Impact Factor ISRA (India) = **1.344**
Impact Factor ISI (Dubai, UAE) = **0.829**
based on International Citation Report (ICR)
Impact Factor GIF (Australia) = **0.356**

Impact Factor JIF = **1.500**
Impact Factor SIS (USA) = **0.438**
Impact Factor РИНЦ (Russia) = **0.179**

SOI: 1.1/TAS DOI: 10.15863/TAS
International Scientific Journal
Theoretical & Applied Science

p-ISSN: 2308-4944 (print) **e-ISSN:** 2409-0085 (online)

Year: 2015 **Issue:** 03 **Volume:** 23

Published: 30.03.2015 **http://T-Science.org**

SECTION 11. Biology. Ecology. Veterinary.

Yaroslava Igorevna Mitaeva
junior researcher,
Nizhny Novgorod State University, Russia
yasya13@mail.ru
Artem Mikhailovich Mozherov
junior researcher, PhD student,
Nizhny Novgorod State University, Russia
Rostislav Andreevich Sokolov
junior researcher, PhD student,
Nizhny Novgorod State University, Russia
Irina Vasil'evna Mukhina
professor Neurodynamics and Neurobiology
Department of Nizhny Novgorod State University,
Head of Central Research Laboratory Nizhny
Novgorod State Medical Academy, Russia

ACTIVATION NETWORK Ca^{2+}-CELL ACTIVITY OF THE HIPPOCAMPUS IN THE LATE NEONATAL ONTOGENESIS

Abstract: *We investigate the spontaneous, ATP- and L-glutamate - induced changes in intracellular calcium in neurons and astrocytes CA3 field of rat hippocampus acute slices. This study allowed us to estimate the dependence of Ca2+ activity of cells of the CA3 field of rats hippocampus of late (R21-25) neonatal period of postnatal ontogenesis from the metabolic state of the cells associated with an increase in the release of neurotransmitters into the synaptic cleft. Furthermore, it was shown that in a mature network, where the spontaneous Ca2+ activity of the cells is low while maintaining excitation of the neural network, adding evoked excitatory neurotransmitters causing strict synchronization of cell activity.*

Key words: *neuron, astrocyte, neuronal-glial networks, CA3 field, ATP, L-glutamate*
Language: *English*
Citation: Mitaeva YI, Mozherov AM, Sokolov RA, Mukhina IV (2015) ACTIVATION NETWORK Ca^{2+}-CELL ACTIVITY OF THE HIPPOCAMPUS IN THE LATE NEONATAL ONTOGENESIS. ISJ Theoretical & Applied Science 03 (23): 168-170.
Soi: http://s-o-i.org/1.1/TAS*03(23)28 ***Doi***: crossref http://dx.doi.org/10.15863/TAS.2015.03.23.28

Information processing in the brain - is the result of the constant interaction between two cellular networks: the neuronal and the glial. Neural networks are integrated through electrical and chemical signals [1-3]. The transmission of information in the glial network is due to the diffusion of ions and molecules to the intercellular space. Although functional value of these alternative signaling pathways is largely unknown, it is increasingly clear that the cell-cell interactions in neuronal-glial networks are essential for normal functioning of the brain. In addition, the study of the functioning of the neuron-glial networks is necessary for understanding the formation of pathological events that determine the outcome of many neurological diseases [4, 5].

Purinergic and glutamatergic receptors play a specific role in signaling in neuronal-glial networks, participate in all varieties of neuron-glial signaling, including Ca^{2+} - signaling as fundamental processes essential for the functioning of cells. Activation of purinergic and glutamatergic receptors causes an increase in intracellular calcium ($[Ca^{2+}]_i$), which is an important messenger of the cellular response in the central nervous system (CNS). On glial cells and neurons expressed metabotropic and ionotropic receptors are mobilizing $[Ca^{2+}]_i$. It is likely that different subtypes of purinergic and glutamatergic receptors play a different role in the physiology and pathology of the cell [6-11].

