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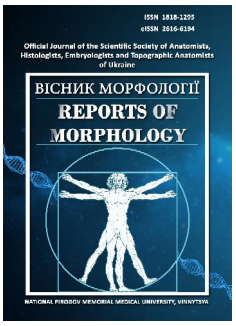

Brain morphometry and its relevance in cerebral small vessel disease

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Cerebral small vessel disease (CSVD) is a heterogeneous group of disorders which affect small perforating vessels of the brain. Clinically CSVD manifest with various constellations of symptoms, like cognitive, functional, affective as well as lacunar stroke or intracerebral hemorrhage. It is responsible for 25 % of all strokes and are the second contributor to dementia after Alzheimer's disease. The gold standard for CSVD diagnostic is neuroimaging. The main key features are white matter hyperintensity (WMH), lacunes, enlarged perivascular spaces (EPVS), brain atrophy. Brain atrophy have been recognized to play a synergistic role in both cerebrovascular and neurodegenerative disorders occurring in the aging brain. It reflects a final common pathway for pathological processes, which progress in time. CSVD progression results in gradual decrease of brain volume, which is seen as changes of ventricles size and cortical sulci span of the brain. But not much is known about its extent, correlates and consequences. The aim of the research is to investigate whether brain morphometric changes correlate with CSVD features. In this study, we included 129 CSVD patients and 165 non-CSVD controls, both with acute stroke. All participants underwent neuroimaging assessment with magnetic resonance imaging (MRI) and computed tomography (CT). We used both univariate and multivariate regression analysis, as well as correlation analysis to identify differences in brain morphometric parameters between groups. Multivariable regression analysis, adjusted for age and sex, revealed significant impact of Evans index (OR 1.09, 95 %; CI 1.01-1.16, p=0.018), the third ventricle index (OR 1.42, 95 %; CI 1.21-1.67, p<0.001), Schaltenbrand and N?rnberger index (OR 1.42, 95 %; CI 1.21-1.67, p<0.001), the fourth ventricle index (OR 1.31, 95 %; CI 1.13-1.51, p<0,001), bicaudate index (OR 1.19, 95 %; CI 1.10-1.30, p<0.001), cella media index (Schiersmann's index) (OR 0.55, 95 %; CI 0.42-0.72, p<0.001), Huckman number (OR 1.05, 95 %; CI 1.02-1.08, p<0.001), width of the longitudinal cerebral fissure in the anterior part of the frontal lobes (OR 1.46, 95 %; CI 1.22-1.75, p<0.001), width of the left insular cistern (OR 1.24, 95 %; CI 1.11-1.39, p<0.001), width of the right insular cistern (OR 1.31, 95 %; CI 1.17-1.46, p<0.001), width of the right and left insular cisterns in sum (OR 1.17, 95 %; CI 1.10-1.25, p<0.001), width of the cerebral fissure in the area of the skull vault (OR 1.49, 95 %; CI 1.21-1.84, p<0.001) on the CSVD presence. Width of the longitudinal cerebral fissure in the anterior part of the frontal lobes in CSVD was 6.13±1.56 mm vs 5.10±1.38 mm in non-CSVD, p<0.001 and width of the right and left insular cisterns in sum in CSVD was 16.98±4.60 mm vs 13.41±4.16 mm in non-CSVD, p<0.001. Width of the cerebral fissure in the area of the skull vault (parietal cortex) was also greater in CSVD patients: 5.04±1.85 mm vs 4.12±1.29 mm, p<0.001. Thus, all ventricular and cortical indices were increased in the group of patients with CSVD. Our results indicate that morphometric indicators of the brain are closely related to CSVD and can be useful for predicting the consequences of a stroke and ascertaining the decline of cognitive functions.

