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## COMPARATIVE PSYCHOMETRIC ANALYSIS OF COGNITIVE FUNCTIONS IN PATIENTS WITH HYPERTENSIVE DISEASE AND HYPOTHYROIDISM

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### Summary

**Aim:** The aim of the study was to determine whether certain cognitive domains exist in the assessment of cognitive functions in HD patients, patients with hypothyroidism and HD patients with concomitant hypothyroidism.

**Material and methods:** The patients were divided into 3 groups according to nosology: Group I – 21 patients with hypertensive disease (HD); Group II – 18 patients with hypothyroidism, Group III – 19 hypertensive patients with concomitant hypothyroidism.

**Results:** It was revealed that patients with HD had a decrease in memory according to the test proposed by A. R. Luria for learning 10 words, ( $p < 0.05$ ), as well as Digit span from Mattisse scale, ( $p < 0.05$ ). In patients with hypothyroidism, a short span of attention was revealed, according to the method of «Selectivity of attention» (G. Munsterberg test), ( $p < 0.05$ ). The analysis of the results showed that considering the interaction of factors (HD and hypothyroidism), the most affected cognitive domains are memory, executive functions and optical-spatial functions, respectively, ( $p < 0.05$ ).

**Conclusions:** To diagnose CI in patients with HD who have problems with the domain of cognitive function memory, it is advisable to use a test for learning 10 words according to the method proposed by A. R. Luria and Digit span from Mattisse scale. In patients with hypothyroidism, attention and executive functions should be determined using the Schulte Tables and the «Selectivity of Attention» method (G. Munsterberg test). With the combined pathology, HD patients with a concomitant hypothyroidism should use Schulte Tables, test for learning 10 words by A. R. Luria and Clock Drawing Test.

**Key words:** cognitive functions, hypertensive disease, hypothyroidism, neuropsychological testing

**Summary:** The level of cognitive-mnemonic functions of 58 individuals aged  $49.84 \pm 0.83$  years was studied. The patients were divided into 3 groups according to nosology: Group I – 21 patients with hypertensive disease (HD); Group II – 18 patients with hypothyroidism, Group III – 19 hypertensive patients with concomitant hypothyroidism. The duration of the disease is  $13.56 \pm 0.79$  years. The control group (CG) involved 18 apparently healthy individuals (AHI) of appropriate age ( $47.84 \pm 0.36$  years), whose selection was carried out with the consideration of the anamnesis, in the absence of hypothyroidism and HD.

At the time of examination, TSH in patients of Group II was  $3.16 \pm 0.79$  mIU/liter, ( $p < 0.05$ ), the stage of compensation was diagnosed in 83.3%, the stage of subcompensation – in 16.7%; in Group III TSH was  $2.92 \pm 0.78$  mIU/liter, ( $p < 0.05$ ), the stage of compensation of hypo-

thyroidism was diagnosed in 85.7%, the stage of subcompensation – in 14.3%. In 84.7% of cases, hypothyroidism was compensated, which was confirmed by the absence of clinical symptoms, as well as normal TSH in serum. In 15.3% of cases, patients did not receive adequate replacement therapy and were subcompensated. After retrospective analysis of medical records, it was found that their levels of TSH were  $7.14 \pm 2.37$  mIU/l and  $8.03 \pm 6.77$  mIU/l, respectively, which corresponded to the stage of decompensation. The average level of office blood pressure (SBP/DBP) in Groups I, III in comparison with CG at the time of examination was SBP  $134.26 \pm 5.23$  mm Hg, ( $p < 0.05$ ); DBP  $84.37 \pm .51$  mm Hg, ( $p < 0.05$ ) Group I; SBP  $145.52 \pm 5.45$  mm Hg, ( $p < 0.05$ ); DBP  $82.41 \pm 3.86$  mm Hg ( $p < 0.05$ ) Group III. Retrospective analysis of medical records revealed insufficient blood pressure control in the

