

CHANGES IN THE DENSITY OF NEURONS AND GLIA OF THE AREA 7 BRAIN CORTEX IN MEN IN THE PROCESS OF AGING

P.A. Agapov, I.N. Bogolepova, L.I. Malofeeva

Research Center of Neurology, Moscow

pavelscn@yandex.ru

In the field of neurosciences, there are many new lifetime morphological findings obtained due to the development of modern methods of neuroimaging in the past two decades [4, 6, 12]. Magnetic resonance tomography revealed *in vivo* the decrease in total brain mass as well as involution of its individual structures which occurs due to atrophy of the gray and white matter of the brain. After 30 years of age, there has been a gradual decrease in the human brain by 2.5% every 10 years on average [2]. Linear characteristics of the brain also change: there is decreasing of them in most of cases, but various brain structures behave differently. Median length and height of the hemispheres and size of many subcortical nuclei is reduced, the volume of the lateral ventricles in the brain increases with age [19], the width of the thalamus also increases in men [9].

In addition to volume changes in the brain there are qualitative and quantitative changes in the nervous tissue in its structural elements [3]. Along with the decrease of brain mass reduction in the number of neurons occurs throughout life, glia/neuron ratio undergo a change; the number of glial cells increases with age in contrast to

the number of neurons which is often associated with compensatory processes involving glial cells [7]. We haven't found articles devoted to age-related changes of the associative cortex of the superior parietal area thus the aim of our work was to investigate age-related changes of cytoarchitectonic area 7 of superior parietal cortex area in brain of men. Area 7 is located near the junction of the frontal and occipital structures and participates in the integration of the motor and visual information. A variety of communication of superior parietal region combine cortical and subcortical structures without having direct connections with primary sensory areas. It is expected that the superior parietal region is involved in the integrative activity of the brain by influencing the structures involved in cognitive processing of information, without the direct analysis of external stimuli which are processed mainly by the primary and secondary sensory cortical fields.

Important functions of the superior parietal region include switching and maintaining of the attention and participation in spatial perception, neural networks of the area 7 capture the visual image, control and tracking of the hand movements [14,

15]. We studied the superior parietal region that is also involved in the control of movement and processing of visual information, retrieving of visual images from memories [20].

MATERIALS AND METHODS

Study of area 7 of brain cortex in men carried on a continuous series of frontal paraffin sections of left and right hemispheres of the brains of 15 men from three age groups (mature group - from 19 to 59 years, elderly group - from 61 to 74 years, senile group - from 75 to 90 years). Staining of micropreparates was made by Nissl method. Thickness of sections was 20 microns. We studied brains of men who do not suffered from mental or neurological disorders. The most typical section of the cortex of the area 7 at the center of the medial surface of the superior parietal region was segregated in accordance to the cytoarchitectonic characteristic. Our attention was drawn to the following morphometric parameters in layers III³ and V of cortex area 7: the profile area of pyramidal neurons, the density of pyramidal neurons, the density of pyramidal neurons surrounded by the satellite glia, the density of the satellite glia and the density of the total glia. The studies were performed with the system of electro-optical analysis "DiaMorph". Only undamaged neurons with nucleus and nucleolus were measured and counted. Statistical data processing was performed in the program Statistica 8.0. Differences between the observed

characteristics were determined using the Mann - Whitney U-test, the differences were considered significant at a significance level of $p \leq 0,05$.

