Scientific Review
UDC 616.853-06: 616.891.6
DOI: 10.17816/pmj41261-67

SPECIFIC DYSPHORIC DISORDERS IN EPILEPSY

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СПЕЦИФИЧЕСКИЕ ДИСФОРИЧЕСКИЕ РАССТРОЙСТВА ПРИ ЭПИЛЕПСИИ

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To analyze affective-somatoform (dysphoric) disorders specific to epilepsy.
Dysphoric disorders can be divided into 3 groups: "periictal" disorders, interictal dysphoric disorder and alternative affective-somatoform syndromes. There are 3 groups of risk factors for affective disorders in epilepsy including depressive and dysphoric: those associated with the disease, those associated with the treatment and those associated with psychosocial aspects. Treatment for depression in epilepsy includes medication and psychotherapy. At the first stage of drug therapy, anticonvulsants are corrected, and at the second, an antidepressant is added. Cognitive behavioral therapy is the most effective method of psychotherapy.
Dysphoric disorders in epilepsy are presented by a wide range of conditions, both paroxysmal and non-paroxysmal, and have their own classification and development factors, which must be taken into account when choosing adequate therapy.
Keywords. Epilepsy, affective disorders, dysphoria, depression.

Осуществлен анализ данных, связанных с аффективно-соматоформными (дисфорическими) расстройствами, специфичных для эпилепсии.

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Дисфорические расстройства можно разделить на три группы: «периктальные» нарушения, интериктальное дисфорическое расстройство и альтернативные аффективно-соматоформные синдромы. Выделяют три группы факторов риска аффективных расстройств, в том числе депрессивных и дисфорических, при эпилепсии: связанные с болезнью, связанные с лечением и связанные с психосоциальными аспектами. Лечение депрессии при эпилепсии включает медикаментозную терапию и психотерапию. На первом этапе медикаментозной терапии проводится коррекция антиконвульсантов, а на втором – добавляется антидепрессант. Из методов психотерапии наиболее эффективна когнитивно-поведенческая терапия.

Дисфорические расстройства при эпилепсии представлены широким спектром состояний как пароксизмального, так и непароксизмального характера, имеют свою классификацию и факторы развития, что необходимо учитывать при выборе адекватной терапии.

Ключевые слова. Эпилепсия, аффективные расстройства, дисфория, депрессия.

The frequency of epileptic seizures and affective disorders is the most important factor in the deterioration of the quality of life of patients with epilepsy. According to a meta-analysis conducted in 2021, the overall prevalence of depression among people over 18 years of age with active epilepsy was 32 %. Moreover, the frequency of depression has doubled in recent years: 16 % in 2000–2005 versus 35 % in 2016–2020 [1]. The types of affective disorders associated with epilepsy are most fully represented in the classification proposed by the International League Against Epilepsy (ILAE) in 2007 [2]. There are affective-somatoform (dysphoric) disorders specific to epilepsy, which we will consider in detail below, and affective disorders comorbid with epilepsy (dysthymia, mild or major depression, etc.), that we will not go into.

It is necessary to recall that the term "dysphoria" (from the Greek *dysphoria* – "irritation", "annoyance") is an antonym of the word "euphoria" and is usually interpreted as a melancholy-angry mood. The founder of the nosological approach in psychiatry E. Kraepelin described periodic dysphorias called Verstimmungszustand as the most common mental disorders in epilepsy back in 1923 [3]. Dysphoria is diagnosed in the presence of at least three of four symptoms: internal tension, irritability, aggressive behavior and hostility [4].

Specific mood disorders in epilepsy are more conveniently classified based on their temporal relationship with epileptic seizures. Affective-somatoform (dysphoric) disorders specific to epilepsy can be divided into three groups: "periictal", i.e. located "around" the seizure, interictal dysphoric disorder and alternative affective-somatoform syndromes. The term "ictus" (from the Latin *ictus* – "blow") is a synonym for the word "seizure". "Periictal" and interictal dysphoric symptoms are similar to each other and differ only in the presence or absence of a relationship between dysphoria and seizures [5]. "Periictal" dysphoric disorders (DD), in turn, are divided into three subgroups: prodromal ("preictal") DD, DD as a manifestation of epileptic seizures and postictal DD.

