Cognitive Deficit in Epilepsy: Experimental Research

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Abstract: The study involved 141 patients with idiopathic epilepsy at the age of 15 to 55 years. The patients were under continuous clinical and neurological observation for 3 years and underwent clinical examination, computer tomography (CT), magnetic resonance imiging (MRI), and electroencephalographic (EEG) monitoring. They also were examined for the higher mental and cognitive function and emotional response. A predominant cognitive deficit with a prevalence of memory, attention and thinking impairments, often accompanied by affective disorders, were revealed during the research. The evident relation between cognitive deficit and the nature of the seizures and their frequency was found. This is unfavorable prognostic factor and criterion indicating the demand of a differentiated approach to anti-epileptic therapy.
[Duchshanova G.A., Chumakov S.A., Zulficarova E.T., Tuksanbayeva G.U. **Cognitive Deficit in Epilepsy: Experimental Research.** *Life Sci J* 2013;10(4):3387-3392] (ISSN:1097-8135). http://www.lifesciencesite.com. 450

Keywords: Epilepsy, cognitive, deficit, affective, memory, thinking, attention.

1. Introduction

Epilepsy is one of the most common nervous system diseases. According to statistics of a number of European countries, the incidence rate of epilepsy is 50-70 cases per 100,000 population per year, prevalence rate equals 10-5 per 1,000 population. There are at least 30 million patients with epilepsy worldwide. The incidence is highest in children and the elderly people. About 5% of the population once in their lifetime (or sometimes more) suffered from epilepsy seizures [1]. The suddenness of epileptic seizures, evident impairments of consciousness and vital functions, as well as their association with severe organic pathology makes epilepsy highly disabling disease and cause high stigmatization of epileptics in the society [2]. The significance of the problem is determined by chronically progredient course of disease that leads to psycho-emotional and intellectual-mental changes, significantly disrupting social adaptation and quality of life of diseased people [3, 4, 5]. Epilepsy curing feature is the need for long-term, sometimes lifelong receiving of anti-epileptic drugs (AEDs) that may lead to side effects and complications [6, 7]. The successes of present-day Epileptology allow one to attribute the epilepsy to curable diseases [8]. Rational anti-epileptic therapy makes it possible to achieve significant results. Important is the impact of antiepileptic drugs on patients' cognitive functions and behavior. In these cases the choice of the drug should be based on its maximum potential efficacy and safety with respect to the possible negative impact on cognitive functions [9, 10]. Clinical course of epilepsy patients is often accompanied by the development of cognitive and behavioral impairment that negatively affect the success of their work and social adaptation and, ultimately, leads to a decrease in quality of life. Pathological changes, revealed by functional MRI, are associated with the pathology of certain neuronal substrates that explains the development of cognitive impairment in epilepsy [11, 12].

The research objective is to study the features of the higher mental and cognitive functions in patients with idiopathic epilepsy.

2. Materials and methods. The present study is based on the results of the trials of 141 patients with idiopathic epilepsy at the age of 15 to 55 years, who were under continuous clinical and neurological observation for 3 years.

Exclusionary criteria: symptomatic and cryptogenic epilepsy, psychotic course of epilepsy, and mental subnormality.

Diagnostication of the disease, the nature and forms of seizures were carried out in accordance with the criteria of the "International classification of epilepsy, epileptic syndromes and similar diseases" (New-Delhi, 1989) and "Classification of epileptic seizures" (Kyoto, 1981).

The studies were conducted in comparative perspective with the control group, which consisted of 45 patients (20 men and 25 women) comparable on the basic parameters.

A clinical study of patients included the following: a detailed analysis of complaints, anamnesis, seizures nature and frequency, disease duration and nature, curing effectiveness, and compliance with antiepileptic drug therapy. In addition, the evaluations of somatic, clinical, neurological, and mental statuses were carried out, as well as electrophysiological and neuroimaging (CT/MRI) studies of the cerebrum. For the study of bioelectric activity of neurons in the cerebrum,

electroencephalography (EEG) with exercise tolerance test (photostimulation, hyperventilation) and video-EEG monitoring were performed.

