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Opinion Article

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Cognitive Impairments in Patients with Epilepsy

Vyacheslav Stepanenko[1*]

[1]*Honorary Doctor of Sciences, Professor (Psychological Sciences) Advisor to the Russian Academy of Natural Sciences (Medical Sciences), Russia*

***Corresponding author**
Vyacheslav Stepanenko, Honorary Doctor of Sciences, Professor (Psychological Sciences) Advisor to the Russian Academy of Natural Sciences (Medical Sciences), Russia

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Cognitive impairment in epilepsy is an important problem. The understanding of the pathogenesis of disorders of higher nervous functions is based on the interaction of several factors, which include the form and duration of the disease, gender differences.

Epilepsy is a disease that belongs to both the field of neurology and the field of psychiatry. This is due not only to the fact that ictal states can manifest as mental disorders, but also to the fact that in the peri- and interictal periods patients may experience changes in cognitive functions and affective personality disorders. This is objectively reflected in the modern definition of epilepsy [1]. In general, neuropsychiatric problems are observed in 30–60% of patients with epilepsy [2, 3]. Psychosocial problems for patients often come to the fore, including cases where seizure control has not yet been achieved [3], as well as cases of controlled disease. In particular, depression in patients with difficult-to-control epilepsy affects quality of life to a greater extent than, say, frequent seizures. In addition, depression can have a significant impact on cognitive functions [4]. Complaints about violations of speech functions, memory, attention, thinking, which patients can present at a doctor's appointment, are in second place after complaints about seizures.

There are certain differences between cognitive and behavioral disorders in childhood and adulthood [1]. In children, epileptic seizures, as well as therapy with antiepileptic drugs (AEDs), affect the development of the structures of the central nervous system and the formation of higher mental functions (HMF), which ensure the adaptation of the child's body to environmental conditions. This leads to pronounced changes in the personal sphere and functions that form the basis of cognitive activity (attention, gnosis, memory, thinking). At the same time, the plasticity of mental processes in childhood makes it possible to compensate for violations with directed correction. In addition, special conditions occur in children - epileptic encephalopathies (early malignant encephalopathies (infantile) and caused by continued activity on the electroencephalogram during slow-wave sleep) [1]. In adults and especially the elderly, a long history of the disease, diffuse or severe local damage to the structure of the brain, and other factors can lead to both intellectual and mnestic disorders up to the degree of dementia, as well as severe mental disorders, which are more rigid to therapy and psychological correction [5].

Modern epileptology has the ability not only to diagnose such disorders in the higher mental sphere, but also to correct them in a timely manner, which, together with effective antiepileptic therapy, can positively influence the general condition and quality of life of the patient. It is the improvement of the quality of life and the social adaptation of the patient that is the main goal of the treatment of epilepsy.

It should be noted that the development of the described disorders is polyetiological [6]. The main group of factors is directly related to the disease itself: age of onset (correlates with reading impairment); the form of epilepsy, the duration of the course, the type, duration and frequency of seizures, their polymorphism (correlate with violations of counting functions); localization of the epileptic focus and other electroencephalographic features, including the presence of continued epileptiform activity during slow-wave sleep (associated with impaired memory, attention, as well as speech functions and disorders in the behavioral sphere); the presence of status epilepticus in history (associated with a delay in the development of various cognitive functions). Gender differences are described (boys with intractable epilepsy are more likely to have learning disabilities). Structural anomalies and their localization (especially cortical dysplasias) detected by neuroimaging and developmental delay may be associated with certain impairments in cognitive functions and behavior [5–7]. However, the correlation between disorders in the higher mental sphere and the localization of the structural focus, as well as regional epileptiform activity, is not always observed [3]. The use of AEDs in mono- or polytherapy is also important. In addition, the described disorders lead to social maladaptation and stigmatization, which, in turn, have a negative impact on disorders in the higher mental sphere, forming the so-called vicious circle.

A unified classification of disorders in the higher mental sphere in patients with epilepsy is being developed at the Research Center for Psychotechnics. In general, cognitive impairment and mental disorders are distinguished. Domestic psychiatrists single out mental disorders in relation to the seizure period, including disorders that are a component of a seizure, in addition, they separate paroxysmal and permanent mental disorders in epilepsy. Paroxysmal mental disorders include epileptic mood disorders (dysphoria, depressive disorders); twilight clouding of consciousness; epileptic psychoses, to permanent mental disorders - various options for changing personality. In addition, the concept of epileptic encephalopathies, which was mentioned above, has been widely developed recently.

