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Shape of cerebral hemispheres: structural and spatial complexity. Quantitative analysis of skeletonized MR images

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For quantitative characterization of the complexity of the spatial configuration of anatomical structures, including cerebral hemispheres, fractal analysis is the most often used method, in addition to which, other methods of image analysis are quite promising, including quantitative analysis of skeletonized images. The purpose of the study was to determine the features of the structural and spatial complexity of the cerebral hemispheres shape using quantitative analysis of skeletonized magnetic resonance images of the cerebral hemispheres. Magnetic resonance brain images of 100 conditionally healthy individuals (who did not have structural changes in the brain) of both sexes (56 women, 44 men) aged 18-86 years (average age 41.72±1.58 years) were studied, 5 tomographic sections (4 coronal sections and 1 axial section) were selected from the set of tomographic images of each brain. During preprocessing, image segmentation was performed to obtain a binary silhouette image, after which silhouette skeletonizing was carried out. Quantitative analysis of skeletonized images included determination of the following parameters: branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points, average branch length, maximum branch length. We divided quantitative parameters of skeletonized images into two groups. The first group included branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points. These parameters were related to each other and to the values of the fractal dimension by positive correlations. The second group of parameters included average branch length, maximum branch length. These parameters were positively correlated, but they had negative correlations with most of the parameters of the first group and with fractal dimension values. Quantitative parameters and fractal dimension turned out to be better parameters for characterizing the spatial and structural complexity of the cerebral hemispheres shape than traditional morphometric parameters (area, perimeter and their derivatives). It was found that the values of most of the investigated guantitative parameters decreased with age; coronal sections were the most representative for characterizing age-related changes. Quantitative assessment of the brain shape, including spatial and structural complexity, can become an informative tool for the diagnosis of some nervous diseases and the differentiation of pathological and normal age-related changes.

Keywords: brain, cerebral hemispheres, morphometry, skeletonizing, fractal dimension.

Introduction

One of the urgent tasks of modern neuroscience and neuromorphology is the development and improvement of methods of objective assessment of various morphological parameters of nervous system structures. Most of the morphometry methods used in modern neuromorphology and medicine in general provide determination of basic geometric parameters - linear dimensions, area, volume and various indices that are derivatives of these parameters [1, 20]. The informativeness of these indicators is quite high when studying structures whose shape is close to the shape of simple geometric figures - a sphere, a prism, a cylinder, etc. However, for the assessment of some natural structures that have an irregular shape, such parameters are not enough, so the search for morphometric algorithms continues.

The shape of the cerebral hemispheres is irregular,

which is due to many factors, including the number, size and complexity of the configuration of convolutions and sulci. These parameters determine such an important characteristic of the shape of the cerebral hemispheres as spatial and structural complexity - the greater the number of convolutions and sulci and the more complex their configuration, the more complex the spatial configuration of the brain as a whole.

For the quantitative characterization of spatial and structural complexity, such a quantity as the fractal dimension is used, which is determined by means of fractal analysis [14]. Using this method, research was carried out on the cortex of the cerebral hemispheres [4, 10, 24] and its outer surface [8, 11], as well as the white matter of the cerebral hemispheres [3, 5, 19, 21, 22, 26-28] and cerebellar white matter [13, 15].

A fairly common image preprocessing method used for fractal analysis is skeletonization [9]. This processing method involves eroding the silhouette image with the formation of its digital skeleton [7, 9, 17, 18]. During the construction of a digital skeleton, an automatic algorithm detects all the vertices of the figure being skeletonized (in the case of cerebral hemispheres, such points are the vertices of the gyri) and connects them using the smallest possible number of short straight segments, forming a network inside the silhouette.

In the works of various researchers, skeletonization was used as a method of image preprocessing for fractal analysis of the white matter of the cerebral hemispheres [3, 5, 21, 22, 26-28]. Skeletonization was also used to analyze magnetic resonance imaging of the cerebral hemispheres using the "Peak Width of Skeletonized Mean Diffusivity" method [2, 6, 13, 23].

In addition to fractal analysis itself, in some cases quantitative analysis of digital skeletons of various biological structures is performed, which can be used both as an independent morphometric method and in combination with fractal analysis [7, 9, 17, 18]. Quantitative analysis of skeletonized images was used in the study of tree-like structures (most often - the dendritic tree of neurons) [7, 17, 18]. Previously, we performed a quantitative analysis of skeletonized images of human cerebellar white matter [15]. However, according to the scientific literature available to us, quantitative analysis of skeletonized images of the cerebral hemispheres has not been performed before. In our previous work [16], we performed a fractal analysis of skeletonized magnetic resonance (MR) images of the cerebral hemispheres. This work is a continuation of the previous one and includes quantitative analysis of skeletonized images.

