

**AGE-RELATED CHANGES IN THE CYTOARCHITECTONICS OF BRODMANN
AREA 44 IN THE ELDERLY AND SENILE AGE WOMEN**

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Studies of the aging human brain is the priority field of modern biology and medicine. In recent decades, different types of neuroimaging techniques have been developed. They allow studying the human brain in health and disease *in vivo* [3, 4, 8, 11, 13]. Nowadays, the number of works about age-related changes of gray and white matter volume, thickness and surface of the cortex, ventricular volumes, and intrasulcular space both in whole human brain and in individual regions has increased dramatically [15-17, 19, 22, 23].

The involution of verbal functions occurs later other functions of the human brain [1]. Over the last decade fMRI-models of the functional anatomy of speech are developed. It has been established that the tasks associated with expressive (motor) speech activate opercular part of inferior frontal gyrus (Brodmann area 44, BA 44) and other brain structures [10, 18]. The results of cytoarchitectonic research have a great importance to resolve the problem of structural changes in the aging brain in women. However they are very fragmentary and limited in the literature

[6, 7, 12, 20].

In this work we present data of cytoarchitectonic study of speech motor cortex (BA 44) women in the mature, elderly and senile age.

Material and methods

The cytoarchitectonics of BA 44 in women was studied on the series front total sections of the left and right hemispheres. We divided women in three age groups: group 1 - mature age (19-33 years), group 2 - elderly age (62-73 years), group 3 - senile age (80-87 years). As a result 30 hemispheres of the brain, 10 in each group were studied. Sections 20 mkm thick were stained with cresyl violet by the Nissl method in modification of laboratory of anatomy and architectonics of the brain. All the tested persons did not have psychiatric and neurological disorders.

We used modern morphometric methods. The following cytoarchitectonic characteristics of BA 44 were studied: thickness of the cortex, area of profile field neurons of the layers III and V, their class composition, the density of neurons and whole glia, density of satellite glial cells and neurons surrounded by them. Glial

index was calculated.

The thickness of the cortex BA 44 was measured by ocular micrometer on a microscope MBS-9 (8x4). The measurement was taken at the top of gyrus in 30 fields of view. The area of profile fields neurons was studied using the system of optical-electronic input and image analysis "DiaMorph" (Russia). In the layers III and V was measured at 100 neurons, which clearly the nucleus and nucleolus were identified.

The density of neurons, whole glia, density of satellite glial cells and neurons surrounded by them were calculated in 0.001 mm^3 of brain substance. The study was conducted on a microscope «Аxcioskop» (Germany) with the adjustment at Abercrombie [2]. In each layer at 30 fields of view were studied. In the role of satellite gliocytes were considered the cells that were located at the distance diameter of gliocytes core from the bodies of neurons or the primary divisions of the dendrites.

Processing of quantitative data was performed using Student's t-test in the program Statistica 8. Differences were considered significant as $P < 0.05$

Results and discussion

Cytoarchitectonic study of

inferior frontal gyrus of the brain cortex in women showed that in all the cases BA 44 takes opercular part of this gyrus. The variability and features in macroscopic and cytoarchitectonic structure of speech motor cortex in mature age women in detail were describe in our previous works [5].

Investigation of age-related changes of inferior frontal gyrus showed that elderly women don't have signs of atrophic process at the macroscopic level in all the cases. Gyrus have convex form and densely adjoin to each other. In women at senile age the expanding of the inferior frontal, precentral and lateral grooves were observed in some cases. It is more shown in the left cerebral hemisphere, which leads on the speech function (Fig. 1).

BA 44 well differentiates among the other structures of the frontal area in mature, elderly and senile age women. The most typical cytoarchitectonic signs are poor development and blurriness of borders of the granular layers II and IV, weak expression of the horizontal stratification and well defined vertical striation of the cortex, clear separation of layer III in three sublayer, presence in sublayer III large number of the large pyramids .

