Epilepsy & Behavior 53 (2015) 15–19

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

# Reevaluating the prevalence and diagnostic subtypes of depressive disorders in epilepsy

Mariusz S. Wiglusz [a,*], Jerzy Landowski [a], Lidia Michalak [b], Wiesław J. Cubała [a]

[a] Department of Psychiatry, Medical University of Gdańsk, Poland
[b] Regional Epilepsy Outpatient Unit, Copernicus Hospital, Gdańsk, Poland

ARTICLE INFO

*Article history:*
Received 15 July 2015
Revised 20 September 2015
Accepted 21 September 2015
Available online 26 October 2015

*Keywords:*
Major depressive disorder
Epilepsy
Depressive disorders
DSM-IV-TR
SCID-I
Epidemiology

ABSTRACT

*Objective:* Depressive disorders are common among patients with epilepsy (PWE). The aim of this study was to estimate the prevalence of different forms of depressive disorders among PWE treated in the outpatient setting.
*Methods:* A group of consecutive PWE that visited the epilepsy outpatient clinic was invited to participate in the study. Ninety-six patients met inclusion criteria and were examined by a trained psychiatrist using standardized measures.
*Results:* A diagnosis of a current major depression was established in 21 (22.3%) out of 96 participants. Furthermore, almost 20% of the study group fulfilled criteria for mood disorder categories other than MDD, adding up to over 40% of PWE suffering from any mood disorder category. Older age and later age at seizure onset, as well as unemployment, were associated with an increase in the odds of MDD diagnosis.
*Study limitations:* A number of limitations are to be considered: the sample size is relatively small, and the findings may not be representative of PWE in general because our population represents a sample coming from a single outpatient clinic with a higher ratio of drug-resistant epilepsy.
*Conclusions:* Major depression as well as other forms of depressive disorders are common among PWE. Unemployment, age, and age at seizure onset are important factors associated with major depression among PWE.


## 1. Introduction

Depression is the most frequently reported psychiatric comorbidity in patients with epilepsy (PWE) with point prevalence ranging from 11% to 62% [1–3].

The diverse methodologies across the studies substantially contributes to the variation in epidemiological data [4] with a limited number of studies using a standardized structured psychiatric interview to produce a diagnosis. Also, various factors associated with epilepsy including type of epilepsy, course of illness, frequency and severity of seizures, and antiepileptic drugs' (AEDs) side effects could affect the accuracy of psychiatric diagnosis. Moreover, there is also variability in sample size population, study population (inpatients, outpatients, surgical patients, etc.), and often lack of control groups [4]. Furthermore, the symptomatology of mood disorders in epilepsy is often atypical, intermittent, and pleomorphic and fails to meet DSM-IV-TR diagnostic categories. Additionally, there are different subtypes of depressive disorders as defined in Appendix B of DSM-IV-TR (for further study) with limited data on their prevalence in PWE.

Also, data on the prevalence of depression among PWE in a Polish population are limited with the sole systematic study conducted by Grabowska-Grzyb et al. [5], who investigated the prevalence and association of depression with various demographic and seizure-related variables in PWE.

To address these factors, we designed a study in a defined cohort of consecutive PWE from a tertiary reference outpatient epilepsy clinic to assess the prevalence of comorbid depressive disorders. It was hypothesized that the point prevalence of major depressive disorder (MDD) together with other forms of depressive disorders systematically assessed with a structured clinical interview for DSM-IV-TR would be higher in PWE as related to previously reported data.

## 2. Methods

### 2.1. Study population

Over a 1-year period, a consecutive series of 118 PWE were screened for study participation, with 96 patients enrolled meeting all inclusion/exclusion criteria. The patients were referred to a regional epilepsy outpatient unit (the only one in the area) by neurologists and general practitioners of Gdańsk province (population of 2,298,811) to receive a second opinion regarding the diagnosis and/or treatment, being the standard procedure in Poland. The population of PWE was

* Corresponding author at: Department of Psychiatry, Medical University of Gdańsk, Dębinki 7 St. Build. 25, 80-952 Gdańsk, Poland. Tel.: +48 58 349 26 50; fax: +48 58 349 27 48.
*E-mail address:* mwiglusz@gumed.edu.pl (M.S. Wiglusz).

http://dx.doi.org/10.1016/j.yebeh.2015.09.029
1525-5050/

representative of the surrounding area because of the regional, hierarchical organization of health care in Poland.

All individuals underwent a complete neurological examination on selection. Inclusion criteria were as follows: (1) confirmed diagnosis of active epilepsy according to the International League Against Epilepsy criteria [6] by a trained epileptologist; (2) ages 18–65 years; (3) stable antiepileptic treatment in the last 2 months; and (4) willingness to provide a written informed consent to undergo the experimental procedures. Exclusion criteria included (1) neurologic somatic-related factors — last seizure within 24 h prior to examination; more than 10 seizures in the last month; major brain damage with mass effect; neurosurgical treatment of epilepsy; unstable somatic disease or serious neurological disorder; and nonepileptic seizures and (2) psychiatry related factors — mental retardation; dependence or abuse of alcohol and/or other drugs in the past 6 months; and diagnosis of borderline, antisocial, or schizotypal personality disorder. The study protocol was approved by the local bioethics committee at the Medical University of Gdańsk. All patients provided a written informed consent for participation in the study.