The purpose of the study is to determine the features of the structural and spatial complexity of the shape of the cerebral hemispheres using quantitative analysis of skeletonized magnetic resonance images of the cerebral hemispheres.

Materials and methods

The study was conducted in compliance with the basic bioethical provisions of the Council of Europe Convention on Human Rights and Biomedicine (from 04.04.1997), the Helsinki Declaration of the World Medical Association on Ethical Principles of Scientific Medical Research with Human Participation (1964-2008), as well as the Order of the Ministry of Health of Ukraine № 690 from 23.09.2009. The conclusion of the Committee on Ethics and Bioethics of the Kharkiv National Medical University confirms that the research was conducted in compliance with human rights, in accordance with the legislation in force in Ukraine, meets international ethical requirements and does not violate ethical norms in science and standards for conducting biomedical research (minutes of the meeting of the Committee on of ethics and bioethics of the Kharkiv National Medical University № 10 dated November 7, 2018).

Magnetic resonance (MR) tomograms of the brain of 100 conditionally healthy individuals (who did not have structural changes in the brain) of both sexes (56 women, 44 men) aged 18-86 years (average age 41.72±1.58 years) were used as the research material.

Selection and pre-processing of images was carried out according to the algorithm described in our previous work [16]. From the set of tomographic images of each brain, 5 tomographic slices were selected (4 in the coronal projection, 1 in the axial projection). The sections had the following localization: the 1st coronal section was located at the level of the most anterior points of the temporal lobes, the 2nd - at the level of the corpus mamillare, the 3rd - at the level of the lamina quadrigemina, the 4th - at the level of the splenium corpori callosi, the axial tomographic section was located at the level of the thalamus.

The parameters of the investigated images were as follows: the size for examining coronal sections - 512x400 pixels, for axial sections - 512x800 pixels; resolution is 128 pixels per inch. The absolute scale of a digital image is 3 pixels (voxels) = 1 mm. During preprocessing, image segmentation was performed to obtain a binary silhouette image (Fig. 1B), after which the silhouette was skeletonized using the "skeletonize" tool of the Image J program (see Fig. 1C). Fractal analysis of skeletonized images was then carried out using the box counting method, for which the "fractal box count" tool of the Image J program was used. The same stages of image processing and analysis were used in our previous work [16].

The next stage of research, to which this work is devoted, was the quantitative analysis of skeletonized images, for which the "analyze skeleton" tool of the Image J program was used (Fig. 2). The following parameters were determined in each of the digital skeletons: branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points, average branch length, maximum branch length. The branches parameter characterizes the number of branches, the junctions parameter characterizes the number of branch connections. Shape of cerebral hemispheres: structural and spatial complexity. Quantitative analysis of skeletonized MR images



Fig. 1. Pre-processing of the magnetic resonance image of the brain: A - non-segmented coronal section after removal of background structures, B - binary silhouette image after segmentation, C - skeletonized image.

The end-point voxels parameter corresponds to the number of end points of the branches of the digital skeleton, junction voxels - the number of voxels forming the junction of branches, slab voxels - the number of voxels forming the branches. The triple points parameter characterizes the number of connections connecting three branches, quadruple points - four branches. The average branch length parameter is the arithmetic average value of the absolute length of all branches, and the maximum branch length parameter is the maximum among the values of the absolute length of all branches of the digital skeleton.

Traditional morphometric parameters belonging to Euclidean geometry were also determined: These parameters were determined on two types of images. The 1st type of images are tomographic sections as a whole (see Fig. 1, A), the perimeter of which corresponds to the contour of the visible surface of the cerebral hemispheres, and the area corresponds to the brain tissue as a whole, including the content of the sulci. The following indicators were determined on these images: P_0 (perimeter), S_0 (area), P_0/S_0 (ratio of perimeter to area), SF_0 (form factor). The 2nd type of images are segmented silhouette images (see Fig. 1, B), the perimeter of which corresponds to the contour of the pial surface of the cerebral hemispheres (including the



Fig. 2. Quantitative analysis of the skeleton image of the cerebral hemispheres: end-point voxels are highlighted in blue, junction voxels are in pink, slab voxels are in red.

contour of the depth of the furrows), and the area corresponds to the brain tissue as a whole (not including the contents of the sulci). The following indicators were determined on these images: $P_{\rm s}$ (perimeter), $S_{\rm s}$ (area), $P_{\rm s}/S_{\rm s}$ (perimeter to area ratio), SF_{\rm s} (form factor). The formula SF=(4 π x A)/P² was used to determine the form factor for both types of images. The ratio of the perimeter and area of the segmented silhouette image to the corresponding parameters of the section as a whole (P_{\rm s}/P_{\rm 0} and S_{\rm s}/S_{\rm 0}) were also calculated.