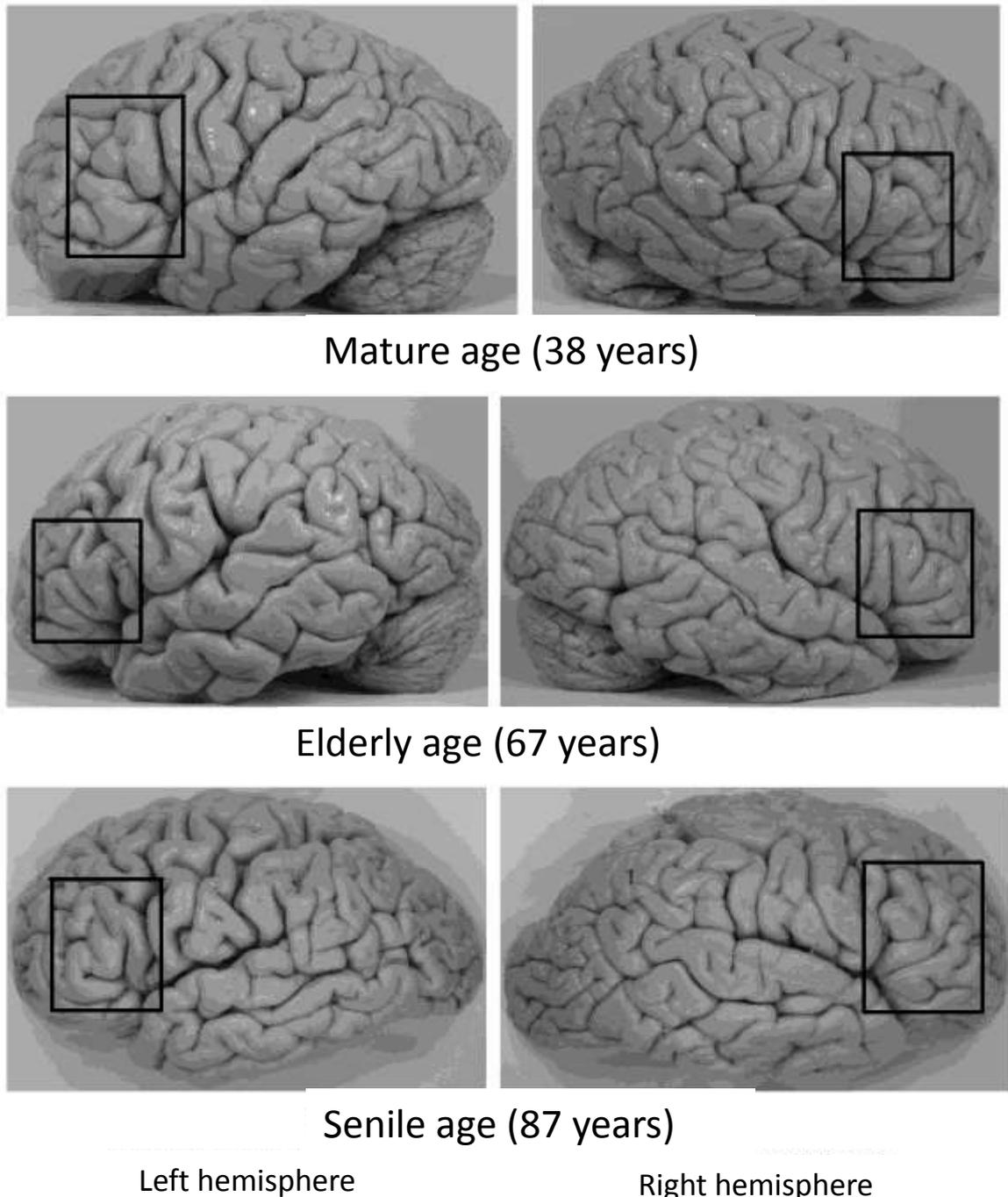


Fig. 1. The macroscopic structure of speech motor cortex in mature, elderly and senile age women (speech motor cortex marked with a square).