Key words: *brain morphometry, cerebral small vessel disease, Evans index.*

Introduction

Cerebral small vessel disease (CSVD) is a heterogeneous group of disorders which affect small perforating arteries, arterioles, capillaries, venules and veins (vessels of 5 mcm - 2 mm. in diameter) of the brain [5]. It affects brains parenchyma through chronic changes of perfusion, hypoxia, ischemia, blood-brain barrier

dysfunction, inflammation and endothelium abnormalities, which results in progressive changes of vessel walls such as hyalinosis (accumulation of plasma proteins in subendothelial space), hyperplastic arteriolosclerosis, segmental arteriolar desorganisation, microaneurisms formation, chronic vessel wall degeneration etc. [16]. These changes may affect both white and grey matter of the brain. As a consequence - gradual decrease of brain volume, which is seen as brain atrophy and changes of ventricles size and cortical sulci span of the brain. Clinically CSVD manifest with various constellations of symptoms, like cognitive, functional, affective as well as lacunar stroke or intracerebral hemorrhage. It is responsible for at least 20-25 % of all strokes and are the second contributor to dementia after Alzheimer's disease [15]. CSVD affects not only subcortical brain parenchyma, but also the cortex with cerebral microbleeds or microinfarcts etc. [9].

The key standard for CSVD diagnostic is neuroimaging. The main features are white matter hyperintensities (WMH), lacunes, enlarged perivascular spaces (EPVS), brain atrophy, recent lacunar infarcts, cerebral microbleeds, microinfarcts, superficial cortical siderosis [3]. Among these, brain atrophy have been recognized to play a synergistic role in both cerebrovascular and neurodegenerative disorders occurring in the aging brain. It reflects a final common pathway for pathological processes, which progress in time. But not much is known about its extent, correlates and consequences [14].

There are several types of brain atrophy, such as global cortical atrophy, deep atrophy, total atrophy, mediotemporal hippocampal atrophy, precuneus atrophy etc. [21], which helps better classified brain changes for diagnostics, treatments and prognostics purposes. Therefore, more precise and thorough measurement of the brain morphology can shed light on underlying pathology and give clues for better prevention strategies.

The aim of the research is to investigate whether brain morphometric changes correlate with CSVD features.

Material and methods

Subjects

It was a prospective cohort study based on specialized stroke department (Stroke Unit) № 22 of the Vinnytsia Regional Psychoneurological Hospital named after acad. O.I. Yushchenko. Committee on Bioethics of National Pirogov Memorial Medical University, Vinnytsya (Protocol № 6 from 3.10.2022) found that the studies do not contradict the basic bioethical standards of the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant WHO regulations and laws of Ukraine.

Between December 2016 and December 2019 294 patients with acute stroke were recruited (age: 61.94±10.11 years old; 115 females). 129 (44 %) stroke patients with CSVD (age: 65.78±8.28 years old; 46 females) and 165 (56 %) stroke patients without CSVD (age: 58.93±10.42 years old; 69 females). The inclusion criteria for CSVD patients included diagnosis of WMH of presumed vascular origin, lacunes of presumed vascular origin, EPVS based on current MRI consensus standards [18]. The total CSVD burden was assessed by amended CSVD score (0-3 scale, scores calculated based on the severity of WMH, lacunes, EPVS (we used CSVD score without atrophy) that was approved in variety of studies [12].

Image Acquisition

120 patients underwent Magnetic Resonance Imaging (MRI), 174 - Computed Tomography (CT). Some of the subjects were imaged only with either MRI or CT, some of them - both with MRI and CT. MRI was performed on a Philips Achieve 1.5 T. The brain scanning protocol consisted of a T1-weighted, T2-weighted, FRAIR and DWI sequences, slice thickness was 3.5-5 mm. CT was performed on a General Electric CT/e (Italy) with a tomographic section thickness of 3-7 mm.

Measurements of the brain morphometry

We calculated such brain parameters as Evans index, the third ventricle index, Schaltenbrand and Nürnberger index, the fourth ventricle index, the bicaudate index, ventricular index, the cella media index (also known as Schiersmann's index), the Huckman number [19]. We multiplied the indices by 100 for better representation. We also measured the width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, the width of the right and left insular cisterns and their sum, the maximum width of the cerebral fissure in the area of the skull vault and the maximum width of the cerebellar fissure [4]. We assessed such CSVD featurea, as WMH, lacunes, EPVS. The severity of WMH was assessed using the Fazekas scale. The scale grades the severity from 0 to 3 [20]. A lacune typically is a lesion 3-20 mm in diameter that affects the subcortical white matter and the deep grey matter of the brain and brainstem. An enlarged PVS is a dilated space, <3 mm in diameter, with an ovoid, round, or linear shape, filled with CSF that surrounds perforating arterioles and venules, as they course from the subarachnoid space through the brain parenchyma [1]. Distinguishing among WMH, lacune, and enlarged PVS can occasionally be challenging by imaging. A marginally hyperintense rim seen with FLAIR is suggestive of a lacune instead of enlarged PVS. The typical anatomical location of enlarged PVS may be the best differentiating feature [21]. Total CSVD burden assessed by simple validate method, if there were one or more lacunes, one point was added, one point was added when the deep WMH Fazekas score reached 2 or periventricular WMH Fazekas score reached 3, if the number of EPVS at the basal ganglia or centrum semiovale level reached >10, one point was added [8].

