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Subtypes of interictal depressive disorders according to ICD-10 in patients with epilepsy

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ABSTRACT

Background and purpose: The purpose of the study was to evaluate the frequency of interictal depressive symptoms and different subtypes of depressive disorders according to 10th revision of the International Classification of Diseases (ICD-10) criteria in patients with epilepsy and its association with the type of epilepsy.

Material and methods: 289 outpatients with epilepsy (169 females, 120 males) aged 18–82 years completed Beck Depression Inventory (BDI). Subjects who scored >11 in BDI were further evaluated by the psychiatrist according to the ICD-10 diagnostic criteria.

Results: 41.9% (121) of the 289 participants scored >11 in BDI. 104 (85.9%) patients who scored >11 in BDI had comorbid mental disorders according to ICD-10 criteria. The most common were organic mood disorders (F06.3 – 31.4%), depressive episode (F32 – 22.3%) and dysthymia (F34.1 – 9.1%) There were no differences in the prevalence of depression and subtypes of depression in patients with certain epilepsy types. Depression was diagnosed before entering the study in only one third of patients with final diagnosis of depression.

Conclusions: Our results confirm the prevailing view that interictal depression is common in epilepsy patients. Depression remains underrecognized and undertreated in patients with epilepsy.

1. Introduction

Depression is one of the most frequent psychiatric disorders in epileptic patients [1–4]. The relationship between depression and epilepsy has been extensively studied in recent decades. A large body of research indicates that there is the increased risk of patients with epilepsy of developing depression compared with healthy controls. The prevalence of interictal depressive disorder in epileptic patients has been shown to range between 9% and 62% [1,5], depending on the sample population and the methods of assessment, and is higher than in a matched population of normal controls. The psychiatric comorbidities in people with epilepsy have important clinical

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and therapeutic implications. There is much evidence that the presence of depression in patients with epilepsy exerts a stronger impact over quality of life than other clinical variables, including types and frequency of seizures [6]. Proper diagnosis and treatment of depression in epilepsy are important issues in the modern treatment of epilepsy. However, in many cases depression remains unrecognized or untreated in both children [7] and adults with epilepsy [3,8,9].

Patients with epilepsy can demonstrate classic symptoms of a depressive disorder that meet the criteria for a DSM V (Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition) or ICD-10 (10th revision of the International Classification of Diseases) diagnosis of depression or dysthymia. A large proportion of interictal depression, however, does not present in this manner and fails to meet criteria of any of the DSM-III (Diagnostic and Statistical Manual of Mental Disorders, Third Edition), DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition), DSM V or ICD-10 affective disorders [10,11]. Interictal depression in epileptic patients frequently presents as a pleomorphic cluster of symptoms of depression with an intermittent, chronic course. Differences of the clinical manifestations of certain types of depression between patients with epilepsy and nonepileptic patients may be a cause of the underrecognition of depression in patients with epilepsy. The development of new, improved criteria of depression in ICD-11 (including organic mood disorders) is actively ongoing [12]. In most studies evaluating patients with epilepsy the prevalence of depression is assessed by means of structured or semi-structured interviews administered by trained investigators and not after clinical interview with the qualified psychiatrist. Due to a pleomorphic pattern of depressive symptoms diagnosis should be set by a psychiatrist familiar with complex psychopathology of patients with epilepsy.

The aim of our study was to assess the occurrence of depressive symptoms and further evaluate different subtypes of depressive disorders according to ICD-10 criteria in patients with epilepsy and interictal depressive symptoms. The additional aim was to find an association between depressive profile and the type of epilepsy.