All patients underwent a special neuropsychological study, based on A.R. Luria methods, which enabled to assess the status of higher mental functions.

Neuropsychological methods included a series of tests to study praxis, gnosis, memory, and the peculiarities of patients' ability to programe and monitor their own behavior, the study of indicators of non-specific features of mental processes, such as the mental alertness, task performance, exhaustion, the mobility of nervous processes, and the mentality. The study of emotional response and behavior was conducted using standardized Spielberger - Hanin test methods (Situation/TraiAnxietInventory, STAI, 1970.) .

3. Research results and discussion. According to the level of education, the patients were distributed as follows: out of 141 patients, 25 people (17.7%) had higher education, 37 (26.2%) – undergraduate education, 43 (30.5%) – vocational secondary education, 28 (19.8%) – secondary-level education, and 8 (5.7%) – incomplete secondary education, i.e. patients with undergraduate education and vocational secondary education accounted for the majority – 80 people (56.7%).

The disease of the majority of patients on the record was characterized by various manifestations: the number of patients with monomorphic epilepsy seizures was by 16.4% greater than that for the patients with polymorphic seizures (58.2% and 41.8%, respectively). Simple or complex partial seizures and generalized convulsive seizures prevailed among monomorphic seizures; at that, the latter occurred or became more frequent under the influence of precipitating factors (stress, alcohol, dream deprivation, the cessation of AEDs administration, etc.).

Simple and complex partial seizures were observed in 12.0% of patients. Among them 6.3% of simple seizures were accompanied by somatosensorial and somatomotor impairments without generalization, with a saved mentality; the simple seizures of remaining patients were held in the form of affective disorders with uprush of fear. The patients with complex partial seizures often manifested vestibular aura, vegetal-vestibular aura, or vegetal-viscerogenic aura before the seizure. Generalized convulsive seizures were observed in 124 (88%) patients. After the seizures, 5% of patients showed aggression, fear, and anxiety, always accompanied by emotional pain (Fig. 1).

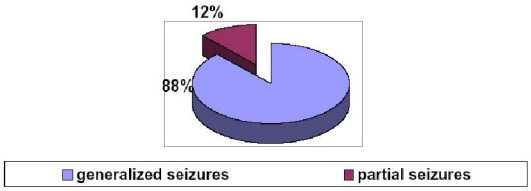

Figure 1. Clinical forms of seizures.

When analyzing seizures frequency, it was observed that frequent seizures (1 or more per week) where observed in 40.4% of cases. Among them frequency of up to 4 seizures a week was observed in 24.8% of cases, while daily seizures were observed in 15.6% of cases. Medium frequency seizures (1-3 times per month) were observed in 71 patients (50.3%), whereas rare seizures (1-2 times per year) were observed in 13 patients (9.2 %).

Dream period was the most common time of seizures for 74 patients (52.4%), while seizures in wake period were observed in 43 (30.4%) patients, who mostly showed partial and generalized seizures. The generalized seizures were dominating during the dream-wake period in 24 patients (17.0%). It should be noted that partial (simple and complex) seizures dominated during the dream period, partial or generalized seizures occurred during wake period, and the generalized seizures occurred mainly during the dream-wake period (Fig. 2).

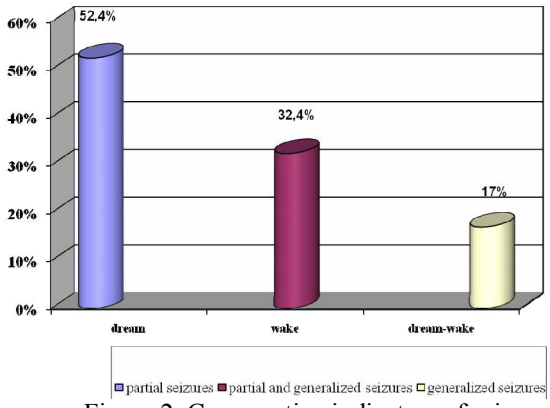

Figure 2. Comparative indicators of seizures in various forms of epilepsy in the dream-wake cycle (%).

