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MODEL OF PERSONALIZED NON-PHARMACOLOGICAL PROGRAM OF COGNITIVE DISORDER CORRECTION IN PATIENTS WITH EPILEPSY AND THE ASSESSMENT OF ITS EFFICACY

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Abstract

Cognitive dysfunction shows higher incidence in people, suffering from epilepsy, than in general population and most likely they are related to common patho-biological processes. The use of medication in patients with epilepsy for treating cognitive functions is limited due to the potential risk of more frequent seizures. Therefore, non-pharmacological methods of cognitive correction are becoming especially important for this category of patients.

Aim. The aim of the research is to study the specifics of non-dementia cognitive disorders in patients with epilepsy and to develop a set of activities for their prevention and non-pharmacological correction.

Materials and methods. The study included 146 patients (61 women and 85 men), their average age was 40,73. We applied clinical anamnestic, sociodemographic, clinical-psychopathological, psycho-diagnostic and statistical research methods. The following psycho-diagnostic techniques were used: Montreal Cognitive Assessment (MoCA), Munsterberg test, MiniMult test, Hamilton depression and anxiety rating scales (HRDS, HARS) and the quality of life scale. 63 patients completed a 3-month computerized online

cognitive training with daily sessions, out of which 33 patients also participated in psychoeducational activities.

Results. The findings of studying patients with epilepsy using the Montreal Cognitive Assessment (MoCA) showed low levels of all parameters while the total score in the patients with epilepsy with cognitive non-dementia disorders was 20,72 versus 27,36 in healthy persons; the analysis of HRDS, HARS showed high anxiety and depression symptoms levels, lower quality of life level was also observed, the average indicator was 69,45, whereas in the control group the level of life quality was 78,60. There was marked adherence to cognitive training in the patients with epilepsy compared to the healthy group.

Conclusion. Reliable improvement of cognitive functioning was found in the patients under consideration after 3 months of the training. The computerized cognitive functions training in current conditions showed its benefits owing to the opportunity to complete it online. It may be advised to be introduced as a part of the social rehabilitation system for patients with epilepsy, who have cognitive non-dementia disorders.

Key words: epilepsy; cognitive training; computerized training; cognitive disorders.

Relevance. Epilepsy is one of the most common neurological diseases, which may be complicated with behavioral, cognitive and mental disorders. According to the statistic sources, currently some 65 million people suffer from epilepsy worldwide.

Mental disorders show higher incidence in people, suffering from epilepsy, than in general population, regardless of the time of seizures commencement; the latter appearing before or after the development of mental disorders, which implies their interrelations and potentially common etiology (Kanner AM, 2017; Salpekar JA, Mula M., 2019) [1, 2, 3].

The co-existence of mental disorders in patients with epilepsy is not merely a coincidence or common comorbidity, but it rather reflects interrelated pathobiological processes (Martsynkovskiy I.A., 2015; Helmstaedter C, Witt JA., 2017; Josephson CB et al., 2017; Bermeo-Ovalle A., 2019) [4, 5, 6, 7]. The recent trend shows obvious pathomorphosis of mental disorders alongside epilepsy, when the specific weight of psychoses has decreased significantly, whereas the number of epilepsy forms with non-psychotic disorders increased (Gromov S., Kissin M. et al., 2006; Maryenko L. Et al., 2014) [8, 9]. Despite the fact that the main manifestation of epilepsy is the availability of seizures, comorbid mental disorders are a bigger burden for patients and affect quality of their lives (Holmes GL., 2015) [10].

In 70-80% patients, chronic epilepsy is comorbid with cognitive disorders (Helmstaedter C, Witt JA, 2017) [5]. The development and manifestations of cognitive disorders comorbid with epilepsy are dependent on the disease etiology, localization and nature of cerebral damage, patients' age, the type and frequency of seizures, hereditary and psychosocial factors of the patients' environment, consequences of surgeries, as well as adverse effects of anti-epileptic drugs (Elger CE, Helmstaedter C, Kurthen M., 2004; Korostiy V. Et al., 2018; Karlov VA., 2019) [11, 12, 13].

Cognitive impairment is presented at earlier stages, before the diagnostics of epilepsy (Osler M et al., 2018) [14]. Another important fact to be identified is in the differences of ageing processes in patients with epilepsy, which may be accelerated due to the loss of the neuroplasticity and cognitive reserves, the so-called "accelerated cognitive ageing" (Breuer LE et al., 2016; Pardoe HR et al., 2017; Hwang G et al., 2020) [15, 16, 17].

