Cognitive impairments in patients with chronic cerebral ischemia

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Abstract Cognitive impairments, such as memory and intelligence, attention and mental performance, usually suffer in diffuse brain damage, in particular in chronic cerebral ischemia. However, they can also occur in focal brain lesions, such as cerebral infarcts, reaching the degree of dementia. The aim of the study was to investigate the peculiarities of non-dementia cognitive disorders in patients with the consequences of cerebral infarction. We examined 30 patients with chronic cerebral ischemia with cerebral infarction at the age of 58-66 years (M=62.4) and a similar comparison group was chosen. The main results of the cognitive status assessment in patients with CHEM with suffered cerebral infarction showed a decrease in short-term visual and figurative memory, more so in men and with increasing age. There were also decreased productivity of attention, decreased level of abstract thinking, and weakened connection between logical thinking and attention, more pronounced in men and in the older age group. With a disease duration of more than 3 years, the volume of figurative memory and the abstract component of thinking decreased. The main conclusions are: cognitive disorders developing against the background of CIM worsen to a greater extent in men, in persons older than 60 years and in 3 years from the moment of cerebral infarction; short-term medication therapy has no significant effect on cognitive dysfunction, the significance of these results determines the need for long-term, at least 6 months, rehabilitative medication therapy.

Keywords: memory, attention, thinking, chronic cerebral ischemia.

1.   Introduction

Chronic cerebral ischemia (CCI), according to epidemiological data, is one of the most common diseases of the central nervous system. The development of CCI is caused by atherosclerotic lesion of cerebral vessels and arterial hypertension, often by their combination [1,2].

The progressive vascular lesion of the brain is caused by the involvement of long perforant vessels in the pathological process with the development of pathomorphological changes in the subcortical nodes and white matter of the brain in the form of infarcts, microhemorrhages and leukoareosis [3,4]. Destruction of prefrontal-subcortical connections leads to the development of cognitive disorders [5].

The most often clinical picture of CCI is accompanied by non-dement cognitive disorders, early treatment of which determines a favorable rehabilitation prognosis and long-term maintenance of patients' ability to work. Memory and intellect, attention and mental performance, emotional and volitional spheres related to integrative functions usually suffer in diffuse brain damage, in particular

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in chronic brain ischemia. However, they can also be affected by focal brain lesions such as brain infarcts. Non-dement cognitive disorders in the form of attention deficit, memory impairment, slowness of attention, rapid exhaustion during mental work, narrowing of interests, often occur acutely after a cerebral infarction, although after the first episode of a vascular accident they rarely reach the degree of dementia [6,7,8].

The frequency of demented cognitive disorders in patients who have suffered cerebral circulatory disorders reaches, according to some data, 30%, and it increases with age. The cause of marked cognitive disturbances reaching the degree of dementia can be extensive lesions of cortical and subcortical structures, single, relatively small infarcts located in functionally important areas of the anterior-medial parts of the optic tubercle and adjacent areas in the cerebellar hemispheres. Most often demented cognitive disorders are observed in subcortical arteriosclerotic encephalopathy (Binswanger type), less often in other types [9,10].

The criteria for non-dement cognitive disorders, according to ICD-10, are: the presence of cognitive impairment according to the patient or his immediate surroundings; evidence of a decline in cognitive abilities in comparison with the initial, higher level, obtained from the patient or his immediate surroundings; objective evidence of memory impairment or other cognitive functions, obtained through neuropsychological tests; preservation of everyday skills, social activity [11].

The aim of the work was to study into peculiarities of non-dement cognitive disorders in patients with the consequences of brain infarction.