Statistical processing of the data was carried out using the Microsoft Excel 2016 program. The data was processed using the tools of variational statistics. The following statistical parameters were calculated for each variation series: arithmetic mean (M), its error (mM), minimum (Min) and maximum (Max) values. The significance of statistical differences between the values of the fractal dimension of tomographic sections of different localization was assessed using the Kruskal-Wallis KW test with Bonferroni correction and Dunn's post-hoc test for multiple comparisons. To determine the relationship between the obtained values, the Pearson correlation coefficient (r) was calculated, the significance of which was assessed using the Student's test.

Results

The statistical parameters and the distribution of the values of the quantitative parameters of the skeletonized images of the cerebral hemispheres are shown in Table 1 and Figure 3. When comparing the values of the quantitative parameters of the skeletonized images of five different tomographic sections, it was determined that the values of all parameters, except quadruple points, were statistically significantly different in sections of different localization (p<0.001), the number of quadruple points in different tomographic sections did not differ statistically significantly (p=0.191). When comparing the values in pairs, it was found that the values of the parameters branches, junctions, junction voxels, slab voxels and triple points of the 1st coronal section and axial section were statistically significantly different from each other and differed from the corresponding values of the rest of the tomographic

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Parameter		Tomographic section						
		Coronal 1	Coronal 2	Coronal 3	Coronal 4	Axial		
	М	95.30	125.08	120.57	116.47	150.18		
Dranaboo (NI)	m	1.58	2.73	2.53	2.21	4.41		
Branches (N)	Min	61	69	70	77	86		
	Max	146	202	224	208	317		
	М	48.62	63.94	62.01	59.80	77.13		
	m	0.91	1.54	1.47	1.26	2.41		
Junctions (in)	Min	30	34	34	37	43		
	Max	76	108	124	109	168		
	М	41.85	54.73	52.35	50.48	65.61		
End-point	m	0.54	0.85	0.71	0.71	1.49		
voxels (N)	Min	29	36	36	38	42		
	Max	58	80	72	79	114		
	М	156.4	199.3	193.5	186.0	234.5		
Junction	m	3.3	5.5	5.1	4.3	8.3		
voxels (N)	Min	94	100	102	116	127		
	Max	260	364	396	344	578		
	М	1755	2655	2680	2651	4209		
Slab voxels	m	20	32	28	26	60		
(N)	Min	1337	1998	2116	2185	3090		
	Max	2214	3359	3418	3235	6398		
	М	45.51	60.29	58.98	56.56	73.41		
Triple points	m	0.80	1.36	1.34	1.16	2.17		
(N)	Min	30	34	32	35	42		
	Max	65	95	115	99	153		
	М	2.300	3.060	2.440	2.460	3.137		
Quadruple	m	0.173	0.251	0.179	0.173	0.311		
points (N)	Min	0	0	0	0	0		
	Max	8	15	9	10	18		
	М	8.342	9.372	9.754	10.03	12.50		
Average	m	0.095	0.094	0.104	0.10	0.17		
branch length (mm)	Min	6.71	7.42	6.74	7.01	8.23		
	Max	13.14	12.05	12.50	12.61	16.14		
	М	27.26	33.90	37.44	40.33	50.88		
Maximum	m	0.51	0.55	0.61	0.62	0.91		
branch length (mm)	Min	17.76	24.01	20.82	26.75	32.26		
	Max	39.80	50.69	57.25	51.96	82.51		

Table 1. Statistical parameters of the distribution of the values of the quantitative parameters of cerebral hemispheres skeletonized images.

sections (p<0.001); the values of the 2nd, 3rd and 4th coronal sections did not differ statistically significantly from each other (p>0.05). The values of the end-point voxels and average branch length parameters of the 1st coronal section and axial section were statistically significantly different from each other and differed from the

corresponding values of the rest of the tomographic sections (p<0.001); the values of the 2nd and 3rd coronal sections, as well as the 3rd and 4th coronal sections did not differ statistically significantly from each other (p>0.05), however, the values of the 2nd and 4th coronal sections differed statistically significantly from each other (p<0.05). No statistically significant difference was found between the values of the "maximum branch length" parameter of the 3rd and 4th coronal sections (p=0.017, the level of statistical significance α =0.050 with Bonferroni correction was α =0.005); the values of the remaining tomographic pairs were statistically significantly different from each other (p<0.01).

