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Mental disorders in patients with epilepsy

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Summary

Mental disorders occur in patients with epilepsy significantly more frequently than in the general population or in those with other chronic diseases. The specificity of epilepsy as a condition of the central nervous system with complex somatic, psychic and social consequences contributes to co-occurrence of these disorders. Moreover, common pathomechanisms are suggested for epilepsy and mental disorders, associated with disturbances of bioelectrical activity and neurotransmission in certain areas of the brain. The authors present a review of main groups of mental disorders observed in epileptic patients: psychotic, affective, anxiety, personality, and conduct disorders. They discuss their epidemiology and clinical presentation, with a particular focus on their risk factors and temporal relation to epileptic seizures. They also highlight problems associated with differential diagnosis and optimal therapeutic strategy. Mental disorders have a significant impact on the quality of life and functioning of patients with epilepsy. Further exploration of interrelationships between these illnesses, as well as cooperation between neurologists and psychiatrists promote an early and precise diagnosis of mental disturbances in this group of patients and their effective treatment.

Key words: epilepsy, mental disorders

Introduction

The frequency of mental disorders among patients with epilepsy is significantly higher than in the general population or among people with other chronic diseases (Table 1).

Table 1. **The incidence of mental disorders in patients with epilepsy and risk of mental disorders in patients with epilepsy compared with the general population (odds ratio [OR]) [5, 7, 16, 19, 21–25, 27–29, 36–39, 43, 49, 52, 53, 59]**

Mental disorders	Incidence in patients with epilepsy	Risk of mental disorder compared with population risk (OR)
General	26–36%	2
Psychotic	5.6% Ictal 30-40% Postictal 2% Interictal 5.2%	7.8
Depressive	23% Preictal 46% Ictal < 1% Postictal 43% Interictal 10–42%	2.8
Bipolar	6–14% Bipolar disorder – 2%	2–17
Anxiety	11–25% Preictal 10–15% Ictal 10–13% Postictal 45% Interictal 18–29%	Approx. 2
Personality	Approx 20%	
Conduct	43% Psychogenic non-epileptic seizures 12–32%	

An opposite tendency has also been observed: patients with a history of affective or anxiety disorders are more often diagnosed with epilepsy [1]. Several hypotheses have been proposed on potentially common pathomechanisms of epilepsy and mental disorders, mainly associated with disturbances in bioelectrical activity and neurotransmission in certain areas of the brain [2, 3]. The development of mental disorders is greatly promoted by the specificity of epilepsy (sudden and unpredictable character of seizures) and its consequences, including somatic (neurological deficit, risk of trauma) and psychosocial aspects (cognitive dysfunction, worsening of social relations, stigma). Mental disorders can constitute a part of an epileptic seizure, retain a temporal relationship with seizures (peri-ictal) or emerge independently (interictal). Some types of disorders (panic attacks, psychogenic seizures) may require differentiation from epileptic seizures, although in some patients they may coexist. Mental disorders among patients with epilepsy substantially affect their quality of life and general functioning, thus require an interdisciplinary therapeutic approach, with the cooperation of neurologists and psychiatrists. The choice of pharmacological treatment should include therapeutic efficacy in both diseases, their potential interactions and adverse effects.

1. Psychotic disorders

The risk of psychotic disorders (ICD-10 – F06.0–F06.3, F06.8) in patients with epilepsy is 7.8 times greater than in the general population (Table 1). Their highest incidence is observed in patients with symptomatic epilepsy due to structural brain lesions: developmental malformations (e.g., errors in neuronal migration), neuroinfections, cerebro-cranial trauma or neurosurgical procedures [4, 5]. The most predisposed patients are those with temporal lobe epilepsy (TLE).

1.1. Peri-ictal psychoses

Ictal psychoses usually take the form of a nonconvulsive status epilepticus and only rarely occur as short, self-limiting episodes. Their symptoms include: aggravation, aggression or 'freezing', sometimes hebephrenic or catatonic syndrome accompanied by disturbed consciousness (to a various degree) [6, 7]. In 30–40% of patients, disorders of perception occur during epileptic seizures. The type of illusions or hallucinations (visual, auditory, olfactory, tactile or general somatic sensations) depends on the localization of the epileptic focus. Epileptic hallucinations are characterized by preserved insight. Approximately 20% of patients (especially with an epileptic focus in the temporal region) experience hallucinations associated with the course of time (speeding, slowing, stopping) or memory (*déjà vu*, *déjà vécu*). Concurrently, approx. 1% of patients with epilepsy experience a so-called dreamy state,

feeling of depersonalization, derealization, 'thought insertion' or mystical sensations during a seizure [7].

