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## Psychiatric disorders as "hidden" contraindications for presurgical VEEG in patients with refractory epilepsy: A retrospective cohort study in a tertiary center

Gerardo Maria de Araujo Filho <sup>a,\*</sup>, Ana Eliza Romano Furlan <sup>a</sup>, Ana Elisa Sa Antunes Ribeiro <sup>a</sup>, Lucia Helena Neves Marques <sup>b</sup>

<sup>a</sup> Department of Psychiatry and Medical Psychology, Faculdade de Medicina de São José do Rio Preto (FAMERP), São Paulo, Brazil
<sup>b</sup> Department of Neurological Sciences, Faculdade de Medicina de São José do Rio Preto (FAMERP), São Paulo, Brazil

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#### ABSTRACT

Given the high frequency of psychiatric disorders (PDs) observed among patients with epilepsy, studies have highlighted the necessity of psychiatric evaluation for these patients, especially for those with refractory temporal lobe epilepsy with mesial temporal sclerosis (TLE-MTS) who are surgical candidates. Current evidence highlights the safety of video-electroencephalography (VEEG) as a means of investigation in patients with TLE-MTS and PDs. However, the presence of such disorders has still been seen as a contraindication for presurgical evaluation with VEEG in some epilepsy centers mainly because of the risk of negative behavioral events. The present retrospective cohort study performed in a Brazilian tertiary epilepsy center aimed to identify whether the presence of a PD remains a contraindication for presurgical VEEG. Clinical, sociodemographic, and psychiatric data from 41 patients who underwent VEEG as part of their presurgical evaluation were compared to data from 32 patients with refractory TLE-MTS who had not undergone VEEG. Psychiatric diagnoses were determined using the DSM-IV and ILAE criteria. Psychiatric disorders were diagnosed in 34 patients (46.6%). Major depressive disorder was the most frequent PD and was observed in 22 patients (30.1%). Anxiety disorders were observed in 14 patients (19.2%). Of the 41 patients (56.2%) who underwent presurgical VEEG, only 12 (29.2%) were found to have a PD during the presurgical psychiatric evaluation compared to 22 of the 32 (68.7%) who did not undergo VEEG (p = 0.001; RR = 2.35). The present findings suggest that the presence of a PD alone should not be a contraindication for VEEG monitoring and epilepsy surgery.

atrist as a member of the team.

2. Methods

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### 1. Introduction

Studies in the literature have observed a prevalence rate of comorbid psychiatric disorders (PDs\_ of 20-40% in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS), which rises to 70% in groups with refractory forms of epilepsy [1–6]. Mood disorders are the most common (24–74%), followed by anxiety (10–25%), psychotic disorders (2–9%), and personality disorders (1–2%) [2–5]. Given the high prevalence of presurgical PDs in this population, the psychiatric outcomes of such patients have become of particular interest to researchers [3,4]. Moreover, the correlation between the presence of presurgical PDs and poorer postsurgical seizure outcomes in patients with refractory epilepsy who underwent surgery has been increasingly recognized [5–10].

\* Corresponding author at: Faculdade de Medicina de São José do Rio Preto, Av. Brigadeiro Faria Lima, 5416, São José do Rio Preto, São Paulo CEP: 15090-000, Brazil. Fax: +55 17 3201 5734.

E-mail address: filho.gerardo@gmail.com (G.M. de Araujo Filho).

All patients were followed in the outpatient clinic of a tertiary center (Epilepsy Section of the Faculdade de Medicina de São José do Rio Preto,

Given the high frequency of psychiatric comorbidity observed among patients with refractory TLE-MTS, studies have also highlighted

the necessity of careful psychiatric evaluation as part of the presurgical

and postsurgical protocols in tertiary epilepsy centers [1–6]. Despite re-

cent studies indicating that the sole presence of a PD would not be a risk

factor for evaluation with video-electroencephalography (VEEG), the

presence of a PD has remained a relative contraindication for presurgical

VEEG in some epilepsy centers mainly because of the risk of negative

behavioral events, such as aggressiveness, attempted suicide, or psycho-

motor agitation [11,12]. The present retrospective cohort study aimed

to determine whether PDs have remained a "hidden" contraindication

for presurgical VEEG in a Brazilian tertiary epilepsy center with a psychi-









São Paulo, Brazil) from January 2013 to November 2014 and underwent psychiatric evaluation. The eligibility criteria included patients who were older than 18, had an electroclinical diagnosis of TLE based on the ILAE classification [13], had been receiving follow-up care with the Epilepsy Center for at least six months, and had been referred for presurgical psychiatric evaluation before VEEG. All patients were seen by the same clinical team. Exclusion criteria included the presence of other clinical or neurological diseases besides epilepsy, cognitive impairments precluding evaluation, and patients who already had VEEG performed before psychiatric evaluation. Any clinical or social factors other than psychiatric evaluations recorded in patients' files that had precluded the use of VEEG were also considered as exclusion criteria. Patients with any PD at the time of psychiatric evaluation that precluded the use of VEEG were excluded, as were those who declined the procedure. Patients with a putative diagnosis of psychogenic nonepileptic seizures (PNES) were not included in the study because this diagnosis must be confirmed using VEEG.