Prodromal (preictal) DD is experienced by up to a third of patients with temporal lobe epilepsy, most often it occurs before secondary generalized seizures [6; 7]. Among the dysphoric symptoms, anxiety and irritability predominate, occurring several hours, less often – days before the onset of the sei-

zure [8]. After the epileptic seizure, these disorders usually disappear. Preictal depression is considered as a manifestation of subclinical epileptiform activity or is explained by the activation of biological mechanisms involved in the development of both pathological conditions: depression and seizure [9].

DD as a manifestation of epileptic seizures is represented by affective non-motor focal seizures. They most often occur in mesial temporal lobe epilepsy. For them, as for other types of seizures, three clinical signs are characteristic: suddenness (but provocateurs are possible), stereotypy (but polymorphism is possible) and short duration (but the development of postictal disorders or epileptic status is possible). Affective seizures can occur in the form of paroxysmal anxiety, panic-type fear, dysphoria, anger and rage, agitation with aggression; euphoria occurs less frequently.

Postictal DD occurs in the first 72 hours (three days) after an attack or series of attacks. It occurs in patients with poorly controlled focal seizures. Among the postictal symptoms, in addition to irritability and depressed mood, there are anxiety and neurovegetative symptoms and / or cognitive disorders, psychotic disorders occur less frequently. The origin of this type of depression is associated with inhibitory mechanisms involved in stopping the attack [9].

The second group of DD specific to epilepsy is interictal dysphoric disorder (IDD). The best-known test for early detection of IDD and its differentiation from periictal mental disorders is the Interictal Dysphoric Disorder Inventory (IDDI) proposed by M. Mula et al. [10]. It consists of 38 questions grouped into eight sections by the number of IDD symptoms. The eight main IDD symptoms are combined into three large groups: affective symptoms (anxiety, fear), depressive symptoms (depressed mood, anergia, pain, insomnia), and specific symptoms (paroxysmal irritability and, rarely, euphoria). To diagnose IDD, at least three symptoms out of eight of “moderate” or “severe” degree, causing “moderate” or “severe” distress are required [11]. It is important to note that this test is a screening test and does not replace a clinical examination.

To identify depression in patients over 18 years of age, neurologists have also proposed the “Neurological Questionnaire of Depressive Disorder in Epilepsy”, consisting of only six questions, the Russian version of which was validated by M. Zinchuk et al. in 2020 [12]. The assessment of patients' responses varies from 1 to 4 points. The optimal point for identifying a current depressive episode is more than 12 points.

To quantitatively assess the dynamics of depressive manifestations, the Hamilton Depression Rating Scale (HDRS/HRSD) is used [13]. Testing is performed by a clinician. 17 signs are an indicator of the severity of depression. Four additional signs carry information about auxiliary symptoms that may require special treatment.

IDD usually occurs two years or more after the onset of epilepsy. Episodes of dysphoria occur without external provocateurs, last from several hours to two days and recur at intervals from several days to months [14]. However, it should be clarified that some interictal disorders may be indistinguishable from periictal ones [14]. The very existence of IDD is still a subject of controversy [15], and some authors believe that IDD as a nosological diagnostic unit is questionable

[7; 16]. It is also important that the clinical manifestations of IDD are very similar to premenstrual dysphoric disorder, and in women with epilepsy this can be a source of errors [17]. IDD is considered a risk factor for sudden suicide attempts and interictal psychoses [9; 18]. Epileptic schizophrenia-like psychoses are a more severe form of IDD [7].

The third group of DDs specific to epilepsy are alternative affective-somatoform syndromes. Synonyms for this term are: the phenomenon of forced (violent) normalization of the EEG (Landolt syndrome), described by H. Landolt in 1953 [19], and "alternative psychosis" in patients with epilepsy [20]. The phenomenon of forced normalization of the EEG is the emergence of psychopathological disorders associated with the cessation of epileptic seizures, occurring in a patient with uncontrolled epilepsy when changing antiepileptic therapy after establishing control over seizures (remission for at least a week) and normalization of the EEG (a decrease in the number of spikes on the EEG by half) [21]. The nature of this phenomenon has not been fully clarified. The following hypotheses are considered for its origin: subcortical (deep) EEG discharges, changes in the balance of neurotransmitters or a decrease in the level of folic acid, a specific type of channelopathy, etc. Possible manifestations of Landolt syndrome are: anxiety, depression, dysphoria, ADHD in children; derealization, depersonalization and schizophrenia-like manifestations; twilight disorder of consciousness.

