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Cerebral hemispheres volumetric characteristics in patients with cognitive impairments with underlying metabolic syndrome

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Abstract
The Research Objective: The research objective is to perform volumetric study (volume determining of particular cerebral hemispheres structures in см³) in patients with mild and moderate cognitive impairments with underlying MS and to compare the findings to the patients' volume without MS.
Research methods and materials: The brain and its liquor system of 47 patients (29 patients with MS - the main group and 18 patients without MS - control group) were evaluated by means of volume try method (measuring volume of particular cerebral hemispheres structures) with MRI scanner Toshiba Vantage Titan 1,5 Tl. Workstation Vitrea was used for images post-processing.
The cerebral substance volume; the cerebral alba volume; the cerebral grey substance volume; the number of infarctions; the volume of infarctions; cortex volume of temporal lobe; cortex volume of frontal lobe; the cerebral alba volume of frontal lobe; the cerebral alba volume of temporal lobe; lateral cerebral ventricles volume; volume of the right and left hippocampus; "leukoaraiosis" volume; the corpus callosum square were measured. All measurements of volume indicators were determined in см³.
We performed general, clinical neurologic and neuropsychological examinations of the patients. The presence of cognitive impairments was determined.
Research findings and discussion: Cognitive impairments in patients of the main and control groups manifested themselves in memory loss, disturbance of attention, slowing of mental processes according to the MOCA and MMSE scales and Schulte's table. The main group's result according to MOCA scale was Me=26,5 points [25; 28], whereas the control group's result was Me = 27,5 points [26; 29]. Cognitive functions indicators according to MOCA scale were inversely dependant on the indicators of glycated hemoglobin increase. There was defined a significant (P <0,05) decrease of cerebral substance volume, alba and grey cerebral substances volume, as well as of alba and grey cerebral substances volume in temporal lobe of patients with cognitive impairments with underlying MS as compared to the patients without MS. Patients with MS had a significantly enlarged cerebral ventricular system volume as compared to the patients without MS. Besides, there was observed a decrease in volume of corpus callosum square $P < 0,05$ in some patients.
Conclusions: There was defined a significant decrease of alba and grey cerebral substances volume, as well as of alba and grey cerebral substances volume in frontal and temporal lobes of patients with cognitive impairments with underlying MS as compared to the patients without MS.

Keywords: Metabolic syndrome, cognitive impairments, cerebral substance volume, dementia.

1. Introduction
The metabolic syndrome (MS) impact on the development and progression of cognitive impairments spike the interest in the problems of diagnosis, treatment and prevention of cerebrovascular diseases (CVDs). In medicine, the vascular dementia belongs to chronic CVDs (V. Hachinski "multi-infarct dementia" [1]). In 1993 V. Hachinski introduced the medical term "vascular cognitive impairments" to define the cognitive impairments resulting from CVDs. Modern scientific literature presents a disputable opinion as for associating MS with cognitive impairments. A number of authors associate MS with cognitive functions decline and developing dementia of vascular and neurodegenerative origin. Some researches reveal the link between the hypertension, type 2 diabetes and MS [2]. Research on individuals taking care of their relatives with Alzheimer's disease, performed within 8 years, has shown that chronic distress of care givers with MS predisposed them to cognitive functions decline. Moreover, chronic stress connected with the care for a close person, predisposed a care giver to CVDs developing [3]. Patients with pre-diabetes and hyperinsulinemia, MS with hypertension, dyslipidemia and obesity are known to have worse cognitive functions and they tend to decline faster [4, 5]. MS itself even without diabetes predispose an individual to

Alzheimer's disease developing [6, 7]. Diabetes mellitus and MS are associated with a higher risk of micro- and macro-vascular complications as well as with cerebrovascular phenomena leading to cognitive functions decline. Risk of dementia developing in patients with type 2 diabetes and hypertension is higher than in case of with type 2 diabetes only or just hypertension [6, 8], and the combination of type 2 diabetes and hypertension makes the risk of vascular dementia development sixfold [6, 9, 10]. Co-existence of cerebrovascular pathology and type 2 diabetes together enhances correlation between moderate cognitive impairment and dementia [6, 11]. Obesity in middle-aged people is associated with cognitive functions decline at later stages of their life. Leptin homeostasis impairment elevates the count of extracellular β-amyloid and phospho-tau (animal models) [12]. In case of Alzheimer's disease, the decline in circulating leptin count has an invert correlation to cognitive deficit. Hyperlipidemia is associated with a higher risk of cognitive deficit [13].