Up to the XX century. It was believed that patients with epilepsy have reduced intellectual abilities. Within the framework of intellectual disorders, a gross deficit of the mnestic-intellectual sphere was considered - mental retardation and epileptic dementia. However, in our Center it was shown that the IQ of these of patients varies widely, sometimes reaching quite high values, and only a small number of patients have a progressive deterioration in the intellectual-mnestic sphere [5]. In some patients, there is a total impairment of the HMF to the degree of epileptic dementia (more often in elderly patients) or mental retardation is diagnosed, mainly in patients with malignant epileptic encephalopathies of early childhood. In turn, 20% of people with intellectual disabilities can be diagnosed with epilepsy, which is associated in most cases with structural disorders of the brain [4].

A group of epileptic syndromes, for which a decrease in intelligence is pathognomonic, are early malignant encephalopathies in children with manifestation of seizures, mainly in the first year of life [1]. In the majority of surviving patients, intellectual impairment, manifesting almost simultaneously with the onset of seizures or associated with mental retardation, is one of the main symptoms of the disease; the development of intellectual disorders in the future may acquire the character of a plateau [3]. Intellectual impairments are noted in patients with such rare diseases as the Kozhevnikov-Rasmussen syndrome, progressive forms of epilepsy with myoclonus. In children with electrical status epilepticus of slow-wave sleep, the intellectual deficit, which is noted even in the absence of seizures, may regress as epileptiform activity decreases on the EEG. If therapy is started late, intellectual impairment may become persistent. However, it has now been convincingly shown that even in cases where therapy was prescribed on time, intellectual deficits may persist in the future. The results of numerous studies demonstrate that both in children and adults with good seizure control against the background of drug antiepileptic therapy, the prognosis for the intellectual sphere is favorable.

Previously, cognitive deficits were also considered as an integral symptom of the clinical picture of epilepsy. Later it was shown that not all patients with epilepsy develop cognitive impairment. Male sex, etiology of epilepsy and localization of the focus of epileptogenesis in the brain, the presence of interictal epileptiform activity, the use of antiepileptic drugs, the course of the disease, local structural changes, continuous spike-wave complexes in slow-wave sleep, hydrocephalus and atrophy of the brain substance are associated with the development of cognitive impairment. [3, 6]. According to M.G. Harbord, cognitive and behavioral disorders are 3 times more likely to occur in children with previous intellectual disabilities than in children with normal intelligence.

In general, cognitive impairments, like psychiatric disorders, can be transient (ictal or postictal), prolonged, or permanent (interictal). In addition, partial cognitive impairments can be distinguished, specific (for example, speech disorders in Landau-Kleffner syndrome) and total, as mentioned above. It should be added that against the background of ongoing antiepileptic therapy, cognitive disorders most often have a dose-dependent effect. transient or prolonged, however, chronic side effects of AEDs with permanent, in some cases progressive cognitive impairment may also develop. In most episodes, transient cognitive impairments transform into permanent and even progressive ones in the long course of epilepsy resistant to antiepileptic therapy.

The nature of ictal and peri-ictal cognitive impairments in most cases is associated with the localization of the focus of epileptiform activity on the EEG and with the localization of a structural defect in the brain, and in children such disorders are more pronounced than in adults. Ictal cognitive impairment can be manifested by speech disorders, memory impairment, which are differentiated from transient global amnesia and the onset of dementia in elderly patients. Ictal cognitive impairment may be associated with the non-convulsive status of focal seizures and absences. Such conditions can be difficult to diagnose, especially in elderly patients, in patients with the onset of epilepsy and with pre-existing cognitive impairments. During the status of absences, both mild cognitive decline and severe cognitive impairment can occur. During the status of focal seizures, cognitive impairment occurs, correlating with the localization of the focus of cortical dysfunction. Postictal cognitive impairments are variable, as a rule, there is a positive dynamic of recovery after the end of the attacks. Interictal cognitive impairment in patients with epilepsy is quite variable, and it is impossible to single out any particular type of cognitive impairment, since it may depend on the location and nature of brain damage, age of onset of pathology, antiepileptic therapy, and disorders such as depression.