The use of medication in patients with epilepsy for treating cognitive functions is limited due to the potential risk of more frequent seizures. Therefore, non-pharmacological methods of cognitive correction are becoming especially important for this category of patients.

The most effective non-pharmacological cognitive function correction methods are cognitive-behavioral therapy, diet, physical exercise, meditation, cognitive training and psychoeducational activities. Non-pharmacological correction methods can improve cognitive functions owing to the neuroplasticity – the ability of brain to change "physical" structure depending on the environment by reorganizing neural networks [18, 19]. Learning new things encourages maintaining already existing neural networks and the development of new ones, which is the prevention of cognitive disorder progression [20].

Cognitive training is carried out by applying special programs and techniques to training attention, memory, and other cognitive functions to support the optimal intellectual state, the development of cognitive skills, which are at the low level and teaching compensatory or renewal strategies.

The use of online platforms has been gaining popularity. Online methods have an additional therapeutic value for expanding patients' health-related abilities. For the patients with a high level of stigmatization or for those who consider their condition not severe enough for formal psychiatric treatment, distance interventions enable gradual mental health improvement. The application of online cognitive training is becoming especially relevant during quarantine restrictions. In this study, it was decided to consider the efficacy of

applying computerized online training and psychoeducational events in the patients with epilepsy.

Aim. The aim of the research is to study the specifics of non-dementia cognitive disorders in patients with epilepsy and to develop a set of activities for their prevention and non-pharmacological correction.

Materials and methods. We studied the specifics of clinical and psychopathological manifestations in patients with epilepsy. The study included 146 patients (61 women and 85 men), their average age was 40,73 (clinical group – CG). We applied clinical anamnestic, sociodemographic, involving the “questionnaire of social functioning and life of patients with epilepsy”, clinical-psychopathological, psycho-diagnostic and statistical research methods. The following psycho-diagnostic techniques were used: Montreal Cognitive Assessment (MOCA), Munsterberg test, MiniMult test, Hamilton depression and anxiety rating scales (HRDS, HARS) and the quality of life scale. The statistic processing of the collected data was performed using Student’s t-test, Mann–Whitney U-test, Kruskal–Wallis test, Wilcoxon signed-rank test, and Spearman's rank correlation coefficient. The differences were considered statistically significant under $p < 0,05$.

The research involved 3 consecutive stages. At the first stage, a cross-section study was carried out to identify socio-demographic indicators, specific clinical manifestations, availability of affective disorders, level of cognitive impairment, psychological features and the life quality of patients with epilepsy. The collected data were compared with the indicators of the control (healthy) group.

Out of 146 examined patients, the biggest group had secondary education – 56 (37,93%), incomplete secondary education – 31 (21,38%), and vocational education – 40 (27,59%), 11 (7,59) patients went to a specialized school, only 8 (5,52%) patients had higher and incomplete higher education, which is related to the fact that most of them were from rural areas 108 (73,97%).

According to the gender, age and clinical indicators under analysis, all the research groups did not show any statistically significant differences ($p < 0,05$).

Results. Clinical-psychopathological specifics of the patients, suffering from epilepsy, are represented by thought, memory and attention disorders. They typically show circumstantial, “sticky” and detailed thinking. Generalization level was low, difficulties with distinguishing between the primary and secondary things were observed. It was hard for the patients to switch over from one topic to another, anchoring on secondary details was common.

Mnemonic disorders in patients with epilepsy are in their low ability to acquire, keep and reproduce new information. This category of patients is characterized by impaired memory of recent and remote events, accompanied with the inertia of mental processes.

Patients are easily affected, become irritated, need special politeness and correctness in communication, while others, vice versa, flattered communicating with the doctor.

The cognitive disorder assessment was carried out using the Montreal Cognitive Assessment (MoCA). According to the collected results, clinical group patients showed executive function level lowered by 1,72, with Mann–Whitney U-test reliability of $p < 0,001$, considerable decrease was observed in a series of subtraction – by 2,78, with Mann–Whitney U-test reliability of $p < 0,001$, attention indicators were lower by 0,59, with Mann–Whitney U-test reliability of $p < 0,001$ and significant impairment of delayed reproduction was observed – by 1,12 with Mann–Whitney U-test reliability of $p < 0,001$. The total score of the cognitive function assessment in the patients with epilepsy was 20,72 versus 27,36 among the healthy persons, the difference was 6,64, with Mann–Whitney U-test reliability of $< 0,001$. The findings are given in diagram 1.