Statistical analysis

We used univariable and multivariable regression analysis to establish the associations between morphometric data and CVSD features. Logistic regression was used in case of binomial, multinomial or ordinal dependent variable. Linear regression was used in case of

linear dependent variable. All multivariable analyses were adjusted for age and sex. Continuous variables were presented as mean ± standard deviations (SD). The results are shown as odds ratio (OR) and 95 % confidence intervals (CI) or as a beta-coefficient in case of linear regression. A p value <0.05 was considered statistically significant. Two groups comparison were performed by Student's t-test in Welch modification in normal distribution or Mann-Whitney U test if the variables were not normally distributed. Multiple group comparison were performed by ANOVA in normal distribution or Kruskal-Wallis test if the variables were not normally distributed. Categorical variables were presented as percentages and were compared with Pearson's chi square test or Fisher's exact test (if the number of observation were <5). Pearson or Spearman correlation were used to establish associations between two variables. Statistical analyses were performed by The jamovi project (2022). Jamovi (Version 2.2.5) [Computer Software]. Sydney, Australia and Microsoft Excel.

Results

Age of CSVD-patients was 65.76±8.28 years old, non-CSVD - 58.93±10.42 years old. Among 129 CSVD patients 83 (64.3 %) were males, 46 (35.7 %) - females. Among 165 non-CSVD patients 96 (58.2 %) were males, 69 (41.8 %) - females. 45 (34.9 %) CSVD patients had a previous stroke history, while 26 (15.7 %) non-CSVD reported about previous stroke. Hospitalization time for

Table 1. Brain morphometry depending on the CSVD presence.

Brain measurement	CSVD, 129	non-CSVD, 165	p
Evans index	28.12±4.23	26.40±3.47	<0.01
The third ventricle index	5.796±1.681	4.490±1.671	<0.01
Schaltenbrand and Nurnberger index	18.97±6.64	25.47±9.58	<0.01
The fourth ventricle index	12.85±2.24	12.18±1.41	<0.05
Bicaudate index	16.86±3.43	14.33±3.17	<0.01
Ventricular index	1.599±0.261	1.683±0.251	<0.01
Cella media index (Schiersmann's index)	4.719±1.030	5.538±1.193	<0.01
Huckman number	60.05±9.55	54.61±8.54	<0.01
Width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, mm	6.130±1.560	5.097±1.377	<0.01
Width of the right insular cistern, mm	8.226±2.499	6.432±2.379	<0.01
Width of the left insular cistern, mm	8.705±2.553	6.982±2.397	<0.01
Width of the right and left insular cisterns in sum, mm	16.98±4.60	13.41±4.16	<0.01
Maximum width of the cerebral fissure in the area of the skull vault, mm	4.887±1.668	3.899±1.167	<0.01
Maximum width of the cerebellar fissure, mm	2.625±1.265	2.505±1.063	>0.05

Table 2. Brain morphometry depending on the lacunes presence.

Brain measurement	Presence of lacunes, 68	Lacunes-free, 225	p
Evans index	27.53±4.25	27.05±3.81	>0.05
The third ventricle index	5.937±1.779	4.802±1.721	<0.01
Schaltenbrand and Nurnberger index	18.80±7.20	23.78±9.21	<0.01
The fourth ventricle index	13.01±2.28	12.31±1.68	<0.05
Bicaudate index	16.56±3.41	15.10±3.49	<0.001
Ventricular index	1.626±0.283	1.653±0.251	>0.05
Cella media index (Schiersmann's index)	4.686±0.991	5.323±1.213	<0.01
Huckman number	59.18±9.80	56.33±9.19	0.014
Width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, mm	6.181±1.638	5.367±1.468	<0.01
Width of the right insular cistern, mm	8.693±2.453	6.774±2.468	<0.01
Width of the left insular cistern, mm	9.044±2,504	7.352±2.517	<0.01
Width of the right and left insular cisterns in sum, mm	17.84±4.40	14.13±4.46	<0.01
Maximum width of the cerebral fissure in the area of the skull vault, mm	5.037±1.853	4.124±1.294	<0.01
Maximum width of the cerebellar fissure, mm	2.936±1.477	2.448±1.020	<0.01

Table 3. Brain morphometry depending on the WMH severity.