RESULTS

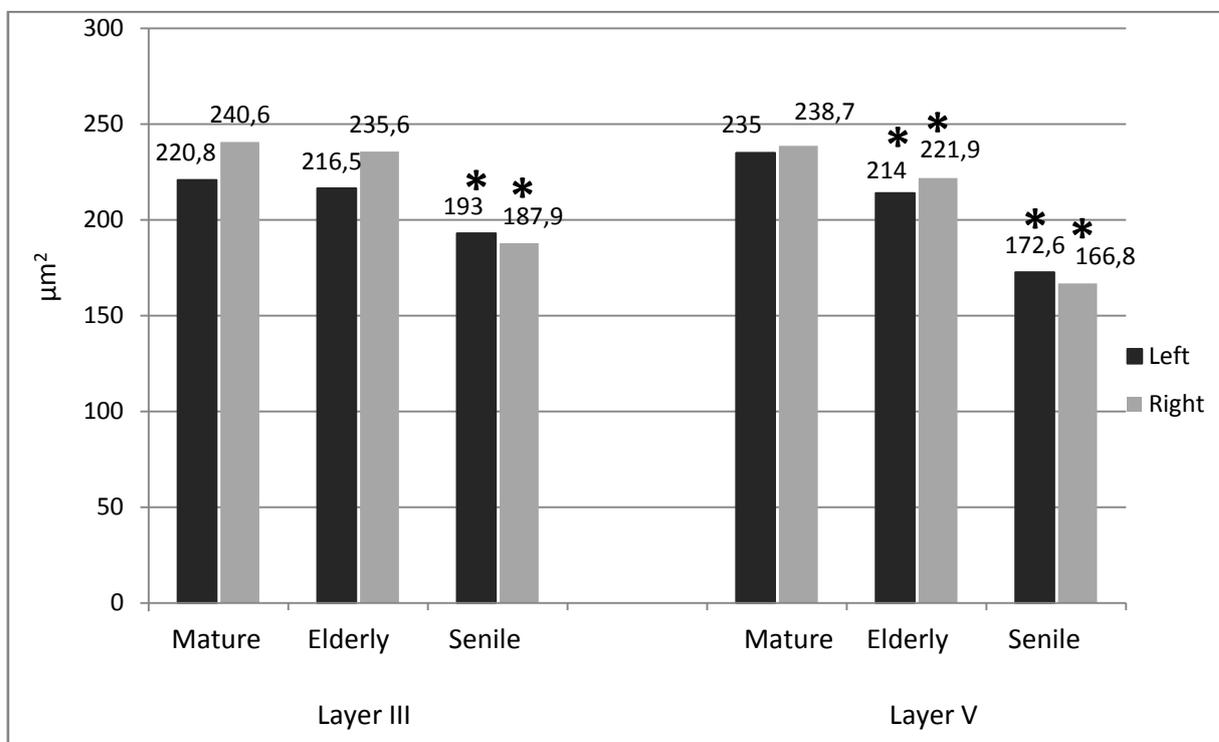
We found hemispheric asymmetry in sizes of the profile area of pyramidal neurons of the III³ layer in the group of men of mature age, so that its average value in the left hemisphere was $220.8 \mu\text{m}^2$, while the right hemisphere $240.6 \mu\text{m}^2$ [1]. Value of the III³ layer was $216.5 \mu\text{m}^2$ in the left hemisphere, while the right hemisphere was demonstrating $235.6 \mu\text{m}^2$ in a group of elderly men. Comparing the average size of the profile areas between two groups of men, it is possible to note a slight smaller value of neuron's area in the second group, but these differences are not statistically significant so they can be neglected.

Analysis of the average values of the profile area of pyramidal neurons of the layer III³ in senile group showed a significant decrease in the size of neurons in comparison with groups of men younger age (mature and elderly) - in the left hemisphere the average value of the profile area of neurons - $193.0 \mu\text{m}^2$, and the right - $187.9 \mu\text{m}^2$. The value of the profile areas of pyramidal neurons in the layer V of the group of elderly men is reduced significantly compared to men of mature group. Its value was in the left hemisphere - $235 \mu\text{m}^2$, in the right hemisphere - $238.7 \mu\text{m}^2$, and a group of elderly men of similar value indexes were lower -

214.0 μm^2 in the left hemisphere and 221.9 μm^2 in the right hemisphere.

There is a significant reduction in the profile area of pyramidal neurons by

26% and 30% on the left and right respectively of 172.6 μm^2 and 166.8 μm^2 in the group of senile men (Figure 1).



* - age differences at $p \leq 0.05$

Fig.1 The profile area of pyramidal neurons in V and III³ layers of the area 7 in male brain cortex (μm^2).

Density of neurons in 0.001 mm^3 of brain in the group of mature men was at 27.2 neurons in the left hemisphere and 27.8 neurons in the right hemisphere in layer III³ of brain cortex. There is a statistically significant decreasing in the number of neurons in the left hemisphere till 25 to 0.001 mm^3 neurons in the brain matter and in the right hemisphere is at approximately the same level in the group of elderly men (26.5 neurons in 0.001 mm^3 of brain). Neuronal density decreases by 21% and 22% and is about to 21.3 neurons in the left and 21.6 in the right in the brain substance 0.001 mm^3 in the senile group.