At the first stage of the correlation analysis, we determined the nature and strength of correlation relationships between the values of similar parameters of the digital skeleton determined on different tomographic sections (Fig. 4). We established that the values of most of the quantitative parameters of the four coronal sections were connected by a statistically significant positive correlation (except for the values of maximum branch length), while the strongest correlation was found between the values of the adjacent coronal sections - 1st and 2nd, 2nd and 3rd, 3rd and 4th. The values of most parameters of the axial section did not have a statistically significant correlation with the similar parameters of the coronal sections. The strongest correlation between adjacent coronal sections was found when conducting a correlation analysis of the following parameters: branches, junctions, end-point voxels, junction voxels, slab voxels, triple points. At the same time, the correlation between adjacent sections was not detected or was weak when conducting a correlation analysis of the values of the following parameters: quadruple points, average branch length, maximum branch length.

At the second stage of the correlation analysis, we investigated the correlation relationships between the values of various quantitative parameters of skeletonized images; we calculated the values of the correlation coefficients both for all the examined sections and separately for each tomographic section (Fig. 5). It turned out that there are significant positive correlations between the values of most parameters, these are the following parameters: branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points (at the same time, correlations between the parameters branches and junctions were close to functional). However, the values of average branch length and maximum branch length, which are positively correlated in all sections, are in most cases negatively correlated with the rest of the parameters (at the same time, average branch length has stronger correlation connections, and correlations between maximum branch length and values of other parameters are in many cases weak and not statistically significant).

At the third stage of the correlation analysis, we investigated the relationships between the values of the



Fig. 3. Distributions of values of quantitative parameters of cerebral hemispheres skeletonized images.

quantitative parameters of the skeletonized images and the traditional morphometric characteristics of the cerebral hemispheres (Fig. 6). It was established that the values of perimeters (P_0 , P_s), area (S_0 , S_s) of non-segmented and segmented images, as well as their ratio (P_s/P_0 , S_s/S_0) are related to most quantitative parameters (with the exception of average branch length and maximum branch length) by positive correlations, while parameters $\mathsf{P}_0/\mathsf{S}_0$ and SF_s are related to the same parameters by negative correlations. Attention is also drawn to exceptions from the general regularity: $\mathsf{S}_s/\mathsf{S}_0$ parameter of axial sections, unlike coronal sections, is related to the values of the quantitative parameters of the digital skeleton by negative, not positive, correlations; and when examining the sample, which



Fig. 4. Correlations of the values of quantitative parameters of skeletonized images of different localization tomographic sections; values of Pearson's correlation coefficients (r) are given.

includes all sections, negative correlations between the P_s/S_s parameter and most of the studied quantitative parameters are revealed. The rest of the morphometric parameters are related to the values of the quantitative parameters by correlations of different strength and direction, which differ in different tomographic sections (see

Fig. 6).

At the fourth stage of the correlation analysis, we investigated the correlations between the values of the fractal dimension, the quantitative parameters of the skeletonized images, and the traditional morphometric characteristics (Table 2). The parameters branches,



Fig. 5. Correlations of the values of quantitative parameters of skeletonized images of the cerebral hemispheres; values of Pearson's correlation coefficients (r) are given.



Fig. 6. Correlations of the values of quantitative parameters of skeletonized images and traditional morphometric parameters of the cerebral hemispheres; values of Pearson's correlation coefficients (r) are given.

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Parameter of skeletonized image	Tomographic section							
	Coronal 1	Coronal 2	Coronal 3	Coronal 4	Axial	All sections		
Branches	0.668***	0.871***	0.867***	0.834***	0.821***	0.229***		
Junctions	0.677***	0.869***	0.871***	0.851***	0.822***	0.261***		
End-point voxels	0.276**	0.631***	0.604***	0.521***	0.736***	-0.015		
Junction voxels	0.678***	0.851***	0.858***	0.812***	0.813***	0.327***		
Slab voxels	0.339***	0.811***	0.743***	0.668***	0.743***	-0.271***		
Triple points	0.628***	0.843***	0.857***	0.830***	0.806***	0.217***		
Quadruple points	0.414***	0.656***	0.560***	0.456***	0.630***	0.364***		
Average branch length	-0.403***	-0.759***	-0.770***	-0.699***	-0.757***	-0.724***		
Maximum branch length	-0.063	-0.203*	-0.162	-0.205*	0.013	-0.469***		
P ₀	-0.305**	-0.102	-0.166	-0.244*	-0.036	-0.605***		
S ₀	-0.348***	-0.025	-0.209*	-0.211*	0.060	-0.505***		
P ₀ /S ₀	0.315***	-0.078	0.177	0.137	-0.126	0.311***		
SF ₀	-0.171	0.172	-0.029	0.116	0.081	0.191***		
P _s	-0.085	0.355***	0.041	0.062	0.395***	-0.433***		
S _s	-0.201*	0.064	-0.136	-0.110	-0.182	-0.511***		
P _s /S _s	0.125	0.261**	0.138	0.149	0.526***	0.582***		
SFs	-0.002	-0.341***	-0.070	-0.095	-0.468***	-0.185***		
P _s /P ₀	0.059	0.462***	0.137	0.221*	0.476***	0.234***		
S _s /S ₀	0.256*	0.203*	0.133	0.236*	-0.146	-0.111**		

Table 2. Correlation relationships of fractal dimension values with the values of quantitative parameters of skeletonized images and traditional morphometric parameters of the cerebral hemispheres.

