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Clinical Research

Interictal dysphoric disorder in patients with localization-related epilepsy: Diagnostic relationships with DSM-IV psychiatric disorders and the impact of psychosocial burden

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ABSTRACT

Background: Some patients with epilepsy develop intermittent and pleomorphic affective–somatoform symptoms, termed interictal dysphoric disorder (IDD). Other psychiatric disorders have been extensively investigated in patients with epilepsy, but there are few clinical studies investigating the comorbidity patterns of IDD and common psychiatric disorders (PDs). In particular, the impact of IDD on the psychosocial burden of patients remains unclear.

Methods: The participants were 128 adult Japanese outpatients with localization-related epilepsy (LRE). In order to determine the comorbidity patterns for IDD and PDs, we conducted a comprehensive diagnostic investigation for IDD and DSM-IV psychiatric disorders. Based on these analyses, participants were divided into groups according to the comorbidity patterns for IDD and PDs in order to compare both suicide risk and quality of life (QOL).

Results: The findings indicated that 19.5% of participants had IDD, and 55.5% had PDs. Younger age at epilepsy onset and refractory complex partial seizures were associated with IDD, but the duration and type of epilepsy were not. Patients with IDD were more likely to have comorbid PDs as follows: mood disorders (odds ratio, OR: 8.30; 95% confidence interval, CI: 3.15–21.83), anxiety disorders (OR: 8.81; 95% CI: 3.30–23.49), and psychotic disorders (OR: 7.72; 95% CI: 2.83–21.06). Group comparisons demonstrated that there were no patients with IDD but without PD. Furthermore, patients with IDD and with PDs had a significantly higher suicide risk and lower QOL compared to the other groups, even after adjusting for the influences of confounding factors.

Conclusion: Interictal dysphoric disorder adds extreme psychosocial burden and is associated with multiple PDs in patients with LRE. The present study suggests that IDD has a specific prognostic significance. However, whether IDD is nosologically independent from conditions diagnosed using standardized psychiatric diagnostic systems such as DSM-IV must be further assessed by future research.

1. Introduction

Epilepsy often occurs in comorbidity with psychiatric disorders (PDs) which may contribute to increased suicide risk and decreased quality of life (QOL) for patients with epilepsy. Community-based studies of adult patients with epilepsy have revealed PD prevalence rates ranging from 5.9 to 55.5%. Depressive disorders are 2.0- to 2.9-fold more prevalent in patients with epilepsy, anxiety disorders are 1.9- to 15-fold more prevalent, and psychotic disorders are 2-fold more prevalent [1,2]. Furthermore, mood disorders and anxiety disorders are independently associated with adverse effects on health-related QOL in patients with epilepsy [3,4]. Depression and adverse events associated with antiepileptic drugs (AEDs) are the strongest predictors of QOL for patients with epilepsy [5,6].

However, patients with epilepsy who present with atypical psychiatric symptoms often fail to meet the established psychiatric diagnostic categories listed in Diagnostic and Statistical Manual of Mental Disorders — 4th Edition (DSM-IV). Kraepelin [7] found that periodic interictal dysphoric episodes represented the most common form of all psychiatric changes associated with epilepsy and introduced the concept of periodische Verstimmung (periodic dysphorias) in the early 1920s. Although the dysphoric episodes are clearly characterized by depressive mood, irritability, pain, anxiety, insomnia, and euphoric mood, whether this group of intermittent pleomorphic symptoms (IPS) has specific clinical and prognostic features is the topic of ongoing debate.

In 1995, Blumer et al. [8] redefined Kraepelin's periodic dysphorias as “interictal dysphoric disorder” (IDD), adding anergia and fear to the original 6 IPS symptoms. The 8 key symptoms were grouped into 3 categories: labile depressive symptoms (anergia, depressive mood, insomnia, and pain), labile affective symptoms (anxiety and fear), and specific symptoms (euphoric moods and paroxysmal irritability). Blumer et al. [9] stated that IDD occurred without external triggers

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and without clouding of consciousness, beginning and ending rapidly and recurring regularly and uniformly (every few days to every few months and lasting a few hours up to 2 days). Blumer et al. [9] concurrently developed the Seizure Questionnaire (SQ), a self-report questionnaire used to assess the 8 affective–somatoform symptoms.

Mula et al. [10] later developed the Interictal Dysphoric Disorder Inventory (IDDI), a 38-item self-report questionnaire for evaluating the frequency, severity, global impairment, and time course of the disorder associated with seizures. Using the IDDI, they suggested diagnostic criteria for IDD; of the 8 key symptoms, 3 or more symptoms of at least moderate severity and distress are required for diagnosis. Studies using SQ or IDDI have reported the prevalence rate of IDD as 9–34% in patients with epilepsy and as 18% in patients with refractory localization-related epilepsy [8,10–13].

Our clinical observations suggest that some patients with epilepsy present with clinically specific IPS meeting criteria for IDD. However, the clinical significance of IDD in patients with epilepsy must be elucidated. First, it is unknown whether IDD influences the severity and patterns of comorbid PDs in patients with epilepsy. Previous reports have ranged from IPS presenting with subthreshold symptoms [14,15] to IDD presenting with mood and anxiety disorders [9,16]. Second, it is unknown whether IDD contributes to the psychosocial burden of patients with epilepsy. In order to determine the comorbidity patterns of IDD and PDs in adult patients with localization-related epilepsy, a comprehensive diagnostic investigation for interictal psychopathology was performed. In order to evaluate the impact of IDD on psychosocial functioning, suicide risk and QOL were compared between patients with different comorbidity patterns for IDD and PDs.