The duration of the disease of 68 (48.2%) patients was mainly 6-10 years, whereas 24.8% of patients were diagnosed epilepsy during a period of 5 years.

The clinical signs of focal cerebrum lesions in majority of patients (85- 60.3%) with both partial and generalized seizures either lacked, or manifested individual stigmas or scattered microfocal neurological symptoms.

The clinical picture was dominated by vegetative and vegetative-visceral disturbances that manifested by faintness, fluctuations in blood pressure, vascular lability, increased dermographism of vagotonic or mixed types. Only 27 patients (19.1%) with complex partial, concomitant partial and generalized seizures manifested moderately. This pathology signs of the oculomotor nerve, trochlear nerve, trigeminal nerve, and abducens cranial nerve in the form of a medial or divergent strabismus, impaired convergence of eyeballs and adaptation of pupillary response, hyperreflexia of tendon and periosteal reflexes, expansion of their reflex zones, the presence of not pronounced pathologic plantar muscle reflexes, and oral automatism reflexes. In half of the cases they were combined with the facial and hypoglossal nerves disorders of the central type, and sense shock of encephalitic conduction type. Ten patients (7.0%) with partial type seizures showed pathology of VIII cranial nerve, which was manifested in loss of hearing, mixed horizontal and rotatory nystagmus, and rotatory vertigo. Impaired coordination in the form of static and dynamic ataxia was found in 9 patients (6.4%) with generalized seizure types (Table 1).

Table 1. Major neurological syndromes in patients with epilepsy in the interictal period.

Symptoms (syndromes)	Absolut.	%
Scattered microfocal symptoms and vegetal disturbances	85	63.3
Pathology of the cranial nerves	37	26.1
Impaired coordination symptoms	9	6.4

Note that, rough neurological deficit, associated with epilepsy, was not identified when analyzing the nature of the neurological manifestations. Neurological symptoms were diagnosed in nearly 70% of patients with both partial and generalized types of seizures. The main neurological manifestation is a scattered microfocal cerebral affection syndrome, combined in certain cases with moderate signs of the cranial nerves dysfunction. The appearance of neurological symptoms in the setting of existing epilepsy is probably due to deposit of intercurrent diseases or complication of epileptic seizures, or evolution of epileptic status, and, consequently, the formation of ischemia focuses in the brain parenchyma.

Electroencephalographic studies were conducted over time to all patients. EEG changes were observed in 127 patients (90.0%), epileptic activity was detected in 64 patients (45.3%) with repeated numerous records. When carrying out electroencephalographic monitoring in the interictal period, epileptic electrical activity (adnations, sharp waves, spike-and-wave or sharp-slow wave combinations) was observed in 78 patients (55.3%).

The focal epileptic activity was recorded in 57 (40.4%) patients, mainly in the frontal region - 31 (21.9%), fronto-temporal lobe - 17 (12.0%), and the temporoparietal region - 9 (6.3%). Bitemporal focal activity was observed in 33 (23.3%) patients (Fig.3). The comparative clinical analysis of the patients of this subgroup (with ambilateral epileptic activity) suggests formation of bitemporal epileptic foci in the patients' cerebrum, mainly in cases, where a medical history revealed the presence of neuroinfections and repeated traumatic brain injuries suffered by the patients in childhood. At the longer duration of the disease (over 6 years) and the prevalence in the clinical presentation of generalized seizures with a characteristic evolution, when in the debut both simple and complex partial seizures with aura and secondary generalization were observed, the evolution of the seizures occurs subsequently with the loss of aura sensation and a gradual removal of focal component in the seizures, which were mostly generalized.