Cytoarchitectonics of BA 44 in women cortex in all groups is sufficiently similar at a visual level and generally changes only in senile age. At this age cortex of BA 44 in women becomes more finer and sparse, small foci of devastation cell are observed (Fig. 2).

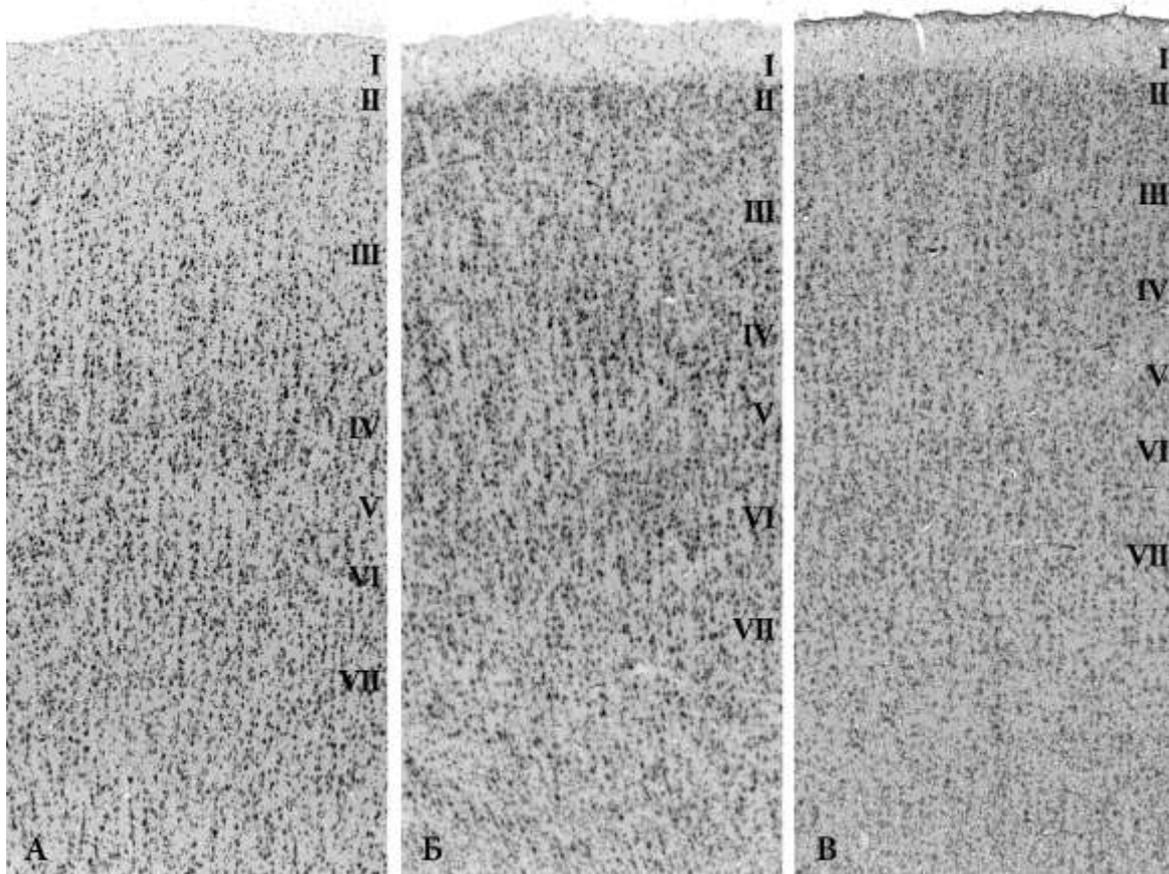


Fig. 2. Cytoarchitectonics of BA 44 in mature (A), elderly (Б) and senile (В) age women. Staining with cresyl violet by the Nissl method.

