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Structural and Volumetric Characteristics of Cerebral Damage in Patients with Metabolic Syndrome

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Abstract.

The objective of the research was to identify volumetric brain indicators (hippocampal volume) in patients with chronic cerebral ischemia secondary to metabolic syndrome (MS) in comparison with patients suffering from chronic cerebral ischemia without MS; to identify the hippocampal index as well as medial, lateral and upper perihippocampal indices in patients with MS in comparison with those in patients without MS.

Materials and methods. Hippocampal volume of 47 patients (29 patients with MS - the main group and 18 patients without MS – the control group) was evaluated by means of volumetric method. During 49 studies (28 - the main group and 21 - the control group) the size of the hippocampus and perihippocampal cerebrospinal fluid space was measured.

Results and discussion. We determined a significant increase (*p<0.05 in comparison with the control group) ɜin the lateral perihippocampal cerebrospinal fluid space (cm) in the main group in comparison with the control group (Me [Q1, Q3]): on the right it was 2.90 [2.75 ; 2.96] vs. 2.21 [1.82; 2.05] in the control group (p<0.05); on the left it was 2.97 [2.75; 2.96] vs. 2.275 [2.15; 2.76] in the control group (p>0.05). A significant decrease in the index of the right and left hippocampus was determined in patients with MS in comparison to the patients of the control group (Me [Q1,Q3]): on the right it was 0.50 [0.41; 0.54] vs. 0.594 [0.58; 0.61]; on the left it was 0.56 [0.52; 0.60] vs. 0.61 [0.58; 0.63] in the control group (p<0.05). A significant difference in the increase of the medial and upper perihippocampal indices on either side was defined in the main group in comparison with the control one. Lateral perihippocampal index did not significantly differ from the control group (p>0.05). Determination of the hippocampal volume (right and left) showed that it was significantly lower in patients with MS than in patients without MS (Me [Q1,Q3]): on the right it was 3.293058* [2.92616; 3.04016] in the main group, and 3.93 [3.72750; 4.29722] in the control group; on the left it was 2.84 [2.65; 3.02] * in the main group, and 3.55 [3.22, 3.7] in the control group. Components of MS cluster in patients with chronic cerebrovascular pathology are likely to contribute to the development of atrophic processes. The combination of hypertension, insulin resistance, dyslipidemia, etc. accelerate the processes of hippocampal atrophy more than each of these separate components determined in patients with chronic cerebral ischemia without MS.

Conclusions. Thus, the degree of hippocampal atrophy in patients with chronic cerebrovascular diseases secondary to MS was defined to be significantly higher in comparison with patients without MS. To improve diagnosis of cerebrovascular diseases in patients with MS, it is possible to apply the identification of the hippocampal index and perihippocampal indices if it is not possible to determine the volume of brain structures.

Keywords: cerebral ischemia; metabolic syndrome; volumetry; hippocampus

Problem statement and analysis of the recent research

High disability progression, increase in human mortality, as well as increased number of young people in the structure of brain ischemia and the progression of cognitive impairments spike the interest in the problems of diagnosis, treatment and prevention of cerebrovascular diseases.

According to the results of a recent study on stroke performed in the USA (Greater Cincinnati/Northern Kentucky Stroke Study–GCNKSS), in the community numbering1.3 million people at the age of 20-54 years, the rate of patients with stroke increased by 19% in 2005 being 13% in 1993-1994, and the average patients' age with initial stroke decreased

to 69 years in 2005 being 71 in 1993-1994. Probable explanation of this fact may be the change in demographic characteristics of causative risk factors for developing stroke - for example, increased obesity among children and young adults, sedentary lifestyle and unhealthy diet which can result in premature development of cerebrovascular diseases due to high blood pressure and the development of diabetes. According to the results of the National Health and Nutrition Examination Survey (NHANES) designed to assess the health and nutritional status of adults and children in the United States prevalence of risk factors for stroke among adults at the age of 20-54 years was almost double: prevalence of diabetes increased from 2% in 1988-1994 to 4% in 2005-2006, high blood cholesterol level increased from 11% to 21%, obesity increased from 19% to 34%. In this regard, metabolic syndrome problem including hypertension, insulin resistance, visceral obesity, hypercholesterolemia and diabetes mellitus takes centre stage.