Notes: the table shows the values of Pearson's correlation coefficients (r); * - p<0.05; ** - p<0.01; *** - p<0.001.

Table 3. Correlation relationships between age and the values of quantitative parameters of skeletonized images of the cerebral hemispheres.

Parameter of skeletonized image	Tomographic section							
	Coronal 1	Coronal 2	Coronal 3	Coronal 4	Axial	All sections		
Branches	-0.502***	-0.386***	-0.248*	-0.387***	0.151	-0.160***		
Junctions	-0.507***	-0.384***	-0.269**	-0.414***	0.153	-0.175***		
End-point voxels	-0.301**	-0.291**	-0.058	-0.162	0.145	-0.057		
Junction voxels	-0.435***	-0.385***	-0.246*	-0.411***	0.140	-0.178***		
Slab voxels	-0.508***	-0.452***	-0.312**	-0.370***	0.010	-0.093*		
Triple points	-0.522***	-0.374***	-0.274**	-0.415***	0.166	-0.168***		
Quadruple points	-0.167	-0.255**	-0.046	-0.059	0.007	-0.097*		
Average branch length	0.120	0.231*	0.128	0.307**	-0.290**	0.040		
Maximum branch length	-0.114	-0.185	-0.151	0.098	-0.025	-0.038		
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Notes: the table shows the values of Pearson's correlation coefficients (r); * - p<0.05; ** - p<0.01; *** - p<0.001.

junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points were associated with the values of the fractal dimension by positive correlations; the parameters average branch length, maximum branch length were related to the values of the fractal dimension of most slices by negative correlations. Traditional morphometric parameters, in comparison with the quantitative parameters of skeletonized images, had a lower correlation strength with the values of the fractal dimension, the strength and directionality of which differed depending on the tomographic section (see Table 2).

At the fifth stage of the correlation analysis, we determined the presence and nature of correlation relationships between age and the values of quantitative parameters of skeletonized images of the cerebral hemispheres (Table 3). It turned out that most of the quantitative characteristics (except for quadruple points and maximum branch length and partially average branch

length) of all coronal sections had statistically significant negative correlations with age (however, the corresponding parameters of the axial section did not have significant relationships with age).

Discussion

Structural and spatial complexity is an important parameter that allows you to qualitatively add to the arsenal of morphological characteristics for the study of structures of irregular shape, including cerebral hemispheres. In most meanings, structural complexity and spatial complexity are very close and practically synonymous concepts and characterize the complexity of the spatial configuration. In addition to this value, structural complexity describes the complexity of not only the form, but also the actual internal structure of certain anatomical formations and can characterize the number and variety of elements that make up the studied structure (for example, the branches of the digital skeleton). An increase in structural complexity leads to an increase in the complexity of the spatial configuration (form), and therefore to an increase in spatial complexity.

Despite the relative novelty of fractal analysis as a morphometric method, the fractal dimension has become the "gold standard" for evaluating the structural and spatial complexity of the configuration of various natural structures, including the cerebral hemispheres [3-5, 8, 10, 11, 16, 19, 21, 22, 24, 26-28].

The spatial and structural complexity and, accordingly, the value of the fractal dimension of the cerebral hemispheres can be influenced by various factors. In this paper, we analyzed the correlations of fractal dimension values of skeletonized images of the cerebral hemispheres with two groups of parameters: with traditional morphometric parameters (perimeter, area, and their derivatives), and with quantitative parameters of skeletonized images. Most traditional morphometric parameters had no statistically significant correlations or weak correlations with fractal dimension values. Most of the quantitative parameters of skeletonized images had statistically significant strong or moderate correlations with fractal dimension values. Therefore, it can be considered that the quantitative parameters of skeletonized images are representative for evaluating the spatial and structural complexity of the cerebral hemispheres, in contrast to traditional morphometric parameters.

We divided the quantitative parameters of skeletonized images into two groups. The first included branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points. These parameters were related to each other and to the values of the fractal dimension by positive correlations. The second group of parameters includes average branch length, maximum branch length. These parameters are connected with each other by positive correlations, but with most of the parameters of the first group and with the values of the fractal dimension, they had negative correlations.