Postictal psychoses occur within 24 hours to 7 days after a single or cluster seizures (lucid interval – a period of clear consciousness and normal functioning) and last for at least 15 hours, up to even 7–8 weeks [7]. They can present as affective disorders (depressive, manic), aggressive and destructive behavior sometimes leading to auto-mutilation, suicide attempts or hurting others. Hallucinations and delusions appear seldom, whereas negative symptoms (such as alogia, anhedonia, apathy, flattened affect or withdrawal) are usually absent. Psychotic symptoms may be associated with disturbed consciousness [6, 7]. Almost half of patients experience just one episode of postictal psychosis during lifetime, other may have a relapse and 14% develop interictal psychosis [8].

Some classifications describe also preictal psychoses, appearing in a prodromal phase of an epileptic seizure or preceding it by a few hours to a few days. Some authors suggest that they should be treated as separate epileptic seizures with exclusive psychotic symptomatology [6].

1.2. Interictal psychoses

Interictal psychoses do not imply an immediate association with epileptic seizures and their duration stretches from a few weeks to even months. They are often named schizophrenia-like. Characteristic symptoms involve hallucinations (mostly auditory, less commonly visual), delusions, religious and mystical experiences. Contrary to schizophrenia, they are not accompanied by disturbances of affect or negative symptoms. Disorders of consciousness are not observed [7].

There is another category of so-called alternative psychoses, induced by successful antiepileptic treatment. They can be revealed after introducing a new, efficient anticonvulsant drug or conducting a successful operation, resulting in both clinical (absence or decrease of seizures frequency) and EEG (forced normalization) improvement [6]. These psychotic episodes proceed usually with productive symptoms (hallucinations, delusions) or anxiety [7]. Approximately 30–40% of patients with an alternative psychosis experience also incidents of interictal psychosis, independent from the treatment [9].

1.3. Pathogenesis

Spreading of paroxysmal activity within the structures of the limbic system (unseizable in standard EEG, but recorded with the use of deep electrodes) is considered as the background for peri-ictal psychoses [10]. According to another hypothesis, a psychotic episode is a manifestation of a self-limiting autoimmune encephalitis subsequent to a transitional increase in permeability of the blood-brain barrier, leading to systemic blood antigens exposure [4].

The phenomenon of ‘kindling’ is considered as a pathomechanism for interictal (also alternative) psychoses. Repetitive bioelectrical discharges in the limbic system overstimulate the dopaminergic system (through excessive dopamine secretion and/or increased sensitivity of dopamine receptors), which may lead to the development of psychotic disorders [3]. Another theory suggests that perinatal hypoxia or injury, past neuroinfection or trauma may result in synaptic reorganization, reduced neuronal plasticity and changed catecholaminergic, GABA-ergic and glutaminergic transmission in susceptible parts of the brain (e.g., the limbic system), favoring both epileptic seizures and psychotic disorders [11]. Frequent family history of psychiatric disorders in this group of patients suggests the role of genetic factors in a common background of epilepsy and psychotic disorders (e.g., CYFIP1 mutations) [12].

The risk of psychotic disorders increases in patients with certain types of epileptic seizures (mostly focal temporal or secondarily generalized), early onset and longer duration of the disease, frequent or cluster seizures and concomitant cognitive dysfunction [4, 7].

1.4. Treatment

The treatment of ictal psychoses consists in interrupting a seizure or status epilepticus according to practical guidelines [7]. Effective anticonvulsant treatment may prevent relapses of postictal psychosis. In its acute phase, benzodiazepines are used and – in case of failure – neuroleptics (e.g., risperidone, olanzapine, quetiapine) [13].

In 15% of patients with interictal psychosis spontaneous remissions are observed; among the remaining ones antipsychotic treatment limits the duration of psychotic episodes. Risperidone is mostly recommended, as it lowers the seizure threshold less than other neuroleptics, while clozapine is contraindicated [11].