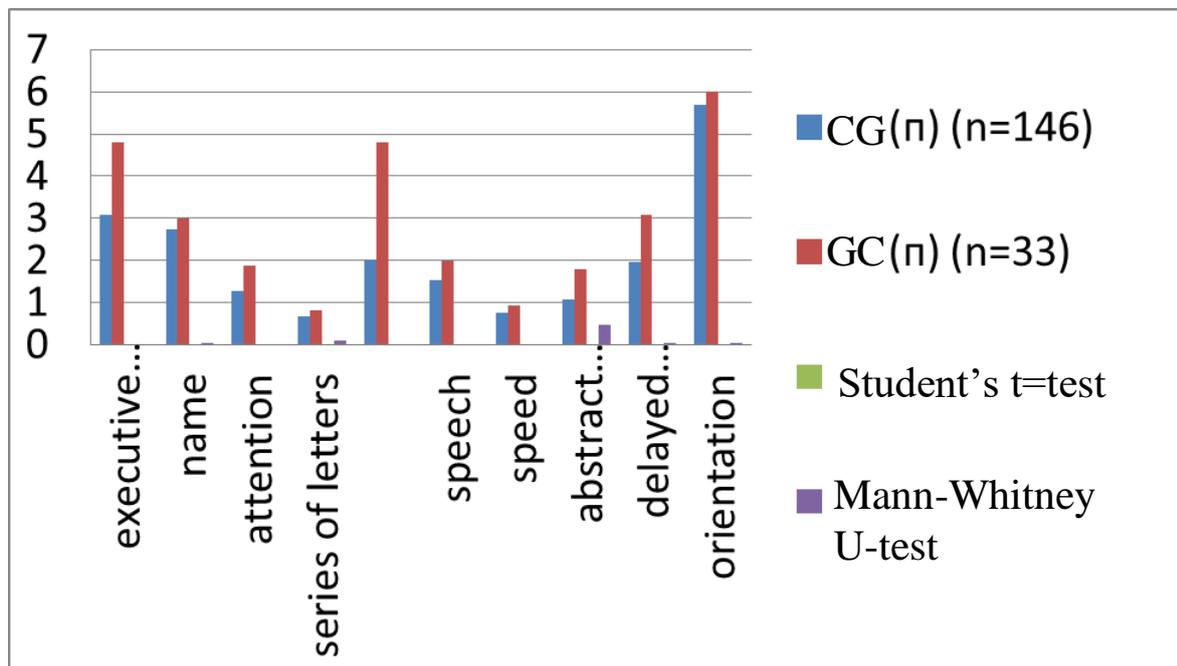


Diagram 1. The findings of cognitive functions assessment in CG and control by individual MoCA test indicators

The study of attention selectivity was performed using Munsterberg test, where only 9 examined patients (6,16%) showed normal indicators, 35 (23,97%) patients refused from the

test while the rest – 102 (69,87%) had low test indicators. The total score in the clinical group was 7,72, which is 13,28 lower than that in the control group, where the attention selectivity indicator was 21, with Mann–Whitney U-test reliability of $p < 0,001$.

The availability of affective disorders was examined using clinical Hamilton depression and anxiety rating scales (HRDS, HARS). Average depression indicators in the clinical group were 7,14, which is 3,33 higher, than in the control group – 3,81, with Mann–Whitney U-test reliability of $p < 0,001$. According to the test results, mild depression was found in 34 (23,29%) patients with epilepsy, moderate depression – in 4 patients (2,74%), severe – in 2 patients (1,37%), highly severe – in 1 (0,68) patient.

Average anxiety indicators in the clinical group were 14,17, which is 3,84 higher than those in healthy persons, whose average anxiety level was 10,33, with Mann–Whitney U-test reliability of $p < 0,001$. Moderate anxiety level was identified in 10 patients (6,85%), high – in 17 patients (11,64%).

According to the Hamilton anxiety rating scale (HARS), 11,64% patients had high anxiety rate, 6,85% - moderate anxiety rate. According to the Hamilton depression rating scale (HDRS): 28% - had depressive symptoms: 23,29% - mild depression, 2,74% - moderate depression, 0,68% - severe depressive signs. The test results are shown in diagram 2.