The VEEG consisted of 2–6 days of continuous monitoring with 32-channel EEG. Electrodes, including sphenoidal electrodes, were placed on the temporal lobe according to the 10-10 system. Mesial temporal sclerosis was determined to be present if atrophy, increased T2-weighted signal, decreased T1-weighted signal, and disrupted internal hippocampal structure were present and accompanied by observations of amygdala atrophy and/or temporal pole signal changes upon visual inspection of the MRI images. The epileptogenic zone was determined by predominantly ipsilateral interictal epileptiform discharges (80% cutoff) and seizure onset recorded during the prolonged VEEG monitoring. Refractoriness to medical treatment was considered present if seizures persisted after the utilization of at least two firstline medications for partial seizures at the highest tolerated dose for at least 6 months. An initial precipitant injury (IPI) was defined as the occurrence of severe cerebral events that required medical intervention and/or hospitalization during the first year of life before the appearance of epilepsy. Febrile seizures, meningoencephalitis, head trauma, or severe perinatal hypoxia were considered IPIs.

#### 2.2. Psychiatric evaluation

A single psychiatrist (GMAF) conducted the clinical interviews using the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) Axis I criteria [14]. Because each patient could have more than one Axis I psychiatric diagnosis, both the number of patients diagnosed and all comorbid PDs diagnosed were considered in the analysis. The presence of other specific psychiatric diagnoses commonly associated with epilepsy, which are not covered by the DSM-IV but are well described in the literature, such as interictal dysphoric disorder (IDD) and epilepsy psychoses, was evaluated using the ILAE criteria. These criteria were also used to differentiate postictal psychosis (PIP) from interictal psychosis (IIP) [15]. Data concerning the lifetime history of psychotropic treatment, defined as any past treatment with psychiatric drugs, were collected from patients during the first clinical interview. Information about the familial history of epilepsy and PDs was also obtained from patients through broad questions regarding whether any first-degree relative was in treatment for epilepsy and/or any PD at the time of the clinical interview.

#### 2.3. Statistics

Statistical analyses were performed using the version 14.0 of the Statistical Package for Social Sciences software (SPSS 10.0, Chicago, Illinois). Bivariate statistical analyses were performed using the most suitable statistical test for each situation (chi-square ( $\chi^2$ ), Fisher's exact test, or Student's t-test for unequal variances). For statistical comparisons, patients were divided into two groups according to the use of VEEG monitoring as an indispensable presurgical evaluation that always occurred (or did not occur) as part of the service routine following psychiatric evaluation. A p-value < 0.05 was considered significant.

#### 3. Results

After written informed consent was obtained, the clinical and sociodemographic data of 73 consecutive surgical candidates with refractory TLE-MTS (48 females; 57.8%) who met the eligibility criteria were collected. Patients' clinical and sociodemographic characteristics are shown in Table 1. Mesial temporal sclerosis occurred more frequently on the left side (39 patients; 53.4%). Thirty-one patients (42.5%) had a history of IPI, with febrile seizures the most frequent (12 cases; 38.7%). There were also ten cases of head trauma (32.2%), five of perinatal hypoxia (16.1%), and two of meningoencephalitis (6.4%). Sixty-nine patients (94.5%) were using at least two medications at the time of evaluation. Carbamazepine (CBZ) was the most frequently used AED and was prescribed to 55 patients (75.3%), followed by phenobarbital (PB) (35; 47.9%), valproate (15; 20.5%), topiramate (TPM) (10; 13.7%), oxcarbazepine (OXC) (7; 9.6%), and phenytoin (PHT) (7; 9.6%). Benzodiazepines (BZDs), particularly clobazam (CLB), were the most common adjunctive drugs and were prescribed to 26 patients (35.6%).

Among the 73 patients, Axis I psychiatric diagnoses were observed in 34 (56.6%). Major depressive disorder (MDD), which included all diagnoses of depression within the present cohort, was the most common PD and was diagnosed in 22 patients (30.1%). Fourteen patients (19.2%) had anxiety disorders, all of them presenting generalized anxiety disorder (GAD). Psychotic disorders were observed in seven patients (9.6%), all of which had IIP. Somatoform disorders (excluding the nonconfirmed presence of PNES) were observed in five patients (6.8%). Fourteen patients fulfilled the criteria for two Axis I disorders. Interictal dysphoric disorder

#### Table 1

Clinical and demographic data of patients with refractory epilepsy who did or did not undergo video-electroencephalography.

Clinical/demographic data	Total	VEEG	Non-VEEG	р
Number of patients (%)	73 (100)	41 (56.2)	32 (43.8)	-
Female gender (%)	42 (57.5)	20 (48.7)	22 (68.7)	0.22 <sup>a</sup>
Age (mean $\pm$ SD)	$41.4 \pm 12.10$	$41.0 \pm 12.57$	$42.4 \pm 12.66$	0.42 <sup>b</sup>
Age at epilepsy onset (mean $\pm$ SD)	$13.9 \pm 13.32$	$12.0 \pm 9.17$	$16.8 \pm 13.31$	0.37 <sup>b</sup>
Epilepsy duration (mean $\pm$ SD)	$26.1 \pm 13.32$	$28.4 \pm 13.50$	$25.1 \pm 14.30$	0.61 <sup>b</sup>
Lifetime psychiatric treatment (%)	34 (46.5)	10 (24.3)	24 (75.0)	0.02 <sup>*,a</sup>
Family history of epilepsy (%)	22 (30.1)	12 (29.2)	10 (31.2)	0.93 <sup>a</sup>
Family history of PD (%)	13 (17.8)	4 (9.7)	9 (28.1)	0.03 <sup>*,C</sup>
Presence of IPI (%)	31 (42.5)	19 (46.3)	12 (37.5)	0.55 <sup>a</sup>
Patients with PDs (%)	34 (46.6)	12 (29.2)	22 (68.7)	0.001 <sup>*,a</sup>

IPI: initial precipitant injury, PDs: psychiatric disorders, and SD: standard deviation.

\* p < 0.05.

<sup>a</sup> Chi-square.

<sup>b</sup> Student's t-test.

<sup>c</sup> Fisher's exact test.

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