Contents lists available at ScienceDirect

Epilepsy & Behavior

Clinical Research

Clinical and sociodemographic variables associated with interictal dysphoric disorder and interictal personality in patients with drug-resistant temporal lobe epilepsy: A controlled study

Gerardo Maria de Araújo Filho *, Bruna Tarifa, Raquel Espagnolla Santos, Ana Laura de Oliveira Dias, Júlia Rodrigues Leandro Ulliano, Lucia Helena Neves Marques

Faculdade de Medicina de São José do Rio Preto (FAMERP), Brazil

ABSTRACT

Psychiatric disorders (PD) have an elevated prevalence and an important negative impact on patients with epilepsy (PWE) since they are associated with lower quality of life and clinical refractoriness. However, it is also necessary to identify behavioral conditions possibly associated with epilepsy that are not part of the standard psychiatric classifications, such as Interictal Dysphoric Disorder (IDD) and Interictal Personality (IP). The frequency of IDD and IP in patients with drug-resistant temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS) was assessed. The Brazilian versions of the Neurobehavioral Inventory (NBI) and Interictal Dysphoric Disorder Inventory (IDDI) were applied to patients and to a control group. Psychiatric standard assessment was conducted through the Diagnostic and Statistical Manual for Psychiatric Disorders – 5th edition (DSM-5). The value of p considered significant was < 0.05. Ninety-five patients (51 women; 53.6%) and 50 controls (29 women; 58.0%) were assessed. Axis I PD were observed in 41 patients (43.1%). Interictal Dysphoric Disorder was observed in 18 patients (18.4%) and IP in 36 (37.9%). Interictal Dysphoric Disorder was associated with left-sided MTS (OR = 3.22; p = 0.008), previous psychiatric treatment (OR = 4.29; p = 0.007), and more than one AED used (OR = 2.73; p = 0.02) while presence of bilateral MTS (OR = 3.27; p = 0.008), longer disease duration (OR = 3.39; p = 0.006), and presence of Major Depressive Disorder (OR = 4.73; p = 0.004) were associated with IP. In the present study, there was a high prevalence of IDD and IP in patients with drug-resistant TLE-MTS; studies should be conducted to identify the presence of behavioral conditions that are not present in the conventional psychiatric classifications.

© 2017 Elsevier Inc. All rights reserved.

1. Introduction

Epilepsy is a chronic neurological disease characterized by recurrent epileptic seizures that affects nearly 1% of the world population. Psychiatric disorders (PD), which have been associated with all epileptic syndromes, contributes to lower quality of life [1–3]. Studies have observed a prevalence of PD of 20–40% in populations with temporal lobe epilepsy (TLE), rising to 70% in patients with drug-resistant epilepsy [4–10]. Mood disorders, particularly depression, are the most common PD diagnosed (24–74%), followed by anxiety disorders (10–25%), psychoses (2–9%), and personality disorders (1–2%) [4–10]. Other behavioral disorders specifically associated with epilepsy may occur, such as the Interictal Dysphoric Disorder (IDD) and specific features of personality disorders such as the Interictal Personality (IP), formerly known as Gastaut-Geschwind Syndrome [4–7].

However, there is still a controversy in the literature about the existence of such behavior patterns specifically associated with epilepsy, as well as how and where they should be described and classified [8–13]. The development of instruments to assess more precisely the possible existence of PD specifically associated with epilepsy which are not part of the current diagnostic criteria in psychiatry, as well as the subclinical presentation of psychiatric symptoms in these patients, has been of great importance [14–19]. The *Neurobehavioral Inventory* (NBI) and the *Interictal Dysphoric Disorder Inventory* (IDDI) are assessment tools especially developed to estimate the presence of symptoms associated with IP, IDD, and depression in patients with epilepsy, respectively [17–19]. This study assessed the frequency of IDD and IP in patients with drug-resistant epilepsy, and their association with possible clinical and sociodemographic aspects.

2. Methods

2.1. Patients

After the study was approved by the local ethics committee and an informed consent was signed, interviews were conducted between September 2014 and September 2016 with 95 patients treated in a

tertiary center (outpatient clinic of the Faculdade de Medicina de São José do Rio Preto - FAMERP) diagnosed with drug-refractory temporal lobe epilepsy and mesial temporal sclerosis (TLE-MTS). Exclusion criteria were presence of non-refractory epilepsy, presence of other brain lesions observed on magnetic resonance imaging besides MTS, and/or inability to answer the questionnaires due to cognitive dysfunction. For comparison purposes, the assessments were also applied to 50 healthy individuals from the community (control group).

2.2. Instruments

All patients and controls underwent standard psychiatric assessment using the criteria of the Diagnostic and Statistical Manual for Psychiatric Disorders – 5th edition (DSM-5) and the diagnostic criteria of the International League Against Epilepsy (ILAE) for Interictal Psychosis (IIP) [14,15]. In addition, both groups were assessed through the Brazilian versions of the following instruments:

a) NBI [17]: this instrument assesses IP characteristics which are historically associated with patients with epilepsy (viscosity, emotions, hypermoralism, spirituality, hyposexuality, and dependency). The inventory is composed of 100 true or false items. Each set of 5 statements investigates one of 20 domains (the numbers in parentheses below correspond to each of the statements in the NBI): writing tendency (6,18,53,62,98), hypermoralism (19,41,49,75,83), religious convictions (13,24,48,94,99), anger and temper (20,25,36,43,91), orderliness (5,14,21,42,71), hyposexuality (7,10,52,77,84), fearfulness (16,40,57,64,86), feelings of guilt (4,55,61,70,80), seriousness (29,45,66,88,100), sadness (33,38, 73,85,92), emotions (9,23,54,69,89), suspicion (12,17,22,34,63), interest in details (26,50,58,67,81), cosmic interests (37,46,51,72,76), sense of personal destiny (1,11,27,32,97), persistence and repetitiveness (35,44,60,78,90), hatred and revenge (56,68,82,87,96), dependency (3,15,28,39,93), happiness (2,31,59,65,79), and physical well-being (8,30,47,74,95). More than two items checked true in more than nine domains, or a total sum over 20 items checked true, are considered elevated scores.