Therefore, the increase in the spatial and structural complexity of the shape of the cerebral hemispheres, which is reflected in the increase in the values of the fractal dimension, is accompanied by an increase in the number and decrease in the length of the branches of the digital skeleton, an increase in the number of connections and end points of the branches, and the number of voxels forming the skeleton. Therefore, the digital skeletons of the hemispheres, which have more convolutions and a more complex shape, are characterized by higher values of the fractal dimension and consist of a relatively large number of relatively short branches. Conversely, the digital skeletons of the hemispheres, which have a less complex configuration, have smaller values of fractal dimension and consist of a small number of relatively long branches. Similar regularities were also revealed as a result of quantitative analysis of skeletonized images of cerebellar white matter [15].

The relatively large age range of the studied sample allowed us to analyze correlations between age and quantitative parameters of skeletonized images. We found that the values of most of the studied parameters decrease with age. This is consistent with a decrease in the values of the fractal dimension and other morphometric parameters of the brain as a result of atrophic changes during normal aging [5, 16, 20, 27] and caused by neurodegenerative diseases [10]. Reducing the volume, smoothing the surface and expanding the grooves of the brain in the complex can lead to a simplification of the spatial configuration of the brain, which in turn will lead to a simplification of the configuration of digital skeletons. However, the described changes were not detected when analyzing the parameters of axial slices and when examining the sample that includes all slices. Therefore, it can be considered that coronal sections are more representative for characterizing age-related changes. A similar regularity was found in our previous work in the study of age-related dynamics of fractal dimension [16].

The number of endpoints of the digital skeleton allows us to indirectly characterize the number of convolutions forming the studied silhouette of the hemispheres. The number of gyri after the completion of their formation is an invariable anatomical characteristic, so the number of endpoints almost does not change during life. The existing weak negative correlations with age can be explained by the fact that sometimes gyri with a complex shape can form not one, but several points of the digital skeleton. Simplifying the shape of the convolutions and the overall silhouette may in some cases lead to a slight reduction in the number of endpoints.

Conclusion

Quantitative analysis of skeletonized images of allows to supplement the arsenal of morphometric methods of both morphology and clinical neuroscience. Quantitative parameters and fractal dimension of skeletonized images are the most relevant morphological parameters for characterizing the spatial and structural complexity of the shape of the cerebral hemispheres. Quantitative assessment of the shape of the brain, including spatial

References

- [1] Avtandilov, G. G. (1990). *Медицинская морфометрия [Medical morphometry].* Москва: Медицина - Moscow: Medicina.
- [2] Baykara, E., Gesierich, B., Adam, R., Tuladhar, A. M., Biesbroek, J. M., Koek, H. L., ... & Duering, M. (2016). A Novel Imaging Marker for Small Vessel Disease Based on Skeletonization of White Matter Tracts and Diffusion Histograms. *Annals of neurology*, 80(4), 581-592. doi: 10.1002/ana.24758
- [3] Esteban, F. J., Sepulcre, J., de Mendizabal, N. V., Goni, J., Navas, J., de Miras, J. R., ... & Villoslada, P. (2007). Fractal dimension and white matter changes in multiple sclerosis. *NeuroImage*, 36(3), 543-549. doi: 10.1016/ j.neuroimage.2007.03.057
- [4] Esteban, F. J., Sepulcre, J., de Miras, J. R., Navas, J., de Mendizabal, N. V., Goni, J., ... & Villoslada, P. (2009). Fractal dimension analysis of grey matter in multiple sclerosis. *Journal* of the neurological sciences, 282(1-2), 67-71. doi: 10.1016/ j.jns.2008.12.023
- [5] Farahibozorg, S., Hashemi-Golpayegani, S. M., & Ashburner, J. (2015). Age- and sex-related variations in the brain white matter fractal dimension throughout adulthood: an MRI study. *Clinical neuroradiology*, 25(1), 19-32. doi: 10.1007/s00062-013-0273-3
- [6] Frey, B. M., Petersen, M., Schlemm, E., Mayer, C., Hanning, U., Engelke, K., ... & Cheng, B. (2021). White matter integrity and structural brain network topology in cerebral small vessel disease: The Hamburg city health study. *Human brain mapping*, 42(5), 1406-1415. doi: 10.1002/hbm.25301
- [7] Greenblum, A., Sznitman, R., Fua, P., Arratia, P. E., Oren, M., Podbilewicz, B., & Sznitman, J. (2014). Dendritic tree extraction from noisy maximum intensity projection images in C. elegans. *Biomedical engineering online*, 13, 74. doi: 10.1186/1475-925X-13-74
- [8] Ha, T. H., Yoon, U., Lee, K. J., Shin, Y. W., Lee, J. M., Kim, I. Y., ... & Kwon, J. S. (2005). Fractal dimension of cerebral cortical surface in schizophrenia and obsessive-compulsive disorder. *Neuroscience letters*, 384(1-2), 172-176. doi: 10.1016/ j.neulet.2005.04.078
- [9] Jelinek, H. F., & Fernandez, E. (1998). Neurons and fractals: how reliable and useful are calculations of fractal dimensions?. *Journal of neuroscience methods*, 81(1-2), 9-18. doi: 10.1016/s0165-0270(98)00021-1
- [10] King, R. D., George, A. T., Jeon, T., Hynan, L. S., Youn, T. S., Kennedy, D. N., ... & the Alzheimer's Disease Neuroimaging Initiative (2009). Characterization of Atrophic Changes in the Cerebral Cortex Using Fractal Dimensional Analysis. *Brain imaging and behavior*, 3(2), 154-166. doi: 10.1007/s11682-008-9057-9
- [11] Lee, J. M., Yoon, U., Kim, J. J., Kim, I. Y., Lee, D. S., Kwon, J. S., & Kim, S. I. (2004). Analysis of the hemispheric asymmetry using fractal dimension of a skeletonized cerebral surface. *IEEE transactions on bio-medical engineering*, 51(8), 1494-1498. doi: 10.1109/TBME.2004.831543
- [12] Liu, J. Z., Zhang, L. D., & Yue, G. H. (2003). Fractal dimension in human cerebellum measured by magnetic resonance imaging. *Biophysical journal*, 85(6), 4041-4046. doi: 10.1016/ S0006-3495(03)74817-6