relevant groups, the average level of SBP/DBP in Groups I and III was  $154.38 \pm 5.11$ , ( $p < 0.05$ )  $96.47 \pm 3.49$   $0.05$  mm Hg;  $158.26 \pm 5.64$ , ( $p < 0.05$ )  $98.42 \pm 4.93$ , ( $p < 0.05$ ) mm Hg, respectively. To simplify the diagnosis of cognitive-mnemonic disorders for all groups, the following psychometric methods were used: «Learning 10 words» – the method of A. R. Luria, Schulte Tables, Clock Drawing Test, Digit span from Mattis scale and «Selectivity of attention» (G. Munsterberg test). It was revealed that patients with HD had a decrease in memory according to the test proposed by A. R. Luria for learning 10 words, ( $p < 0.05$ ), as well as Digit span from Mattis scale, ( $p < 0.05$ ). In patients with hypothyroidism, a short span of attention was revealed, according to the method of «Selectivity of attention» (G. Munsterberg test), ( $p < 0.05$ ). The analysis of the results showed that considering the interaction of factors (HD and hypothyroidism), the most affected cognitive domains are memory, executive functions and optical-spatial functions, respectively, ( $p < 0.05$ ). It should be noted that in patients of Group II there is an increase in the time of Schulte Tables completion, in comparison with Group I, ( $p < 0.05$ ). In addition, there was an increase in time spent for words searching, the number of errors and omissions in finding and underlining words by the method of «Selectivity of attention». The results of the study revealed a significant decrease in memory, ( $p < 0.05$ ), the presence of moderate cognitive impairment (CI) in patients of Group III compared with Group I, ( $p < 0.05$ ). Thus, in HD patients with concomitant hypothyroidism, a significant slow processing speed and executive function disorders were found, as well as memory loss, impaired optical-spatial functions, in comparison with Group II, ( $p < 0.05$ ).

**Conclusions.** To diagnose CI in patients with HD who have problems with the domain of cognitive function memory, it is advisable to use a test for learning 10 words according to the method proposed by A. R. Luria and Digit span from Mattis scale. In patients with hypothyroidism, attention and executive functions should be determined using the Schulte Tables and the «Selectivity of Attention» method (G. Munsterberg test). With the combined pathology, HD patients with a concomitant hypothyroidism should use Schulte Tables, test for learning 10 words by A. R. Luria and Clock Drawing Test. The study of cognitive functions in patients with HD and hypothyroidism is appropriate even in the compensation of the disease, because, as the study showed, in patients with lifelong pathology the level of TSH and blood pressure fluctuates, which affects cognitive functions: 3.6% of HD patients and 7.2% of patients with hypothyroidism suffer from cognitive disorders. In the future, this will make it possible to identify patients with CI among the patients with HD and hypothyroidism and to treat the disorders.

