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The structure of neural psychological disorders in patients with symptomatic and idiopathic epilepsy

Abstract: Symptomatic and idiopathic forms of epilepsy have several differences in neural psychological values. The most expressed cognitive deficit in the form of cognitive disorders is characteristic for patients with symptomatic epilepsy. The absence of inter-hemisphere asymmetry of P300 wave amplitude was revealed in cases of idiopathic and symptomatic forms, indicating functional disorders.

Keywords: epilepsy, cognitive disorders, cognitive-induced potentials

The problem of epilepsy is still in the center of scientist-neurologist attention. It is linked with not only variety of neural physiologic peculiarities of the disease, diversity of clinical progress, but also with various complications developing together with regular administration of antiepileptic agents [2; 3].

Recently the number of publications, dedicated to the study of cognitive functions in cases of various neurologic

diseases, is increasing. The problem of cognitive deficit increase was considered in close link with progressing of the pathologic process, including epilepsy in adults. In 30–50% of patients with epilepsy psycho-neurological disorders [1] were observed. Among these disorders there were cognitive, affective and behavior ones and disorders of the highest psychic functions, including those linked with inadequate and inopportune administration of antiepileptic agents (AEA) [6; 9].

Cognitive disorders take one of the leading places in clinical progress of epilepsy. The most often manifestations of cognitive dysfunction in case of epilepsy is depression, disorder of memory, attention and bradiphenia during the period between seizures [5]. In fact, as it is reported in literature references, the presence of more than 100 general tonic-clonic seizures in anamnesis in the majority of cases leads to development of cognitive disorders or pre-dementia disorders [7].

As it is mentioned in references, study of the link of cognitive disorders with personal and psychopathologic characteristics of the patients with various forms of epilepsy and various kinds of seizures gains scientific interest [4; 8]. Besides that, the problems of antiepileptic agents' effect on aggravation of cognitive disorders are not studied well, and it of great importance for clinical neurology.

The aim of the research: is to study the impact of common clinical characteristics of epilepsy (its form and duration, type of seizures, etc.) on the development of cognitive disorders.

Materials and methods of the research: the study was based on the results of checking of 264 patients with epilepsy.

The study of cognitive disorders was performed in all patients with epilepsy ($n=264$). Control group involved 30 clinically healthy people of the corresponding age and sex.

Taking into account clinical progress, semiology of seizures, data of neural visualization and electroencephalographic tests the following forms of epilepsy were isolated in the main group: idiopathic (55 patients) and symptomatic one (209 patients).

The first group (group 1) involved 55 patients with idiopathic epilepsy (IE; $n=55$): 27 men (49.1%) and 28 women (50.9%). The age varied from 18 to 52 years of age; the average age was 34.3 ± 1.8 years.

The second group (group 2) included 209 patients with symptomatic epilepsy (SE; $n=209$): 123 men (58.9%) and 86 women (41.1%) aged from 20 to 60 years old; average age was 42.5 ± 1.1 years.

For the revealing of interictal cognitive dysfunction all patients underwent neural psychological checkings using common neurological practical tests. The test included in the protocol were aiming detection of cognitive disorders the most often met in cases of epilepsy, such as disorders of memory, attention, concentration (mini mental status examine — MMSE, repeating of digitals (DS), 5 words remembering test, verbal activity test, watch-drawing test).

The study of acoustic cognitive induced potential (ACIP) or P300 was done in compliance with standard strategy «odd-ball paradigm». MEDELEC «Sapphire premier» four-channel electromyography was used for the study. Calculation of P300 peaks was performed automatically with markers set in the progress of the analysis. Measurement of latent periods of N2, P3 peaks, interval between N2 — P3 peaks was done in milliseconds (ms), N2/P3 complex amplitude in micro Volts (mkV) as a sum of amplitude values of N2 and P3 peaks from isoline. Maximal positive component

with latency equal to 300ms and more was taken for P300. Measurements of P300 in central leads underwent quantitative analysis.

Statistic processing was performed with the help of «Statistics» package. Correlation dependence was calculated by means of quadrates method (Pirson's method).

Results of the research: The progress of paroxysmal syndrome differed by its significant severity degree in the majority of the patients: benign or little progradient progress, with achievement of remission or decrease of severity and polymorphism of seizures, detected in 158 patients (59.8%). At the moment of checking the frequency of seizures more than one per month was registered in 82.6% of the patients, and in 29.9% of the examined patients polymorphic seizures were noted.

39.7% of the patients administered polytherapy with anticonvulsive agents. Only 53 patients (20.1%) didn't get any AEA.