2. Material and methods

One hundred and twenty-eight Japanese patients with epilepsy were consecutively recruited from our clinic between December 2010 and December 2014. The inclusion criteria were the following: (1) diagnosis of localization-related epilepsy according to International League Against Epilepsy (ILAE) criteria; (2) age of at least 18 years; and (3) a Mini-Mental State Examination (MMSE) [17] score of greater than 20. The exclusion criteria were the following: (1) clinical diagnosis of dementia, (2) current pregnancy, and (3) severe intellectual disabilities. All participants gave written informed consent, and the study was approved by the ethics committee of National Defense Medical College.

2.1. Interview and assessment

Sociodemographic and clinical information was collected, including age at assessment, gender, education level, employment status, marital status, number of people living together, past history of febrile seizures, family history of epilepsy, and family history of psychiatric disorders. Epilepsy-related information was also collected, including age at epilepsy onset, seizure control during the last 12 months, seizure types and frequency during the last 3 months, and medication history. Characterizations of the epilepsy type and localization, as well as lateralization of the epileptic focus, were based on clinical seizure semiology, video-electroencephalography (EEG) data, and brain magnetic resonance imaging (MRI). Remission was defined as the absence of all types of seizures for 12 months.

Mini-Mental State Examination, the 17-item Hamilton Depression Rating Scale (HAMD) [18], and the Adverse Events Profile (AEP) [19] were administered in order to assess general cognitive function, severity of depressive symptoms, and subjective perceived adverse effects of AEDs, respectively.

Interictal dysphoric disorder diagnoses occurred according to the Japanese version of the IDDI, which is based on Blumer's criteria subsequently reelaborated by Mula, if at least 3 of the 8 key symptoms were at least moderate or severe in magnitude and were also producing moderate to severe distress for the patient. Periictal dysphoric symptoms were excluded from IDD diagnosis. The internal consistency of the Japanese version of the IDDI was assessed using Cronbach's alpha coefficient.

Diagnoses of interictal PDs were made according to the Japanese version of the Mini-International Neuropsychiatric Interview (MINI) [20]. This is a short, structured diagnostic interview for current DSM-IV psychiatric disorders including major depressive disorder, bipolar I/II disorder, dysthymic disorder, panic disorder with or without agoraphobia, social anxiety disorder, obsessive–compulsive disorder, posttraumatic stress disorder, generalized anxiety disorder, psychotic disorder, alcohol abuse/dependence, drug abuse/dependence, anorexia nervosa, bulimia nervosa, and antisocial personality disorder. It also provides lifetime DSM-IV psychiatric disorders including major depressive disorder, bipolar I/II disorder, panic disorder, and psychotic disorder. The Japanese version of the MINI has been validated previously [21].

The severity of current suicide risk was determined using the total score of the MINI suicidality module (MINI-SM). This module is comprised of 6 items with varied weighting: recent suicidal thoughts (score: 1), self-harm ideation (2), suicidal ideation (6), suicide planning (10), suicide attempt (10), and previous suicide attempt (4). According to the broadest definition, suicidality was defined as nonzero MINI scores. Although suicide risk is often classified as no (0), low (1–5), moderate (6–9), or high (≥10), we used the total score of this module as an ordinal variable in order to more precisely assess the severity of suicide risk.

Health-related QOL (HRQOL) measures were obtained using the Japanese version of the World Health Organization QOL Questionnaire—26 (WHOQOL-26) [22]. The Japanese version of the WHOQOL-26 has previously been validated [23]. The WHOQOL-26 consists of 26 items classified into 5 domains: physical, psychological, social relationship, environment, and general QOL. Each item is rated on a 5-point Likert scale, and the overall score is calculated as the mean of 26 question scores.

2.2. Statistical analyses

In order to identify the clinical factors associated with IDD, demographic and clinical differences between the patients with or without IDD were first tested using χ^2 and Fisher's exact tests for categorical variables and by Student's t tests for continuous variables.

In order to clarify the impact of IDD on QOL and suicide risk, participants were then divided into 4 groups (IDD with or without PDs, PDs without IDD, and no psychopathology). The total score of the MINI-SM and overall WHOQOL-26 scores were compared between groups using Kruskal–Wallis test with Steel–Dwass post-hoc test and one-way analysis of variance (ANOVA) with Scheffe's post-hoc tests, respectively.

Then, univariate and multivariate logistic regression analysis was conducted to ascertain which variables significantly predicted suicidality.

Lastly, in order to eliminate the effects of confounding factors, we performed analysis of covariance (ANCOVA), with clinically relevant variables affecting QOL as covariates.

3. Results

The participants were 128 patients with epilepsy (69 women, 59 men) between 18 and 85 years of age (mean = 42.6 ± 14.2 years, median = 40) and with seizures occurring over a period of time ranging from 2 to 74 years (mean = 22.9 ± 12.4 years, median = 24). Seventy-six (59.3%) patients had temporal lobe epilepsy, 34 (26.6%) had frontal lobe epilepsy, and 18 (14.1%) had other types of localization-related epilepsy. Thirty-three (34.7%) patients had a history of febrile seizures. The mean number of AEDs used was 2.0 ± 1.0. Sixty-five (50.8%) patients achieved a remission period of 12 months or more while the remaining 63 patients (49.2%) had refractory seizures. Seizure types were as follows: 15 (11.7%) had simple partial seizures (SPS); 35 (27.3%) had complex partial seizures (CPS); and 10 (7.8%) had secondarily