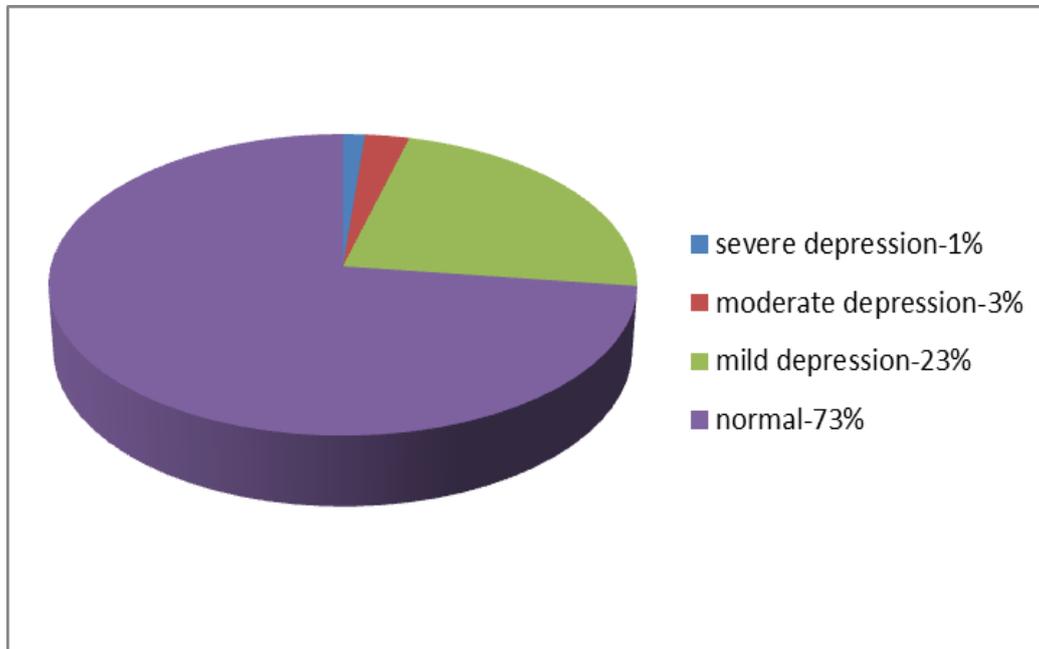


Diagram 2. HDRS rating scale assessment results.

The decrease in the quality of life was found in the clinical group, where the average score was 69,45, while in the control group the life quality rate was 78,60. Thus, the

difference was 9,15, which is significant and reliable (Student's t-test 0,001, Mann-Whitney U-test - 0,002). The life quality in patients with epilepsy is lower than in healthy persons, which is explained by the factors of epileptic disease impact, seizures, patients' lower functioning level, higher level of anxiety and depressive disorders, and cognitive impairment. The results are given in diagram 3.