Gradual decrease in the density of neurons is observed with aging in the layer V of cortex area 7. The density of layer V neurons in 0,001 mm^3 of brain matter is 27.3 in the left hemisphere and 29.2 in the right hemisphere. The density of neurons is reduced by 14%

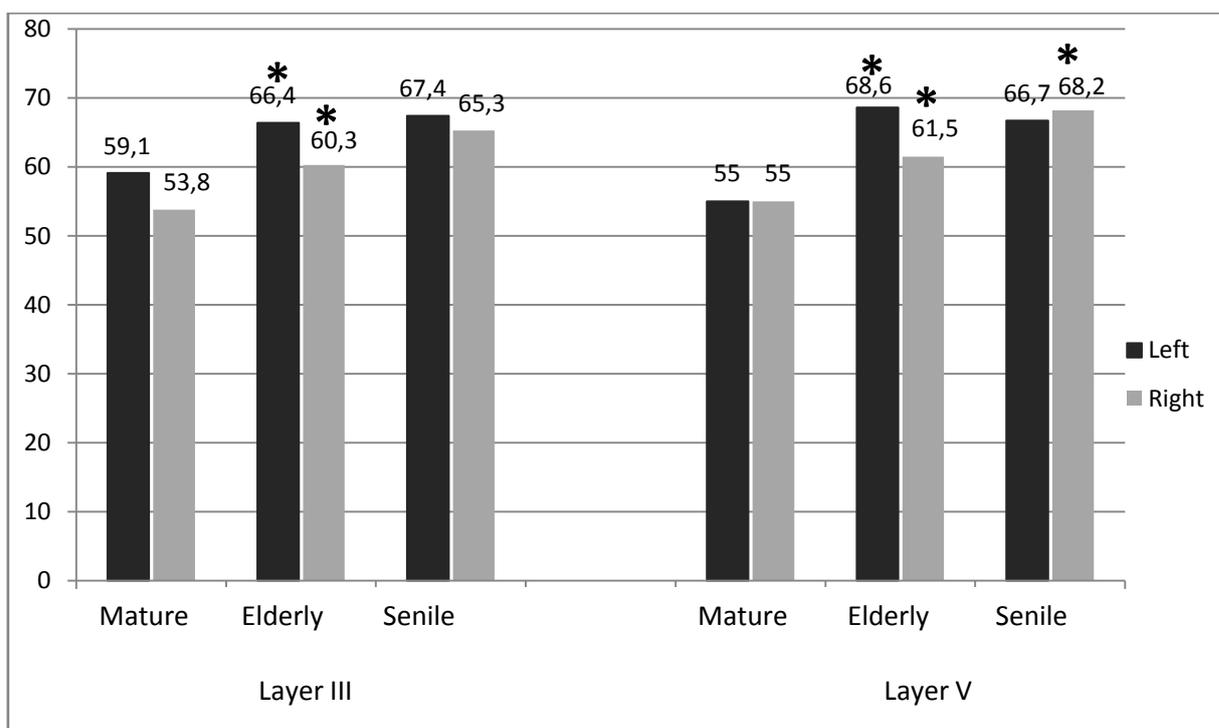
and is 23.6 and 24.9 of neurons respectively in 0.001 mm^3 of brain in the elderly group. In the senile group density decreases by 10%, reaching a value of 20.7 in the left hemisphere and 21.6 neurons in the right hemisphere in 0.001 mm^3 of brain.

There is a downward trend for the density of neurons surrounded by the satellite glia in III3 layer in each age group, but revealed differences are not statistically significant. The most significant changes in the density of neurons surrounded by the satellite glia occur in men of senile age, where it is reduced in comparison with a group of mature men to 20-21%, amounting to 9.9 in the left hemisphere and 10.1 in the right hemisphere in 0,001 mm³ of brain. The density was 13.2 neurons surrounded by the satellite glia in the left hemisphere and 12.9 neurons surrounded by the satellite glia in the right hemisphere in 0,001 mm³ of the brain, and in a group of elderly men, respectively 11.9 and 12.3 neurons surrounded by the satellite glia in 0.001 mm³ of the brain. The density of neurons surrounded by the satellite glia in layer V significantly reduced in senile group - 23% which result in 8.9 neurons on the right and 9.8 on the left in 0.001 mm³ of brain. Their density in the group of mature men is 11.6 (left) and 12.8 (right), in elderly age, respectively, 10.8 and 12.8 of neurons surrounded by the satellite glia in 0.001 mm³ of the brain.

