50 (19.0 $\pm$ 12.8)
Duration of epilepsy in years (mean $\pm$ SD)	2 to 59 (26.9 $\pm$ 12.2)
Presence of initial precipitant injury (%)	39 (36.7%)
Previous psychiatric history (%)	37 (35%)
Familiar psychiatric history (%)	17 (16%)
Familiar epilepsy history (%)	34 (32%)
Psychiatric disorders (axis I) (%)	65 (61.3%)

PD were found in 65 patients (61.3%). Mood disorders were the most frequent (32 patients; 30%), followed by interictal (15 patients; 14%) and postictal (10 patients; 9.4%) psychosis. Six patients performed criteria for two axis I disorders, all of them with left MTS and presenting major depression and postictal psychosis. The psychiatric diagnoses are described in Graphic 1.



**Graphic 1.** Prevalence of psychiatric disorders in a series of patients with mesial temporal sclerosis.

A comparison of clinical data regarding the presence of PD and some clinical and socio-demographical characteristics was performed. This was made analysing the presence of PD (as a group and individually) and the clinical and socio-demographical variables found in the group. All comparisons were made through an application of an adequate statistical test (chi-square, Students' t test or Fisher's exact test). Previous and familiar psychiatric histories were significantly associated to PD in this group ( $p < 0.05$ ). PD as a group were not associated to epilepsy duration, but postictal psychosis was related to less than 20 years of disease ( $p < 0.05$ ), while mood disorders and interictal psychosis separately were associated to  $> 20$  years of epilepsy ( $p < 0.05$ ). Postictal and interictal psychosis were significantly associated with left side ( $p < 0.05$ ), while PD as a group and mood disorders were not associated to any side.

## DISCUSSION

The aim of this study was to conduct an evaluation of the frequency and types of PD in a series of patients with refractory TLE related to MTS treated in a tertiary center through the use of standardized instruments based on the modern psychiatric nosography, estimating its frequency and correlating with socio-demographical and clinical variables such as seizure frequency, time without treatment, number of AED and duration of epilepsy. We also studied the correlation of PD to the laterality of MTS.

About six per cent of epileptic patients in general appear to suffer from a PD. This number rises to 10-20% in populations with TLE or refractory epilepsy.<sup>(1)</sup> Mood disorders, particularly depression, are the most common (24-74%), followed by anxiety disorders (10-25%), psychoses (2-7%) and personality disorders (1-2%). However, accurate estimates of psychiatric comorbidity are hard to find, because it is characterized by considerable heterogeneity and varies according to a variety of factors, like type of the study, severity and chronicity of epilepsy, the methodology applied (e.g., diagnostic instruments), the

population setting and subgroup of epileptic patients studied (e.g., focal or primary generalised epilepsies).<sup>(1,8)</sup> Nevertheless, there are evidences that epilepsy places the patient at increased risk of developing PD, and adequate controlled studies existing in literature show a higher risk in relation to normal control groups, but this is not always confirmed when epileptic patients are compared to patients with other chronic medical conditions, like arthritis, cancer and heart disease.<sup>(6)</sup> Thus, more controlled studies are necessary to clarify how important is the contribution of epilepsy condition itself in predisposing to PD.

Studies in literature have highlighted the association between TLE and PD, particularly mood, anxiety and psychotic disorders.<sup>(4,11,12)</sup> Risk factors associated to PD in TLE are clinical refractoriness, MTS and bitemporal lesions.<sup>(2,13)</sup> Limbic involvement is a possible explanation for the high frequency of PD in this group of patients,<sup>(2,13)</sup> possibly because the role of limbic structures in emotions and behaviour. In our study there was a high frequency of PD, particularly mood and psychotic disorders, confirming other data in the current literature about these patients.<sup>(2,13)</sup>

MTS on left side was significantly correlated to psychosis, suggesting the existence of specific anatomic alterations in psychotic symptoms associated to TLE.<sup>(13,14)</sup> The left side was already related to epileptic psychosis in past studies, and patients with left temporal lobe epileptogenic lesions are specially disposed to develop psychosis.<sup>(14)</sup> In fact, postictal psychosis is characterized by antecedent seizures, lucid intervals, short episodes and mild confusion with subsequent amnesia. In contrast, interictal psychosis occurs between epileptic episodes, is long lasting and the psychopathology is usually more distinguishable. In our study patients with epilepsy for a shorter time ( $< 20$  years of disease) developed more postictal psychosis, while those with longer time of disease ( $> 20$  years) developed more interictal psychosis, suggesting that these two types of psychosis related to epilepsy could have different physiopathology and probably the disease may contribute by different ways to the development of these pictures, although there is insufficient biologic evidence to support this premise.<sup>(15)</sup> Nevertheless, studies in literature had already confirmed that psychosis associated to epilepsy should not be defined as a single and simple condition but rather as a complex condition with several possible subcategories.<sup>(15)</sup> There was a significant correlation between PD and past ( $p < 0.05$ ) and family ( $p < 0.05$ ) psychiatric history in our study. These findings were also consistent to data in literature.<sup>(15)</sup>

In the present study, we conclude that there was a high prevalence of PD in patients with refractory TLE

associated to MTS. The most common were mood and psychotic disorders. Psychosis was significantly associated to left side. These findings are concordant with data in current literature relating the prevalence of PD in TLE,<sup>(1,4)</sup> confirming the existence of anatomic alterations, and also a possible left laterality effect in the mesial temporal lobe structures in patients with epileptic psychosis.<sup>(1,4,8,13,14)</sup>

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