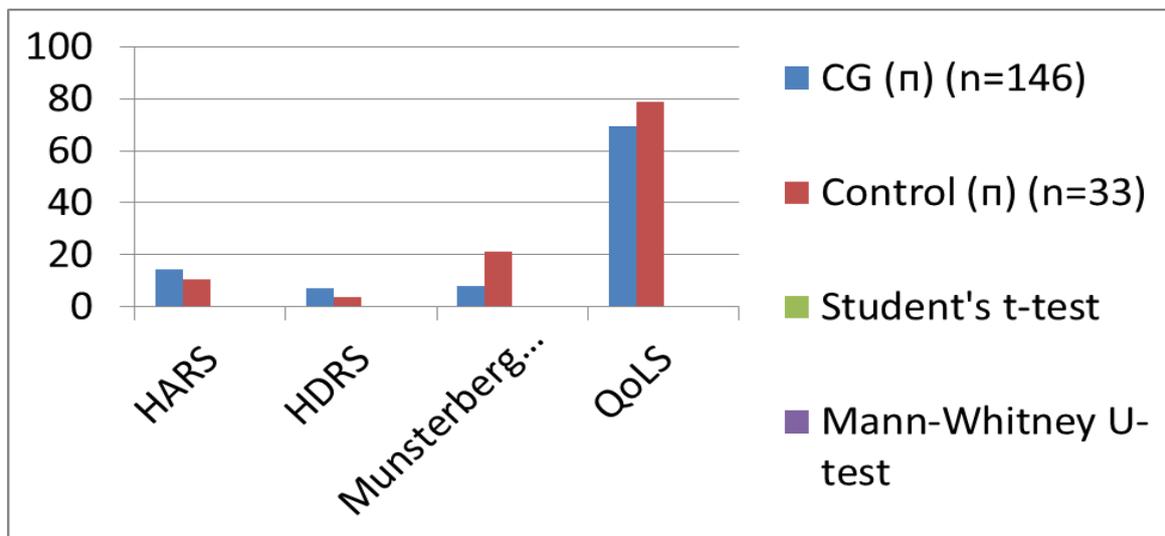


Diagram 3. Results of clinical and control group indicators assessment by HARS, HDRS, Munsterberg test and quality of life scale.

A significant part of the patients showed reduced social contacts and low social activity as well as limited personal mobility. Patients with epilepsy presented higher level of social disadaptation and prevailing subordinate position in their families. Most patients did not have any hobbies, showed low need of reading. Most patients were satisfied with their living conditions, but noted average or below average level of income. Patients with moderate cognitive impairment mainly showed groundlessly high subjective assessment of the quality of life. Low working capacity of the patients also affected the quality of their life.

At the second stage, 3 research groups were set up. They included 96 patients with present cognitive non-dementia level disorders, which included the patients with epilepsy and non-dementia level of cognitive impairment and a control group of healthy persons. Over three months patients of research group (RG) 1 competed a cognitive online training and psychoeducation alongside anticonvulsant therapy; patients of research group (RG) 2 competed a cognitive online training and anticonvulsant pharmacotherapy; the persons of the comparative group underwent basic therapy while healthy persons of the control group competed a cognitive online training.

A cognitive disorder pathogenetic model in patients with epilepsy was developed. It was proven that the factors of cognitive disorder development in patients with epilepsy was the lack or incompleteness of psychopharmacological remission, availability of the periods of frequent seizures in their anamnesis, low level of education, the abuse of alcohol and other psychoactive substances along with epilepsy pharmacotherapy.

Prognostically significant factors are low level of patient compliance, low level of life quality, lack of regular intellectual activities, high level of anxiety and depression under psycho-diagnostic scale tests. The grounds for cognitive disorders in patients with epilepsy are minimum brain neurological dysfunction and metabolic disorders.

At the third stage, control testing was carried out in the four groups under research (96 patients and 33 healthy persons) and the efficacy of applying cognitive training and psychoeducation was assessed in terms of patients' and health persons' cognitive functions and quality of life, anxiety and depression levels. The research design is shown in figure 1.

The study involved the development and testing of pathogenetic grounded personalized program of non-pharmacological correction of cognitive disorders in patients with epilepsy, which includes: individual program of computerized cognitive functions training with the monitoring of task performance and the dynamics of mental functioning, differentiated use of psychoeducational techniques, aimed at improving compliance and reduction of risk factors impact.

Following the results of the completed assessment of the efficacy of applying a 3-month computerized online training and a psychoeducational program, the effectiveness of the holistic application of psychoeducation was found. Patients of RG1 under the MoCA test results showed improved cognitive functions (1,4, $p<0,001$), better indicators of attention selectivity under Munsterberg test (0,63, $p<0,001$), lower anxiety levels under HARS (1,45, $p<0,001$), lower depression levels under HRDS (1,7, $p<0,001$) and higher subjective assessment of the quality of life (2,77, $p<0,05$). Patients of KII2, following the MoCA test results, showed improved cognitive functions (0,73, $p<0,001$), better indicators of attention selectivity under Munsterberg test (0,27, $p<0,05$), lower anxiety levels under HARS (4,27, $p<0,05$), lower depression levels under HRDS (2,32, $p<0,05$) and higher subjective assessment of the quality of life (1,21, $p<0,05$).

The MoCA test results of the patients from the comparison group showed lower cognitive functions (0,22, $p<0,05$), better indicators of attention selectivity under Munsterberg test (0,15, $p<0,05$), higher anxiety levels under HARS (2,61, $p<0,001$), lower depression levels

under HRDS (2,49, $p < 0,001$) and higher subjective assessment of the quality of life (1,0, $p < 0,05$).