The destructive changes of individual neurons at elderly and senile women in BA 44 are observed: deformation of the body, core, total tigrolysis, accumulation of lipofuscin in neurons. The number of cells-shadows and glial nodules increases with age in all layers of the cortex, particularly in the lower layers (V and VI).

The thickness of the cortex of BA 44 at senile women very slightly decreases for 1.4% compared with mature age in the left hemisphere of the brain, and for 2.5% in the right ($P > 0,05$). More significant decrease of thickness of the cortex of BA 44 is

observed at senile age women in both hemispheres – for 6.9% and 7.5%. Its value significantly differs from this at mature age ($P > 0,05$) (Fig. 3).

Age-related changes were also identified in our study of area of profile field neurons in layers III and V of BA 44. It is reduced in the layer III in left and right hemispheres at elderly age women compared with mature age on average for 6.5% and 9.5%, at senile age for 21.4% and 16.8% ($P < 0,05$). Age-related reduction of neurons sizes in the layer V of BA 44 is less significant – for 2.1% and 7.8% at the elderly age, 11.9% and 15.7% at senile age (Fig. 4).

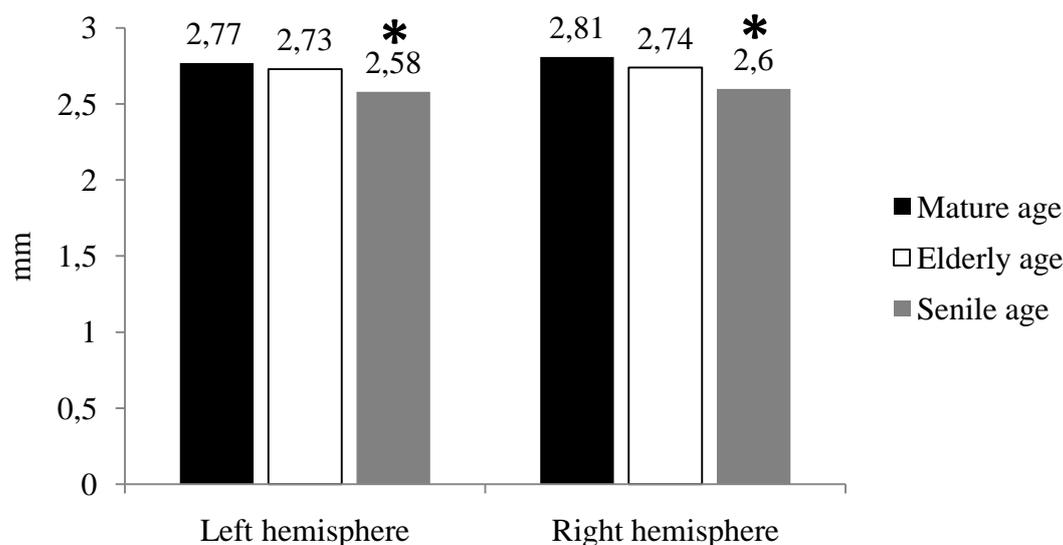


Fig. 3. The thickness of the cortex of BA 44 in mature, elderly and senile age women (mm). * - age-related differences of group 3 from group 1 at the $P < 0.05$.