**Key words:** cognitive functions, hypertensive disease, hypothyroidism, neuropsychological testing.

## INTRODUCTION

The issue of early diagnosis of cognitive disorders is extremely relevant in modern medicine, especially in patients with several diseases that may affect the state of cognitive functions, which directly or indirectly adversely affect blood supply to the brain and/or metabolism, in particular hypertension and hypothyroidism. Studies have shown that one of the most common pathogenetic factors in the formation and development of cognitive impairment (CI) is HD, especially its long course which leads to CI of varying degrees; cerebrovascular pathology on the background of HD is one of the main causes of cognitive decline [5]. Studies of Systolic Hypertension in Europe trials, PROGRESS, LIFE, SCOPE, MOSES have shown that normalization of blood pressure (BP) significantly reduces the risk of developing and progressing of CI [6]. However, according to the analysis of studies, there is no convincing evidence that a decrease in blood pressure in patients with HD without cerebrovascular disease in the anamnesis prevents the development of CI [7]. Despite the widespread world's reports about the need to control blood pressure, the XVIII European Cardiac Congress in Birmingham presented disappointing data on the detection of HD, the attitude of patients to their condition and the quality of health care [12]. It was found that among all patients who suffer from HD, only about 50% know they are sick. Among those aware, only half receive antihypertensive treatment. And of this half, only one in two is treated adequately, which is 12.5% of the cohort of people with HD [13]. On the basis of the Kharkiv city polyclinic, a long-term prospective study was conducted with the aim to study the course of HD, the adequacy of antihypertensive drugs and complications of HD in patients with diseases of the internal organs [1]. The results of the study (described in 2010) revealed the presence of polypragmatism in the treatment of high blood pressure, frequent use of second-line drugs (25.1%), lack of practice of titrating doses of antihypertensive drugs to optimal, underestimation by doctors of more careful blood pressure control and lack of timely dose adjustment of antihypertensive drugs for HD patients who take drugs for the treatment of comorbidities that can increase blood pressure and as a result – a fairly low percentage of achieving the target blood pressure in patients (36.6%), i.e. only a third of cases. Among all causes of cognitive impairment, metabolic disorders account for about 5%, in particular, thyroid dysfunction with the development of hypothyroidism. Moreover, given its duration and severity, the prevalence of CI in this pathology varies, according to various authors, from 1.3% to 10.3% (Niafar M. et al., 2009; Catherine M. Otto, et al., 2012). Some authors [8\9] hold the view that cognitive functions are restored by compensating for hypothyroidism, but there is another opinion: CI that developed in thyroid hormone deficiency is irreversible or partially reversible [9]. According to the results of study of thyroid pathology in Ukraine and Poltava region in recent years, the prevalence of hy-

pothyroidism in 2005–2013 has been studied; it was found that doctors underestimate the need for more thorough diagnosis and lack of timely dose adjustment [4]. It should be noted that prolonged deficiency of thyroid hormones causes cognitive deficits, which leads to disability and reduced quality of life of patients. Our previous studies identified insufficient control of blood pressure in patients with hypertension and thyroid-stimulating hormone (TSH) in patients with hypothyroidism. According to the retrospective analysis of medical documentation of patients with HD, we found insufficient blood pressure control; the average level of systolic/diastolic blood pressure (SBP/DBP) was  $159.20 \pm 8.36 / 98.00 \pm 8.54$ ;  $162.50 \pm 6.34 / 101.04 \pm 10.01$  mm Hg, respectively, for patients with hypertension and HD patients with concomitant hypothyroidism. Analyzing TSH level, it was found that at the time of examination the patients were at the stage of compensation (TSH =  $3.96 \pm 1.09$  mIU/l;  $4.12 \pm 0.78$  mIU/l, respectively, for patients with hypothyroidism and HD patients with concomitant hypothyroidism). We also assessed TSH levels in patients with a confirmed history of hypothyroidism. A retrospective analysis of the data was performed and it was found that in the examined patients the average level of TSH was insufficiently corrected, TSH =  $7.14 \pm 2.37$  mIU/l;  $8.03 \pm 6.77$  mIU/l, for patients with hypothyroidism, HD patients with concomitant hypothyroidism, respectively. Given that HD and hypothyroidism are important risk factors for CI, moreover, these diseases can be mutually burdensome, it is especially important to study cognitive function in people with combined pathology to determine whether these two pathologies have an additive effect on CI. Thus, based on our results, which show that HD patients had a significantly lower score in the memory domain, patients with hypothyroidism had a significantly lower score in the domain of attention and executive functions, and analysis of the results showed that taking into account the interaction factors (HD and hypothyroidism) it was found that 40% of the most affected cognitive domains are memory and speech, and 60% of patients have impaired executive functions, as well as optical-spatial functions, respectively. Based on the results, the following psychometric methods were used to screen for cognitive-mnemonic disorders: a test for learning 10 words according to the method proposed by A. R. Luria and Digit span from Mattis scale for patients with HD; for patients with hypothyroidism – the method of «Selectivity of attention» (G. Munsterberg test), Schulte Tables; for HD patients with concomitant hypothyroidism – a test for learning 10 words according to the method proposed by A. R. Luria, Schulte Tables and Clock Drawing Test. The set of neuropsychological techniques should be simple enough to diagnose CI regardless of the medical diagnosis of the test subject, but at the same time it should be sensitive to relatively minor CI, which in the absence of timely correction can lead to more severe disorders with dementia. The aim of the study

was to determine whether certain cognitive domains exist in the assessment of cognitive functions in HD patients, patients with hypothyroidism and HD patients with concomitant hypothyroidism.