Cardiac, neurological and endocrinological diseases resulting from metabolic syndrome cause mortality, disability and dramatic decrease in quality of lifestyle. Scientists and doctors' interest spike in the metabolic syndrome during the last decades is associated with the importance of preventing type 2 diabetes and cardiovascular diseases due to atherosclerosis. Metabolic syndrome prevalence increases annually. Nowadays the WHO experts consider this situation to be a new pandemic of the XXI century spanning industrialized countries.

The most significant argument for studying the impact of MS on the occurrence, clinical manifestations and prognosis of ischemic stroke is its atherogenic potential of cardiac and cerebrovascular complications due to atherosclerosis. Many studies have shown that patients with MS often develop early signs of carotid and coronary arteries atherosclerosis. It indicates that the causes of myocardial infarction, ischemic stroke and peripheral vascular diseases have a common origin. Thus, the studies [5, 6, 2] showed that treatment regimens do not only prevent coronary conditions and the need for revascularization, but also reduce the incidence of ischemic stroke and peripheral vascular diseases.

It is considered that pathogenesis of chronic cerebral ischemia results from increase in pathobiochemical abnormalities caused by decreased levels of oxygen in arterial blood (hypoxemia) on the one hand and the influence of suboxide oxygen intermediates (oxidative stress) on the other hand. As a result, patients with chronic cerebral ischemia having chronic disorders of cerebral perfusion, systemic blood flow, microcirculation and hypoxemia develop micro-lacunar ischemic zones. Chronic brain hypoperfusion causes changes primarily in white matter forming foci of demyelination damaging *astro*- and *oligodendroglia* with microcapillary compression and results in apoptotic foci. These pathologic processes in chronic cerebral ischemia result in clinical changes manifested as both subjective and objective symptoms occurring due to disorders of cortico-striate and cortico-stem connections. The clinical picture of chronic cerebral ischemia is manifested by a combination of cognitive disorders, emotional disorders and focal neurological symptoms, the character of which is mostly determined by localization of changes in brain substance and their severity [4]. One of the severest manifestations of chronic cerebral ischemia is vascular dementia [1].

Regarding the occurrence of cognitive impairment in patients with MS, there are disputable points of view presented in scientific literature. Several authors associate MS with decline in cognitive function and developing dementia of neurodegenerative and vascular origin. The studies revealed connection of dementia with hypertension, diabetes and metabolic syndrome. It was determined that patients with prediabetes, hyperinsulinemia, metabolic syndrome with hypertension, dyslipidemia and obesity have worse cognitive capabilities and they reduce faster [7, 8]. Even MS itself without diabetes contributes to the development of Alzheimer's disease [3, 9].

Characteristic morphometric changes according to brain MRI and CT occur in acute cerebrovascular accidents and other organic damages, which reveal features specific to a particular process. MRI does not usually reveal any pathological changes caused by chronic ischemia. The significance of microfocal changes has not been cleared out yet. According to the published data, they can comply with natural brain aging and are common to most people over 65 years old. Structural brain damage in patients with chronic cerebral ischemia affected by MS has been insufficiently studied and existing data are disputable.

The objective of the research was to identify volumetric brain indicators (hippocampus) in patients with chronic cerebral ischemia affected by MS and compare them to those of the patients with chronic cerebral ischemia without MS; to identify the hippocampal index as well as medial, lateral and upper perihippocampal indices in patients with MS in comparison with those in patients without MS.

Materials and methods

Hippocampal volume of 47 patients (29 patients with MS - the main group and 18 patients without MS – the control group) was evaluated by means of volumetric method (measuring volume of brain structures) using the Toshiba Vantage Titan 1.5T MRI machine. The Vitrea workstation was used for image post-processing. We used MR sequences: T1 - weighted image, T2- weighted images, Isotropic, Flair, DWI, T2*, FSBB. The volume of the right and left hippocampus was determined. All measurements of volume indicators were determined in cm^3.