In approx. 0.5% of patients with epilepsy (especially women and patients with temporal lobe epilepsy), psychotic disorders may be evoked by the use of antiepileptic drugs, most often phenytoin, zonisamide and levetiracetam, least often – carbamazepine (Table 2). The prognosis in such cases is better than in other type of epilepsy-related psychoses, provided an appropriate modification of the treatment [14, 15].

Table 2. **The effect of antiepileptic drugs on mental disorders [14, 15, 30, 34–36, 49, 60]**

Mental disorders	Recommended antiepileptic drugs	Contraindicated antiepileptic drugs
Psychotic	-	Levetiracetam Phenytoin Zonisamide
Affective	Lamotrigine Carbamazepine Oxcarbazepine Valproic Acid	Levetiracetam Topiramate Clonazepam Vigabatrin Tiagabine
Anxiety	Pregabalin Tiagabine Valproic Acid Benzodiazepines	Levetiracetam Ethosuximide Zonisamide
Conduct	-	Levetiracetam

2. Affective disorders

The incidence of affective disorders (ICD-10 – F06.3) in patients with epilepsy is 2.8 times higher than in the general population [16] (Table 1).

2.1. Peri-ictal affective disorders

Peri-ictal affective disorders are associated almost exclusively with focal seizures, mostly originating from the temporal lobe. Preictal depressive disorders, characterized by mood depression, anxiety and irritability, precede a seizure by a few days to a few hours [7, 17]. Ictal depressive disorders (sudden, short-lasting mood depression of varying severity, not related to any environmental factors) may constitute a regular part of an epileptic seizure. They are often accompanied by: anhedonia, guilt, suicidal thoughts. Such episodes are rare (< 1%) [7, 17]. Postictal depressive disorders, which are much more frequent (43%), may be present immediately after a seizure or develop within a few days time and last up to 24 hours. Symptoms of depression (low mood, anhedonia, feeling of hopelessness and helplessness, guilt, irritability, suicidal thoughts in 30% of cases) may be accompanied by anxiety disorders [18, 19].

Preictal bipolar/dysphoric disorders (mood instability with euphoria and irritability) may begin about 3 days before the seizure, exacerbate during its course and usually subside within 24 hours [20]. Postictal mania or hypomania, characterized by racing

thoughts, psychomotor acceleration, elevated mood,euphoria or deconcentration, develop after a few days after a seizure and last up to several days. They are observed mostly in patients with focal epileptic seizures [19].

2.2. Interictal affective disorders

Interictal depression is the most frequent affective disorder in patients with epilepsy (10–42% – percentage comparable to other chronic diseases) [21–25]. It consists of typical features: mood depression, psychomotor slowness, suicidal thoughts and/or tendencies, somatic symptoms (masked depression – e.g., sleep disorders, menstrual cycle disturbances, unspecific pain symptoms, dyspepsia, etc.). Depression can be diagnosed if symptoms persist for more than 2 weeks. In contrast to depression not associated with epilepsy, guilt consciousness, helplessness and circadian mood fluctuations occur rarely and the dynamics of the symptoms may be different (acute onset) [7, 26].

Approximately 2% of patients with epilepsy are diagnosed with bipolar disorder (ICD-10 – F06.31) [27, 28], while 6–14% present with bipolar symptoms (ICD-10 – F06.33) [23, 28, 29]. The morbidity is twice as high than in other chronic diseases (e.g., migraine, asthma, diabetes) and 20 times higher than in the general population [23, 27, 29]. No negative influence was observed of the coexistence of epilepsy and bipolar disorder on either of these diseases [30]

Interictal dysphoric disorders (DD) occur with exacerbations and remissions. Their characteristic features (diagnosis is possible with at least 3 of the following) include: mood depression, anergy, pain syndromes, insomnia, panic attacks, anxiety, irritability, euphoria [31, 32].

2.3. Pathogenesis

The background for peri-ictal disorders is hypothesized to be associated with a disturbance in the bioelectrical activity of the brain before and during an epileptic seizure and spreading of epileptic activity i.a. to the limbic system [7]. Decreased neuronal excitability subsequent to hyperpolarization, decreased level of neurotransmitters (glutamate, endogenous opioids, adenosine) and postictal focal hypoperfusion are thought to play an important role [18].