During clinical research studies with 823 patients participating, which took place in Amsterdam [14], there were obtained some results. The relationship between patients' cognitive dysfunction and atherosclerosis was studied. The risk of cognitive dysfunction developing in case of MS as a general condition was compared to the risk of cognitive dysfunction developing under the circumstances of separate factors (for example hypertension, diabetes mellitus, dyslipidemia, etc.)

MS was proved to cause a higher risk of memory impairment (2.0, 95% Cl1.1 -3.3), but not of the executive dysfunction.

It is rather reasonable to predict that MRI pictures showed the presence of some cognitive impairment signs in patients with MS. However, the role of minute affected areas present in patients frequently, has not been cleared out yet. Referring to the data provided in scientific publications, these minute affected areas may correspond to the brain natural aging, and they are common in people over 65. Specific researches on MS impact on the brain revealed that there developed some periventricular, subcortical and hyper intensive affected areas, silent lacunar infarctions and leukoaraiosis [15]. There is some evidence that the presence of subcortical affected areas in patients' Alba results in cognitive deficit developing [15].

A number of scholars consider that the association between decline of information processing speed and affection of Alba in patients with MS can be greatly caused by the MS impact itself, and not only by age-related changes in patients' brain [16].

The Research Objective: The research objective is to perform volumetric study (volume determining of particular cerebral hemispheres structures in см³) in patients with mild and moderate cognitive impairments with underlying MS and to compare the findings to the patients' volume without MS.

Research methods and materials: The brain and its liquor system of 47 patients (29 patients with MS - the main group and 18 patients without MS - control group) were evaluated by means of volumetry method (measuring volume of particular cerebral hemispheres structures) with MRI scanner Toshiba Vantage Titan 1,5 Tl. Workstation Vitrea was used for images post-processing. We used MR sequences: T1 - weighted image, T2- weighted images, Isotropic, Flair, DWI, T2 *, FSBB.

While analyzing the obtained findings, the following parameters were evaluated: the cerebral substance volume; the cerebral alba volume; the cerebral grey substance volume; the number of infarctions; the volume of infarctions; cortex volume of temporal lobe; cortex volume of frontal lobe; the cerebral alba volume of frontal lobe; the cerebral alba volume of temporal lobe; lateral cerebral ventricles volume; volume of the right and left hippocampus; "leukoaraiosis" volume; the corpus callosum area.

All measurements of volume indicators were determined in см³. Considering the fact that the cerebral volume can change with the age, we took into account indicators of those patients who were of the same age: the main group (patients with MS) – patients' age – Me = 62 (Q1=54,Q3=70); control group (patients without MS) – Me= 64 (Q1=56,Q3=70). In this way we could avoid age error of a measurement.

We performed clinical neurologic examination (complaints, medical history, neurologic status), cardiovascular examination, measuring blood pressure, ECG, complete blood count, urinalysis, glucose test, blood clotting test, atherogenic index test, C-reactive protein test, bilirubin test, ALT level test, AST level test, cholesterol test, triglyceride test, HDL and LDL tests, HOMA–IR and Hb1Ac index tests to all patients. Patients were also determined their anthropometric measures like weight, height in cm, waist and hips volume in cm. Patients' BMI was also calculated. MS presence was determined in patients by ATR III requirements. Neuropsychological test included: screening – psychological status assessment according to MMSE scale, according to Montreal scale of cognitive functions assessment MOCA; according to Spielberger anxiety scale; according to Beck's depression inventory.

Mental alertness test included number search with the help of Schulte tables, the time spent for performing this task was also evaluated.

Tatistic analysis of findings was performed by means of contemporary calculus methods applying statistic packages "Statistica-6" and "Exel 2003". Student's parametric test and U non- parametric test (Mann – Whitney – Wilcoxon criterion) were used to guarantee data deviation reliability.

Research findings and discussion: Both mild and moderate cognitive impairments were found in patients of the main and control groups. Indicators of psychological status assessment ranged from 24 to 30 points.

The main group's result according to MMSE scale was Me=26 points, Q1=25,0 Q3=28, whereas the control group's result was Me= 27 points, Q1=25; Q3=28.The most significant cognitive impairments manifested themselves in memory loss, disturbance of attention and slowing of mental processes. Sensitivity of Montreal cognitive assessment scale (MOCA) to detect mild cognitive impairment allows to use it for revealing mild cognitive disorders. Therefore, results analysis was carefully conducted by means of the MOCA scale. These results are shown in Table №1. Impairments were observed in the following cognitive spheres: attention and mental alertness, memory, optical-spatial skills, abstract thinking and calculating. The most significant cognitive impairments manifested themselves in attention and mental alertness, memory, somewhat milder in visual-constructive skills.