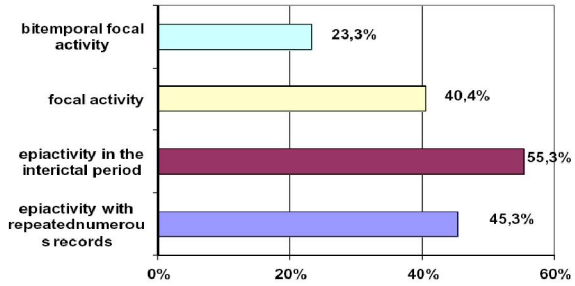

Figure 3. Epiactivity options.

During the neuroimaging study (CT, MRI) the patients with different types of epileptic seizures showed lesions mainly in the form of diffuse changes of the brain substance in the frontal-temporal leads, expansion of subarachnoid clefts, sulcuses, signs of atrophy or sclerotic changes of the hippocampal region, botryoid expansion of cerebrospinal fluid space of the anterior mediobasal part of the temporal lobe, cystic and scars lesions with the expansion of the lateral ventricles of the cerebrum, subarachnoid spaces, or the formation of a single or multiple cyst encapsulations.

The absence of neuroimaging changes was detected in 17.7% of patients. Coincidence of found cerebral affection lesions and clinical symptoms has occurred in patients with symptomatic epilepsy.

The variety of neuroimaging phenomena and their combination in the conducted research allowed

one to determine the relationship of the brain substance lesions with clinical implications and neurological disorders.

The cognitive functions are commonly understood in modern neuroscience as the most complex cerebrum functions that allow for rational perception of the world. These include memory, attention, sensation (gnosis), motor skills (praxis), language behavior, and analytical abilities (executive function).

In the course of neuropsychological studies, we noted that in general, cognitive impairment occurred in 132 (93.6%) patients. At that, moderately pronounced and slight changes of memory, attention, and thinking were dominated. Among them, the mild imparaments were found in 74 (56.0%) patients, moderately pronounced impairments – in 43 (32.5%) patients, and the pronounced impairments – in 15 cases (11.4%) (Fig. 4).

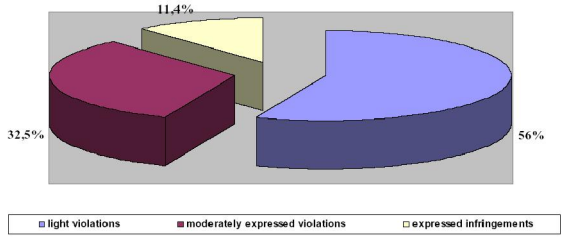

Figure 4. Structure of cognitive disorders in patients with epilepsy, %.

Disorder of mnestic activity was a leading impairment of the higher mental functions in more than 90% cases. Mnestic functions, such as attention and thinking, were impaired in patients with frequent seizures, differing by nature of paroxysmal states. We revealed the correlation of the reduction of mnestic functions and thinking with the seizures types. Complex partial and polymorphic seizures have a great impact on the hypomnesia, attention, and thinking.

Changes in memory were observed in the most of the patients - 132 (93.6%). The repeated studies of the remaining 9 (6.3%) patients did not show any memory impairment. At the beginning of the study before anti-epileptic therapy, 74 (56.0%) patients had mild impairments, 43 (32.5%) patients showed moderately pronounced changes in memory, 15 (11.4%) cases revealed pronounced changes in memory. When studying mnestic functions by memory recall of ten words, the memorization productivity in patients with moderately pronounced impairment was 6.2±2.1 words, in patients with pronounced memory impairment - 5.6±2.0 words as compared with the control group. When studying long-term memory in delayed reproduction of the words after 60 minutes in comparison with the control group, 37 (27.9%) patients out of 43 patients reproduced 5.3 ± 2.0 words, and 52.2 % of the patients – 4.4 ± 1.5 words.