We observed a dramatic reduction in the density of the satellite glia in the senile group: 11 satellite glial cells in 0.001 mm³ of brain in the left hemisphere (a decrease of 33%) and 11.8 of satellite glial cells in 0.001 mm³ of brain in the right hemisphere of the brain (26%).

The density of the total glia increases with the aging unlike other brain cortex parameters of the area 7. Density of the layer III³ is 59.1 glial cells in 0.001 mm³ of the brain in the left hemisphere and 53.8 glial cells in the right hemisphere. There is a significant increase of 12% in the left and right hemisphere in the elderly group, reaching a value of 66.4 and 60.3 glial cells in 0.001 mm³ of the brain. Density remains approximately at the same level in the senile age group, increasing slightly in the right hemisphere: 67.4 glial cells on the left, 65.3 glial cells on the right in 0.001 mm³ of brain.

There are same changes in the density of total glia in the layer V of the cortex of the brain of the area 7 as in III3 layer (Fig. 2).



* - age differences at $p \leq 0.05$

Fig. 2. The density of the total glia in V and III3 layers of the area 7 in male brain cortex.

DISCUSSION

There is reduction in the density of neurons in the process of brain aging in layers III and V of the area 7 of the brain cortex in men which is most expressed in senile age. The observed reduction in the number of neurons is consistent with other studies thus show that the number of neurons in the brain is reduced from 10% to 30% in total in the end of life [17]. The density of neurons surrounded by the satellite glia also decreased in both cytoarchitectonic layers, but approximately by the same value in each age group in contrast to density of neurons. Number of satellite glia decreased in the same principle as the number of neurons surrounded by satellite glial cells - that is a gradual

decrease in the number of them in the aging process.

The observed decrease in the values of the density of neurons and glial satellite is consistent with other work studying age-related changes of cytoarchitectonics in the human brain [5]. Some authors attribute the death of neurons from neural tissue hypoxia caused by the degradation of brain microvascular system [18]. We describe the uneven rate of decline in the number of neurons found in the works of other authors. For example, N.S. Orzhekhovskaya also revealed a higher rate of reduction in the number of neurons in senile age and more stable satellite glia in the aging process [8], which is probably due to compensatory mechanisms involving glial cells.

Furthermore glial cells have a higher RNA synthesis activity and higher resilience as compared with neurons, according to the other studies [11].

There is involving in the process of aging of all body systems and especially hormonal system that affects the physiological state of the nervous system. For example, the level of testosterone that in elderly men decreases in two or more times, according to Janowsky J.S. and others, influences on the behavior organization [16], in particular on the activity of interaction with the environment that is directly related to the functional significance of the superior parietal region and cytoarchitectonic area 7. There is only one morphometric parameter of area 7 whose value increased with aging – the density of total glia. We found a significant increase in its density in the elderly group by 25%, however, in the next age group, the density of total glia remains approximately at the same level. This trend is described in many articles devoted to age-related changes of cytoarchitectonic structure of the brain [10, 13].

References

1. Agapov P.A., Bogolepova I.N. [Hemispheric asymmetry and gender differences profile of the field 7 cortex neurons in superior parietal region of the human brain]. // Fundamental'nye issledovaniya. - 2013. - №8-2. - P. 338-342. (In Russ).
2. Baybakov S.E., Gayvoronskiy I.V., Gayvoronskiy A.I. [Comparative analysis of morphometric parameters of the adult brain (according to the magnetic resonance tomography)]. // Vestnik Sankt-Peterburgskogo universiteta. - 2009. – №11-1. - P. 111-117. (In Russ).
3. Bogolepova I.N., Amunts V.V., Orzhekhovskaya N.S., Malofeeva L.I. [Some patterns of structural changes in the cortex and subcortical structures of the human brain under aging process]. // Zhurnal Nevropatologii i psikiatrii imeni S.S. Korsakova. - 1985. – №85-7. - P. 965-968. (In Russ).
4. Bogolepova I.N., Krotenkova M.V., Malofeeva L.I., Konovalov R.N. et al. [Human brain cortex [architectonics](#): MRI Atlas]./ - Moscow: Izdatel'skiy kholding «Atmosfera». - 2010. – 216 p. (In Russ).
5. Bogolepova I.N., Malofeeva L.I. [Age-related changes in neuron-glia relationships of speech-motor cortex area in elderly men]. // Morfologicheskie vedomosti. - 2014. - №2. - P. 13-18. (In Russ).
6. Bogolepova I.N., Malofeeva L.I., Konovalov R.N., Krotenkova M.V. et al. [Structural asymmetry of Broca area in women's brain]. / Materialy Vserossiyskoy konferentsii «Sovremennye napravleniya issledovaniy funktsional'noy mezhpolutsharnoy

