The cerebral cortex occupies a special position among the structures of the CNS. The systematic study of the regularities of its cellular structure, the investigation of the structural features of the various divisions of the cortex, and the delineation of such structural units as the territory, region, field, and subfield, have been implemented over the course of many decades. The now classic works of I. N. Filimonov, Yu. G. Shevchenko, E. P. Kononovaya, G. I. Polyakov, I. A. Stankevich, S. A. Sarkisov, et al., have led to the development of maps of the cytoarchitectonics of the human cerebral cortex, maps which have fundamental significance both for the resolution of theoretical questions of the localization of cerebral functions, and for a whole series of practical problems of neuropathology and psychiatry. The development and deepening of the fundamental investigations in the realm of the physiology of higher nervous activity which has been taking place in recent years [1, 3], impact special significance to quantitative investigations of the features of the organization of the higher divisions of the brain which are the structural basis of its integrative activity, and require the acquisition of quantitative information regarding brain organization. It is clear that this is a necessary link in the investigations of the structural bases of the mechanisms of the disturbance of brain activity, especially of its higher mental functions.

The architectonic approach, in relation to the introduction of new investigational methods into neuromorphology, has undergone, as it were, a second birth [4, 7]. It is associated above all with a significant leap forward in the objectivization of the classical features of the cytoarchitectonic scheme, and with the promise of the development of the most complex quantitative methods of analysis of the spatial organization of the structures of the brain.

The quantitative description of the structure of the cortex requires the observation of a number of conditions for the acquisition of stable quantitative assessments. The formalized (standard) determination of the boundaries between the cellular elements and the neuropil, the taking into account of the instability of the conditions of staining, and the averaging of the measured values across a series of sections and across a representative spatial interval within the limits of each of them, are such conditions. It can be shown experimentally that the assessments of even the most simple morphometric characteristics, for example, of the volumetric ratio of the cellular elements located within the limits of any layer of the cortex, acquire stability only over an averaging interval of the order of 2.5-3 mm, which is accompanied also by a corresponding reduction in the coefficient of variation (Fig. 1).

To carry out a study observing the stated requirements, a special automated methodology, involving a number of stages, was developed. The first of these stages is the planning of the study at a slight magnification, and the setting up of a schema of the scanning of a series of sections. The second stage, the measurement proper in an automated mode, includes the procedures of focusing, of search for the boundaries of the cellular elements under study, and of the sorting out of artifacts, and the demarcation of cellular elements located close to one another. As the result of measurements which are carried out by a scanning screen moving along the column of neurons, and oriented along the layer, profiles describing the character of changes of three principle morphometric parameters of the cellular elements (volumetric ratio, number of cross sections, and their average size) are obtained, from the surface of the cortex down to the transition to the white matter.

Fig. 1. Character of the behavior of estimates of mean volumetric ratio of cellular elements (A), and the coefficient of variation (B) as a function of the length of the segment of averaging along the layer. Along the abscissa, the length of the segment of averaging (in μm); along the ordinate, mean volumetric ratio and coefficient of variation (in %).

At the final stage of the analysis, it is necessary to compare the obtained morphometric result with the object under study. In our case this is achieved by the superposition of the obtained curves on the image of one of the sections to the same scale, in order to describe them and to draw the boundaries of the layers. Using a special program, the research morphologist is enabled in an interactive mode to describe the available curves, to isolate characteristic sections, to demarcate them, and to establish their correspondence with specific layers and sublayers of the cortex. In the course of such an analysis, information regarding the thickness of the layers and the mean values of the parameters characterizing each layer or sublayer is obtained.

The methodology described here is realized in the form of a complex of programs for the TAC television image analyzer produced by Leitz. The programs are written in FORTRAN-4, using a library of subprograms controlling the apparatus's transformations of the images. The algorithms for the processing of the latter are based on the principles of mathematical morphology [8]. The total scanning area for one preparation was 50-120 mm², the number of analyzed fields of view was 1000-1800, and the expenditure of machine time was 6-8 h per preparation.

Using the programs developed, the brain of individuals who had died unexpectedly or suddenly as a result of acute cardiovascular insufficiency was studied. Autopsies were done up to six hours after death. Blocks from the frontal pole (field 10), from the lower third of the opercular convolution (field 44), and the occipital lobe, and from the lower wall of the calcaneous fissures (field 17), were dissected from the whole brain. The material was processed by conventional methodologies. In all, 16 cases, ranging in age from 27 to 84 years, were studied.