2. Material and methods

2.1. Study participants

Patients consecutively selected from the outpatient epilepsy clinic, Department of Neurology of University Hospital in Cracow between September 2009 and August 2010, entered this study after giving informed consent. All patients underwent previously a detailed clinical and laboratory investigation, including electroencephalography or video-electroencephalography (video-eeg) and high-resolution brain magnetic resonance imaging (MRI) (or computed tomography if MRI was contraindicated), so as to categorize their epilepsy syndrome according to the 1989 International League Against Epilepsy classification [13]. Characterization of epilepsy and seizure type relied on the assessment of the video-eeg data. If the video-eeg was normal, subjects with a clinical diagnosis of simple or complex partial seizures were considered to have focal epilepsy, whereas those with only generalized events were considered to have an unknown epilepsy type. Inclusion criteria were age older than 18 years, established epilepsy for >1 year and signed informed consent. Study exclusion criteria were as follows: (1) history of psychogenic non-epileptic seizures, (2) history of drug or alcohol abuse, (3) clinical seizure in the previous 72 h, as in most cases ictal and post-ictal depressive symptoms ameliorate within 2–3 days [14], (4) changes in antiepileptic drugs (AEDs) regimen during the preceding month, (5) serious chronic medical or neurological illnesses, (6) a Mini-Mental State Examination (MMSE) <24, (7) moderate or severe mental retardation (IQ < 50). Thereby, all patients with significant cognitive dysfunction were excluded from the study and patients who entered the study had the cognitive capacity to give informed consent and complete study questionnaires.

Demographic and clinical data were collected by interviews and from information in patients' medical files. Information including sex, age, marital status, education, occupation, comorbidities, medication history, family history of epilepsy and/or depression, epilepsy onset age, type of epilepsy, seizure types and frequency, AEDs treatment, past history of psychiatric illness or treatment was recorded by means of the questionnaire, created for that purpose. Previous diagnosis of depression was coded as present if documented in the clinical record or if the patient was currently taking antidepressant medication.

2.2. Protocol

All subjects were administered Beck Depression Inventory, 21 item version (BDI-II), a widely used and well validated 21-item self-report inventory of depressive symptoms. BDI-II has been recently tested in 205 patients with epilepsy from five epilepsy centers and was found to have a high sensitivity and specificity as a screening instrument of major depressive episode. Total score >11 is suggestive of depressive disorders according to the study of Jones and coworkers [15].

Patients who scored >11 in Beck Depression Inventory were referred to a psychiatrist to confirm a diagnosis of depression. All patients with previous diagnosis of depression or taking antidepressant medication were also referred to a psychiatrist. Psychiatric diagnoses were made in accordance with ICD-10 [16] after clinical interviews with the qualified psychiatrists from our team (D.D and M.S). All procedures were approved by an institutional bioethical board.

2.3. Statistical analysis

The statistical analyses were performed using SPSS for Windows v. 14. The Student's *t*-test was used for continuous variables. The χ^2 test and Fisher exact test was used for dichotomous and other categorical variables. $p < 0.05$ was considered as significant. Continuous data are presented as mean ± standard deviation (SD) while non-continuous variables are given as percentages.

3. Results

301 patients attending the outpatient epilepsy clinic of the University Hospital in Cracow met inclusion criteria and

Table 1 – Cohort characteristics (289 patients).

Average age (years)	35.7 (±14.9)
Male, *n* (%)	120 (41.52%)
Single	163 (56.40%)
Unemployed	178 (61.59%)
Average age at epilepsy onset	20.86 (±15.24)
Duration of epilepsy (years)	14.67 (±11.37)
Type of epilepsy	
Idiopathic generalized	63 (21.80%)
Focal	189 (65.40%)
Unknown epilepsy type	37 (12.80%)
Seizure frequency	
>1/week	58 (20.07%)
<1/week, >1/month	49 (16.96%)
<1/month, >1/year	92 (31.83%)
<1/year	90 (31.14%)
Epilepsy therapy	
Monotherapy	161 (55.71%)
Polytherapy	128 (44.29%)

entered this study after giving informed consent. 132 patients who scored >11 in Beck Depression Inventory were referred to a psychiatrist to confirm a diagnosis of depression. 11 patients, who scored >11 in BDI-II withdrew their consent for psychiatric assessment, so they were excluded from further analysis. 31 patients had previous diagnosis of depression, they were currently treated with antidepressants, mostly with selective serotonin re-uptake inhibitors (SSRIs). All of them scored >11 in BDI-II. In total 121 patients underwent psychiatric assessment. Final cohort consisted of 289 patients (169 females, 120 males) ranging between 18 and 82 years of age (mean = 35.7 ± 14.9), most patients had focal seizures (65.4%). Seizure frequency was lower than one per year in only 90 patients (31.14%); the remaining patients had higher seizure frequency. Most patients (55.71%) were on one antiepileptic drug. The most commonly used AEDs were valproate, levetiracetam, carbamazepine, lamotrigin, topiramate and oxcarbazepine. The mean BDI-II score in the whole cohort was 11.53 (±9.68). Table 1 lists the subject demographic and seizure data, and Table 2 detailed information on epilepsy treatment.

