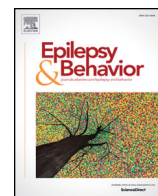




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## Suicide risk, temperament traits, and sleep quality in patients with refractory epilepsy☆

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### ABSTRACT

**Objectives:** The objective of the study was to access the suicide risk (SR) in patients with refractory epilepsy and its association with temperament and sleep quality.

**Methods:** A total of 50 consecutive patients referred for epilepsy surgery evaluation in the Porto Alegre Epilepsy Surgery Program were included. All patients had a detailed neurologic and psychiatric evaluation, including video-electroencephalogram (VEEG), high-resolution magnetic resonance imaging (MRI), and neuropsychologic assessment. In addition, structured questionnaires were applied: module C of the MINI-plus (International Neuropsychiatric Interview-Brazilian version 5.0.0), Affective and Emotional Composite Temperament Scale (AFECTS), and Pittsburgh Sleep Quality Index (PSQI).

**Results:** Ten patients (20.0%) showed an increased SR. The most frequent location of the epileptic focus was in the temporal lobe (50%;  $n = 25$ ). Final diagnosis on VEEG comprised epilepsy in 74.0% ( $n = 37$ ), psychogenic nonepileptic seizures (PNES) in 8.0% ( $n = 4$ ), and both in 12%. Thirty patients (60.0%) received surgery indication. Mood disorders were the main psychiatric diagnosis, found in 19 subjects (70.4%), with major depressive disorder (MDD) encountered in 15 patients (55.6%). In the group, SR was more frequent in patients with sleep disorders ( $p = 0.001$ ) and elevated scores of high emotional sensitivity ( $p = 0.003$ ).

**Conclusion:** In this cohort of patients with highly refractory epilepsy, there was a significant association between SR, sleep disorders, and high emotional sensitivity. Careful evaluation of these factors should be performed in these patients to fully access SR.

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### 1. Introduction

Psychiatric comorbidities are commonplace in epilepsy, occurring in 10 to 40% of patients [1,2]. Often, psychopathologies are underdiagnosed and remain untreated, leading to significant morbidity [3]. Suicide poses a public health challenge, with over a million suicides worldwide every year. Suicide represents one of the main causes of death in epilepsy, representing 5 to 11% of deaths in this group [4]. In the United States, such numbers are significantly higher than the rate of suicide in the general population (1.5 to 11.6/100.000) [1,2,4]. Since early 2000s, there has been a better understanding in the shared physiopathology of psychiatric disorders and epilepsy [5]. Such relationship is known as the ‘bidirectional hypothesis’, in which a shared cerebral deregulation

that interferes in behavioral functioning and mood regulation, also leads to neuron excitability and an increased risk of seizures. This concept helps understand the high prevalence of psychiatric disorders both prior and after the diagnosis of epilepsy [6].

An increasing amount of evidence suggests an increased risk of suicidal behavior in patients with psychogenic nonepileptic seizures (PNES) [6,7]. Psychogenic nonepileptic seizure is the main differential diagnosis in patients with supposedly refractory epilepsy, and its coexistence with epilepsy, particularly refractory, has been recently recognized as a diagnostic and therapeutic challenge [6]. Mood disorders contribute to four times increase in the risk of suicide in these patients [2,3,8]. Another important factor in patients with epilepsy (PWE) is sleep quality and psychiatric comorbidities, especially related to suicide risk (SR). Evidence suggests a protective effect of sleep in epilepsy, mostly based on the clinical and laboratorial observation of increased seizures and epileptiform discharges after sleep deprivation. Alterations in the sleep–wake cycle may also contribute to an increased risk of suicidal behavior [9,10]. Mood and anxiety disorders are the most frequent psychiatric comorbidities found in epilepsy [9,11]. In these patients, symptoms may not fulfill strict diagnostic

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criteria from International Statistical Classification of Diseases and Related Health Problems (ICD-10) or Diagnostic and Statistical Manual of Mental Disorders (DSM 5), requiring other instruments to fully evaluate their emotional characteristics [2,11,12]. Temperament traits may be evaluated as protective or harmful for suicidal behaviors [13–15]. Lara et al. [11] proposed an alternative instrument of assessment (the so-called Affective and Emotional Composite Temperament (AFECT) model) that integrates emotional temperament (Cloninger) [16] and affective temperament (Kraepelin and Akiskal) [17,18]. Our study aimed to assess SR, temperament traits, and sleep quality in a cohort of patients whose epilepsy is highly refractory evaluated for epilepsy surgery.