- asimmetrii i plastichnosti mozga». Moscow. - 2010. - P. 94-97. (In Russ).
7. Goryaynov S.A., Protsky S.V., Okhotin V.E., Pavlova G.V. et al. [About astroglia in the brain and pathology]. *Annaly klinicheskoy i eksperimental'noy nevrologii.* - 2013. - V.7. - №7. - P. 45-52. (In Russ).
 8. Orzhekhovskaya N.S. [Neuron-glia relationships in the human brain frontal cortex in a normal and pathological aging (Alzheimer's disease)]. // *Arkhiv anatomii, gistologii i embriologii.* - 1986. - V.91 - №11. - P. 5-12. (In Russ).
 9. Pavlov A.V. [Linear skull parameters and the individual structures of the human brain changing in age aspect according the MRI data]. // *Rossiyskiy mediko-biologicheskii vestnik im. akademika I.P. Pavlova.* - 2011. - №1. - P. 20-25. (In Russ).
 10. Pavlov A.V., Zherybat'eva S.R., Lazutina G.S., Ovchinnikova N.V. [Histological characterization of people mammillary bodies architectonic in different ages]. // *Nauchnye vedomosti Belgorodskogo gosudarstvennogo universiteta. Seriya: Meditsina. Farmatsiya.* -2016. - V. 33. - №5 (226). - P. 104-108. (In Russ).
 11. Pevzner L.Z. [Functional and biochemical characteristics of glia]. // *Uspekhi sovremennoy biologii.* - 1969. - V. 6. - 3(6). - P. 340-360. (In Russ).
 12. Piradov M.A., Tanashyan M.M., Krotenkova M.V., Bryukhov V.V. et al. [State-of-the-art neuroimaging techniques]. // *Annaly klinicheskoy i eksperimental'noy nevrologii.* - 2015. - V.9. - №4. - P. 11-19. (In Russ).
 13. Seroukh A.G., Maslovskiy S.Yu. [Age-related differences in neuronal-glia-capillary relationship in manual postcentral gyrus area of the female brain.] // *Morfologiya.* - 2009. - V. 3. - №3. - P. 177-181. (In Russ).
 14. Andreasen N.C., O'Leary D.S., Cizadlo T., Arndt S. et al. Remembering the past: two facets of episodic memory explored with positron emission tomography. // *Am J Psychiatry.* - 1995. - V. 152. - № 11. - P. 1576-1585.
 15. Connolly J.D., Goodale M.A., Desouza J.F., Menon R.S. et al. A comparison of frontoparietal fMRI activation during anti-saccades and anti-pointing. // *J. Neurophysiol.* - 2000. - V. 84. - № 3. - P. 1645-1655.
 16. Janowsky J.S., Oviatt S.K., Orwoll E.S. Testosterone influences spatial cognition in older men. // *Behav. Neurosci.* - 1994. - V. 108. - P. 325-332.
 17. Pakkenberg B., Gundersen H.J. Neocortical neuron number in humans: effect of sex and age. *J.*

- Comp. Neurology. - 1997. – V. 384. - P. 312-320.
18. Raz N., Rodrigue K.M., Acker J.D. Hypertension and the brain: vulnerability of the prefrontal regions and axecutive functions. // Behavioral Neuroscience. - 2003. - V. 17. - P. 1169-1180.
19. Resnick S.M., Pham D.L., Kraut M.A., Zonderman A.B. et al. Longitudinal magnetic resonance imaging studies of older adults: a shrinking brain. // J. Neurosci. - 2003. - V. 23. - №8. - P.3295-3301.
20. Voisin J.I., Rodrigues E.C., Héту S., Jackson P.L. et al. Modulation of the response to a somatosensory stimulation of the hand during the observation of manual actions. // Exp. Brain Res. - 2011. - V. 208. - № 1. - P. 11-19.