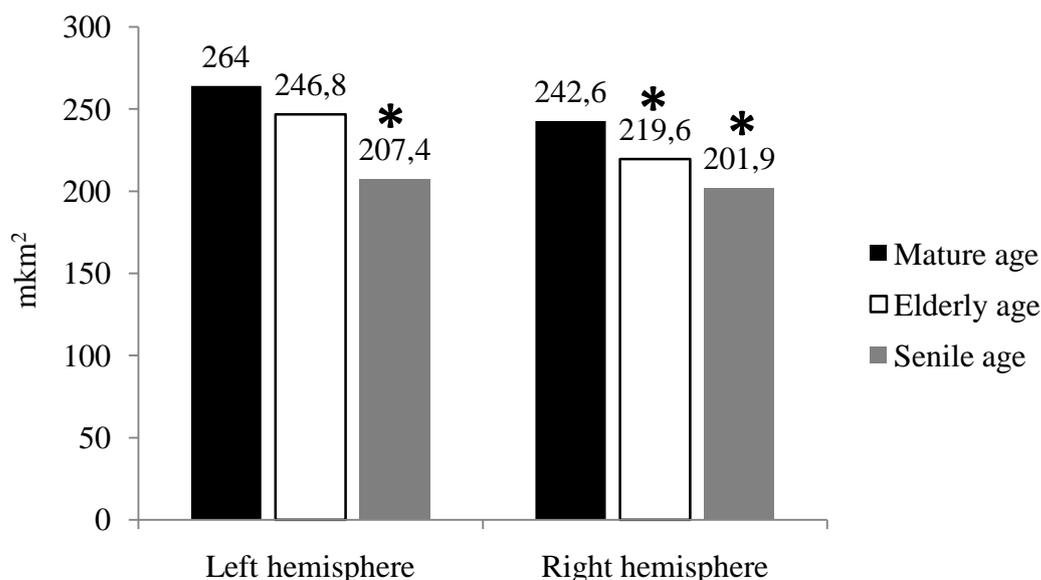


Fig. 4. The area of profile field neurons in layers III of BA 44 in mature, elderly and senile age women (mkm²). * - age-related differences of groups 2 and 3 from group 1 at the $P < 0.05$.

Neuron-glia relationships in the speech motor cortex change during women aging. The density of neurons in the associative layer III significantly decreased in senile age – for 10.2% and 12.4% ($P < 0,05$). These changes are less significant in the projection layer V and amount to only 4.5% in the left

hemisphere of the brain and 5.6% in the right ($P > 0,05$). At senile age in the cortex of Broca's area number of cells-shadows, glial nodules and foci of devastation cells increase that indicates neuronal death. Density of neurons in 0,001mm³ of the brain is dramatically reduced not only in layer III (22.2% and

22.4%), but even more in the layer V (30.8% and 33.8%) in the left and right hemisphere of the brain.

Age-related changes the value of this parameter at senile age women

compared to mature age in both layers of the cortex of BA 44 are statistically significant ($P < 0.05$) (Fig. 5).