The research of the volume of certain brain structures is a complex, time-consuming process and requires long-term patient's exposure to the MRI scanning. The literature describes a technique proposed by Scheltens et al, based on the assessment of the medial temporal lobe, including the hippocampus, and the volume of the cerebrospinal fluid space, in particular, temporal horn of the lateral ventricle and vascular slit [10]. According to this method the study (MRI) of the brain was performed by means of Siemens MAGNETOM Avanto 1.5Tl MRI Scanner. T2WI, T2blade dark-fl, T1WI scans of the brain were performed in axial, coronal and sagittal projections. In 49 patients (28 patients of the main group and 21 patients of the control group) transverse and vertical size of the hippocampus, transverse and vertical size of the whole perihippocampal cerebrospinal fluid space and transverse size of the medial, lateral (temporal horn) and vertical perihippocampal spaces were measured. Both right and left hemispheres were measured. Then the hippocampal index was calculated; set of transverse and vertical diameters of the hippocampus was divided by the plurality of transverse and vertical diameters of the whole perihippocampal space (Fig.1).The medial perihippocampal index was calculated in the following way: the width of the medial cerebrospinal fluid space was divided by the full-width of perihippocampal cerebrospinal fluid space. The lateral perihippocampal index was calculated in the following way: the width of the lateral cerebrospinal fluid space was divided by the full-width of perihippocampal cerebrospinal fluid space. The superior perihippocampal index was calculated in the following way: the height of the outer cerebrospinal fluid space was divided by the full-height of perihippocampal cerebrospinal fluid space.

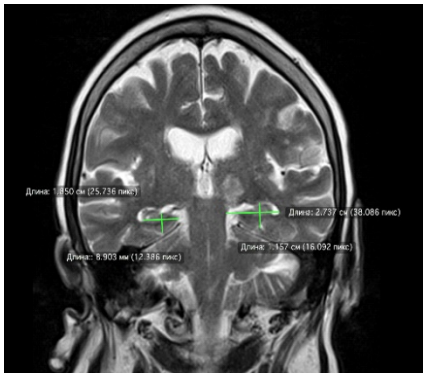

Fig.1. Transverse and vertical size of the hippocampus (on the left) and transverse and vertical size of the whole perihippocampal cerebrospinal fluid space (on the right)

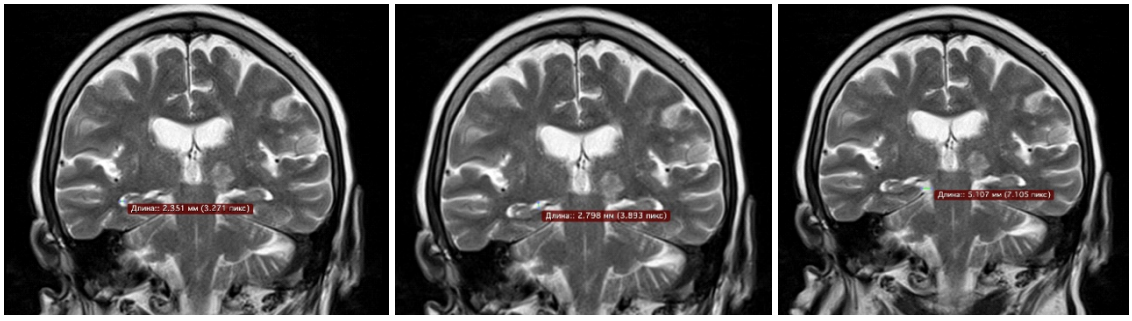

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Fig.2. Measuring the size of the medial cerebrospinal fluid space
Fig.3. Measure the size of the outer cerebrospinal fluid space
Fig.4. Measuring the size of the lateral cerebrospinal fluid space

Results and discussion

While measuring the size of the transverse perihippocampal cerebrospinal fluid space (cm), a significant increase (* $p < 0.05$ in comparison with the control group) in this index was determined in the main group in comparison with the control group (Me [Q1, Q3]): on the right it was 2.90 [2.75 ; 2.96] vs. 2.21 [1.82; 2.05] in the control group; on the left it was 2.97 [2.75; 2.96] vs. 2.275 [2.15; 2.76] in the control group.

Table 1

Hippocampal index in patients with chronic cerebrovascular pathology

	Main Group		Control Group	
	Me [Q1,Q3]		Me [Q1,Q3]	
	right	left	right	left
Hippocampal index	0.50[0.41;0.54]*	0.56[0.52;0.60]*	0.594[0.58;0.61]	0.61[0.58;0.63]

Note: *p<0.05

In patients with metabolic syndrome a significant decrease in the hippocampal index (right and left) in comparison with the control group was determined.

