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Cognitive and clinical variables associated with interictal dysphoric disorder in patients with epilepsy

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ABSTRACT

Purpose: The relationship between interictal dysphoric disorder (IDD) and cognitive impairment in adult patients with epilepsy (PWE) is poorly studied.
Methods: The Interictal Dysphoric Disorder Inventory (IDDI) with cognitive and clinical aspects was compared with Quality of Life in Epilepsy Inventory (QOLIE-31) and Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) scores of 117 PWE at significance level $p < 0.05$.
Results: Interictal dysphoric disorder occurred in 25 (21.4%) PWE, and it was significantly associated with the presence of psychiatric disorders (PD) (α^2; $p = 0.007$), presence of major depressive episodes ($p = 0.03$), lower educational level, older individuals, and those with a lower performance in the category fluency test (VF) (9.7 ± 5.1 vs. 12.2 ± 4.2; *t*-test; $p = 0.037$). There was a negative correlation between QOLIE-31 and IDD. The predictive factors for the occurrence of IDD were the presence of PD ($p = 0.014$) and lower performance in the VF ($p = 0.013$).
Conclusion: The occurrence of IDD was high. Interictal dysphoric disorder was found in different epileptic syndromes, and it was associated with the presence of PD, depressive episodes, lower performance in VF, and lower quality of life (QoL).

1. Introduction

Interictal dysphoric disorder (IDD) is a condition characterized by labile depressive symptoms, labile affective symptoms, and specific symptoms (paroxystic irritability and instable euphoric moods) with pleomorphism that has been found in 9–34% of patients with epilepsy (PWE) and a higher incidence in focal refractory epilepsies [1–4]. In the literature, the relationship between IDD, quality of life (QoL) [4–6], and clinical aspects [2,4–7] in PWE is described. We did not find any studies that evaluated the relationship between IDD and cognitive aspects.

Cognitive impairment often described in PWE is related to the disease itself, location of the epileptogenic area, seizure recurrence, or psychosocial aspects [8,9]. Studies evaluating the relationship between psychiatric disorders (PD) and cognitive impairment in epilepsy are rare [10–12].

Thus, the aim of this study was to evaluate the occurrence of IDD in PWE and the relationship with sociodemographic, clinical and cognitive aspects, and QoL.

2. Methods

2.1. Patients

From August 2016 to February 2017, during routine medical appointments at the outpatient clinic of neurology of PUC-Campinas, Campinas, Brazil, 117 consecutive PWE aged +18 years were invited to participate in the study. Those who agreed to participate answered a sociodemographic (age, gender, education level, marital status) and clinical characteristics questionnaire (age of onset, seizure type and frequency, duration of epilepsy, number of antiepileptic drugs (AED) used, and epileptic syndrome). Seizure control was operationally defined as seizure-free for the last 12 months in this study.

The presence of PD was evaluated using the criteria of DSM-IV and ICD-10 at the medical appointment at the psychiatry department of PUC Campinas. The patients were then classified into two groups: with and without PD.

Epilepsy was diagnosed according to the International Classification of Epilepsies and Epileptic Syndromes (ILAE) [13] criteria. Patients with symptomatic focal epilepsies were included in a subgroup of surgery-naive patients with temporal lobe epilepsy with hippocampus sclerosis (TLE-HS) characterized by their clinical aspects, namely the presence of hippocampus atrophy, loss of digitations of the hippocampal head, and

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loss of definition of internal structure as revealed by magnetic resonance imaging.

Patients who had difficulty understanding the questions in the instruments due to low educational level or mental disabilities, those with a history of cancer or stroke, progressive neurological diseases, or neurodegenerative diseases were excluded from the study.

The interview and the questionnaires were carried out by the author GMAS Tedrus who is an expert in epilepsy and responsible for the medical care provided at the facility.

The study was approved by the Human Research Ethics Committee of PUC-Campinas.

2.2. Assessment

1. Interictal Dysphoric Disorder Inventory (IDDI): The IDDI is a 38-item self-report questionnaire specifically designed to investigate IDD and evaluate IDD symptoms considering its presence, frequency, severity, and global impairment in the previous 12 months. It is possible to obtain a total score and 3 subscale scores for the following: labile depressive symptoms, labile affective symptoms, specific symptoms, and the severity of these symptoms. The diagnosis of IDD is established by the presence of at least three symptoms that range from moderate to severe causing moderate or severe distress [2]. The IDDI was translated and culturally adapted in Brazil in 2010 [14].
2. Quality of Life in Epilepsy Inventory (QOLIE-31): The QOLIE-31 is an epilepsy-specific QoL inventory. This inventory has a total score and measures the following seven domains: worry seizure, overall quality of life, emotional well-being, energy-fatigue, cognitive functioning, medication effects, and social functioning. The overall score ranges from 1 to 100. A higher score indicates higher QoL [15]. It was validated in Brazil in 2007 [16].
3. Mini-Mental State Examination (MMSE) [17]: The MMSE is a screening test to assess cognitive impairment, temporal and spatial orientation, registration and recall of three words, attention and calculation, language, and visual construction. Its maximum score is 30 points. The MMSE has been validated in Brazil in 2003 [18].
4. Brief Cognitive Battery (BCB) [19]: The BCB is the screening cognitive test of low educated individuals. This instrument requires the identification and naming of simple drawings of 10 common objects, followed by the incidental memory of these objects. Subsequently, the drawings are presented on two more occasions, followed each time by the recall of the objects, to obtain the scores of immediate memory and the number of items learned or encoded, called the learning scores. This is followed by an interference phase consisting of a category fluency test (animals in 1 min) and the clock-drawing test. After this interference, (free) delayed recall and recognition of the 10 objects among 20 drawings (with 10 distractors) are evaluated.
5. Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) [20]: The NDDI-E has six items using a 4-point scale from "never" to "always or often". The NDDI-E accurately assesses the patient's affective experience for fast screening and it was validated in Brazil in 2011 [21]. Major depression is suspected when the NDDI-E score is >15, as proposed by the original study and the Brazilian validated version.

