Journal of Psychiatry and Psychiatric Disorders doi: 10.26502/jppd.2572-519X0054

Mini Review Volume 2, Issue 6

Participation of Src-kinase in Age Changes of the Brain Central Zone

Yavisheva Tatiana*, Shcherbakov Sergey

JSC "R-Pharm", Moscow, Russian Federation

***Corresponding Author:** Dr. Yavisheva Tatiana, Laboratory of mechanisms of stem cells regulation, Joint Stock Company "R-Pharm", Moscow, Russian Federation, Tel: +7 905-735-45-90; E-mail: javisheva@rambler.ru

Received: 18 October 2018; **Accepted:** 01 November 2018; **Published:** 06 November 2018

Abstract

In germinal loci of a brain, as well as in tissues of peripheral organs there are morphofunctional zones in which a proliferation and differentiation of cambial cells occur. The hypothalamus with hypophysiotropic region represents the central zone. One of the key proteins of morphofunctional zones is the Src-kinase, participating in transfer of a nervous signal, if it is in its active form. The hypothalamus initially has a high expression of an inactive Src-kinase which is connected with the development of a brain from an ectoderm. With aging due to the influence of the estrogens, which activate the Src-kinase, the resources of an inactive Src in a hypothalamus are exhausted, which leads to violation of release of many hormones including AKTH. Local accumulation in hippocampus of the glucocorticoids, which have inhibitory effect on neurons can lead to neurodegenerative diseases at low congenital level of the Src-kinase in the hypothalamus and also the stresses strengthening emission of glucocorticoids.

Keywords: Central morphofunctional zone; Src-kinase; Age aspect

1. Src-kinase in Age Changes of the Brain Central Zone

Tissues of peripheral organs are constructed as the morphofunctional zones, consisting of two subunits with 12 cambial cells in each, at which division 12 pairs of mother and daughter cells are formed [1]. Between pairs of these cells there is a redistribution of electric charges which leads to emergence of the electric field, stretching daughter cells. As a result, particular loci of chromosomes, fixed to a cell membrane, become accessible to a transcription, i.e. cells are ready to a further differentiation. In the course of daughter cells stretching, the non- receptor Src-kinase is expressed in them, which in the inactive form participates in microtubules cells assembly. These latter together with the intermediate filaments, which synthesis they potentiate, stretch a cell nucleus [2]. Therefore, in case of poor

amount of inactive Src-kinase the formation of a cytoskeleton and a differentiation of cells suffer. In this regard, the expression of necessary amount of this protein in its inactive form in the morphofunctional zones is one of the main functions of cambial cells.

Inactive Src-kinase is a redox-sensitive molecule, therefore it very quickly passes into its active form under the influence of various oxidants [3, 4]. In the active state Src-kinase takes part in the processes of a transcription [4]. Besides, the exocytosis is carried out with its help, because it activates the protein p190RhoGAP, which reduces an expression of one of small G-proteins-RhoA [5]. It leads to the falling of concentration of formins-the multidomain proteins, which are a part of a cell cortex. The relaxation of a cell cortex occurs, and the possibility of splitting off of exocytosis bubbles from a cell membrane appears [1].

The ratio between inactive and active Src-kinase defines also directional differentiation of the cells towards an epitheliocyte or fibroblast-like cells. At a dominance of inactive Src-kinase loci of chromosomes will stretch near telomeres, defining an epithelial differentiation. If the portion of the active Src-kinase begins to increase, then stretching occurs closer to a centromere, and fibroblast-like cells are formed [6].

It appeared that germinal loci of a brain, as well as peripheral organs are constructed as morphofunctional zones [7]. The hypothalamus with its hypophysiotropic region represents the central zone, regulating the most important functions of an organism. At children's and youth an expression of inactive Src-kinase in hypothalamic cells is high which is connected with the development of a brain in the embryonic period from an ectoderm, which initially has a high concentration of this protein. In a neural plate under the influence of a chord there is only a transitional strengthening of the active Src, therefore in neurons inactive Src prevails [6]. In this regard the untwisting of chromosomes in these cells will occur as in epitheliocyte, i.e. closer to telomeres. The function of the neurotransmitters developed by cells of a brain is also directed to strengthening of inactive Src-kinase portion in neurons.

Fast transition of Src-kinase from inactive into the active form under the influence of various factors causes its participation in an exocytosis and transfer of a nervous signal [8]. For example, the starting moment in carrying out a nervous impulse at adrenocorticotropic hormone (AKTH) synthesis is the decrease in a share of inactive Src-kinase under the influence of light in retina photoreceptors and melanopsin cells. It leads to the increase in a share of the active Src-kinase in them, strengthening an exocytosis and decrease in neurotransmitters number, because the stretching of chromosomes loci will be displaced to a centromere, which will cause recession of their synthesis. The reduced number of neurotransmitters and strengthening of an exocytosis in synapses will reduce the concentration of inactive Src-kinase in a brain in each point of a regulatory chain. In a pituitary the development of AKTH, which action is also directed to the decrease in a portion of inactive Src-kinase in cells-targets, starts. It provides the beginning of glucocorticoids synthesis in adrenal glands. Glucocorticoids unlike AKTH increase the concentration of inactive Src-kinase in tissues [8]. Therefore the part of inactive Src-kinase, the quantity of RhoA and, therefore, a cortex rigidity, increase in cells. In process of accumulation they influence over peptidergic neurons of the sexual

center and a pituitary, oppressing an exocytosis and slowing down the development of an gonadotropin-releasing hormone (GnRH) and AKTH. Therefore, the agents causing increase in a part of inactive Src-kinase in a chain of a regulation are inhibitory and vice versa, reducing it-exciting.