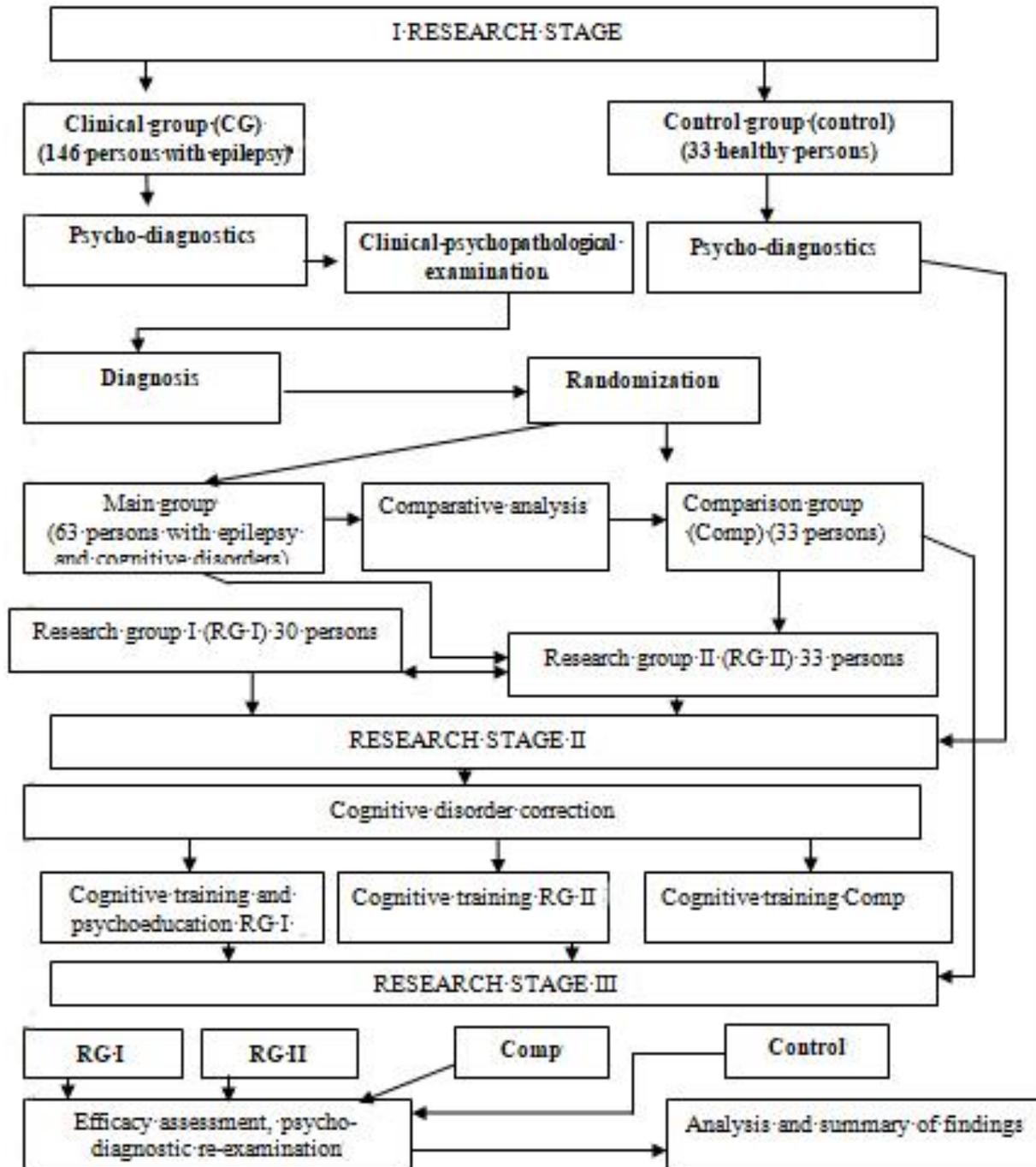


Fig. 1. Design and algorithm of research performance

The MoCA test results of the control group showed better cognitive functions (0,79, $p < 0,001$). The comparative analysis of the research groups before and after the correction is shown in diagrams 4, 5, and 6.