Perseverations and contaminations were another feature of memory disorders in patients with epilepsy. Perseverations occurred in 62 (46.9%) cases, when the patient insensibly reproduced repeatedly the same word. Contamination of incentives at memorizing of 10 words was observed in 51 (38.6%) patients.

Insufficient mental alertness was detected in 72 (54.5%) patients, who spent time on the assignment exceeding the standard time. At that, 45 (34.0%) patients had a span of attention, which was manifested in significant fluctuation of results without trend towards improvement.

The combination of impaired attention and tiredness resulted in increase of number of errors in each successive test stage in 15 (11.4%) patients (Fig. 5).

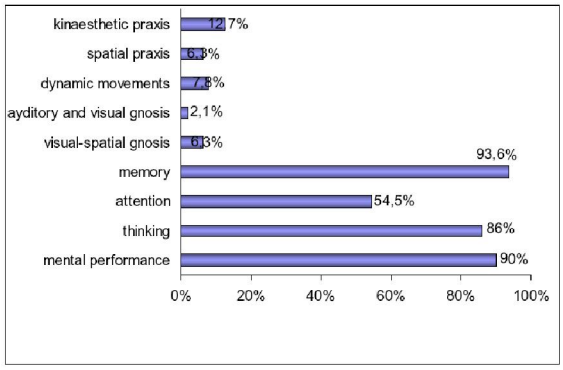

Figure 5. Characteristics of diminution of cerebral competence in patients with epilepsy, (%).

Almost 90% of the cases showed a reduction of the activation and time-varying parameters of activity (1st cerebral block) in the form of reduced mental capacity and rapid tiredness.

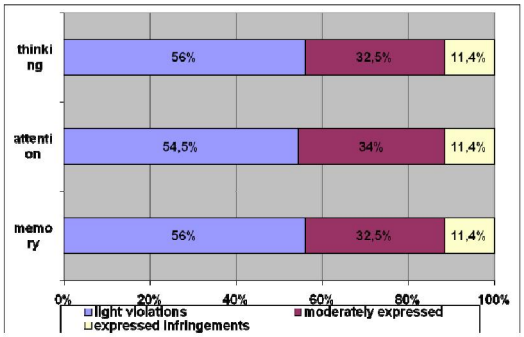

Figure 6. Cognitive function indicators in patients with epilepsy, (%).

Changes in thinking were detected in parallel with the changes in memory (Fig.6). At that, 74 (56.0%) patients had mild impairment of thinking, which manifested as slower pace of intellectual process, decreased reasoning ability, a violation of logical links between concepts and sequences of events. Moderate version of disturbances in cogitativity occurred in 43 (32.5%) patients, while pronounced thinking infringements have been identified in 15 (11.4%) patients. The latter were manifested in inability of the patients to immediately realize the situation, depicted in the picture, to make a visual synthesis, and to differentiate significant and minor details (Table 2).

Table 2. The severity of cognitive impairments in patients with epilepsy.

The severity of cognitive impairments	Memory		Attention		Thinking	
	Abs.	%	Abs.	%	Abs.	%
Mild impairments	74	56.0	72	54.5	74	56.0
Moderately pronounced impairments	43	32.5	45	34.0	43	32.5
Pronounced impairments	15	11.4	15	11.4	15	11.4
Total	132	99.9	132	99.9	132	99.9

Emotional turmoil was detected in 135 (93.1%) patients with different types of seizures in the interictal period. This manifested in diminution of active inhibition, increased distraction, weakness, high sensitivity to external stimuli, accompanied by general hyperesthesia, dream disorders, vegetal changes in the form of blood pressure asymmetry, body temperature, increased heart rate at slow breathing, or vice versa.

Insane violations in form of depressive disorders, mixt anxiety and depressive disorders, and hypochondriacal disorders were found in 97 (68.7%) patients, of which in the prodromal period of seizure affective disorders were observed in 28 (19.8%) patients, in the post seizure period – in 17 (12.0%) patients, and in the interictal period – in 52 (36.8%) patients.