Table 2 – Epilepsy therapy.

Monotherapy	161 (55.71%)
Polytherapy	128 (44.29%)
Specific anticonvulsant use	
Valproate	171 (59.17%)
Levetiracetam	70 (24.22%)
Carbamazepine	62 (21.46%)
Lamotrigin	39 (13.43%)
Topiramate	38 (13.15%)
Oxcarbazepine	36 (12.46%)
Gabapentin	14 (4.84%)
Phenonobarbital	10 (3.46%)
Clonazepam	9 (3.11%)
Phenytoin	8 (2.77%)
Primidon	6 (2.08%)
Vigabatrin	2 (0.69%)
Tiagabine	2 (0.69%)
Ethosuximide	2 (0.69%)
Clobazam	1 (0.35%)

Table 3 – Prevalence data of current ICD-10 psychiatric disorders in patients with depressive symptoms according to BDI-II.

ICD diagnosis	Number (%) 121 (100)
Organic mood [affective] disorders (F06.3)	38 (31.4)
Organic emotionally labile [asthenic] disorder (F06.6)	1 (0.8)
Unspecified organic personality and behavioral disorder due to brain disease, damage and dysfunction (F07.9)	2 (1.7)
Persistent delusional disorders (F22)	1 (0.8)
Depressive episode (F32)	27 (22.3)
Mild depressive episode (F32.0)	14
Moderate depressive episode (F32.1)	13
Dysthymia (F34.1)	11 (9.1)
Recurrent depressive disorder (F33)	8 (6.7)
Recurrent depressive disorder, current episode mild (F33.0)	7
Recurrent depressive disorder, current episode moderate (F33.1)	1
Other mood [affective] disorders (F38)	1 (0.8)
Phobic anxiety disorders (F.40)	1 (0.8)
Mixed anxiety and depressive disorder (F41.2)	1 (0.8)
Adjustment disorders (F43.2)	9 (7.4)
Hypochondriacal disorder (F45.2)	1(0.8)
Neurotic disorder, unspecified (F48.9)	3 (2.5)
No psychiatric disorder	17 (14.1)

104 (85.9%) patients who scored >11 in BDI-II had comorbid mental disorders diagnosed during psychiatric interview, according to ICD-10 criteria, whereas 17 (14.1%) patients did not have any current ICD-10 diagnosis. The most common were organic mood disorders (38 patients, 31.4%), depressive episode (27 patients, 22.3%) and dysthymia (11 patients, 9.1%) (Table 3). Among patients with depressive episode 14 suffered from mild depression, 13 from moderate depression. In almost all patients (7/8) with recurrent depressive disorder, current episode was mild. In 31 patients with previous diagnosis of depression, diagnosis was confirmed in 23 patients (organic mood disorders in 11, depressive episode in 9, recurrent depressive disorder in 3). Of the remaining 8 patients, 4 had no psychiatric disorder; unspecified organic personality and behavioral disorder due to brain disease, damage and dysfunction were diagnosed in 2 patients, persistent delusional disorders in 1 and adjustment disorders in 1.

Depression (F32, F33 and F06.3) was diagnosed in 73 patients (60.3% of patients with BDI-II >11; 25.3% of the final cohort). The mean BDI-II score in patients with depression was 20.20 (±6.94) and was significantly higher than in the whole cohort ($p < 0.05$). Table 4 presents types of depression in patients with different epilepsy syndromes. There were no differences in the prevalence of depression ($p = 0.141$) and subtypes of depression in patients with certain epilepsy types ($p = 0.188$).

10.4% patients (30 out of 289) had recent suicidal thoughts. These patients marked the answers 1 (''I have thoughts of killing myself, but I would not carry them out'' – 29 patients) or 2 (''I would like to kill myself'' – 1 patients) in question 9 of the BDI. All patients with recent suicidal ideation scored >11 in BDI, the mean BDI score was 26 (±7.82).

Table 4 – Subtypes of depression in epilepsy syndromes.