and structural complexity, can become an informative tool for the diagnosis of some nervous diseases and the differentiation of pathological and normal age-related changes.

- [13] Low, A., Mak, E., Stefaniak, J. D., Malpetti, M., Nicastro, N., Savulich, G., ... & O'Brien, J. T. (2020). Peak Width of Skeletonized Mean Diffusivity as a Marker of Diffuse Cerebrovascular Damage. *Frontiers in neuroscience*, 14, 238. doi: 10.3389/fnins.2020.00238
- [14] Mandelbrot, B. B. (1983). *The fractal geometry of nature*. N.Y.: W. H. Freeman&Co.
- [15] Maryenko, N., & Stepanenko, O. (2021). Characterization of white matter branching in human cerebella: quantitative morphological assessment and fractal analysis of skeletonized MR images. *Biomedical Research and Therapy*, 8(5), 4345-4357. doi: 10.15419/bmrat.v8i5.673
- [16] Maryenko, N. I., & Stepanenko, O. Y. (2022). Fractal dimension of skeletonized MR images as a measure of cerebral hemispheres spatial complexity. *Reports of Morphology*, 28(2), 40-47. doi: 10.31393/morphology-journal-2022-28(2)-06
- [17] Milosevic, N. T., & Ristanovic, D. (2006). Fractality of dendritic arborization of spinal cord neurons. *Neurosci Lett*, 396(3), 172-176. doi: 10.1016/j.neulet.2005.11.031
- [18] Orlowski, D., & Bjarkam, C. R. (2012). A simple reproducible and time saving method of semi-automatic dendrite spine density estimation compared to manual spine counting. *J Neurosci Methods*, 208(2), 128-133. doi: 10.1016/ j.jneumeth.2012.05.009
- [19] Pantoni, L., Marzi, C., Poggesi, A., Giorgio, A., De Stefano, N., Mascalchi, M., ... & Diciotti, S. (2019). Fractal dimension of cerebral white matter: A consistent feature for prediction of the cognitive performance in patients with small vessel disease and mild cognitive impairment. *NeuroImage Clinical*, 24, 101990. doi: 10.1016/j.nicl.2019.101990
- [20] Podgorski, P., Bladowska, J., Sasiadek, M., & Zimny, A. (2021). Novel Volumetric and Surface-Based Magnetic Resonance Indices of the Aging Brain - Does Male and Female Brain Age in the Same Way?. *Frontiers in neurology*, 12, 645729. doi: 10.3389/fneur.2021.645729
- [21] Rajagopalan, V., Das, A., Zhang, L., Hillary, F., Wylie, G. R., & Yue, G. H. (2019). Fractal dimension brain morphometry: a novel approach to quantify white matter in traumatic brain injury. *Brain imaging and behavior*, 13(4), 914-924. doi: 10.1007/s11682-018-9892-2
- [22] Rajagopalan, V., Liu, Z., Allexandre, D., Zhang, L., Wang, X. F., Pioro, E. P., & Yue, G. H. (2013). Brain white matter shape changes in amyotrophic lateral sclerosis (ALS): a fractal dimension study. *PloS one*, 8(9), e73614. doi: 10.1371/ journal.pone.0073614
- [23] Raposo, N., Zanon Zotin, M. C., Schoemaker, D., Xiong, L., Fotiadis, P., Charidimou, A., ... & Viswanathan, A. (2021). Peak Width of Skeletonized Mean Diffusivity as Neuroimaging Biomarker in Cerebral Amyloid Angiopathy. *AJNR. American journal of neuroradiology*, 42(5), 875-881. doi: 10.3174/ ajnr.A7042
- [24] Roura, E., Maclair, G., Andorra, M., Juanals, F., Pulido-Valdeolivas, I., Saiz, A., ... & Villoslada, P. (2021). Cortical fractal dimension predicts disability worsening in Multiple Sclerosis patients. *NeuroImage. Clinical*, 30, 102653. doi: 10.1016/j.nicl.2021.102653
- [25] Schneider, C. A., Rasband, W. S., & Eliceiri, K. W. (2012). NIH