Brain measurement	WMH Fazekas 3, 106	WMH Fazekas 0-2, 188	p
Evans index	28.42±4.08	26.44±3.64	<0.01
The third ventricle index	5.946±1,.96	4.565±1.709	<0.01
Schaltenbrand and Nurnberger index	18.14±5.51	25.15±9.60	<0.01
The fourth ventricle index	12.92±2.23	12.22±1.54	<0.01
Bicaudate index	17.32±3.44	14.38±3.10	<0.001
Ventricular index	1.580±0.235	1.684±0.263	<0.01
Cella media index (Schiersmann's index)	4.596±0.984	5.508±1.179	<0.01
Huckman number	61.00±9.22	54.74±8.71	<0.01
Width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, mm	6.284±1.549	5.137±1.384	<0.01
Width of the right insular cistern, mm	8.180±2.549	6.677±2.452	<0.01
Width of the left insular cistern, mm	8.829±2.633	7.123±2.387	<0.01
Width of the right and left insular cisterns in sum, mm	17.07±4.75	13.80±4.25	<0.01
Maximum width of the cerebral fissure in the area of the skull vault, mm	4.946±1.667	3.987±1.258	<0.01
Maximum width of the cerebellar fissure, mm	2.649±1.316	2.507±1.055	>0.05

Table 4. Correlation analysis of brain morphometrics and CSVD features.

Brain measurement	WMH	Total SCVD	Amount of lacunes	EPVS BG	EPVS CS
Evans index	0.34***	0.23***	0.06	0.14	0.07
The third ventricle index	0.48***	0.40***	0.28***	0.29**	0.18*
Schaltenbrand and Nurnberger index	-0.9***	-0.40***	-0,.8***	-0.29**	-0.18*
The fourth ventricle index	0.16**	0.21***	0.20***	0.24**	0.05
Bicaudate index	0.47*	0.37***	0.19**	0.26**	0.11
Ventricular index	-0.28***	-0.21***	-0.06	-0.12	0.02
Cella media index (Schiersmann's index)	-0.41***	-0.39***	-0.24***	-0.21**	-0.05
Huckman number	0.37***	0.31***	0.14*	0.20**	0.09
Width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, mm	0.34***	0.35***	0.23***	0.26**	0.31***
Width of the right insular cistern, mm	0.34***	0.36***	0.33***	0.43***	0.23*
Width of the left insular cistern, mm	0.38***	0.35***	0.28***	0.35***	0.27*
Width of the right and left insular cisterns in sum, mm	0.41***	0.42***	0.35***	0.45***	0.29**
Maximum width of the cerebral fissure in the area of the skull vault, mm	0.36***	0.35***	0.25***	0.33***	0.50***
Maximum width of the cerebellar fissure, mm	0.12*	0.13*	0.22***	0.28**	0.24*

Note: *p<0.05; **p<0.01; ***p<0.001.

CSVD patients was 10.05±4.62 days, for non-CSVD - 8.94±3.72 days.

Brain morphometry measurements in accordance to CSVD, lacunes and WMH presence are shown in tables 1, 2, 3 respectively. Correlation analysis of brain morphometrics and CSVD features are shown in Table 4.

Multivariable regression analysis, adjusted for age and sex, revealed significant impact of Evans index (OR 1.09, 95 %; CI 1.01-1.16, p=0.018), the third ventricle index (OR 1.42, 95 %; CI 1.21-1.67, p<0.001), Schaltenbrand and Nürnberger index (OR 1.42, 95 %; CI 1.21-1.67, p<0.001), the fourth ventricle index (OR 1.31, 95 %; CI 1.13-1.51, p<0,001), bicaudate index (OR 1.19, 95 %; CI 1.10-1.30, p<0.001), cella media index (Schiersmann's index) (OR 0.55, 95 %; CI 0.42-0.72, p<0.001), Huckman number (OR 1.05, 95 %; CI 1.02-1.08, p<0.001), width of the longitudinal cerebral fissure in the anterior part of the frontal lobes (OR 1.46, 95 %; CI 1.22-1.75, p<0.001), width of the left insular cistern (OR 1.24, 95 %; CI 1.11-1.39, p<0.001), width of the right insular cistern (OR 1.31, 95 %; CI 1.17-1.46, p<0.001), width of the right and left insular cisterns in sum (OR 1.17, 95 %; CI 1.10-1.25, p<0.001), width of the cerebral fissure in the area of the skull vault (OR 1.49, 95 %; CI 1.21-1.84, p<0.001) on the CSVD presence.