**Materials and methods.** To achieve the goal, we used the results of our published work on the study of neuropsychological structure of patients with HD, patients with hypothyroidism and HD patients with concomitant hypothyroidism. Retrospective analysis of medical records revealed insufficient long-term control of blood pressure and TSH, which in the future became the cause of CI in this group of patients [14]. A comprehensive clinical and neurological examination of 58 patients (27 men and 31 women), mean age –  $47.84 \pm 0.36$  years, disease duration –  $13.56 \pm 0.79$  years was carried out. The CG involved 18 people representative of age and sex ratio without a history of HD, hypothyroidism. Patients were divided into 3 groups by nosology: Group I – 21 patients with HD who received antihypertensive therapy; Group II – 18 patients with hypothyroidism who received L-thyroxine at a dose of 100–150 mg, Group III – 19 HD patients with concomitant hypothyroidism who received appropriate treatment. Data used to select patients with HD were the following: stage of the disease, the degree of increase in blood pressure, disease duration, the level of SBP and DBP. Patients with HD received basic therapy (antihypertensive). The diagnosis of hypothyroidism was made by an endocrinologist according to the recommendations of the American Association of Clinical Endocrinologists and the American Thyroid Association for the Diagnosis and Treatment of Hypothyroidism in Adults [10]. Hypothyroidism caused by autoimmune thyroiditis was revealed in 9 (50%) individuals, as a result of thyroid surgery – in 5 (27.7%) patients, and in 4 (22.3%) individuals hypothyroidism occurred spontaneously. At the time of examination, the stage of compensation of hypothyroidism was diagnosed in 5 (27.8%) patients, subcompensation – in 13 (72.2%) patients. Exclusion criteria: history of traumatic brain injury and stroke, mental illness, diseases of the blood system, cancer, persistent atrial fibrillation, chronic obstructive pulmonary disease (respiratory failure of the I–II stages), Diabetes mellitus, renal failure and hepatic failure in the stage of decompensation. The study was conducted on the basis of the Endocrinology and Neurology departments of the Ivano-Frankivsk Regional Clinical Hospital, as well as on the basis of the Hypertension department of the Ivano-Frankivsk Regional Clinical Cardiology Dispensary. All patients gave informed consent before enrollment in the study. Assessment of patients' condition was performed on the basis of an algorithmic standard thematic map, which included sections of clinical and neuropsychological testing. General clinical examination included examination by a physician, endocrinologist, ECG, laboratory tests. Neuropsychological research included: Schulte Tables to assess executive functions, the rate of sensorimotor responses, the amount of active attention, training

status and fatigue of patients, «Learning 10 words» – the method of A. R. Luria and digit span from Mattis scale, which allowed to study the processes of memorization, preservation and reproduction of information [5]; attention studies were performed using the «Munsterberg Technique» [3]. Disorders of spatial functions were most clearly manifested when performing Clock Drawing Test [3]. Statistical processing of the obtained data was performed using the statistical data analysis package Statistica 6.0. The non-parametric Kolmogorov-Smirnov criterion was used to assess the statistical significance of the difference

between the groups. Changes in indicators under  $p < 0.05$  were considered probable.

**Results of research and discussion.** The main complaints of patients during the examination were the following: «I cannot remember new information», «I can't do mental arithmetic», «I lose my mind», «I don't listen after 10 minutes of conversation», «It's hard to concentrate», «I think slowly», «Brain fog», «I can't perform several tasks simultaneously», «I have lost confidence in the right choice», «I postpone decisions» (Table I). A decrease in memory, impaired attention and psychomotor slowing were registered in Group III.