Cognitive disorders were observed in 76.4% of the patients with IE and 88.5% patients with SE. That group included patients with expressed mnestic-intellectual defect, which defined the severity of the clinical progress, but not reaching dementia degree.

Clinical manifestations of cognitive disorders were mostly decrease of memory and concentration of attention, difficulty to summarize, abstract, predict, slow speed of thinking, difficult perception of a new material and its understanding. Majority of the patients had partial disorders of orientation in time. The aforesaid disorders often served to be the cause of social disadaptation.

Total point according to MMSE in that group was average 25.1 ± 3.4 versus 29.5 ± 0.1 in the control group ($P < 0.05$).

According to MMSE scale in both groups of the patients there was significant decrease of the values in comparison with the control group. In the majority of the cases both with SE and IE we observed slight and moderate cognitive disorders (62.7% and 58.2% correspondingly).

On the basis of the achieved results we concluded, that SE was accompanied by more explicit cognitive disorders. It can possibly be linked with morphologic disorders of cerebral structures and high frequency of epileptic seizures and, as a result, longer administration of AC, and that was confirmed by correlation analysis.

Correlation link of the MMSE test results with the frequency of seizures was $r = +0.628$, and with the term of the disease — $r = +0.795$, i. e. there is close direct correlation link.

Patients with epilepsy had decrease in the values of praxis, especially explicit in the cases of SE. With the qualitative analysis we could determine that patients with IE reliably more often (19.1%; 40 patients; $P < 0.05$) depicted clock dial with certain time indication in comparison with the patients with SE (9.1%; 5 patients).

Analysis of the values of the verbal activity test showed diminishing of the number of indirect associations in the patients with idiopathic epilepsy, testifying expressed cognitive dysfunction.

Comparative characteristics of the verbal activity test showed reliable low values of semantically mediated associations and phonetically mediated associations in the patients with SE.

Diminishing of the number of semantically mediated associations was one of the earliest symptoms of dementia, which was more characteristic for SE and it was linked with dysfunction of temporal-limbic system (3.9 ± 0.29 and 4.1 ± 0.34 ; $P < 0.05$). Patients with IE had prevailing subcortical-frontal dysfunction, as the quantity of phonetically mediated associations diminished faster, than the number of semantically mediated ones (8.1 ± 0.23 and 5.7 ± 0.19 ; $P < 0.05$).

The next stage of our work was the study of tests of 5 words remembering and repetition of numerals in the reverse order. Patients with epilepsy had reliable decrease of these values, especially expressed with SE.

Thus, 78.5% patients with epilepsy had cognitive disorders such as disorder of memory, attention, praxis, space orientation, which were more expressed in the cases of SE.

Patients with IE had dysfunction of attention, praxis, memory and speech, while in the cases of SE these disorders were more expressed. Besides that, in cases of SE we registered disorders of thinking and gnosis.

Detected expression of cognitive defect was in the direct correlation with the duration of the disease and frequency of seizures. It should be noted, that in the patients with IE correlation dependence was average ($r = +0.68$), while in the patients with SE it was weak ($r = +0.271$).

The terms of therapy using anticonvulsants were different: from 0 to 5 years of therapy in 128 patients (48.5%), from 5 to 15 years in 103 patients (39.0%), more than 15 years in 33 patients (12.5%). Duration of the therapy of the patients with IE in the majority of the cases was more than 5 years 61.8%, while in the cases of SE from 0 to 5 years (51.2%). We revealed correlation link with duration of the disease and expression of cognitive disorders.

Thus, the achieved results of the study showed that cognitive disorders together with convulsive seizures were one of the leading clinical symptoms of the various forms of epilepsy.

In the system of objective evaluation methods for cognitive disorders, the most adequate for the modern time are neurophysiologic strategies providing reliable and objective evaluation of the status of cerebral systems, and particularly study of P300 [7].

The data of cognitive induced potentials (CIP) were analyzed among 72 patients with epilepsy, and thirty-eight of them had SE and thirty-four — IE. The control group involved 20 healthy people, with corresponding age and sex.

With the help of the achieved data we could reveal heterogeneous severity and quality characteristics of alterations. In the study of LP P3, in compliance with the data

achieved by us, reliable differences between the values of the control group and the type of epilepsy were determined ($P < 0.01$).

We observed reliable rise of that value in the patients with epilepsy in comparison with the values of the control group ($P < 0.05$). Besides that we registered reliable rise of P3 in the patients with SE to 18.5 ms in the C3 lead and to 20.2 ms in C4 lead ($P < 0.05$).

There was no reliable difference in the values of N2-P3 interval in the patients with epilepsy compared with the control group.