Discussion

In this study we explored brain morphological alterations in a cohort of stroke patients with and without CSVD. We measured such indicators, as Evans index, the third ventricle index, Schaltenbrand and Nürnberger index, the fourth ventricle index, bicaudate index, ventricular index, cella media index (Schiersmann's index), Huckman number, width of the longitudinal cerebral fissure in the anterior part of the frontal lobes, width of the right and left insular cisterns and its sum, width of the cerebral fissure in the area of the skull vault, width of the cerebellar fissure. The results of the present research strongly support that brain atrophy is a key marker in CSVD.

Our study revealed that compared with the control group, the CSVD group showed significantly increased almost all deep indicators as well as cortical sulci span (except width of the cerebellar fissure). Lacunes and WMH separately also reflected similar results, however in lacunes group Evans index and ventricular index did not show significance. Explanation for it might be that WMH affects brain parenchyma more diffuse than lacunes. In the other words - CSVD and its features, like WMH and lacunes promote diminish of the brain volume, both white and grey matter. Our results showed that CSVD should be considered a whole-brain disease as deep and cortical morphometrics were both significantly altered. Decreasing of white matter volume may lead to loss of functional connectivity. It can disrupt white matter tracts or U-fibers that mediate cortical-cortical or cortical-subcortical connections [17]. Besides, some researches showed that local white matter lesions may influence the grey matter in remote areas [13]. So white and grey matter lesions complement each other [10].

According to our findings, width of the longitudinal cerebral fissure in the anterior part of the frontal lobes in CSVD was 6.13±1.56 mm vs 5.10±1.38 mm in non-CSVD, $p<0.001$ and width of the right and left insular cisterns in sum in CSVD was 16.98±4.60 mm vs 13.41±4.16 mm in non-CSVD, $p<0.001$. Width of the cerebral fissure in the area of the skull vault (parietal cortex) was also greater in CSVD patients: 5.04±1.85 mm vs 4.12±1.29 mm, $p<0.001$, which suggests diffusion cerebral cortex involvement during CSVD progression. The prefrontal and temporal cortex is a set of functionally connected regions that plays crucial roles in internal cognitive processing like working memory, attention and language, processing speed, autobiographical memory etc. [7] and its damage can cause cognitive deterioration. Early injury of temporal lobes in CSVD might be the reason of more serious cognitive decline [12], that's why measurement of width of the insular cisterns might be useful for patients selection for early cognitive decline prevention, like acetylcholinesterase inhibitors etc., whether it is neurodegeneration or vascular origin. It is necessarily to find out relationships between cortical and deep indices impact on cognitive functions as well as stroke outcome.

We also found out that EPVS CS mostly associated with width of the cerebral fissure in the area of the skull vault ($r=0.50$, $p<0.001$), but much less associated with ventricles size. It is known that beta-amyloid angiopathy mostly associated with EPVS at centrum semiovale [12]. Hence, predominantly cerebral fissures enlargement in the area of the skull vault might reflect beta-amyloid pathology of the brain.

For further investigations, measurements of ventricle size and cortical sulci span may be of interest, particularly for disentangling the effect of primary neurodegeneration from that of CSVD. It is also interesting, whether some particular index cause a specific neuro-cognitive, functional or affective change.

Conclusions

1. Brain morphometric indices is highly associated with CSVD and are key markers in it.

2. Different indices may reflect different underlying pathology, which can be useful for diagnostic and prognostic purposes.

3. Brain indices may be treated as a marker of CSVD progression. It might be useful for patients selection for early treatment or preventive strategies.