## 2. Methods

We performed a prospective study of all patients admitted for diagnostic and presurgical evaluation of refractory epilepsy at the Epilepsy Monitoring Unit (EMU) of the Porto Alegre Epilepsy Surgery Program (PAESP) from January 2017 to October 2017.

### 2.1. Inclusion criteria

We screened all patients from 18 to 70 years of age, and all were included after agreeing to participate in the study and signing a written informed consent form.

### 2.2. Exclusion criteria

Patients were excluded if they had any of the following conditions: 1) Active psychosis; 2) Current drug abuse (i.e., cannabis, alcohol, cocaine...) and drug-related mental illnesses; 3) Severe cognitive impairment; 4) Unable or unwilling to sign the consent form or to participate in the study.

### 2.3. Ethics

Our study was approved by our Ethics Committee at Pontificia Universidade Católica do Rio Grande do Sul (CAAE69516317.0.0000.5336). All patients in the study signed a written informed consent form.

### 2.4. Data collection

All patients had a detained neurologic and psychiatric assessment, as part of their evaluation for possible epilepsy surgery. This included a careful semiological evaluation of the seizure type and epilepsy, as well as a prolonged video-electroencephalographic (VEEG) study and a 3 T brain MRI. In addition, all had thorough neuropsychologic and psychiatric evaluations. We also applied structured validated questionnaires, including the following: a) Standardized sociodemographic questionnaire; b) Module C of the MINI-plus questionnaire (International Neuropsychiatric Interview-Brazilian version 5.0), regarding SR and evaluation [19]. This score ranges from 1 to 33. Scores from 1 to 5 indicate low risk (suicide ideation), 6 to 10 represents moderate risk (suicide plan), and > 10 implies high SR (with previous suicide attempt). In our sample, SR were categorized in two groups, according to module C as present (moderate and high scores) or absent (low scores); c) Affective and Emotional Composite Temperament Scale (AFECTS) [11], a self-reporting instrument, developed and validated by Lara et al. This scale is comprised of two parts: 1) Emotional Section divided in nine dimensions: volition, impulse, anger, fear, emotional sensibility, maturity, control, anxiety, and stability; 2) Affective section comprised of brief descriptions of 12 affective temperaments: [depressive, anxious, apathetic (internalizing); cyclothymic, dysphoric, volatile (unstable); obsessive, euthymic, hyperthymic (stable); irritable, unhinged, and euphoric (externalizing)]; d) Pittsburgh Sleep Quality Index (PSQI), a self-reporting instrument, previously validated

in Portuguese [20]. This questionnaire evaluates sleep quality over a 1-month period, and it is comprised of 19 self-reported questions and five questions directed to the patient's spouse, composing seven composite scores ranging from 0 (no difficulty) to 3 (severe difficulty). The score is calculated by the sum of all items and ranges from 0 to 21, where lower scores denote 'good sleepers', moderated scores indicate 'poor sleepers' quality, and high scores indicate sleep disorder.

### 2.5. Statistics analysis

Descriptive data will be reported using Chi-square test and *t*-test analyses. Residue analyses were performed to detect categories with higher-than-expected values. Quantitative variables were analyzed by *t*-student test. Statistical analyses were performed by SPSS software v. 20 (IBM Corp., Armonk, NY). A *p* value of  $\leq 0.05$  was considered statistically significant.