2.3. Data analysis

Continuous variables were analyzed using descriptive statistics (mean, standard deviation, frequency, and percentage (%)). Categorical variables were tabulated by the absolute (n) and percentage (%) frequencies. The independent *t*-test (for categorical data) was applied to check for significant differences in the mean scores between the groups on the individual dimension, and Pearson's correlation coefficients (for continuous data) were calculated to check the linear association among the variables.

Based on the significant correlations, logistic regression was used to determine the relationship between the predictor variables and binary or continuous outcome variables (dependent variables) using variables at $p < 0.10$ in the prior correlation analyses (independent variables). The data were treated by the software IBM SPSS Statistics, version 22. The significance level adopted was 5% ($p < 0.05$).

3. Results

The study included 117 PWE (50.4% were females). The mean age of the sample was 43.0 (±16.3) years, and the mean education level was 6.4 (±4.1) years. The age at first seizure was 19.5 (±14.5) years, and the mean disease duration was 23.4 (±15.1) years.

The epilepsies were generalized idiopathic epilepsies in 25 (21.3%) cases, symptomatic focal epilepsies and probably symptomatic focal epilepsies in 59 (50.4%) and 33 (28.2%) cases, respectively. The TLE-HS was observed in 38 (32.4%) cases.

Twenty-five (21.3%) PWE met the criteria established for IDD. As recommended by Mula et al. [2], patients were considered to have IDD if they had at least three core symptoms that were moderate or severe and caused moderate to severe distress in the previous 12 months.

In the 117 PWE, the values found for total score and severity total score were as follows: 4.2 ± 2.2 and 3.4 ± 2.2, respectively. The subscale scores were the following: labile depressive symptoms: 3.2 ± 2.2; labile affective symptoms: 9.2 ± 2.2; and specific symptoms: 5.2 ± 2.2.

3.1. IDD and sociodemographic, clinical, and cognitive aspects

The PWEs that presented IDD were significantly older and had a lower level of formal education when compared with those without IDD.

The clinical aspects according to the occurrence of IDD are shown in Table 1. There was no difference in the occurrence of IDD according to

Table 1
Occurrence of IDD according to sociodemographic and clinical aspects of the 117 PWE.

	IDD		*p*
	Present (n = 25)	Absent (n = 92)	
Age (y)	49.9 (±15.8)	41.0 (±16.1)	**0.039**[*]
Educational level (y)	4.96 (±4.1)	6 9 (±4.0)	**0.045**[*]
Age at first seizure (y)	22.6 (±16.7)	18.6 (±13.8)	0.284
Duration of epilepsy (y)	26.3 (±15.7)	22.6 (±14.9)	0.300
Type of seizure			
Focal (n = 86)	20	66	0.289[a]
Exclusively generalized (n = 31)	5	26	
Epileptic seizure frequency			
Uncontrolled (n = 64)	15	49	0.356[a]
Controlled (n = 53)	10	43	
Antiepileptic drugs			
One (n = 70)	13	57	0.250[a]
≥2 (n = 47)	12	35	
Psychiatric disorders			
Present (n = 43)	15	28	**0.007**[b,*]
Absent (n = 74)	10	64	
Epileptic syndrome			
Generalized idiopathic (n = 25)	4	21	0.563[b]
Probably symptomatic focal (n = 33)	9	24	
Symptomatic focal (n = 59)	12	47	
TLE-HS lateralization			
Right (n = 17)	3	14	0.478[a]
Left (n = 21)	5	16	
NDDI-E (score)			
≤15 (n = 89)	16	73	**0.030**[a,*]
>15 (n = 16)	7	9	

IDD: Interictal dysphoric disorder; TLE-HS: Temporal lobe epilepsy with hippocampus sclerosis; NDDI-E: Neurological Disorders Depression Inventory for Epilepsy.
[a] Fisher's exact test.
[b] Chi-square.
[*] $p < 0.05$.

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