One of the most common cognitive problems in patients with epilepsy is memory impairment. Most researchers associate the occurrence of dysmnesic syndrome with bilateral damage to the temporal lobes of the brain or specific impairments of verbal (with left-sided damage to the temporal lobe) and spatial memory (with right-sided localization of the lesion). In recent years, studies have appeared that indicate that more pronounced specific memory impairment occurs after surgery on the temporal lobes in difficult-to-treat epilepsy [6]. With earlier onset of structural pathology (for example, brain tumors), more pronounced memory impairment is also noted. The problem of studying cognitive impairment in patients with hippocampal sclerosis or lesions of the hippocampus due to other etiology remains particularly relevant. It is assumed that since this structural pathology is a consequence of impaired brain embryogenesis (cortical dysgenesis) or occurs as

a result of prolonged or serial febrile seizures, due to the plasticity of the brain (especially in children), functionally significant zones are formed in intact areas of the ipsi- or contralateral hemisphere. In this regard, in patients with hippocampal sclerosis, memory impairment may be absent. However, most patients with this pathology can be diagnosed with dysmnestic syndrome. It is known that patients' subjective perception of their own disturbances in the mnestic sphere can be more negative than the objective results of neuropsychological testing. This is due, on the one hand, to disturbances in the affective-personal sphere, and, on the other hand, to the fact that in patients with disorders in the mnestic sphere can affect long-term memory, and testing is carried out only at certain short periods of time. Memory impairment during testing may be more pronounced or reappear if the patient had an epileptic seizure within 24 hours before the test [5].

Many researchers advise to improve memory functions as early as possible to provide reliable control over seizures, avoid prescribing drugs of the "old groups" and topiramate, observe sleep patterns, apply techniques to improve memory, use memory aids (paper stickers, notebooks, sound reminder signals etc.). Currently, complex therapy is used to improve memory in patients with epilepsy, but the evidence base for the effectiveness of such drugs is not always available. The main exclusion criteria from the study were: an established diagnosis of drug-resistant epilepsy; a history of pseudo-seizures, events not related to epilepsy, or psychogenic seizures of any other type that resemble epileptic seizures; the presence during the 12 months preceding the start of the study, including within 8 weeks before inclusion in the study, status epilepticus (both convulsive and non-convulsive) or clustering of seizures; the presence of mental illness or affective disorders, mental retardation, autism, schizophrenia; the use of unstable dosages of any antiepileptic drugs within 30 days before the inclusion of the child in the study; concomitant use of other nootropic drugs; severe somatic diseases.

Patients with epilepsy may also suffer from problems associated with impaired attention, in particular in the context of attention deficit hyperactivity disorder (ADHD). According to many authors, ADHD is more common in patients with epilepsy than in the general population. Accordingly, in these patients, a violation of attention is determined. Absence forms of epilepsy can also be accompanied by impaired attention. In general, impaired attention can be observed in patients of both sexes with all forms of epilepsy. Speech disorders in patients with epilepsy are studied less frequently than disorders in the mnestic sphere. However, they can lead to serious consequences in the area of social functioning of patients, including learning. Moreover, speech problems (more often when reading and writing) can occur in patients with epilepsy without intellectual impairment. Most authors associate the occurrence of disorders in the speech sphere with the pathology of the left temporal lobe. Epileptic syndromes with specific speech disorders are described, for example, the Landau-Kleffner syndrome, or aphasia, in which speech disorders in the form of sensory and then motor aphasia that occur in children with previous normal speech development at the age of 4 to 11 years are associated with regional epileptiform activity in the temporal or parietal-occipital regions on the EEG [1]. Diagnosis of this syndrome can be difficult due to the fact that some patients do not develop epileptic seizures. In some patients, seizures, on the contrary, may precede aphasic disorders. If speech disorders occur in patients with epilepsy, antiepileptic therapy can be corrected, classes with a speech therapist are recommended. Symptomatic (nootropic) therapy can also be prescribed, while it is very important to choose drugs that will not lead to a worsening of the course of the underlying disease, to an increase or worsening of seizures. With the localization of the pathological focus mainly in the frontal lobes of the brain, there are such disorders in the cognitive sphere as difficulties in programming actions, making decisions and developing strategies, abstract thinking, and others, which generally determines the ability of individuals to live independently and adapt in society. With regard to the lateralization of the discussed functions in the cortex of the frontal lobes of the brain, numerous studies have been carried out, in particular, the observation, which showed that in this aspect the frontal lobes represent a single area of functioning without a clear difference in sides. This may also be due to the high frequency of occurrence of the phenomenon of the spread of an electric discharge when the focus of epileptogenesis is localized in the frontal lobe from one hemisphere to another. In subsequent works, I report that the most pronounced disorders occur when the pathological process is localized in both hemispheres.

In the treatment of patients with partial, as well as total deficits in the higher mental sphere, a significant role is played by directed psychological correction, supported by antiepileptic therapy [2].

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