The comparison of the individual profiles and sections graphically reflects the presence of stably repeating segments of curves, and of their correspondence to the layers and sublayers of the cortex of the studied fields. Each segment of the cross section finds reflection in a segment of the curve which describes the behavior of the quantitative parameters with respect to the cross section of the corresponding layers and sublayers [6] (Fig. 2). For example, the morphocorticogram (MCG) of field 17 in all of the cases studied demonstrates the uniqueness of its cytoarchitectonics: the relatively weak development of layer III, and the subdivision of layer IV into four sublayers. Layer I is poor in cellular elements, which is reflected in the minimal values of all the parameters studied (2-4% with respect to parameter VA; from 400 to 800 cross sections per 1 mm²; 40-50 μm² with respect to parameter SA). Layer II is represented by a steeply sloped segment with respect to parameters VA and NA, which reflects a sharp increase in the volumetric ratio and number of cellular elements. The average values of the parameters reach the level respectively of 10% and 1500 particles per 1 mm². The mean size of the cross sections increases more smoothly up to 60-80 μm². At the boundary with layer III a peak is observed, mainly due to the condensing of the cellular elements of the neighboring layers.

Layer III is, as a rule, well differentiated from layers II and IV, especially with respect to parameters NA, as the result of some thinning out of neurons. The segments of the curves which correspond to this layer, reflect, with respect to parameter VA, an insignificant increase in the volumetric ratio of cellular elements up to values on the order of 12-13%. In a number of cases one or two zones of local increase is observed in VA and in the number of cells in the central region of the cross section of the layer. The number of cellular elements is, on the average, 1700 per 1 mm². The mean value of the size of the cross sections in layer III continues to increase, and is here, on the average, 80 μm². The local maximum of the mean size corresponds to this layer; however, its value is variable: the coefficient of variation (CV) is equal to 14%.

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Fig. 2. Examples of typical MGS of fields 17 (A), 10 (B), and 44 (C) of the human cerebral cortex according to parameters: volumetric ratio ($V_A$), number of cross sections per unit area of the slice ($N_A$), and mean size of the cross sections of cellular elements ($S_A$). Along the abscissa, distance to the surface (in μm); along the ordinate, volumetric ratio (1), number of cross sections per 1 mm$^2$ (2), and mean area of cross sections (in μm$^2$) (3).

In the segments of the curves corresponding to layer IV it is possible to delineate stably four zones, which correspond to the sublayers described for this layer. The transition toward it always corresponds to a rise in the density of cells to an average value of about 2000 cross sections per 1 mm$^2$. Sublayer IV$^a$ is characterized above all by a decrease in the size of the cross sections approximately down to an average level of 72 μm$^2$, while the volumetric ratio is maintained at a level approximately corresponding to layer III. An insignificant increase, to values on the order of 15%, is observed as a variant.

Sublayer IV$^b$ is characterized by a decrease in both the volumetric ratio and in the number of cross sections of cellular elements. Parameter $V_A$ decreases to 12%, and $N_A$ to 1790 per 1 mm$^2$. The average size, on the contrary, may increase, which corresponds to the appearance of giant cells in the sublayer. This feature is variable, however.

In sublayer IV$^b$ two zones are stably distinguished, to which sublayers IV$^{b\alpha}$ and IV$^{b\beta}$ probably correspond. Sublayer IV$^{b\alpha}$ is set apart because of a local decrease in the number of cross sections and an increase in their mean size. Conversely, for sublayer IV$^{b\beta}$ a decrease in the size and an increase in the number of cellular elements is again characteristic, to which an isolated peak or break in the curve corresponds in a number of cases.

Sublayer IV$^c$ is the most thickly cellular; it is represented by a global maximum of parameter $V_A$ at a level of 16-17% and of $N_A$ at 2200-2500. The mean size of the cross sections remains at the level of layer III.

Layer V, as in the case of sublayer IV$^b$, is characterized by a fall in the volumetric ratio to a level of 9-11%, and also by a sharp fall in the number of cross sections to 1800 per 1 mm$^2$. In this case the mean size either does not change or decreases insignificantly as compared with sublayer IV$^c$ to 72 μm$^2$. Thus the presence in a layer of single large pyramidal neurons does not affect the value of this parameter.