Image to ImageJ: 25 years of image analysis. *Nature methods,* 9(7), 671-675. doi: 10.1038/nmeth.2089

- [26] Zhang, L., Butler, A. J., Sun, C. K., Sahgal, V., Wittenberg, G. F., & Yue, G. H. (2008). Fractal dimension assessment of brain white matter structural complexity post stroke in relation to upper-extremity motor function. *Brain research*, 1228, 229-240. doi: 10.1016/j.brainres.2008.06.008
- [27] Zhang, L., Dean, D., Liu, J. Z., Sahgal, V., Wang, X., & Yue, G.

H. (2007). Quantifying degeneration of white matter in normal aging using fractal dimension. *Neurobiology of aging*, 28(10), 1543-1555. doi: 10.1016/j.neurobiolaging.2006.06.020

[28] Zhang, L., Liu, J. Z., Dean, D., Sahgal, V., & Yue, G. H. (2006). A three-dimensional fractal analysis method for quantifying white matter structure in human brain. *Journal of neuroscience methods*, 150(2), 242-253. doi: 10.1016/ j.jneumeth.2005.06.021

ФОРМА ВЕЛИКИХ ПІВКУЛЬ ГОЛОВНОГО МОЗКУ: СТРУКТУРНА ТА ПРОСТОРОВА СКЛАДНІСТЬ. КІЛЬКІСНИЙ АНАЛІЗ СКЕЛЕТОНОВАНИХ МР-ЗОБРАЖЕНЬ *Мар'єнко Н. І., Степаненко О. Ю.*

Для кількісного характеризування складності просторової конфігурації анатомічних структур, у тому числі великих півкуль головного мозку, найчастіше використовується фрактальний аналіз, крім якого досить перспективними є й інші методи аналізу зображень, у тому числі кількісний аналіз скелетонованих зображень. Мета дослідження - визначити особливості структурної та просторової складності форми великих півкуль головного мозку за допомогою кількісного аналізу скелетонованих магнітно-резонансних зображень великих півкуль головного мозку. У якості матеріалу дослідження було використано магнітно-резонансні томограми головного мозку 100 умовно здорових осіб (які не мали структурних змін головного мозку) обох статей (жінок 56, чоловіків 44) віком 18-86 років (середній вік 41,72±1,58 років). Із набору томографічних зображень кожного мозку було відібрано 5 томографічних зрізів (4 - у корональній проекції, 1 - у аксіальній). Під час попередньої обробки проводилася сегментація зображень із отриманням бінарного силуетного зображення, після чого проводилося скелетонування силуету. Кількісний аналіз скелетонованих зображень включав визначення таких параметрів: branches, junctions, end-point voxels, junction voxels, slab voxels, triple points, quadruple points, average branch length, maximum branch length. Ми розділили кількісні параметри скелетонованих зображень на дві групи. До першої увійшли branches, junctions, endpoint voxels, junction voxels, slab voxels, triple points, quadruple points. Ці параметри були пов'язані між собою та зі значеннями фрактальної розмірності позитивними кореляційними зв'язками. До другої групи параметрів увійшли average branch length, maximum branch length. Ці параметри були пов'язані між собою позитивними кореляційними зв'язками, але з більшістю параметрів першої групи та зі значеннями фрактальної розмірності вони мали негативні кореляційні зв'язки. Кількісні параметри та фрактальна розмірність виявилися кращими параметрами для характеризування просторової та структурної складності форми великих півкуль головного мозку, ніж традиційні морфометричні параметри (площа, периметр та їх похідні). Виявлено, що значення більшості досліджених кількісних параметрів зменшуються з віком, корональні зрізи виявилися найбільш репрезентативними для характеризування вікових змін. Кількісне оцінювання форми головного мозку, у тому числі просторової та структурної складності, може стати інформативним інструментом для діагностики деяких нервових захворювань та диференціювання патологічних та нормальних вікових змін.

Ключові слова: головний мозок, великі півкулі головного мозку, морфометрія, скелетонування, фрактальна розмірність.