For the calculation of ACIP amplitude we summed up the values of N2 and P3 amplitude from isoline. It was linked with the fact, that sometimes it is difficult to determine isoline for each peak because of instability of the registered impulse. As a result in the cases of IE we revealed slight emotional, regulation disorders, reflecting dysfunction of cortical-subcortical structures. It was displayed by the absence of clear inter-hemisphere asymmetry of P300 amplitude. Patients with SE showed more significant disorders, characterized by the absence of inter-hemisphere asymmetry of P300 amplitude and reliable increase of P300 latent period.

Thus, patients with epilepsy had neural physiological values of cognitive induced potentials which objectively reflected the status of the highest cerebral functions. In cases of IE and SE we revealed absence of inter-hemisphere asymmetry of P300 amplitude indicating dysfunctional disorders. The values of the P300 latent period increased in cases of SE, different from IE, and reflect inhibition of cognitive processes.

Expressed decrease of P300 amplitude, which we had detected, inversely correlating with a significantly increased latent period, reflects deficiency of limbic-reticular impact regulation, leading to misbalance of cortical-subcortical relationships, and as a result of which sufficient level of cortex activation compulsory for optimal processing of perceived information and salvation of cognitive problems is not provided.

Conclusions:

1. The character and degree of cognitive deficit expression in the patients with epilepsy depend on the form and duration of the disease. It was established that the most expressed cognitive deficit in the form of cognitive disorders was characteristic for the patients with symptomatic epilepsy.

2. In the patients with epilepsy neurophysiologic values of cognitive induced potentials objectively reflect the status of the highest cerebral functions. In cases of idiopathic and symptomatic forms we revealed absence of inter-hemisphere asymmetry of P300 wave amplitude, indicating functional disorders. Values of P300 latent period were increased in the cases of symptomatic epilepsy, different from idiopathic one, and reflected inhibition of cognitive processes.

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The diffusion weighted magnetic resonance imaging in diagnostics of symptomatic epilepsy in children

Abstract: In this article the possibilities of MR diffusion weighted imaging in symptomatic epilepsy patients have been presented. We determined the quantitative standards of numerical values of diffusion of white matter in children with symptomatic epilepsy of various etiology. The regions with abnormal white matter FA and ADC values not only matched to limbic circle zones, but also to areas of intra- and interhemispheric connections uniting the frontal, temporal, parietal and occipital lobes of the brain. Determining the specific clusters of brain tracts in symptomatic epilepsy, regardless of etiology, is important to predict the prognosis of the disease and the likely possibility of cognitive impairment. The study proved that symptomatic epilepsy is characterized by a variety of changes in the white matter of the brain tracts that lead to the dissociation of certain regions of the brain, interrupting connections between cortical and subcortical regions and inhibiting transfer of information. It can be concluded, that diffusion-weighted imaging are much more sensitive to the structural and metabolic changes occurring in the brain, in comparison with conventional MRI images.

Keywords: Symptomatic epilepsy, MR diffusion, Fractional anisotropy, Average diffusion capacity.

Introduction

In vivo visualization of structural morphological changes of the brain in patients with epilepsy and epileptic syndromes, has been made possible due to the introduction into daily medical practice of neuroradiologist diagnostic methods of research aspects such as: computed tomography and magnetic resonance imaging (CT and MRI) that are classified as “structural” neuroimaging techniques [1, 21–26]. The introduction of MRI in clinical practice has greatly expanded the identification of various structural changes in the brain tissue underlying the formation of the epileptic focus, which usually leads to the subsequent development of epilepsy. MRI allows radiologists to identify of malformations such as lencephaly, periventricular heterotopy, shizencephaly, a focal cortical dysplasia and other brain anomalies [2, 33–39]. But epilepsy do not always manifest on the background of congenital abnormalities of the brain, particularly if they are not localized in the cortical regions of brain. Congenital disorders of brain has a major part in

epilepsy origin, which manifest themselves in early periods of childhood [10, 353–361].

However, in practical medicine, it is not always possible to determine what is the basis of locally-induced epilepsy. Conventional MRI provides information about structural changes not in all cases [5, 95–97]. In this regard, at modern neuroradiology, it became necessary to use functional neuroimaging techniques that allow not only in vivo study the pathological changes of different brain structures, but also capable to clarify some of the mechanisms of epileptogenesis. These methods include diffusion tensor MRI tractography, which is the technology of the future to obtain morphological images of brain.

Diffusion imaging is an MRI method that produces in vivo magnetic resonance images of biological tissues sensitized with the local characteristics of molecular diffusion, generally water (but other molecules can also be investigated using MR spectroscopic approaches) [8, 719]. Diffusion-weighted images are much more sensitive to the structural and metabolic