The following layers of the lower level of the cortex, VI and VII, are characterized by a pronounced rise in parameters $V_A$ and $N_A$. The volumetric ratio increases relatively more sharply, but nevertheless does not reach the level of sublayer IV$^c$, and is 13% on the average.
the number of cross sections increases more weakly, and is characterized on the average by a value of 1670 per 1 mm², which is lower by 25% than sublayer IVc. Layers VI and VII sometimes correspond to layer IV with respect to the size of the cross sections, but more often exceed this level. In that case a global maximum of mean size reaching 100 μm² corresponds to these layers.

On the whole the form of the curve of parameters Vₐ and Nₐ for field 17 is well reproduced from observation to observation. The parameter of mean size of the cross sections of cellular elements has the greatest variability, both with respect to the absolute value and to the ratios characteristic for the different layers. The variability of the form of the Sₐ profile is manifested above all in the different ratios of the values of the mean size which are characteristic for the upper and lower levels of the cortex. In addition, the degree to which the stratification of the field with respect to the given parameter is marked fluctuates: the local minima in sublayers IVa-b and in layer V are not always pronounced. With respect to the remaining parameters, the pattern of the profile is always well marked, i.e., all the characteristic extrema are maintained.

Analysis of the form of the curves which characterize fields 10 and 44 (see Fig. 2b, c) demonstrates that the profiles of the cross section of these fields are significantly different from field 17, but have much in common with each other. For example, the subdivision of layer III into sublayers with respect to the number of cross sections and to the character of the changes of this parameter in relation to the cross section of the layer, is well marked. The differentiating feature associated with the appearance of a local maximum of the value of the mean size of the neurons of field 44 in the zone of layer V, is unfortunately not always present in the curve. The similarity of the behavior of the morphometric values in fields 10 and 44 compel a more detailed examination of the problem of comparing them and of the identification of quantitative differences.

Comparison of the values of morphometric parameters, averaged within the limits of each layer, shows that significant differences between the fields under comparison are, it would seem, lacking. Statistically reliable differences can only be observed between the thickness of V and the morphometric values which characterize layer III. The average of morphometric data with respect to the cross section of a layer (accepted in the majority of studies) is not desirable for the identification of the particular features of the cytoarchitectonic structure of different fields of the cortex. It leads to smoothing out of the relief of the profile, and to an increase in the dispersion of the corresponding assessments as the result of the systematic change in the morphometric parameters. Analysis of the regularities of the change in one or another value with respect to the cross section of each layer and of the entire field as a whole with the use of the MCG appear to be far more informative than the comparison of the averaged values.

The absolute values of the thickness of the cross section of the various fields vary. In addition, the individual variability of the width of the cortex of one and the same field is significant (CV = 30%). Therefore, it is advisable to carry out the comparison of the MCG to relative scale with respect to depth. In addition, comparison of the relative values makes it possible to avoid the experimental determination of the coefficient of tissue shrinkage, which is different for the gray and white matter. In the context of the gradual character of the transition of the gray matter to the white, as well as of the strong deformation of the column of neurons at the level of layers VI-VII, we selected the boundary between layers IV and V, corresponding to the well reproduced maximum of the MCG with respect to parameters Vₐ and Nₐ, as the reference point for the calculation of relative depth (Fig. 3). For the construction of a generalized curve characterizing the structure of one field or another, the amplitude of the given maximum was used for the norming of each of the curves before averaging.

Analysis of the profiles of two comparable fields demonstrates that the character of the layer-wise change of both the number of neurons and the volumetric ratio differs reliably with respect to all the layers of the cross section, with the exception of sublayer III (see Fig. 3). These differences are reliable (p < 0.01). Above all the comparative analysis of the profiles of field 10 and 44 quantitatively corroborates the relatively lesser development of the granular layers II and IV in field 44. In these zones the volumetric ratio of cells is smaller by 20% (layer IV), and the number of neurons, by 12 and 25% (respectively in layers II and IV). Throughout the cross section of layer IV in field 10, the number of elements is increased by 30%, but in field 44, by only 5%. In keeping with this, the fall in values between layers III and IV is more marked in field 10.
In addition to the absolute differences in the volumetric ratio and the number of neurons in the field under comparison, differences are detected in the character of the rearrangement of the structure of fields with respect to the cross section of layer III. If within the limits of sublayer III¹ the relative differences in the volumetric ratio of cells is insignificant, and a coincidence is observed with respect to the number of cellular elements, then, beginning from the boundary of sublayer III², a marked lag in the increase in both $V_A$ and $N_A$ in field 44 is observed in field as the distance to the surface increases.