Table 1

Frequency of subjective complaints of patients (M ± m)

Subjective complaints of patients	Control Group, n=18	Group I, n=21	Group II, n=18	Group III, n=19
<b>Memory</b>				
«I cannot remember new information»	11.11±7.41	14.29±7.64	44.44±11.71* •	57.89±11.33×
« I can't do mental arithmetic «	5.56±5.40	19.05±8.57	22.22±9.80	31.58±10.66
<b>Attention</b>				
«I lose my mind»	16.7±8.78	14.29±7.64	33.33±11.11	42.11±11.33×
« I don't listen after 10 minutes of conversation «	5.56±5.40	14.29±7.64	44.44±11.71* •	36.84±11.07
<b>«Psychomotor speed»</b>				
«It's hard to concentrate»	11.11±7.41	9.52±6.41	44.44±11.71* •	52.63±11.45×
«I think slowly»	11.11±7.41	9.52±6.41	61.11±11.49* •	68.42±10.66×
«Brain fog»	0.00	9.52±6.41	50.00±11.79* •	52.63±11.45×
<b>Executive functions</b>				
«I can't perform several tasks simultaneously»	11.11±7.41	19.05±8.57	27.78±10.56	31.58±10.66
«I've lost confidence in the right choice»	11.11±7.41	9.52±6.41	27.78±10.56	26,32±10.66
«I postpone decisions»	11.11±7.41	9.52±6.41	27.78±10.56	26.32±10.66

Notes:\* reliability of the difference between the data compared to CG, ( $p < 0.05$ );

• reliability of the difference between the data of Groups I and II, ( $p < 0.05$ );

× reliability of the difference between the data of Groups I and III, ( $p < 0.05$ ).

A detailed neuropsychological examination was performed, which makes it possible to compare cognitive functions according to individual domains (Table II).

Having selected batteries of tests for rapid assessment of cognitive functions with the consideration of the specific clinical situation, we have registered in HD patients a decrease in memory according to the test for learning 10 words according to the method proposed by A. R. Luria ( $p < 0.05$ ), as well as Digit span from Mattis scale ( $p < 0.05$ ). In patients with hypothyroidism, according to the method of «Selectivity of attention» (G. Munsterberg test), a short span of attention was noted ( $p < 0.05$ ). For an extended assessment, Schulte Tables were chosen, the result of which demonstrates the state of the domain of the patient's executive functions and proves a short span of attention.

Taking into account the interaction of factors (HD and hypothyroidism) the analysis of results showed that the most affected cognitive domains are memory, executive functions and optical-spatial functions, respectively ( $p < 0.05$ ). Analyzing the data, it should be noted that patients of Group II spent more time for searching words, they made more errors and omissions while searching and underlining words according to the method of «Selectivity of attention» in comparison with Group I ( $p < 0.05$ ). In addition, they spent more time filling Schulte Tables, which also confirms a short span of attention and instability of executive functions. The results of studies revealed moderate CI in patients of Group III in comparison with Group I ( $p < 0.05$ ). Thus, patients with a combination of HD and hypothyroidism showed a significant decrease in memory, executive functions, impaired optical-spatial functions in comparison with Group II ( $p < 0.05$ ).