2. Materials and Methods

We studied the features of cognitive functions (memory, attention and thinking) of 30 patients diagnosed with CCI: «CCI. Consequences of brain infarction. Moderate cognitive impairment», of them 13 (43%) were women and 17 (57%) men. The median age was 62.4 years (58.1; 66.6). The study was conducted in the neurological department of a multidisciplinary hospital. The patients received a traditional course of neurotropic therapy (drugs improving the cerebral blood flow and rheological properties of blood, neurometabolic drugs). The study took into account such parameters as sex, age, education level, disease duration, duration of inpatient treatment of patients.

The main study group included 30 patients with stage II CCI coupled with previous cerebral infarction with moderate cognitive impairment. The comparison group consisted of 30 patients with CCI without cerebral infarction, distributed by sex, age, and educational level approximately corresponding to that of the patients.

We also took into account the distribution according to the duration of the disease: 16 persons (53%) with the disease duration (brain infarction) up to 3 years and 14 persons (47%) with more than 3 years. The educational level of the patients was distributed as follows: secondary education - 11 persons (37%), specialized secondary education - 10 persons (33%), higher education - 9 persons (30%). During the study we also took into consideration the time of patients' examination: during the first days of the admission (first 2-4 days) - 8 persons (27%) and by the end of inpatient treatment (12-14 days) - 22 persons (73%).

In the course of study we evaluated the peculiarities of memory, attention, and thinking and made a comparative analysis of cognitive dysfunction depending on the duration of the disease and the therapy being conducted. All investigations were conducted with the informed consent of the patients according to article 21 of the Constitution of the Russian Federation, the Declaration of Helsinki of the World Medical Association «Ethical principles for medical research with people as subjects of research».

TESTING METHODS

Verification of the diagnosis in the patients was carried out on the basis of clinical and neurological examination, neuro-psychological examination and computer tomography of the brain. The study used psychodiagnostic techniques to assess memory and thinking: «Memory for numbers» (Luria, 1995),

«Memory for images» (Chris, 1974), «Münsterberg test» (Münsterberg, 1934), «Singling out essential features» (Rubinstein, 1951), «Missing details or completion of pictures» (Wexler, 1955).

The NUMBER MEMORY METHODOLOGY is designed to evaluate short-term visual memory, its volume and accuracy. The task consists of showing the examinees for 20 seconds a table with twelve two-digit numbers which should be memorized and after the table is removed to write them down on a blank. Evaluation of test results was carried out with the help of memory coefficient (C), where $C = a / n$, (a - the number of correctly reproduced numbers, n - the total number of presented numbers).

The methodology MEMORY FOR IMAGES is designed to study figurative memory. Its essence is that the examinee is exposed to a table with 16 images for 20 seconds. The images should be remembered and reproduced on the form within 1 minute. The test results were evaluated using memory coefficient (C), where $C = a/n$, (a - the number of correctly reproduced images, n - the total number of presented images).

The MUNSTERBERG TEST is designed to determine selectivity and concentration of attention. The stimulus material contains a random sequence of letters in the form of several lines without spaces and 25 words placed between the letters. We estimated the net productivity index $E=AN$, (N - the number of underlined words within 2 minutes, A - accuracy index ($A=n/n+0$), where n - number of words underlined within 2 minutes, 0 - number of mistakes within the same period) and error rate per person $Ker=m/n$, where m - number of wrongly underlined words recorded during the test, n - total number of words.

The DISTINGUISHING SUBSTANTIAL FEATURES technique reveals the testee's ability to separate substantial features of objects or phenomena from unimportant, secondary features. In addition, the presence of a number of assignments, which are identical in nature of performance, makes it possible to judge the consistency of the examinee's reasoning. The task contains 20 rows of words and the examinee must demonstrate his or her ability to grasp the abstract meaning of certain concepts. We evaluated the net productivity index $E=AN$, (N is the number of correct answers, A is the accuracy index ($A=n/n+0$), where n is the total number of answers, 0 is the number of errors during the same period) and the error rate per person $Ker =m/n$, where m is the number of erroneously selected images recorded during the study, n is the total number of images.