Hyperactivation of the hypothalamic-pituitary-adrenal axis and disturbances in neurotransmission in the CNS (decreased serotoninergic activity and GABA/glutaminergic imbalance) are considered as potential common pathomechanisms of epilepsy and depression [33].

Furthermore, the phenomenon of ‘kindling’ (‘arousal’ of epileptic activity as a consequence of repetitive – and consequently perpetuated – changes in the level of neurotransmitters) and hyperexcitability of neurons caused by excessive cellular sodium ions influx have been suggested as a common basis for epilepsy and bipolar

disorder [20]. The last hypothesis is supported by the mood stabilizing effect of sodium channel blocking anticonvulsant drugs [30].

The probability of depression in patients with epilepsy increases with certain types of seizures (especially focal with impaired consciousness) and their insufficient control, but is also related to retained feeling of shame after a seizure or fear of being hurt due to it [19, 34]. Multiple risk factors for the occurrence and severity of depression are associated with antiepileptic treatment: depressogenic effect of some agents (levetiracetam, topiramate, clonazepam, vigabatrin, tiagabine), withdrawal of mood stabilizing drugs (lamotrigine, carbamazepine, valproic acid) or cytochrome P450 induction (phenytoin, carbamazepine) – especially in the case of simultaneous intake of antidepressant drugs metabolized by this cytochrome (tricyclic antidepressants, sertraline) [26, 34, 35] (Table 2).

Occurrence of affective disorders may be also promoted by genetic predisposition (e.g., polymorphism of genes responsible for GABA-ergic transmission homeostasis), chronic stress, other psychosocial factors (unemployment, low education and/or economic status, stigmatization) [34].

2.4. Treatment

Treatment of peri-ictal disorders consists mostly in effective control of seizures. In interictal depression and bipolar disorder, specific pharmacological treatment and psychotherapy (especially cognitive behavioral therapy) are recommended. Adverse effects, mechanisms of action and potential interactions of anticonvulsant and antidepressant drugs should be taken into consideration. The safest antidepressant drugs (with regard to lowering seizure threshold) are selective serotonin reuptake inhibitors (especially escitalopram, citalopram, sertraline) and moclobemide, whereas bupropion, maprotiline and tricyclic antidepressants should be avoided. As it was mentioned above, some anticonvulsant drugs (lamotrigine, carbamazepine, oxcarbazepine, valproic acid) have a positive effect on mood stabilization [26], while those potentially exacerbating depression should be refrained from (levetiracetam, topiramate, clonazepam, vigabatrin, tiagabine) [34, 35].

3. Anxiety disorders

Anxiety disorders (ICD-10 – F06.4) occur in patients with epilepsy twice more often than in the general population (Table 1).

3.1. Peri-ictal anxiety disorders

Preictal disorders, comprising nervousness, fear, anger, irritability, emotional instability may precede focal epileptic seizures, usually of temporal symptomatology

[36]. In 10–13% of patients with epilepsy, short-lasting (up to a few minutes) sudden-onset anxiety episode may constitute a part of a seizure [37, 38]. Their clinical image depends on the localization of the epileptogenic focus. In patients with temporal lobe seizures anxiety may vary in intensity (from restlessness/uncertainty to panic), are accompanied by autonomic dysfunction and the feeling of discomfort in the chest or head or migrating from the epigastrium to the throat; sometimes depersonalization and memory illusions co-occur. In patients with frontal lobe seizures, intensive anxiety appears usually at night and wakes the patient from their sleep [7, 36]. Postictal anxiety disorders are observed in 45% of patients with focal epileptic seizures. They develop within 12–72 hours after a seizure and can last for up to 24 hours. Their most common features are: worrying, agoraphobia, fear of recurrence of seizures, obsessions and compulsions, frequently followed by depressive or dysphoric symptoms [19].

Differentiation of panic attacks and focal epileptic seizures containing features of anxiety may be a diagnostic challenge. Analysis of their course (epileptic seizures last shorter, are accompanied by automatisms, disturbances of consciousness and positive psychotic symptoms) may be helpful. However, recording of paroxysmal activity in EEG during an incident is the basis for a diagnosis [36].