Depressive disorders were noted in 26 (18.4%) patients, whose condition was characterized by depressed and melancholic mood, apathy, adynamia, and anxious feeling. Hypochondriacal depression was diagnosed in 55 (38.9%) patients.

Mixt anxiety and depressive disorders, as well as hypochondriacal disorders, manifested in 16 (11.3%) patients in the form of apprehension, unmotivated fears of their own health and health of their relatives, anxiety, and experience were extended to the broad scope of psychopathologic manifestations and gathered peculiar interpretation of abnormal esthesia (Fig.7).

Anxious feeling was noted almost in all the seizures components, beginning with precursor of the aura, the seizure, and after the seizure, in which the anxiety manifested most often as a component element.

In 17.7% of patients, short episodes of dysphoria often were preceded the epileptic seizure; normally, their duration did not exceed a few hours or days.

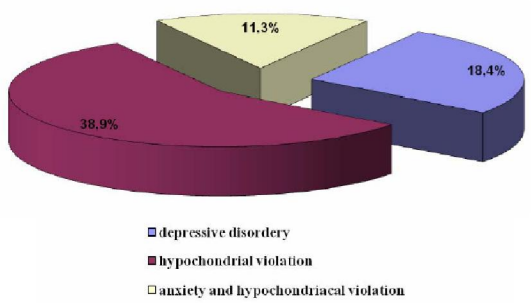

Figure 7. Types of insane violations in patients with epilepsy, (%).

Analysis of the results of the higher mental functions identified certain patterns depending on the presence of neurological symptoms. More pronounced changes in thinking, memory, and mentality were observed also in 70% of the patients with diagnosed neurological symptoms. Thus, among 26.9% of patients with partial and secondarily generalized seizures, confirmed in EEG by focal epileptic activity, mild impairments of kinetic praxis were observed in 12.7% of patients; the light changes in motor acts dynamics were detected in 7.8% of patients; 6.3% of patients manifested minor impairments of the visual-spatial organization of motor acts. Also, minor changes in the auditory gnosis were detected in 2.1% of patients, and visual-spatial gnosis - in 6.3% of patients.

In the process of neuropsychological research it was found that in 68.7% of epileptic patients with affective disorders in form of depressive, hypochondric, mixt anxiety, and depressive dysphoria, hypochondriacal disorder prevailed in the interictal period. Such changes do not imply an irreversible epileptic defect and depend on the biological and social factors. Their compensation through remedial measures and rehabilitation actions has an impact on the course of disease.

Memory impairment was the most frequent diminution of cerebral competence in more than 90% of patients. To a greater degree, a mnestic functions, attention, and thinking were impaired in patients with frequent seizures, differing in nature of paroxysmal states. We have identified the correlation between cognitive decline and the types of seizures. Complex

partial or polymorphic seizures are combined with more pronounced cognitive deficit.

4. Conclusions

The pathology of higher mental functions in epilepsy is characterized mainly by cognitive deficit with dominated memory impairments, alterations of attention and thinking, often accompanied by affective disorders, which testifies on the dysfunction of the 1st structural and functional block of the cerebrum.

Analysis of a cognitive functions level of patients with epilepsy is an objective criterion in assessing the severity of the disease; the growth of cognitive deficit is an unfavorable prognostic criteria.

The severity of cognitive deficit depends on the frequency and nature of seizures; frequent complex partial and polymorphic seizures are accompanied by more severe cognitive impairment that is confirmed by electroencephalographic monitoring.

Assessment of the cognitive function dynamics is an important component in differentiated therapeutic approach of patients with epilepsy and in the prescription of an adequate anti-epileptic product group. It should be taken into account in the outpatient care in health care institutions.

Acknowledgement

The study was conducted in South Kazakhstan State Pharmaceutical Academy under the R&D grant funding program of the Ministry of Science and Education of the Republic of Kazakhstan.

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12/18/2013