b) IDDI [18]: this instrument was developed to diagnose IDD, which is determined by the presence of eight key symptoms divided into three dimensions: depressive symptoms (depressed mood, anergy, pain, insomnia), affective symptoms (fear/panic, anxiety), and so-called "specific" symptoms (irritability and euphoria). At least three of the key symptoms producing considerable social and occupational dysfunction are sufficient to determine the diagnosis. The diagnosis of IDD was not performed if participants met diagnostic criteria for an Axis I disorder.

2.3. Statistical analysis

The collected data were analyzed with mean and standard deviation (discrete variables) or according to their presence or absence (categorical variables). Results obtained were statistically analyzed according to the most appropriate methods (chi-square test, Fisher's exact, Student's t-test, Kruskal-Wallis). The Bonferroni adjustment for multiple comparisons was applied as a *post-hoc* test for statistically significant differences.

Two multivariate analyses through logistic regression models were performed to identify possible clinical and socio-demographic risk factors associated with the presence of IDD and IP, respectively. Variables included in the initial model were gender, age, presence and type of IPI, previous psychiatric treatment, family history of epilepsy and PD, epilepsy duration, age at epilepsy onset, number and types of AED, number and types of Axis I PD, and laterality of MTS. The *odds-ratio* (OR) was calculated for significant risk factors. A P value of <0.05 was considered significant.

3. Results

Clinical and sociodemographic data of patients and controls are shown in Table 1. When compared to controls, the group of patients had significantly more history of previous psychiatric treatment ($p < 0.001$), family history of epilepsy ($p < 0.001$), and family history of PD ($p < 0.001$).

Axis I PD were observed in 41 patients (43.1%). The following diagnoses were observed: Major Depressive Disorder (MDD) (21 patients; 51.2%), Generalized Anxiety Disorder (GAD) (15 patients; 36.5%), Conversion Disorder (9 patients; 9.4%), and IIP (5 patients; 5.2%). Nine patients (9.4%) had two Axis I PD. Six individuals in the control group met criteria for MDD (12%), and five individuals for GAD (10%).

The assessment with IDDI showed the presence of IDD in 18 patients (18.4%), whereas diagnostic criteria for IP were observed in 36 patients (37.9%) accordingly to the NBI criteria. Four individuals in the control group (8%) met the criteria for IDD and four (8%) met the criteria for IP. When compared to the control group, the group of patients had more diagnoses of MDD ($p < 0.001$), GAD ($p < 0.001$), Conversion Disorder ($p < 0.001$), IDD ($p < 0.001$), and IP ($p < 0.001$). Fig. 1 shows PD among both groups.

An analysis of the diagnostic superposition between IDD or IP and Axis I PD was performed; of the 18 patients with IDD, no one had an Axis I PD. Of the 36 patients diagnosed with IP, 15 (41.6%) had an Axis I PD: MDD (10 patients; 66.6%), IIP (three patients; 18.7%) and Conversion Disorder (two patients; 13.4%). In the control group, none of the subjects with Axis I PD demonstrated superposition with IP or IDD diagnoses.

Multivariate logistic regression models were performed to identify possible clinical and socio-demographic risk factors associated with the presence of IDD and IP, respectively. Regarding the presence of IDD, the final adjusted model (sensitivity 71.2%; specificity 89.5%; positive predictive value 66.5%; negative predictive value 75.3%; area under the curve 0.785) observed that the presence of left-sided MTS (OR = 3.22; p = 0.008), previous psychiatric treatment (OR = 4.29; p = 0.007), and more than one AED used (OR = 2.73; p = 0.02) were

Table 1
Clinical and sociodemographic data of controls and patients with drug-resistant temporal lobe epilepsy treated in a tertiary center.

Clinical/sociodemographic data	Patients	Controls	p
Number of participants	95	50	–
Women (%)	51 (53.6)	29 (58.0)	0.87
Age (mean ± SD)	40.3 ± 14.6	41.2 ± 13.8	0.76
Family history of epilepsy (%)	44 (46.3)	3 (6)	<0.001[*]
Previous psychiatric treatment	53 (55.7)	5 (10)	<0.001[*]
Family history of PD (%)	25 (26.3)	4 (8)	<0.001[*]
Age at first seizure (mean ± SD)	17.5 ± 11.9 years	–	–
Epilepsy duration (mean ± SD)	25.3 ± 7.4 years	–	–
Most frequently used AEDs (%)	Carbamazepine: 58 (61.0)	–	–
	Phenobarbital: 41 (43.1)		
	Clonazepam: 25 (26.3)		
	Lamotrigine: 21 (22.1)		
	Clobazam: 18 (18.9)		
Number of AEDs used (%)	One AED: 5 (5.1)	–	–
	Two AED: 79 (83.4)		
	Three AED 11 (11.5)		
Presence of type of IPI (%)	No IPI: 54 (57.1)	–	–
	Head trauma: 11 (11.5)		
	Febrile seizures: 25 (26.3)		
	Meningoencephalitis:5 (5.1)		
MTS lateralization	Left: 54 (56.2)	–	–
	Right: 26 (27.5)		
	Bilateral: 15 (16.3)		

AED: antiepileptic drug; IPI: initial precipitant injury; MTS: mesial temporal sclerosis; PD: psychiatric disorder; SD: standard deviation.
[*] $p < 0.05$.