3.2. Interictal anxiety disorders

Interictal and peri-ictal anxiety disorders (ICD-10 – F06.4) often coexist. Their most common forms are:

- generalized anxiety disorder (3–12.5%) – persistent and systemic fear existing for at least 6 months, often associated with somatic and autonomic symptoms, also sleep and concentration disorders;
- phobia (2–7%) – fear of a certain situation, object or phenomenon, leading to their avoidance. In patients with epilepsy, specific phobias may develop: agoraphobia (4–5%) – often associated with the fear of consequences of an epileptic seizure outside home, and social phobia (6–14%) – caused by the specificity of the disease and feeling of stigmatization;
- obsessive-compulsive disorder (1–3%) – intrusive and unpleasant thoughts, provoking compulsive behavior;

panic attacks (5–21%) – episodes of sudden, intense and short-lasting fear, not provoked by any external stimuli, occurring at least once per week for at least one month [21, 24, 36, 39, 40]

3.3. Pathogenesis

Expansion of the pathological bioelectrical activity within the limbic system, especially the amygdala, is considered to be the background for anxiety disorders.

Similarly to affective disorders, potential common pathomechanisms with epilepsy include: disturbances in serotoninergic, noradrenergic and GABA-ergic transmission; the phenomenon of 'kindling' and dysfunction of the neuronal network integrating the amygdala and other parts of the CNS (the cortex, the cerebellum). The hypothesis of the role of GABA-ergic transmission is supported by the anxiolytic effect of GABA-oriented anticonvulsant drugs (pregabalin, tiagabine, valproic acid, benzodiazepines) [36]. A common genetic background is also considered – e.g., serotonin gene polymorphism [2].

The incidence of anxiety disorders is higher among young people with short history of epilepsy (adaptive mechanisms develop along with the course of the disease and with age) [39]. Other issues promoting anxiety disorders include: female sex, family history of epilepsy, insufficient seizure control (high frequency, unpredictability, risk of trauma), side effects of antiepileptic drugs (levetiracetam, ethosuximide, zonisamide) and psychosocial factors (low education, unemployment, lack of social support) [7, 36].

3.4. Treatment

Treatment of peri-ictal anxiety disorders is based on effective antiepileptic treatment. However, interictal disorders need a modified approach. The safest anxiolytic substances in such patients are: mirtazapine, risperidone, venlafaxine and SSRIs; imipramine, bupropion, olanzapine, quetiapine, clomipramine have a moderate effect, while chlorpromazine is contraindicated. An anxiolytic effect of GABA-ergic anticonvulsant drugs (pregabalin, gabapentin, tiagabine, valproic acid, benzodiazepines) can be used in the therapy [36].

For specific types of anxiety disorders, the following schemes of treatment are recommended:

- generalized anxiety disorder – pregabalin is the medication of choice and in case of failure, paroxetine, venlafaxine and imipramine may be used;
- social phobia – selective serotonin reuptake inhibitors (sertraline, escitalopram, paroxetine) are most efficient;
- obsessive-compulsive disorder – sertraline or clomipramine together with cognitive behavioral therapy are recommended. Sometimes small doses of antipsychotics (risperidone, haloperidol) are needed, but as side effects and interactions of such medications can result in worsening of seizure control, treatment of these patients requires cautious, interdisciplinary care;
- panic attacks – a combination of SSRIs and cognitive behavioral therapy is advised, in milder cases psychotherapy may be sufficient [36].

It should be remembered that some antiepileptic drugs (levetiracetam, ethosuximide, zonisamide) may exacerbate anxiety. Polytherapy also needs consideration of

potential interactions: carbamazepine and phenytoin through cytochrome P450 induction cause a decrease of the serum level of most anticonvulsant drugs, while valproic acid has a contradictory effect [36] (Table 2).