Diagnosis	Idiopathic generalized epilepsy	Focal epilepsy	Unknown epilepsy type
Organic mood [affective] disorders (F06.3)	5 (45.4%)	29 (53.7%)	4 (50.0%)
Depressive episode (F32)	4 (36.4%)	20 (37.1%)	3 (37.5%)
Recurrent depressive disorder (F33)	2 (18.2%)	5 (9.2%)	1 (12.5%)

χ^2: $p = 0.244$.

All patients with newly diagnosed depressive disorder were started on antidepressant drugs (SSRIs and SNRIs), in 3 patients additional psychotherapy was instituted (Table 5).

4. Discussion

In the present study of 289 epilepsy patients, 41.9% (121) of the participants had abnormal BDI-II scores (>11), suggestive of depressive disorders [15]. In comparison the mean BDI score in a group of healthy men in Poland was 7.8. [17]. However, depressive episode or recurrent depressive disorder was diagnosed in 73 (60.3%) patients which constitutes 25.3% of the whole cohort. The percentage is comparable to studies assessing sample of patients with partial and generalized epilepsy [18,19].

There were no statistically significant differences between patients with different epilepsy types with respect to the number of patients diagnosed with depression and separate subtypes of depression. Previous studies found an increased risk of depression in focal epilepsy, especially in temporal lobe epilepsy when compared with other types of epilepsy [20,21]. However, most studies evaluating patients with mixed epilepsy types did not find significant differences in the prevalence of depression between patients with focal and primarily generalized epilepsy [18,19,22,23]. Depression was properly diagnosed and treated before entering the study in only 23 (31.5%) patients with final diagnosis of depression, what is consistent with results of previous studies [9,10]. One of the reasons for the lack of detection of depression in patients with epilepsy appears to be the time pressure. The use of psychometric tools that are self-administered, like BDI-II, can help to resolve this problem. However, these devices do not diagnose the presence of a depression but identify symptoms that can be later categorized using DSM-V or ICD-10 criteria. Yet, the process of diagnosis of depression cannot be restricted to the completion of a rating scale. Self-report methods as BDI have been designed for populations other than patients with acquired brain damage, so their diagnostic value in patients with epilepsy may be limited [24].

Table 5 – Treatment instituted in patients with newly diagnosed depressive disorder.

Treatment	Number
Pharmacotherapy	50
Citalopram	25
Escitalopram	11
Fluoxetine	2
Sertraline	4
Paroxetine	4
Venlafaxine	4
Psychotherapy	3

Patients with "high" scores should be subjected to a more extensive and detailed evaluation. A definite diagnosis of depressive disorder in epileptic patients can be a challenge because a number of symptoms, which are recognized as diagnostic criteria for a depressive episode by the ICD-10 and DSM-V, may occur in temporal relation to seizures or secondary to AED toxicity. Secondly, it is also established that up to 70% of mood disorders identified in patients with epilepsy present with atypical clinical characteristics that do not meet any of the DSM Axis I categories [10]. Self-rating scales, such as BDI-II, are useful to identify the presence of depressive symptoms and quantify their severity. This type of assessment must be followed by a referral for a complete psychiatric interview to set the final diagnosis, regarding multifactorial contributors to psychiatric disturbances, including effects of the underlying central nervous system disorder, relation to seizures, medication effects and psychosocial influences. Other scales or inventories such as Hamilton Depression Rating Scale or Symptom Checklist-27-plus Questionnaire may be also useful [25]. Additional finding of our study is high rate of suicidal ideation (10.4%) in patients with epilepsy. This confirms recent results from Hecimovic et al. [25] and Jones et al. [26]. The rate of current suicidal thoughts was approximately 12% in both studied cohorts.

There are several limitations to our study. First, not all individual were referred to the psychiatrist. The possibility remains that some patients, who scored <11 in BDI-II, suffered from mild forms of depressive disorder. Second, a selection bias toward patients with pharmacoresistant epilepsy in our outpatient clinic may not be negligible. Third, a lack of control groups, such as patients with other chronic neurological disorders, or healthy control subjects, should be noted.

In conclusion, all subtypes of depressive disorders are common in patients with epilepsy. While depression is properly diagnosed only in one third of patients with epilepsy it is crucial to recognize and treat these conditions.

Conflict of interest

None declared.

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Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical

Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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