## 3. Results

A total of 50 patients were included in our study, all of whom consent to participate. Sociodemographic and clinical data are displayed

**Table 1**  
Sociodemographic and clinical data [without SR–with SR (n = 50)].

|  | Without SR<br>[n (%)] | With SR<br>[n (%)] | Total<br>number<br>[n (%)] | OR (CI:95%)              |
|--|-----------------------|--------------------|----------------------------|--------------------------|
| Gender   |                       |                    |                            |                          |
| Male   | 20(50.0)              | 5(20.0)            | 25(50.0)                   |                          |
| Female   | 20(50.0)              | 5(20.0)            | 25(50.0)                   |                          |
| Age (mean $\pm$ SD)                            | 35.8 $\pm$ 12.2       | 31.80 $\pm$ 11.2   | 34.96 $\pm$ 12             |                          |
| Stable relationship                            |                       |                    |                            |                          |
| No   | 17(43.6)              | 5(50.0)            | 22(44.9)                   |                          |
| Yes  | 22(56.4)              | 5(50.0)            | 27(55.1)                   |                          |
| Education, in years<br>(mean $\pm$ SD)         | 10.1 $\pm$ 3.7        | 11.4 $\pm$ 4.4     | 10.4 $\pm$ 3.8             |                          |
| Employment                                     |                       |                    |                            |                          |
| Student  | 5(12.5)               | 1(10.0)            | 6(12.0)                    |                          |
| Working  | 7(17.5)               | 2(20.0)            | 9(18.0)                    |                          |
| Housewife                                      | 10(25.0)              | 4(40.0)            | 14(28.0)                   |                          |
| Unemployed                                     | 7(17.5)               | 1(10.0)            | 8(16.0)                    |                          |
| Retired  | 11(27.5)              | 2(20.0)            | 13(26.0)                   |                          |
| Age at epilepsy<br>onset ( $\leq 18$ years)    | 30(75.0)              | 8(80.0)            | 38(76.0)                   |                          |
| Epileptic<br>focus <sup>a</sup>                |                       |                    |                            |                          |
| Frontal  | 4(10.5)               | 1(12.5)            | 5(10.9)                    |                          |
| Temporal                                       | 19(50.0)              | 6(75.0)            | 25(54.3)                   |                          |
| Multiple foci                                  | 7(18.4)               | 1(12.5)            | 8(17.4)                    |                          |
| Nonlocalizing                                  | 3(7.9)                | –                  | 3(6.5)                     |                          |
| Others foci                                    | 5(13.2)               | –                  | 5(10.9)                    |                          |
| Final diagnosis                                |                       |                    |                            |                          |
| Epilepsy                                       | 31(77.5)              | 6(60.0)            | 37(74.0)                   |                          |
| PNES   | 2(5.0)                | 2(20.0)            | 4(8.0)                     |                          |
| Epilepsy + PNES                                | 4(10.0)               | 2(20.0)            | 6(12.0)                    |                          |
| Inconclusive                                   | 3(7.5)                | –                  | 3(6.0)                     |                          |
| Epilepsy surgery                               | 24(60.0)              | 6(60.0)            | 30(60.0)                   |                          |
| Psychiatric diagnosis<br>(ICD-10)              |                       |                    |                            |                          |
| Yes  | 19(47.5)              | 8(80.0)            | 27(54.0)                   | OR = 1.68<br>(0.57–4.95) |
| No   | 21(52.5)              | 2(20.0)            | 23(46.0)                   |                          |
| Types of psychiatric<br>diagnosis <sup>b</sup> |                       |                    |                            |                          |
| Schizophrenia                                  | 1(5.3)                | –                  | 1(3.7)                     |                          |
| Mood disorders                                 | 13(68.4)              | 6(75.0)            | 19(70.4)                   |                          |
| Depressive disorder                            | 13(68.4)              | 2(25.0)            | 15(55.6)                   |                          |
| Bipolar disorder                               | 1(5.3)                | 3(37.5)            | 4(14.8)                    |                          |
| Anxiety disorders                              | 5(26.3)               | 2(25.0)            | 7(25.9)                    |                          |

SR: suicide risk, VEEG: video-electroencephalogram; PNES: psychogenic nonepileptic seizures, SD: standard deviation, OR: odds ratio, CI: confidence interval, ICD: International Statistical Classification of Diseases and Related Health Problems.

<sup>a</sup> This variable is about 46 patients with epilepsy, excluded PNES.

<sup>b</sup> This variable is about 27 patients with psychiatric disorders.

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