Estrogens, unlike glucocorticoids, have the properties of the excitatory signal, because they reduce the concentration of inactive Src-kinase in tissues, making active Src-kinase by means of G-proteins, which join to its catalytic domain [9]. But the terminal products having such characteristic cannot slow down the development of a hypothalamus GnRH in the regulatory chain. Therefore it is developed constantly, and depending on amplitude and a rhythm of secretion, regulates the production not only of pituitary follicle-stimulating hormone (FSH), but also luteinizing (LH) [8]. Really, in the process of estrogens amount increase in an organism, the portion of the active Src-kinase in the sexual center will increase also. Thus, the exocytosis and, therefore, the frequency and amplitude of secretion of hypothalamus GnRH amplify, which causes the development of FSH. The cells-targets at large emission of hormones stop to react to this stimulus [10]. Therefore, at the increased synthesis of FSH there comes the insensitivity of the ovary cells. It leads to decrease of androgens aromatization, thus the formation of estrogens will fall in ovaries. Influence of estrogens over a brain tissues will weaken, which will cause the increase in a share of inactive Src-kinase in the hypothalamus sexual center. It in turn leads to decrease of the exocytosis, a drop of GnRH emission frequency and the beginning of LH synthesis in a pituitary.

Thus, estrogens, influencing over a brain, steadily exhaust with aging the resources of inactive Src-kinase in the hypothalamus and other departments of a brain having many receptors to estrogens (a pituitary, an epiphysis). At the same time the number of neurotransmitters, including melatonin, rendering inhibitory effect on brain neurons, especially a hypothalamus, which represents the central morphofunctional zone and carries out a regulation of many hormones synthesis, decreases. Therefore, the falling in an expression of inactive S-kinase in this zone leads to violation of hormonal activity of all organism with aging.

On the example of AKTH synthesis it is clear, that such falling in age aspect causes decrease in neurotransmitters number and their inhibitory influence on supra-chiasmatic nucleus (SCN) [6, 8]. Therefore the duration of own cell cycle of SCN is reduced, which leads to the earlier beginning of AKTH synthesis-at 3 a.m., instead of 6-8 a.m. Due to the increase in a portion of the active Src-kinase, the carrying out of a signal in neurons, exocytosis and synthesis of this hormone in a pituitary amplify. In adrenal glands the production of glucocorticoids respectively increases.

It is shown above that the increased quantity of glucocorticoids exert inhibitory impact on carrying out of a signal in nervous tissue, because they increase a share of inactive Src-kinase in the cells and worsen the secretion of mediators in synapses by means of an exocytosis. Interestingly, that the glucocorticoids receptors in a hippocampus are located not diffusively, and locally in the fields CA1-2. According to literature data the field CA1 first of all is exposed to pathological changes at Alzheimer's disease and a senile dementia [11].

Thus, the level of inactive Src-kinase in the central morphofunctional zone is lower, the larger quantity of glucocorticoids is synthesized in adrenal glands and, therefore their inhibitory effect on hippocampus neurons is stronger. Hence, the low congenital level of inactive Src-kinase of a brain and the stresses are the having moment for the development of neurodegenerative diseases.

References

1. Yavisheva TM, Shcherbakov SD. Epithelial-stromal morphofunctional zones: structure and functions. RAMN (publisher) Moscow (2013): 145.
2. Yavisheva TM, Shcherbakov SD. Participation of an inactive and active Src-kinase in formation of a cytoskeleton and melanogenesis in Hep2 cells. International Journal of Current Microbiology and Applied Sciences 5 (2016): 583-593.
3. Aikawa R, Komuro I, Yamazaki T, et al. Oxidative stress activates extracellular signal-regulated kinases through Src and Ras in cultured cardiac myocytes of neonatal rats. J Clin Invest 100 (1997): 1813-1821.
4. Burova EB, Gonchar IV, Nikolsky NN. Stat1 and stat3 activation by oxidative stress in A431 cells involves src-dependent EGF receptor tranactivation. Tsitologiya 45 (2003): 466-477.
5. Arthur WT, Petch LA, Burridge K. Integrin engagement suppresses RhoA activity via a c-Src-dependent mechanism. Curr Biol 10 (2000): 719-722.
6. Yavisheva TM, Shcherbakov SD. Participation of the morphofunctional zones in aging process. Uspekhi gerontologii 25 (2012): 604-611.
7. Yavisheva TM, Shcherbakov SD, Golubeva IS. Some aspects of morphofunctional organization of germinal regions of the hippocampus and the olfactory bulb in young and old mice. International Journal of Innovative Studies in Medical Sciences 1 (2017): 4-11.
8. Yavisheva TM, Shcherbakov SD. To a question of structural and functional organization of the morphofunctional zones in age aspect. Participation of Src-kinase in the work of morphofunctional zones International Journal of Current Medical and Pharmaceutical Research 4 (2018): 3336-3344.
9. Razandi M, Pedram A, Park ST, et al. Proximal events in signaling by plasma membrane estrogen receptors. Journal of Biological Chemistry l4 (2003): 2701-2712.
10. Tepperman J, Tepperman H. Metabolic and endocrine physiology. Mir (publishers) Moscow (1989): 653.
11. Vinogradova OS. Hippocampus and memory. Nauka (publishers) Moscow (1975): 332.

Citation: Yavisheva Tatiana, Shcherbakov Sergey. Participation of Src-kinase in Age Changes of the Brain Central Zone. Journal of Psychiatry and Psychiatric Disorders 2 (2018): 179-182.