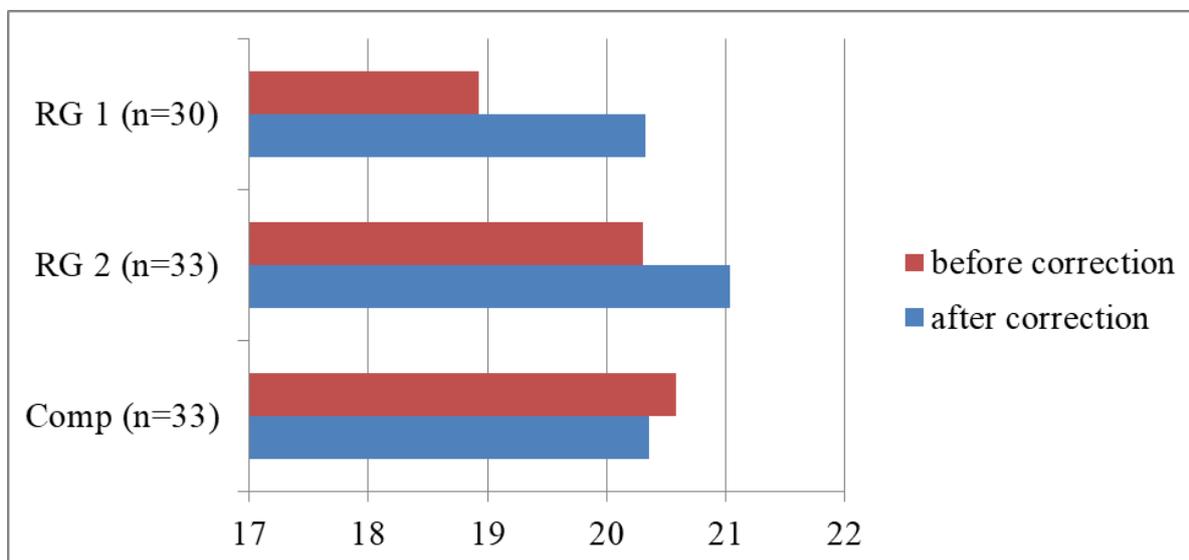


Diagram 4. Cognitive functioning level in research groups 1, 2 and the comparison group before and after the correction under MoCA test results.

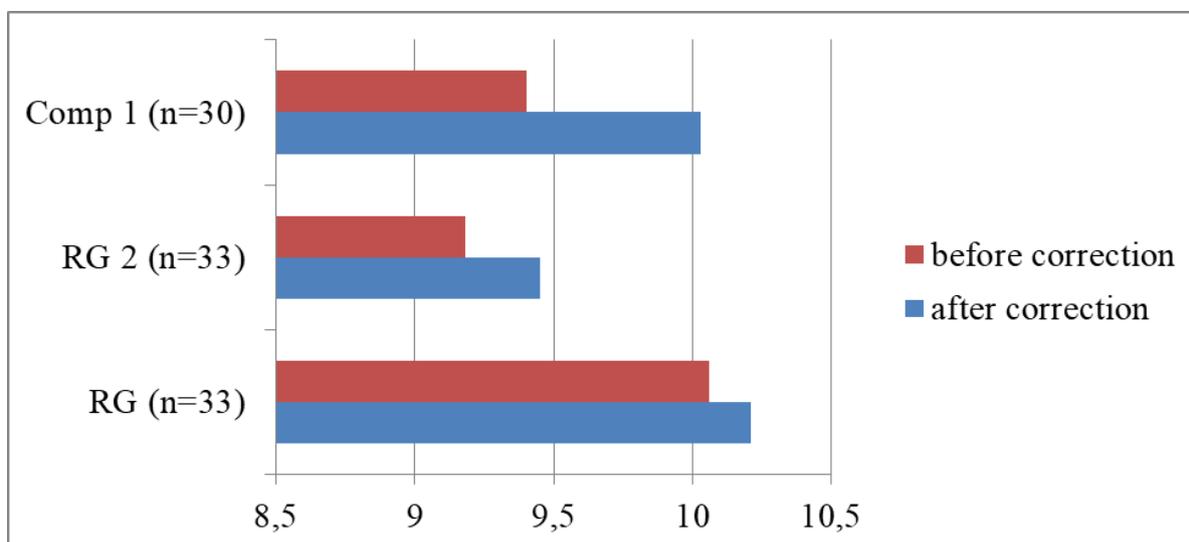


Diagram 5. Attention selectivity level in RG1, RG2 and comparison group before and after the correction *копекції* under Munsterberg test.