There are practically no changes in the values of $V_A$ and $N_A$ in field 44 within the limits of sublayer III² (2 and 0.1%), whereas in field 10 $V_A$ increases by 9%, and $N_A$ by 5%. With respect to the cross section of sublayer III² the same parameters behave differently; the relative increment in $V_A$ in field 44 runs somewhat ahead of the changes in the same value in field 10 (12 and 10%, respectively). The number of neurons in the same sublayer increases more rapidly, approximately by 20%, in field 10, whereas it increases by 17% in field 44. The differences between the sublayers are underscored by the fact that the thickness of sublayer III² of field 44 is 10% greater on the average. Thus, the rearrangement of the structure of layer III in field 10 takes place more energetically as depth increases, while in field 44 it occurs more smoothly.

These differences in the structure of layer III apparently correspond to the significantly greater ramification of the dendritic system of the neurons of field 44 as compared with field 10. The quantitatively scantier distribution of neurons identified within the limits of sublayer III² may be associated with the appearance in this region of the giant pyramidal cells and pyramidal spindles which are characteristic for the architectonic structure of field 44 of man, and are included in the secondary projection-association complex [5].

In addition to the relative differences identified in the structure of the fields under comparison, the data obtained permit the quantitative characterization of the cytarchitectonic features of granular layers II and IV, the quantitative parameters of which in the fields under comparison correlate in different ways. If layer IV predominates in field 10 with respect to the value of the volumetric ratio, and the maximum of the number of neurons in layers II and IV reach a similar level, then in field 44 (despite its relatively poorer expressivity as compared with field 10) layer II is somewhat higher with respect to parameter $V_A$, and significantly exceeds layer IV with respect to the number of neurons. In this connection is is appropriate to recall that the neurons of layer IV are oriented to the perception of thalamic afferent stimuli, while the neurons of layer II take in mainly intercortical and intercerebral inputs. Thus, the results of this comparison correspond to differences in the functional significance of the fields under comparison. Consideration of the described features demonstrates a coincidence with the data regarding the fact that if, within the limits of field 10 a system of neurons predominates which is oriented to the synthesis of non-specific thalamic influences which effect a modulating influence on the integrative processes, then within the limits of field 44 intercortical interactions have a greater significance, which corresponds to its role as the speech-motor associative zone [2].
Thus, as the result of the application of a method which has been worked out of the automated analysis of sections of cortex, a set of characteristic profiles which quantitatively describes the uniqueness of its cytoarchitectonics were obtained for each field investigated. It appears useful to call the aggregate of profiles a field (which were recorded with respect to the set of morphometric parameters within the limits of a statistically representative segment of a section), which reflects the most general and stable regularities of the changes in the structural characteristics of the layer-wise structure of a cortical field, the MCG, and the method itself, automated morphocorticography.

Within the limits of each of the layers, the mean values of the volumetric ratio, sizes and numbers of cells change reliably. The character of these changes is different for each of the layers, which can serve as a criterion of their demarcation.

The comparative characteristics of the quantitative parameters of the fields, which differ with respect to absolute thickness, can be obtained through comparison of their profiles in relative scale. By this means, for example, differences reaching a reliable level (p < 0.01), in the structure of fields 10 and 44, with respect to volumetric ratio and number of cross sections, are identified in layers II, III, and IV, and correspond to the features of their morphofunctional organization.

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STATE OF THE HIPPOCAMPUΣ IN PATIENTS WITH VARIOUS FORMS OF SENILITY

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Research on the structural organization of the brain in persons afflicted with Alzheimer's disease (AD) and senile dementia (SD) is one of the important tasks of biological psychiatry. The increasing interest of psychiatrists and neuromorphologists in this problem can be explained by the increase in the number of AD and SD patients in recent years. Among patients with SD, 13% have AD. According to the data of McLachlan and DeBon [16], in certain regions of the world, 15-23% of the population are more than 65 years old; of these, 11-15% are afflicted, and 60-70% of the afflicted are diagnosed as AD patients.

The structural features of the brain in patients with AD or SD have been studied over a long period. Processes of atrophy have been noted in the cortex of the cerebral hemispheres especially in the temporal and sincipital areas [3, 4, 9, 20]. Some pathomorphological changes in the neurons and glial cells in the cortex of the human brain have been described. Attempts have been made to find the most damaged brain structures in AD and SD: specifically, much attention has been given to Meinert's nucleus and certain other architectonic formations of the brain.