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ЦЕРЕБРАЛЬНА МОРФОМЕТРІЯ ТА ЇЇ КЛІНІЧНЕ ЗНАЧЕННЯ ПРИ ЗАХВОРЮВАННІ МАЛИХ СУДИН МОЗКУ

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Захворювання малих судин головного мозку (ЗМСМ) - це група гетерогенних розладів, що вражають дрібні перфорантні судини головного мозку. Клінічно ЗМСМ проявляється різними симптомами, такими як когнітивні, функціональні, афективні розлади, а також лакунарним інсультом або внутрішньомозковим крововиливом. ЗМСМ є причиною 25 % усіх інсультів та виступає другою причиною деменції після хвороби Альцгеймера. Золотим стандартом діагностики ЗМСМ є нейровізуалізація. Основними ключовими ознаками є гіперінтенсивність білої речовини (лейкоараіоз), лакуни, розширені периваскулярні простори, мозкова атрофія. Доведено, що атрофія мозку відіграє синергічну роль як у цереброваскулярних, так і в нейродегенеративних захворюваннях, що розвиваються у старіючому мозку. Вона відображає кінцевий загальний результат прогресування патологічних процесів, які розвиваються із часом. Прогресування ЗМСМ призводить до поступового зменшення об'єму мозку, що проявляється зміною розмірів шлуночків і борозн мозку. Але про його масштаби, кореляти та наслідки відомо небагато. Мета дослідження - з'ясувати, чи корелюють морфометричні зміни головного мозку з ознаками ЗМСМ. У дослідженні прийняли участь 129 пацієнтів зі ЗМСМ та 165 пацієнтів без ЗМСМ, у котрих розвинувся інсульт. Усі хворі пройшли нейровізуалізаційне обстеження за допомогою магнітно-резонансної та комп'ютерної томографії. Ми використали як однофакторний, так і багатофакторний регресійний аналіз, а також кореляційний аналіз із метою виявлення відмінностей у морфометричних параметрах мозку між групами. Багатофакторний регресійний аналіз, скоректований за віком і статтю, виявив достовірний вплив індексу Еванса (ВШ 1,09, 95%; ДІ 1,01-1,16, p=0,018), індексу третього шлуночка (ВШ 1,42, 95%; ДІ 1,21-1,67, p<0,001), індексу Шалтенбранда-Нюренбергера (ВШ 1,42, 95%; ДІ 1,21-1,67, p<0,001), індексу четвертого шлуночка (ВШ 1,31, 95%; ДІ 1,13-1,51, p<0,001), бікаудального індексу (ВШ 1,19, 95%; ДІ 1,10-1,30, p<0,001), індексу Шеєрсмана (ВШ 0,55, 95%; ДІ 0,42-0,72, p<0,001), числа Хакмана (ВШ 1,05, 95%; ДІ 1,02-1,08, p<0,001), ширини поздовжньої мозкової щілини в передній частині лобових часток (ВШ 1,46, 95%; ДІ 1,22-1,75, p<0,001), ширини лівої острівкової цистерни (ВШ 1,24, 95% ДІ 1,11-1,39, p<0,001), ширини правої острівкової цистерни (ВШ 1,31, 95% ДІ 1,17-1,46, p<0,001), ширини правої та лівої стрівкових цистерн у сумі (ВШ 1,17, 95%; ДІ 1,10-1,25, p<0,001), ширини мозкової щілини в ділянці склепіння черепа (ВШ 1,49, 95%; ДІ 1,21-1,84, p<0,001) на наявність ЗМСМ. Ширина поздовжньої мозкової щілини в передньому відділі лобових часток при ЗМСМ

становила 6,13±1,56 мм проти 5,10±1,38 мм у контрольній групі (p<0,001), сумарна ширина правої та лівої острівкових цистерн при ЗМСМ становила 16,98±4,60 мм проти 13,41±4,16 мм у групі контролю, p<0,001. Ширина мозкової щілини в ділянці склепіння черепа (тім'яної кори) також була більшою у хворих із ЗМСМ: 5,04±1,85 мм проти 4,12±1,29 мм, p<0,001. Таким чином, усі шлуночкові та кортикальні індекси були збільшеними в групі пацієнтів зі ЗМСМ. Дані результати вказують на те, що морфометричні показники головного мозку тісно пов'язані зі ЗМСМ і можуть бути корисними для прогнозування наслідків інсульту та констатації зниження когнітивних функцій.

Ключові слова: *морфометрія мозку, захворювання малих судин мозку, індекс Еванса.*