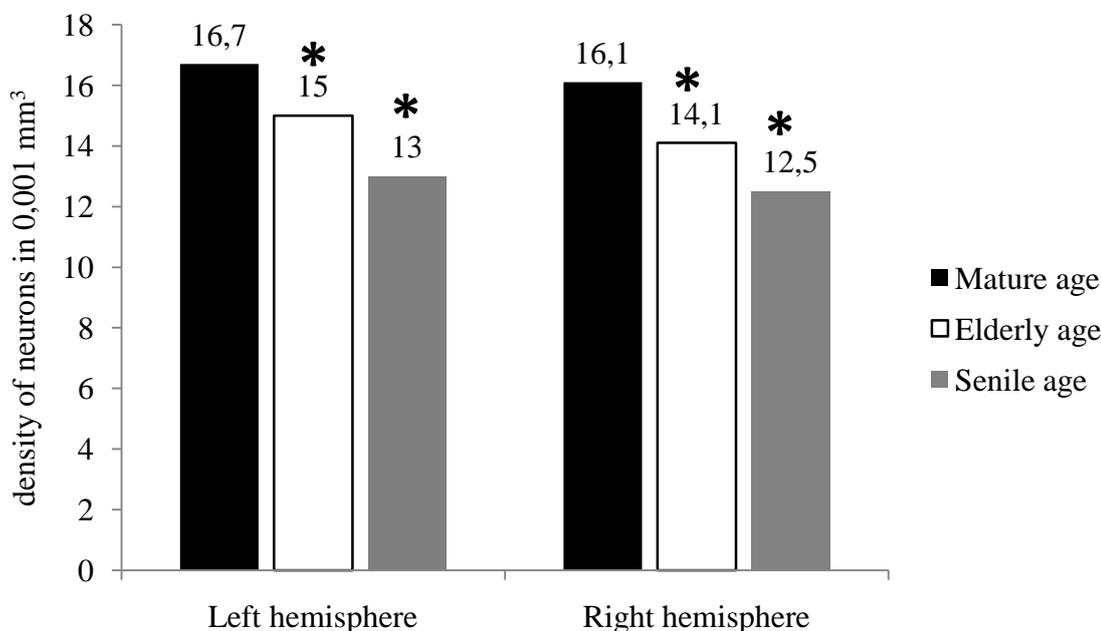


Fig. 5. Density of neurons in the layer III of BA 44 in mature, elderly and senile age women (in 0,001mm³). * - age-related differences of groups 2 and 3 from group 1 at the $P < 0.05$.

The results of our research showed that change in the density of glial cells in layers III and V of BA 44 is observed in women with aging. In recent years much attention is paid to study of glia functions. It is found that neuroglia not only supports nervous tissue homeostasis, the normal functioning of neurons and also participates in the nervous impulse. Satellite gliocytes play an important role in maintaining the functional activity of neurons.

We have found that density of all glial cells in the layer III slight increase

at elderly age women compared to mature age – for 2.4% in the left and 4.7% in the right brain hemisphere ($P > 0.05$). This parameter dramatically increases at senile age women – for 16.0% and 19.5%. The difference density of whole glia between the first and third age group is statistically significant ($P < 0.05$). Increase density of whole glia in the layer V of BA 44 is less significant than in the layer III in groups of elderly and senile age women.

Reducing density of neurons and increase density of glial cells lead to a change of the glial index in aging. It

shows how many glial cells in fall on a one neuron. Thus, it was in the layer III of BA 44 in the left hemisphere 3.4 at mature age, at elderly age – 3.9. Its value was very large at senile age – 5.1. The glial index in the right hemisphere was 3.3, 3.9, 5.0 accordingly to age groups.

Notably that increase of density of all glial cells occurs by increasing the number of free glia, while the density of the satellite glial cells is significantly reduce at the elderly and senile age. In the associative layer III of BA 44 it is reduced for 21.1% and 25.6% at the elderly age women, for 34.1% and 25.0% at senile age women in the left and right hemisphere of the brain. At the same time density of neurons surrounded by satellite glial cells is reduced for 21.1% and 21.0% in the elderly age, and for 33.9% and 30.0% in senile age. Age-related changes of these parameters in the layer V of BA 44 are less pronounced than in the layer III.

Thus, our data suggest that area of speech motor cortex of the women brain is characterized by a slower rate of age-related changes of macroscopic, cytoarchitectonic and morphometric characteristics of its structure. Signs of cortical atrophy BA 44 found only at the group of senile age women. Interestingly that the greatest changes of the morphometric characteristics of BA 44 are expressed in the associative layer III at senile age women. A significant reduction in the density of neurons in

this layer, reducing the number of large neurons may show about impairment of interhemispheric and intrahemispheric interactions of structures, which provide different aspects of speech function.

The literature data suggest that structural changes in the human brain are connected not only with the aging. They are also due to the influence of other endogenous and exogenous factors [21]. The number of chronic diseases increases in elderly and senile age. Stress and decreased levels of sex hormones have a great influence on the state of the brain tissue. Hypertension and cardiac failure are common diseases in old age. Significant changes in the structural elements of the brain and neurons are revealed during severe hypoxia and cerebral ischemia [9, 14]. We believe that we have identified age-related changes cytoarchitectonics speech motor cortex in women is result not only of the aging process, but also the influence of other factors.

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