The MISSING PARTS OR LOSSING PICTURES methodology diagnoses visual observation and the ability to identify salient features. Stimulus material contains 21 cards, which show pictures with a missing part. The solution time of one task is 20 seconds, the right answer is evaluated by 1 point. We calculated the net productivity index $E=AN$, (N - number of points, A - accuracy index ($A=n/n+0$), where n - number of viewed pictures, 0 - number of mistakes during the same period) and error rate per person $Ker =m/n$, where m - number of incorrectly added or incorrectly completed pictures recorded during the study, n - total number of pictures.

Statistical data processing was performed using Statistica 10.0 software. In order to solve the problem of reliability of the obtained data and their comparison, all the results of the study were processed by the method of variation analysis. Estimation of reliability criterion was done using Student's table and probability coefficient p. The results were considered reliable if $p \leq 0,05$.

3.   Results

All patients in the examined groups had cognitive disorders. The following complaints prevailed: decreased memory, difficulty thinking, and impaired attention concentration. The mnemonic functions were investigated using the «number memory» technique. The technique revealed 1.4-fold lower values of short-term visual memory ($p<0,05$) in patients with the consequences of cerebral infarction in comparison with the control group; women memorized more numbers, also in the elder age group from 61 to 70 years (Table 1). In the course of the disease for more than 3 years, the number of remembered numbers and memory coefficient decreased 1.2-fold ($p<0,05$) than in patients with a

shorter duration of the disease. Memory parameters did not differ in the examined group both at the beginning of treatment and at the end, i.e., the course of treatment had no positive effect.

Table 1. Results of the study by method «memory for numbers»

Parameters		The volume of short-term visual memory	
		M	C
Core group (n=30)			
Average value in the group		3.0±1.2*	0.25±0.08*
Gender	Men	2.5±1.0*	0.22±0.09*
	Women	3.4±1.3*	0.28±0.11*
Age, years	51-60	2.3±0.9*	0.19±0.07*
	61-70	4.0±0.8*	0.34±0.15*
Disease duration	Up to 3 years	3.2±0.8* **	0.27±0.09* **
	Over 3 years	2.7±0.7* **	0.22±0.08* **
Examination Time	Start of treatment	2.9±0.7*	0.21±0.06*
	By the end of treatment	2.8±0.9*	0.25±0.09*
Comparison group (n=30)			
Average value in the group		4.3±0.8	0.36±0.06
Gender	Men	4.6±0.6	0.38±0.12
	Women	4.0±0.9	0.33±0.11
Age, years	51-60	4.3±1.1	0.35±0.09
	61-70	5.0±1.3	0.42±0.09

Note: * - reliability of the results in relation to the control group, p<0.05;
** - reliability of the results in the groups as to the disease duration, p<0.05;
*** - reliability of the results in the groups as to the time of study, p<0.05.

The study of the image memory revealed a 1.1-fold decrease in the average values of the memorized images and memory coefficient in the patients compared to the control group; it suffered more in men than in women and was 1.3-fold lower (p<0,05) (Table 2). Image memory naturally worsens with age, but the duration of the disease has no significant effect on it. A course of inpatient therapy insignificantly – 1.1 times - improved the volume of figurative memory.

Table 2. Results of the research on the «memory for images» methodology

parameters		Volume of imaginative memory	
		M	C
Core group (n=30)			
Average value in the group		5.4±0.9*	0.34±0.09*
Gender	Men	5.0±0.9*	0.31±0.09*

	Women	5.9±0.8	0.37±0.08
Age, years	51-60	5.3±0.4*	0.33±0.04*
	61-70	4.8±1.2*	0.30±0.12*
Disease Duration	Up to 3 years	5.4±1.0*	0.34±1.1*
	Over 3 years	5.4±0.9*	0.34±0.7*
Inspection Time	Start of treatment	4,9±0,7* ***	0.31±0.10* ***
	By the end of treatment	5.6±1.0 ***	0.35±0.6***
Comparison group (n=30)			
Average value in the group		6.1±0.6	0.38±0.6
Gender	Men	6.4±0.8	0.40±0.8
	Women	5.8±0.5	0.36±0.10
Age, years	51-60	6.8±0.8	0.43±0.05
	61-70	6.0±0.1	0.38±0.04