Table II

## Indicators of cognitive functions according to neuropsychological testing

	Control Group, n=12	I, n=21	II, n=18	III, n=19
<u>Memory I)</u>				
Luria's Test-1, words	9 [9; 10]	7 [5; 8] *	9 [8; 10]	6 [5; 7] * \ ** \ ***
Luria's Test-6, words	8 [7; 9]	8 [7; 10]	8 [7; 9]	4 [3; 6] * \ ** \ ***
2) Digit span from Mattisse scale	17 [16; 17]	13 [12; 15] *	16 [14; 17]	15 [13; 17] * \ ** \ ***
<u>Attention</u>				
Method «Selectivity of attention», points	14 [12; 16]	11 [9; 13] *	7 [5; 9] * \ **	7 [4; 9] * \ ** \ ***
<u>Executive functions / Schulte Tables /</u>				
-work efficiency, sec	39 [33; 44]	40 [39; 41]	65 [53; 78] * \ **	72 [59; 86] * \ ** \ ***
<u>Optical-spatial functions</u>				
Clock Drawing Test	9 [9; 10]	9 [9; 10]	9 [8; 9]	8 [7; 9] * \ ** \ ***

Notes: \* reliability of the difference between the data compared to CG ( $p < 0.05$ );

\*\* reliability of the difference between the data compared to Group I ( $p < 0,05$ );

\*\*\* reliability of the difference between the data compared to Group II ( $p < 0.05$ ).

Therefore, all patients, according to neuropsychological testing, had a decrease in cognitive functions, but the most pronounced disorders were observed in patients with a combination of HD and hypothyroidism. Testing analysis showed that these patients had a decrease in memory, executive functions and impaired optical-spatial functions. The obtained data are consistent with the results of similar studies. For example, according to Yakovlev O. O. (2013), hypertensive patients with stage II have a decrease in short-term memory with a relative preservation of a long-term one. However, there are other data in the literature: in many cases the decrease in concentration, memory impairment, as well as increased fatigue are observed [11]. There are controversial data on the development of CI in subclinical hypothyroidism. It should be noted that CI in patients with hypothyroidism is characterized primarily by slowed thinking and processing of information – bradyphrenia: the patient needs more than normal time and effort to solve intellectual tasks. Many studies have found a positive association of cognitive decline in subclinical hypothyroidism (Jensovsky J., et al., 2002; Boxel M. P., et al., 2004). Regarding the denial of such a correlation, a number of authors argue that subclinical hypothyroidism does not cause global cognitive dysfunction. But in specific cognitive domains (memory and executive functions) there may be a slight deficit.

Patients with subclinical hypothyroidism and significant cognitive dysfunction may have independent diagnoses that should be evaluated and treated separately (Samuels M. H., 2010; Roberts R. O., 2014; Kim J. M., 2010; Kramer C. K., et al., 2009). It is known that a long-term combination of HD with concomitant hypothyroidism leads to varying degrees of CI [11] and is a common pathogenetic factor in the development of dementia. The relevance of the study of this problem is also justified by

the fact that today there are no clear criteria for the diagnosis of CI in the combination of HD with concomitant hypothyroidism. This comparative analysis of conventional scales for determining CI can be used in planning a diagnostic search to ensure early effective verification of changes in cognitive-mnemonic functions.

## CONCLUSIONS

1. To diagnose CI in hypertensive patients who have cognitive function memory loss, it is advisable to use «10 words learning test» according to A. R. Luria and Digit span from Mattisse scale. In patients with hypothyroidism, attention and executive functions should be determined using the method of «Selectivity of attention» (G. Munsterberg test) and Schulte Tables. Hypertensive patients with a concomitant hypothyroidism should undergo «10 words» method of A. R. Luria, Schulte Tables and Clock Drawing Test.

2. The study proved that patients, who suffer from the mentioned disorders for a long time, have unstable levels of TSH and blood pressure, which affects cognitive function: 3.6% of hypertensive patients and 7.2% of patients with hypothyroidism have cognitive disorders. In the future, this will make it possible to identify patients with CI among patients with HD and hypothyroidism and to treat the disorders. Therefore, the results of the research prove that the choice of neuropsychological techniques should be made with the consideration of the specific clinical situation. This comparative analysis of generally accepted scales for determining CI can be used in planning a diagnostic search to ensure early effective verification of changes in intellectual and mnemonic functions. All this necessitates the use in practice of simple and reliable psychometric tools for early diagnosis of cognitive disorders.

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