### 2.2. Evaluation

All subjects were assessed at the same visit by the same psychiatrist (MSW). Psychiatric diagnosis was based on the Structured Clinical Interview (SICD-I) for DSM-IV-TR [7]. The SCID-I is an internationally validated, structured interview that has been used extensively as a diagnostic tool for DSM-IV-TR psychiatric disorders. The reliability and validity of this instrument have been well established [7]. Hamilton Depression Scale (HAMD-17) was used to measure the severity of depressive symptoms [8,9]. The same trained investigator (MSW) administered SCID-I and HAMD-17 to all of the patients. All participants also completed the Beck Depression Inventory (BDI) [10]. The structured interview was used to obtain information on the disease history and sociodemographic status of patients including gender, age, economic situation, martial status, age at seizure onset, duration of epilepsy, seizure frequency, seizure type, experience of auras and duration of treatment, existence of lesions, and psychiatric history. Results of CT/MRI, EEG, and laboratory tests were available for the majority of subjects. Data were corroborated by referral source records obtained from the epileptologist.

### 2.3. Statistics

Statistical procedures were performed using Statistica 10.0.1011. Frequencies and descriptive statistics were analyzed for each variable. Comparisons between patients with current MDD and patients without MDD were made using Student's t-tests for normally distributed continuous data, Mann–Whitney's U-test for nonnormally distributed data, and Fisher's exact test for categorical data. To explore the influence of factors on the occurrence of depression, we used the logistic regression model in variables that differed significantly on the univariate analysis. A value of $p < 0.05$ was considered to be statistically significant.

## 3. Results

The prevalence of mood disorders in the study group is presented in Table 1. Twenty-one (22%) PWE met criteria for major depressive disorder (MDD). Dysthymic disorder was found in 7 patients, among which 4 patients had cooccurrence of MDD ('double depression'). Globally, 21 patients with MDD and 19 patients with other forms of depressive disorder were identified, producing a total number of 40 patients with any depressive disorder.

In the subgroup with current MDD, the severity of depressive symptoms with HAMD-17 was mild in 5 patients, moderate in 6 patients, severe in 5 patients, and most severe in 5 patients. The subgroup with other depressive disorders (n = 19) was characterized in the majority by mild severity of symptoms (n = 11). Only in one case was moderate severity of depression observed.

**Table 1**
Prevalence of mood disorders in the group of patients with epilepsy (n = 96).

| DSM-IV-TR diagnosis | N (%) |
|---|---|
| Major depressive disorder (MDD)[a] | 21 (22) |
| Single episode | 17 (4) |
| Dysthymic disorder[a] | 7 (7) |
| Depressive disorder NOI | 16 (17) |
| Brief recurrent depressive disorder | 5 (5) |
| Minor depressive disorder | 5 (5) |
| "Mixed" episode[b] | 4 (4) |
| Others | 2 (2) |
| Any depressive disorders | 40 (42) |

[a] 4 cases 'double depression'.
[b] Present symptoms of depression and mania but not fulfilled DSM-IV-TR mixed episode criteria.

Table 2 summarizes the AEDs used and their corresponding psychotropic effects on depression as reported in the literature [11–13]. The most used AED in the study group was carbamazepine (34.2%), followed by sodium valproate (21%), lamotrigine (15.7%), and topiramate (8.5%).

The subgroup with MDD with major depressive disorder and the subgroup without MDD were compared with respect to sex, age, education, family, and social economic and epilepsy-related factors. Drug-resistant epilepsy, defined as two consecutive failures of properly selected, applied and tolerated AEDs, in monotherapy or polytherapy [14], was found in 73% of all patients. Detailed results are summarized in Table 3.

Regarding the sociodemographic characteristics, the patients with MDD were more likely to be unemployed ($p = 0.009$, Fisher's exact test) and older ($p = 0.0008$, Student's t-test). Regarding the epilepsy-related characteristics, the patients with MDD had later seizure onset ($p = 0.0002$, Student's t-test).

These variables were entered into the multivariate logistic regression model (Table 4). The full model significantly predicted MDD ($\chi^2 = 21.189$, df = 3, $p < 0.0001$). Two factors were independently associated with the risk of MDD: unemployment (OR = 3.23, 95% CI = 1.14–9.17, $p = 0.028$) and age at seizure onset (OR = 1.07 for each year, 95% CI = 1.02–1.12, $p = 0.006$).

The demographic and clinical factors of the subgroup without any depressive disorders, the subgroup with MDD, and the subgroup with DD-NOS were compared post hoc (Table 5).

## 4. Discussion

In this consecutive cohort group, the prevalence for any depressive disorder was 42% with the current incidence of MDD observed in 22% of patients and dysthymic disorder in 7% of the subjects. The obtained results correspond with other studies with similar methodology. The point prevalence of major depression ranges from 17% to 28%. In a recent study of a consecutive group of 97 PWE, a MINI-based diagnosis

**Table 2**
Antiepileptic agents used in the study group and their correspondent psychotropic effects regarding depression.

| Antiepileptic drug | Number | Percentage | Psychotropic effect |
|---|---|---|---|
| Carbamazepine | 52 | 34.2% | Neutral |
| Valproic acid | 32 | 21% | Neutral |
| Lamotrigine | 24 | 15.7% | Positive |
| Topiramate | 13 | 8.5% | Negative |
| Oxycarbamazepine | 8 | 5.2% | Neutral |
| Tiagabine | 7 | 4.6% | Negative |
| Vigabatrin | 5 | 3.3% | Negative |
| Phenytoin | 3 | 2% | Neutral |
| Phenobarbital | 3 | 2% | Negative |
| Clonazepam | 3 | 2% | Negative |
| Gabapentin | 2 | 1.3% | Neutral |