Table 1: Test results according to MOCA scale

	Main group (points) (n=29)	**Control group (points) (n=18)**
Me[Q1,Q3]	26,5[25;28] *	27,5[26;29]

* P <0,05 – there is a significant difference as compared to the patients without MS.

There was defined the relationship between the glycated hemoglobin and decrease of cognitive functions according to MOCA scale (Fig 1).

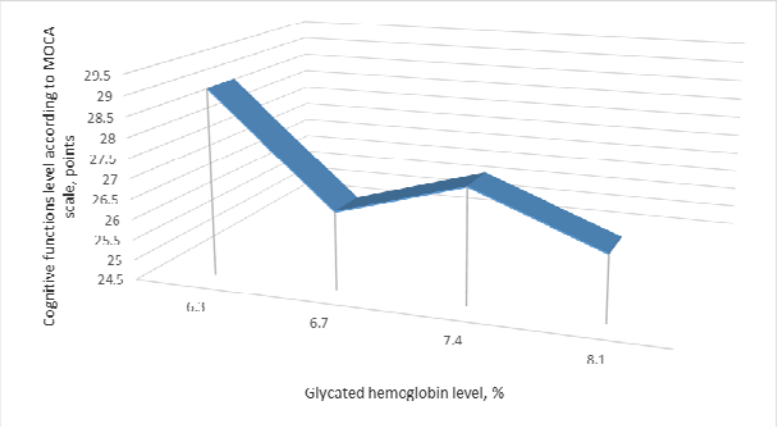

Fig 1: The relationship between cognitive functions according to MOCA scale and the glycated hemoglobin of the patients in the main group was ($P < 0,05$)

Based on data provided in Fig.1, cognitive functions indicators according to MOCA scale are inversely dependant on the indicators of glycated hemoglobin increase.

Measuring volume of particular brain structures by means of MRI, revealed a significant ($P < 0,05$) general volume decrease of cerebral hemispheres substance(alba and grey substances).

Table 2: General Volume of Cerebral Hemispheres Substance (cm³).

Measurement Area	Main group (patients with MS) (n=29) Me (Q1,Q3)	Control group (patients without MS) (n=18) Me (Q1,Q3)	P
General Volume of Cerebral Hemispheres Substance (cm³)	990 [660,1080]*	1200[1100,1480]	< 0,05
Grey Substance Volume (cm³)	368,6 [140;422] *	430 [320;540]	< 0,05
Alba Volume (cm³)	533,3 [140;422] *	672,5[635;720]	< 0,05

* P <0,05 – there is a significant difference as compared to the patients without MS.

Based on data provided in Table №2, indicators of general cerebral substance volume differed. There was defined a significant decrease of cerebral substance volume in patients with cognitive impairments with underlying MS. There was also defined a significant difference between cerebral alba and grey cortex substances volume $P < 0,05$ between patients of the main and control groups

Table 3: The Cerebral Alba and Grey Cortex Volume in Temporal Lobe (cm³).

Measurement Area	Main group (patients with MS)(n=29) Me (Q1,Q3)	Control group (patients without MS) (n=18) Me (Q1,Q3)	P
The cerebral alba volume (cm³)	94,5 [82;107] *	127,5 [115;160] *	<0, 05
The cerebral grey cortex volume (cm³)	99 [82;110] *	125[125;145] *	<0,05

* P <0,05 in comparison to control group

Based on data provided in Table № 3, the volume of alba and grey cerebral substances of temporal lobe differed significantly between patients with and without MS ($P < 0,05$).

Fig 2 Determinig the volume of alba and grey cerebral substances in frontal lobe of 64 year - old patient Sh. with MS (red colour – cortex, blue colour – alba and cerebral substance of temporal lobe).

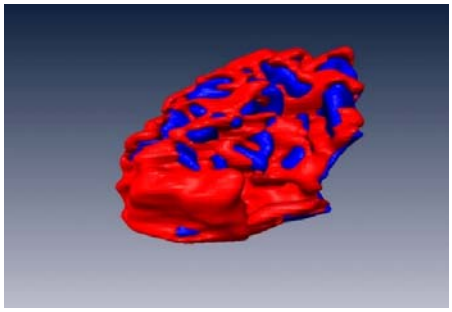

Fig 2: demonstrates cerebral cortex atrophy of the patient with mild cognitive impairments with underlying MS.