*Note: * - reliability of the results in relation to the control group, p<0,05;*
*** - reliability of the results in the groups as to the disease duration of the, p<0,05;*
**** - reliability of the results in the groups as to the time of study, p<0,05.*

Analyzing the results of the Munsterberg test, we found a 1.4-fold decrease in the E index ($p<0,05$) in both men and women compared to the control group; it did not change with age categories or the age of the disease; there was a slight positive dynamics against the background of inpatient treatment (Table 3). The error rate per one person in the Münsterberg method was 1.5 times higher ($p<0,05$) in patients than in healthy subjects; men and patients aged between 61-70 years did more mistakes. The course of traditional therapy reduced this index. The results obtained confirm the decrease in all attention parameters characteristic of CCI, and, first of all, such most important of them as concentration and stability. In addition, these patients were found to have increased distractibility and low selectivity of attention.

Table 3. Münsterberg test results

Parameters		E	K
Core group (n=30)			
Average value in the group		9.4±1.2*	4.0
Gender	Men	8.2±1.0*	4.4
	Women	10.6±1.4*	3.5
Age, years	51-60	9.2±0.9*	3.8
	61-70	9.0±0.7*	4.5
Disease Duration	Up to 3 years	9.1±1.1*	4.3
	Over 3 years	9.4±1.0*	3.9

Inspection Time	Start of treatment	8.9±0.7* ***	5.0
	By the end of treatment	10.1±0.8* ***	3.5
Comparison group (n=30)			
Average value in the group		13.0±0.7*	2.7
Gender	Men's	11.5±0.5*	2.8
	Women's	14.4±0.5*	2.6
Age, years	51-60	13.4±0.6*	2.8
	61-70	13.2±0.9*	1.5

*Note: * - reliability of the results in relation to the control group, p<0.05;*
*** - reliability of the results in the groups as to the disease duration, p<0.05;*
**** - reliability of the results in the groups as to the time of study, p<0.05.*

Studying the abstract component of thinking in patients with CCI revealed a 2.9-fold decrease (p<0,05) in the average value of the index E in men, and also in the age category from 51 to 60 years; its decrease by 1.7 times when the disease had lasted more than 3 years, than before 3 years (Table 4). There was also a 2-fold increase in the mean values of the error rate (p<0,05) and its growth after 3 years of disease.

Table 4. Results of the study according to the method "Distinguishing substantial features"

Parameters		E	K
Core group (n=30)			
Average value in the group		1.8±0.8*	7.5
Gender	Men	1.4±0.9*	7.5
	Women	2.2±1.2*	7.4
Age, years	51-60	1.5±0.6*	7.8
	61-70	2.0±0.7*	7.2
Disease Duration	Up to 3 years	2.2±0.6* **	7.0
	Over 3 years	1.3±0.5* **	8.0
Inspection Time	Start of treatment	1.7±0.6*	7.8
	By the end of treatment	1.9±0.6*	7.9
Comparison group (n=30)			
Average value in the group		5.3±1.0*	3.7
Gender	Men	4.7±1.1*	4.2
	Women	5.9±1.2*	3.2

Age, years	51-60	6.4±0.9*	2.8
	61-70	5.7±1.1*	3.5

*Note: * - reliability of the results in relation to the control group, p<0.05;*
*** - reliability of the results in the groups as to the duration of the disease, p<0.05;*
**** - reliability of the results in the groups as to the time of study, p<0.05.*

The results of the study according to the method «Missing parts», which shows the relationship of thinking with attention, showed that the E index in the patients was 1.9 times lower (p<0,05); in male patients it was 2.2 times lower (p<0,05); it dropped with increasing age (Table 5). The mean error rate in the study group was 1.5 times higher (p<0,05); in men it was 2 times higher (p<0,05); in age 51-60 it was 1.7 times higher (p<0,05).