The causes of affective disorders, including depressive and dysphoric disorders, in epilepsy can be divided into three groups: those associated with the disease, those associated with the treatment and those associated with psychosocial aspects. Among the factors, associated with the disease, the localization of the epileptic focus is dominant. Depression often develops with a focus in the left temporal lobe [22], and postictal mania – with the involvement of the frontal lobe of the non-dominant hemisphere [23].

Factors, associated with the treatment, are divided into two subgroups: prescription of antiepileptic drugs (AEDs) with a "depressogenic" effect (phenobarbital, topiramate, vigabatrin, tiagabine) and/or discontinuation of mood-correcting AEDs (carbamazepine, lamotrigine, valproates) [9]. Mood disorders occur significantly more often in individuals with uncontrolled epileptic seizures with antiepileptic therapy [24].

Factors associated with psychosocial aspects include: rejection and poor adaptation to the diagnosis, unpredictability of the disease course; the need to change lifestyle, prohibition of driving, forced change of job; lack of social support, less often – discrimination based on the diagnosis and other circumstances [25].

Treatment of affective disorders, including depressive disorders, in epilepsy should combine two directions: drug therapy and psychotherapy. Drug therapy is carried out in two stages [9]. At the first stage, correction of AEDs is necessary in order to achieve seizure control and possible replacement of AEDs with a "depressogenic" effect with mood-correcting AEDs. AEDs are used to normalize mood in patients with epilepsy in three cases: if depressive symptoms (including interictal DD) have a temporary connection with recurrent seizures and / or they appeared after the introduction or increase in the AEDs dose with a negative psychotropic

profile, and / or they appeared after the cancellation of mood-correcting AEDs [26].

At the second stage of drug therapy for depression, an antidepressant is added. There are three principles for prescribing antidepressants for epilepsy: choosing a drug with a minimal proconvulsant effect, low doses in the initial period of treatment, slow titration to target doses. Preference is given to selective serotonin reuptake inhibitors (SSRIs): fluoxetine for anergy; sertraline, citalopram for insomnia [27; 28]. Agomelatine can be prescribed, especially with desynchronization of circadian rhythms. Classical antidepressants (tricyclics) are almost never used to treat mood disorders in epilepsy, since their use is associated with the risk of increasing the frequency of epileptic seizures. The duration of treatment with antidepressants is from three to six months, followed by gradual withdrawal of drugs.

Psychotherapy for depression in epilepsy (including online self-treatment programs) is underused, although it has proven its effectiveness [29]. A meta-analysis of 13 studies examining cognitive behavioral therapy (CBT) for depression in epilepsy found that CBT was effective in reducing depression and improving quality of life, but was ineffective in controlling seizures [30].

Conclusions

Affective-somatoform (dysphoric) disorders specific to epilepsy can be divided into three groups according to their temporal relationship with epileptic seizures: "periictal" disorders, interictal dysphoric disorder, and alternative affective-somatoform syndromes (Landolt syndrome). "Periictal" dysphoric disorders, including prodromal ("preictal"), ictal, and postictal disorders, are closely related to the type and frequency of seizures. Interictal dysphoric disorder is actively studied, but its existence as a nosological diagnostic unit is still a matter of debate. The pathogenesis of Landolt syndrome is not fully understood. Treatment of depression in epilepsy should include both drug therapy and psychotherapy. At the first stage of drug therapy, anticonvulsants are adjusted in accordance with the identified type of disorder, and at the second stage, an antidepressant is added. Of the psychotherapy methods, cognitive behavioral therapy is the most effective. Thus, affective disorders in epilepsy are represented by a wide range of dysphoric psychopathological conditions of both paroxysmal and non-paroxysmal nature, have their own classification and development factors, which must be taken into account when choosing adequate therapy.

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Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest.

Author contributions are equivalent.

Received: 11/14/2023
Revised version received: 12/13/2023
Accepted: 03/25/2024

Please cite this article in English as: Malov A.G., Andrusenko A.A., Selyanina N.V. Specific dysphoric disorders in epilepsy. *Perm Medical Journal*, 2024, vol. 41, no. 2, pp. 61-67. DOI: 10.17816/pmj41261-67