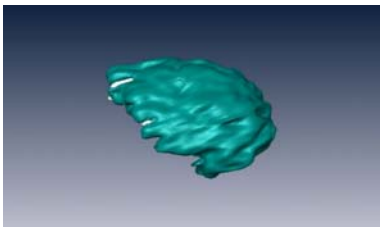

Fig 3: Determinig the volume of alba and grey cerebral substances in frontal lobe of 62 year - old patient S. without MS.

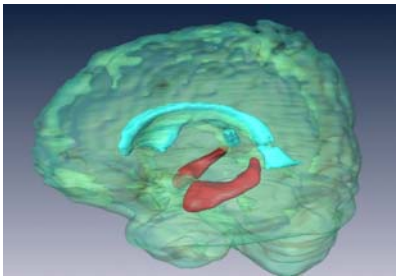

Fig 4: Determinig the lateral cerebral ventricles volume, the volume of hippocampi of 62 year - old patient S. without MS.

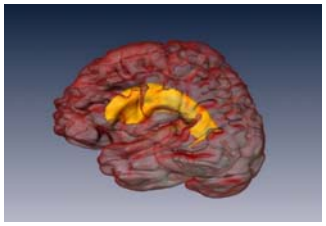

Fig 5: Determinig the lateral cerebral ventricles volume, the volume of hippocampi in 64 year - old patient Sh. with MS.

Figure 4 demonstrates clearly marked cerebral ventricles and hippocampi in patients without MS. Figure 5 demonstrates enlarged cerebral ventricle proving the presence of internal hydrocephaly and it is hardly marked, hippocampi volume is significantly decreased in patient with MS.
Volumes of lateral cerebral ventricles are provided in Table №4

Table 4: The General Volumes of Lateral Cerebral Ventricles (cm³).

Measurement Area	Main group (patients with MS) (n=29) Me (Q1,Q3)	Control group (patients without MS) (n=18) Me (Q1,Q3)	P
The general volumes of lateral cerebral ventricles (cm³)	30,7 [19,4;52] *	21,3[11,2;25,80]	< 0, 05

* *P* <0,05 in comparison to another group.

Data provided in Table №4 prove the patient with MS to have a significantly enlarged volume of ventricular system in comparison to patients without MS.

While determining volumes and measuring particular cerebral structures, there was observed a decrease in volume of corpus callosum square in some patients.

Table 5: Corpus Callosum Square in Researched Groups.

	Main group (patients with MS) (n=29)					Control group (patients without MS) (n=18)				
	Min	***Max***	***Me***	**Q1**	**Q3**	***Min***	***Max***	***Me***	**Q1**	**Q3**
Corpus Callosum Square (см²)	630	707	656,6*	645	685	689	780	734,5	720	760

**P* < 0,05 in comparison to control group

Analyzing data provided in Table №5, we can confirm that in patients with cognitive impairments with underlying MS, a significant decrease of corpus callosum square *P*<0,05 was noticed in comparison to the patients without MS.
Decrease of corpus callosum square is likely to reflect the impairment of associative fibers running through it and playing a significant role in providing an integral cerebral activity, resulting in a discovered correlation between its square changes and the degree of cognitive impairments with underlying cerebrovascular changes. There is an impairment of interhemispheric interaction, and accordingly an impairment of hemispheric coordinated activity.
Obviously, combination of MS components cluster in patients with cognitive impairments anticipates atrophic processes in the strategic areas of the brain more than any separate component determined in patients with cognitive impairments without underlying MS.

Conclusions

- The study has revealed the presence of atrophic processes in the strategic cerebral hemispheres in patients with cognitive impairments without underlying MS.
- Patients with cognitive impairments with underlying MS have been determined a significant decrease of the cerebral cortex volume and of alba substance in their frontal and temporal lobes as compared to the patients without MS.
- Neuropsychological testing also revealed the decrease of cognitive functions in patients of both groups according to MMSE and MOCA scales, but the group where disease developed with underlying MS demonstrated lower indicators (*P*<0,05) as compared to the patients in control group.
- Patients with cognitive impairments with underlying MS, were determined a significant decrease of corpus callosum square (*P*<0,05) in comparison to the patients without MS.

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