Table 2

Lateral, medial and upper perihippocampal indices

	Main Group		Control Group	
	Me [Q1,Q3]		Me [Q1,Q3]	
	right	left	right	left
Medial perihippocampal index	0.18[0.14;0.17]*	0.15[2.75;2.96]*	0.12[2.75;2.96]	0.11[2.75;2.96]
Lateral perihippocampal index	0.08 [0.072;0.78]	0.18 [0.13;0.17]	0.09 [0.06;0.08]	0.17 [0.14;0.16]
Superior perihippocampal index	0.157 [0.12;0.177]*	0.1721[0.136;0.156]*	0.12 [0.09;0.17]	0.1337 [0.11;0.17]*

Note: *p<0.05

A significant increase in medial and superior perihippocampal indices both left and right, was defined in the main group in comparison with the control group (right and left). The lateral perihippocampal index did not significantly differ from that in the control group (p>0.05).

Thus, patients with chronic cerebrovascular pathology secondary to MS, showed higher rate of hippocampal atrophy, which was determined by significant increase in perihippocampal indices and decrease in the hippocampal index in comparison with patients without MS.

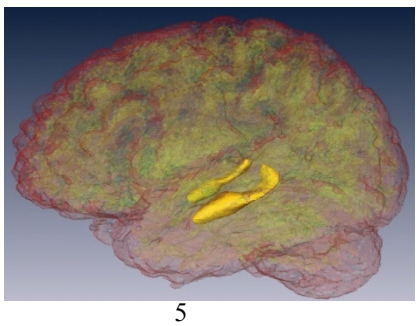
The results of measuring the hippocampal volume proved that hippocampal volume (right and left) in patients with MS was significantly lower in comparison with that in patients without MS (Table 3).

Table 3

Hippocampal volume (left and right) (cm³)

	Hippocampal volume (cm³) main group					Hippocampal volume (cm^3) control group				
	Min	*Max*	*Me*	Q1	Q3	*Min*	*Max*	*Me*	Q1	Q3
Right	2.2229	3.6500	3.293058 *	2.92616	3.04016	3.3692	4.400	3.93	3.72750	4.29722
Left	2.13	3.2500	2.84*	2.65	3.02	2.8	4.1000	3.55	3.2	3.7

Note: *p<0.05



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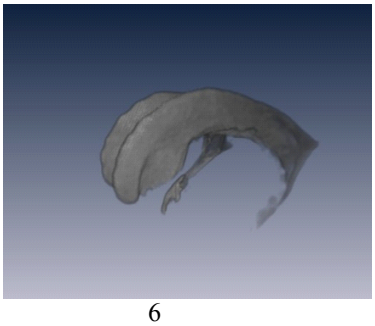

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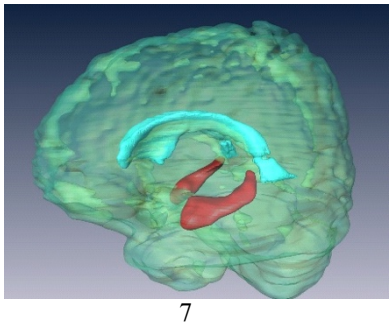

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Fig. 5. Measurement of the hippocampus in 56-year-old female patient L., (the main group).

Fig. 6. Measurement of ventricular and hippocampal volume in 62-year-old female patient S., (the main group) - severe hippocampal atrophy.
Fig. 7. Measurement of ventricular and hippocampal volume 64-year-old male patient P., (the control group).

Conclusions

Thus, the degree of hippocampal atrophy in patients with chronic cerebrovascular diseases secondary to MS was defined to be significantly higher in comparison with patients without MS. To improve diagnosis of cerebrovascular diseases in patients with MS, it is possible to apply the identification of the hippocampal index and perihippocampal indices if it is not possible to determine the volume of brain structures.

Prospects for further research

The obtained results of the study require further research. It is reasonable to conduct measurements of other essential brain structures in patients suffering from CVD secondary to MS and those not affected with MS, and determine possible correlation between indices of their volume and cognitive and affective disorders.

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