4. Personality disorders

4.1. Geschwind syndrome – viscosity

In the 1970s, Norman Geschwind described a syndrome typical for patients with relapsing temporal lobe epileptic seizures. Its dominant feature was so-called viscosity – persistence of emotions or train of thought despite ceasing of the evoking stimulus. It was supposed to lead to a disturbance of thought, impairing the communicativeness of speech, such as: 'circumstantiality' – multiple straying from the main subject to loosely associated subplots and back again – or 'tangentiality' – repetitive answers inconsistent with the question. Viscosity could be observed also in different activities, e.g., prolonged handshake or writing exceptionally long texts (hypergraphy). In such patients, disorders of thought were also described with a tendency towards religious thinking, mysticism, overmoralization, philosophizing, aggression, and a decrease of libido. The traditional description of Geschwind syndrome is nowadays regarded as controversial and some authors even doubt its relevance [41].

4.2. The current classification of personality disorders (ICD-10 – F07.0)

In patients with epilepsy predominating features of personality include: timidity, instability, low self-esteem, insecurity, introversion – leading to avoidance of social interactions. Such description is consistent with the cluster C personality disorders according to DSM (Diagnostic and Statistical Manual of Mental Disorders). Cluster C is diagnosed in 72–100% epileptic patients with concomitant personality disorders [42, 43]. Avoidant (63–100%) and dependent (16–45%) personality disorders are most commonly observed, while obsessive-compulsive ones are less frequent (12–16%) [42, 43]. Factors that promote the development of personality disorders include: longer duration of the disease, greater frequency of seizures, large number of antiepileptic drugs used. The incidence of avoidant and dependent personality disorders is affected mostly by the psychosocial consequences of epilepsy (stigmatization, feeling of loss of control, insecurity, instability) and subsequent social isolation, as well as by the kind of developed defensive mechanisms. These pathomechanisms are escalated in patients with drug-resistant epilepsy because of high frequency of seizures and emerging changes in treatment and/or polytherapy, followed by its side effects [43].

Pathogenesis of cluster C personality disorders is considered to be associated with disturbed serotoninergic transmission of the limbic system, subsequent to sensitiza-

tion caused by repetitive epileptic discharges in this area [44]. This hypothesis may be supported by higher incidence of personality disorders in patients with temporal lobe epilepsy, however, data on this subject are limited [43].

Regarding the incidence (14–22%) and types of concomitant personality disorders, the patients with juvenile myoclonic epilepsy constitute a separate group [45–47]. They are characterized by: immaturity, emotional instability, hedonism, impulsiveness and insubordination. More than half of them (54–85%) present with cluster B personality disorders according to DSM, especially borderline (20–46%) and histrionic (8–35%) ones. Cluster C disorders – dependent (10–21%) and obsessive-compulsive (4–10%) personality disorders are much more rare within this group: [45, 46]. The type of personality disorders in patients with juvenile myoclonic epilepsy can be attributed to structural and functional changes in the frontal lobes, which is supported by neuroimaging (MRI) [48]. Personality disorders develop more often in patients with insufficient seizure control [47].

4.3. Treatment

The treatment of personality disorders is based mostly on psychotherapy. In the case of obsessive-compulsive disorder, SSRIs are also recommended. In patients with juvenile myoclonic epilepsy, optimal anticonvulsant treatment plays a key role, supported by behavioral therapy, which modifies the schemes of conduct and has further positive impact upon seizure control.

5. Conduct disorders

Conduct disorders (ICD-10 – F07.0) in patients with epilepsy usually occur as aggressive and anti-social behavior (43%) [49]. They are more frequent in patients with a frontal epileptogenic focus, which supports the hypothesis of their common structural background with epileptic seizures [50]. The risk of these disorders is increased by factors associated with treatment (polytherapy, use of levetiracetam, insufficient seizure control), concomitant disorders (depression, anxiety, cognitive dysfunction) and psychosocial factors (unemployment, low income, loneliness, stigmatization) [49, 51].

Psychogenic nonepileptic seizures (PNES) are a particular type of conduct disorders. They resemble actual epileptic seizures, but are not caused by pathological bioelectrical brain activity. According to the WHO classification, PNES are a subtype of dissociative (conversion) disorders (ICD-10 – F44). The coexistence of actual and psychogenic seizures in one person (present in 12–32% of cases) may pose as a diagnostic challenge and requires a thorough analysis [52, 53]. PNES misdiagnosed as real epileptic seizures may lead to a false diagnosis of refractory epilepsy and harmful escalation of anticonvulsant treatment. On the other hand, withdrawal from therapy

due to all seizures misclassified as psychogenic ones may result in increase in seizure frequency or even life-threatening status epilepticus.