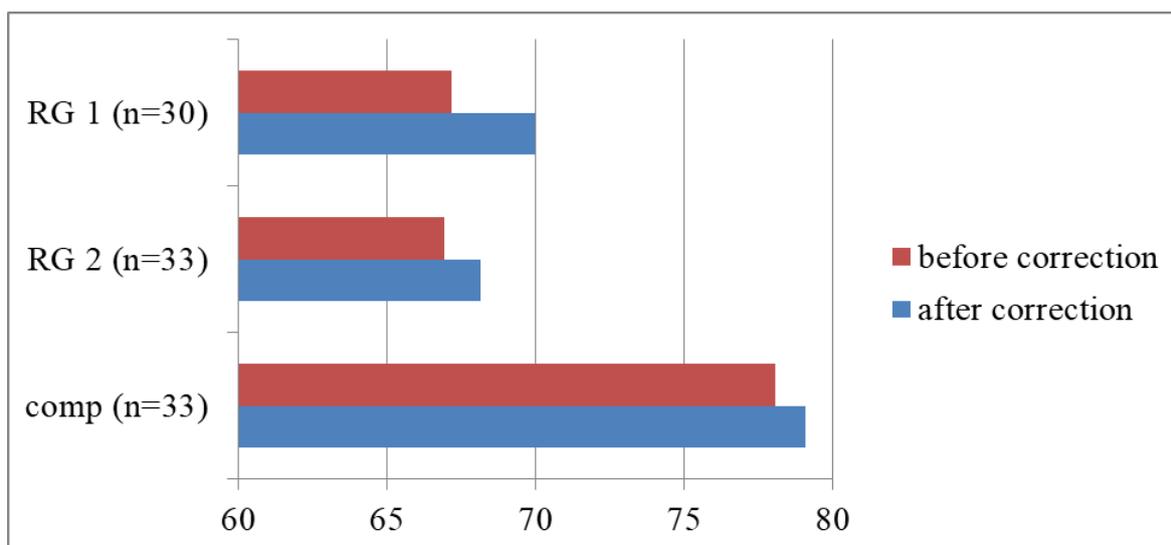


Diagram 6. The quality of life level in research groups 1, 2 and the comparison group before and after the correction.

Better routine compliance and interest in task performance were observed in the patients with epilepsy compared to healthy persons. The introduction of developed non-pharmacological correction of cognitive disorders in patients with epilepsy enables to inhibit the progression of cognitive disorders, and in case of mild cognitive disorders – improve cognitive functions, promotes better quality of life and the renewal of social functioning among patients with epilepsy.

Conclusion. Clinical-psychopathological specifics of the patients, suffering from epilepsy, are presented by the impairment of memory (for both recent and remote events), thinking (inertia of mental processes) and attention (its selectivity). The patients with epilepsy mostly showed expressed cognitive dysfunction (6,64, $p < 0,001$), high anxiety (3,84, $p < 0,05$) and depression levels (3,33, $p < 0,001$) compared to healthy persons. Cognitive dysfunction affects patients' social adaptation and the quality of their lives. The quality of life of the patients with epilepsy is lower than in healthy persons (9,15, $p < 0,05$). Patients with epilepsy presented a lower level of social adaptation and prevailing subordinate position in the family. A significant part of the patients showed lower level of social contacts and low social activity. The factors of cognitive disorder development in patients with epilepsy are the lack or incompleteness of psychopharmacological remission, availability of the periods of frequent seizures in their anamnesis, low level of education, the abuse of alcohol and other

psychoactive substances along with epilepsy pharmacotherapy. The collected data enabled us to develop a pathogenetic model of cognitive disorders formation in patients with epilepsy.

According to the above model, a pathogenetic grounded personalized program of non-pharmacological correction of cognitive disorders in patients with epilepsy was developed and tested. It includes individual computerized cognitive functions training with the monitoring of task performance and the dynamics of mental functions, differentiating use of psychoeducational techniques, aimed at the improvement of compliance and the reduction of risk factor impact. The program test findings in the research category of patients showed reliable improvement of their cognitive functioning level after a 3-month training. The computerized cognitive functions training in current conditions showed its benefits owing to the opportunity to complete it online, and it is advised to be introduced as a part of the social rehabilitation system for patients with epilepsy, who have cognitive non-dementia disorders. The introduction of the developed programs of non-pharmacological cognitive disorder correction in patients with epilepsy enables to inhibit the progression of cognitive disorders, and in case of mild cognitive disorders – improve cognitive functions, promotes better quality of life and the renewal of social functioning among patients with epilepsy.

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