The relevance of the project is defined, first of all, the studying of the fundamental mechanisms of cell-cell interaction in neural networks of the hippocampus, in particular in the CA3 field in health and disease, and, secondly, the need to development of prevention and correction of post-ischemic disruption methods to the neural networks in the acute and chronic phase of circulatory ischemia after a stroke.

In this work, we investigate the spontaneous, ATP- and L-glutamate - induced changes in intracellular calcium in neurons and astrocytes CA3 field of rat hippocampus acute slices, using laser scanning confocal microscope Carl Zeiss LSM 510 Duoscan (Germany). Entries fluorescence kinetics were carried out in full frame (field of view of 400x400 mm), with a digital resolution of 256x256 pixels and a scan rate of 1 Hz. Fluorescence

indicators recorded in the range 500-530 nm (Oregon Green 488 BAPTA-1 AM) and 650-710 nm (Sulforhodamine 101). The fluorescence intensity (ΔF/F) shows the dependence of the concentration of $[Ca^{2+}]_i$ on the time, indicating metabolic activity of cells [15, 16].

Spontaneous $[Ca^{2+}]_i$ signals observed in neurons and astrocytes. Neuron $[Ca^{2+}]_i$ signals are associated with the release of neurotransmitters, synaptic plasticity and electrical excitability. Astrocytes electrically are nonexcitable, therefore $[Ca^{2+}]_i$ signals occur in response to chemical or mechanical stimuli.

To study the mechanism of spontaneous Ca^{2+} oscillations in mature network of neurons and astrocytes were carried out experiments with the addition of excitatory neurotransmitters - ATP and L-glutamate [16]. The neurotransmitters glutamate and ATP control about 80% of synaptic transmission in the hippocampus. Addition of tetrodotoxin in the perfusion solution allows to evaluate the performance of individual synapses and cells.

It has been shown that when added to the perfusion solution P2.- ATP receptor agonist, increases the amount of Ca^{2+} oscillations in the cells of CA3 field of rats hippocampus: in pyramidal neurons by 100% , by 85% on interneurons and doubled in astrocytes. And when added in a perfusion solution agonist of glutamate receptors - L-glutamate was registered an increase in the amount of Ca^{2+} oscillations in the cells of CA3 field of rat hippocampus: in pyramidal neurons by 71% in interneurons by 42% and by 100% in astrocytes.

At rest, in the animal hippocampus extracellular glutamate levels ranging from 1 to 2 mM, and the ATP level of 100 nM. A concentration of these substances in 20 mM considered half-maximal effective concentration, and can be observed at increased activity of the brain, for example during a research of animal behavior. While maintaining the excitation of a neural network, ATP and L-glutamate - dependent activation of synaptic transmission resulted in a significant increase in Ca^{2+} activity in the network as reflected in the presence of synchronization between cells when added excitatory neurotransmitters..

This study allowed us to estimate the dependence of Ca^{2+} activity of cells of the CA3 field of rats hippocampus of late (R21-25) neonatal period of postnatal ontogenesis from the metabolic state of the cells associated with an increase in the release of neurotransmitters into the synaptic cleft. Furthermore, it was shown that in a mature network, where the spontaneous Ca^{2+} activity of the cells is low while maintaining excitation of the neural network, adding evoked excitatory neurotransmitters causing strict synchronization of cell activity. In the works of Tsukamoto-Yasui, Ikegaya, Mazzoni, Sipla aimed at understanding the neural networks in the hippocampus as well it has been demonstrated that about 60% of the neurons respond to sensory irritation, due to the peculiarities of the structure of the hippocampus [3, 12-14].

The scientific significance of the project is to provide new fundamental knowledge about the role of electrical and chemical components of calcium signaling in hippocampus neuronal-glial networks of late neonatal ontogenesis.

Acknowledgements

Funding provided by Grant of the President of the Russian Federation for young scientists and graduate students engaged in advanced research and development in priority areas of modernization of the Russian economy for 2015-2017 (СП-1531.2015.4).

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