Psychogenic nonepileptic seizures appear generally (70–100%) after setting the diagnosis of epilepsy. Their clinical manifestation usually resembles epileptic seizures seen in a particular patient, although they are usually more frequent, have longer duration and a more spectacular course [54, 55]. Neither their subjective perception by the patients, nor the observations of the patients' kin allow to differentiate these types of seizures [56].

PNES occur more often in women (70–80%), coexist mostly with actual focal-onset epileptic seizures (72%) (with the highest risk in frontal lobe epilepsy) seldom with primarily generalized ones (26%). Frontal lobe seizures (e.g., tortional movements of the trunk and head), especially with atypical EEG pattern, can be easily mistaken for PNES and thus should be interpreted cautiously [57].

In 30–70% of patients with epilepsy, the occurrence of PNES is associated with traumatic experiences (e.g., loss of a close person, physical/emotional/sexual abuse, family issues, another somatic disease or trauma). In almost all epileptic patients with PNES (and only approx. 50% of the remaining ones), other psychiatric disorders coexist. These include depression (20–58%) and anxiety disorders (up to 50%), cluster B personality disorders according to DSM (40%), other conversion disorders (20%) [52, 54]. Moreover, patients with both types of seizures usually present with worse cognitive performance, especially in the domain of visual memory [55].

The treatment of psychogenic nonepileptic seizures consists in informing the patient and their kin on the diagnosis and psychotherapy. Such demeanor helps in most of cases to eliminate or reduce PNES and in some patients also to decrease the doses of antiepileptic drugs.

Magaudda et al. [58] proposed a classification of patients with concomitant epileptic and nonepileptic seizures, based on the course of the disease, interrelationships between seizures, and emerging therapeutic possibilities:

(1) patients with refractory focal epilepsy and affective disorders
   - PNES are a consequence of the psychosocial burden of epilepsy (stigmatization, problems with social relationships or employment);
   - treatment is based on cognitive behavioral therapy, alternatively supported by pharmacotherapy.

(2) patients with epilepsy and mental retardation due to early developmental brain damage
   - nonepileptic seizures appear after the reduction of epileptic seizures through effective anticonvulsant treatment and act as their substitute, assuring attention and care from caregivers;
   - treatment consists in education of the caregivers and modifying their behavior;

(3) patients with sufficient pharmacological control of seizures who developed PNES after a traumatic experience
   – cluster B personality disorders and/or anxiety disorders often coexist;
   – treatment is based on psychotherapy.

6. Consequences of mental disorders in patients with epilepsy

The most important consequence of mental disorders concomitant with epilepsy is the problem of suicides. Epileptic patients are more susceptible to suicidal thoughts and tendencies and approx. 0.2–0.4% undertake suicide attempts [1, 34]. The risk of suicide is exceptionally high among patients with temporal lobe epilepsy and in those with frequent, poorly controlled seizures. The risk increases also with coexisting psychotic, affective or anxiety disorders and alcohol and drug addictions. This aspect should be cautiously considered in the case of potential depressiogenic side effects of antiepileptic medications (levetiracetam, topiramate, clonazepam, vigabatrin, tiagabine).

Mental disorders in patients with epilepsy significantly influence their quality of life and various aspects of functioning. They have a huge impact upon patients' perception of oneself and may further increase the feeling of isolation and social stigmatization caused by epilepsy. Psychiatric disorders may also affect the patient's attitude towards the disease and treatment – usually in a negative manner, with an adverse effect on cooperation with the physician, compliance, and subsequently also on seizure control.

The knowledge of determinants and typical symptoms of mental disorders coexisting with epilepsy enables to distinguish a group of patients particularly prone to their development (regarding the type and course of seizures and the patient's situation) and pay a special attention to follow-up of epilepsy course and treatment effects.

Considering a growing number of therapeutic options in epilepsy, but also in psychotic and affective disorders, the knowledge of the medications' mechanisms of action, potential interactions and side effects is required to allow an optimal choice for a specific patient, both in the context of control of seizures and mental disturbances. The cooperation of a neurologist and psychiatrist in this field may ease the resolution of diagnostic problems and settlement of an appropriate therapeutic strategy.

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