Table 5. Results of the study using the «missing parts» methodology

Parameters		E	K
Core group (n=30)			
Average value in the group		3.4±0.9*	2.4
Gender	Men	3.0±0.8*	2.9
	Women	3.8±1.0*	1.8
Age, years	51-60	3.3±0.7*	2.6
	61-70	3.0±0.8*	1.9
Duration Disease	Up to 3 years	3.1±0.6*	2.5
	Over 3 years	3.7±0.4*	2.4
Time Inspection	Start of treatment	3.5±1.1*	2.7
	By the end of treatment	3.6±1.2*	2.4
Comparison group (n=30)			
Average value in the group		6.6±0.7	1.6
Gender	Men	6.6±0.7	1.4
	Women	6.6±0.9	1.8
Age, years	51-60	7.0±1.0	1.5
	61-70	6.6±0.8	1.0

*Note: * - reliability of the results in relation to the control group, p<0.05;*
*** - reliability of the results in the groups as to the disease duration, p<0.05;*
**** - reliability of the results in the groups as to the time of study, p<0.05.*

4.   Discussion

Since cognitive functions are provided by the integrative activity of the whole brain, they can occur at different localization of the ischemic focus [12,13,14]. At the same time, the nature of cognitive

disorders will directly depend on the localization of the brain infarction, and their severity - on its size. Impaired working memory may develop, with patients finding it difficult to retain large amounts of information and quickly switch from one source of information to another. Impaired working memory significantly impairs learning and acquiring new skills, but does not extend to remembering and recalling life events [15].

The results of the assessment of the cognitive status in patients with CCI coupled with cerebral infarction in case history showed a decrease (1.4 times) in short-term visual memory and (1.1 times) in imagery memory; this type of memory is more affected in men; the indexes worsen with age. It was also marked that against the background of CCI there was a decrease of the attention productivity (1.4 times) and increase of the number of mistakes (1.5 times) both for men and women in both age categories. Typical manifestations of cognitive disorders in small caliber vascular pathology are neuropsychological symptoms of frontal dysfunction. One of the first symptoms of frontal dysfunction is delayed thinking: patients need more time and effort to perform various mental exercises, it becomes difficult for them to concentrate [16]. Disorders of voluntary attention are case-specific: Patients have difficulties switching from one stage of activity to another, or, on the contrary, are distracted from the planned program. Perseverations and increased impulsiveness are a consequence of these disorders. Impaired analytic abilities are also case-specific, and patients will have difficulty generalizing concepts or trying to explain the meaning of proverbs and sayings. CCI also affects operational and thinking activity, which is expressed in the suppression of its basic components - comparison, generalization, abstraction, classification [17,18]. The decrease of the abstract thinking level (2.9 times) was revealed in the main group, more expressed in men (3.3 times) with the number of mistakes increasing twice; weakening of the logical thinking connection with attention (1.9 times) was noted, more expressed in men (2.2 times) and in the older age category.

The duration of the disease has a negative effect on cognitive dysfunction, obviously, due to worsening of CCI phenomena. Thus, in the main group of patients with a history of cerebral infarction more than 3 years, the volume of figurative memory decreased by 1.2 times, the abstract component of thinking - by 1.7 times.

5.   Conclusions

Cognitive impairment against the background of CIM worsens more in men, in those over 60 years of age, and 3 years after a cerebral infarction; short-term drug therapy has no significant effect on cognitive dysfunction. Short-term in-patient drug therapy causes a non-significant increase in the mean values of visual memory and attention with a decrease in their error rate. This aspect confirms the necessity of long-term, not less than 6 months, complex therapy [19,20,21].

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