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the first few days after the birth, and by the end of the first postnatal week topographic thalamocortical connections are formed. However, it remains unknown whether the early thalamic inputs are topographically precise at birth or the initial configuration of thalamocortical connections is coarse and overlapping. We attempted to answer this question by studying the development of somatosensory maps in the barrel system of newborn rats in vivo. We have found that early postnatal period is characterized by the oscillatory response in one cortical site induced by alternate stimulation of several whiskers, which means that the receptive fields indeed largely overlap at birth, thus favoring the model of coarse thalamocortical connectivity. Barrel pattern of activity with precise thalamocortical connections emerges in several days by P4. Based on our data we propose that initially thalamocortical projections enter the cortex in a non-precise manner. During development a competition between topographic and non-topographic thalamocortical connections takes place and it is followed by elimination of non-topographic sensory inputs and establishing precise connections between topographically linked groups of thalamic and cortical neurons.

Keywords: barrel cortex, thalamocortical connections, development, protomap

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CHANGES IN KINETICS OF CALCIUM SIGNALS IN RESPONSE TO HIGH FREQUENCY STIMULATION IN CULTURED HIPPOCAMPAL NEURONS

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Dynamic changes in the intracellular free Ca^{2+}concentration ($[Ca^{2+}]_i$) were studied in hippocampal cultured neurons (prepared from hippocampi isolated from 1-day old Wistar rats) using fluorescent Ca^{2+}-indicator dye Indo-1 and somatic whole-cell recordings. The resting $[Ca^{2+}]_i$ was determined to be 43±2 nM; single action potentials evoked Ca^{2+}-transients with peak amplitude of 9±1 nM. During the tetanus stimulation (frequency varied from 30 to 100 Hz, duration - from 2 to 30 s) Ca^{2+}-transient increased their amplitude up to a steady-state level during repetitive stimulation. We identified two groups of neurons basing on Ca-signal dynamics after the end of stimulation: the first group (n=24) with the monoexponential decay of $[Ca^{2+}]_i$ direct after the end of the tetanus; the second group (n=32) with monoexponential delayed $[Ca^{2+}]_i$ decay after the end of the tetanus, the duration of delay varied from 1 to 27 s and depended on duration and frequency of stimulation. Peak amplitudes of Ca^{2+}-transients were statistically different between the first (1820±195 nM, n=24) and the second (2618±165 nM, n=23) groups. A linear dependence between decay time constant and frequency of stimulation was found for the second group of neurons only. In all cases when the delayed decay was observed the decay time constant changed reliably after arising delayed decay; the average rise made up 41±8%. We suppose dynamic changes and essential rise in the intracellular free Ca^{2+} concentration arise from the presence of intracellular low-affinity buffer. This statement is to be further tested using pharmacological approach.

Keywords: calcium signals, Indo-1, hippocampal cultured neurons

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INVESTIGATION OF THE NEW TISSUE-SPECIFIC INHIBITORS OF ACETYLCHOLINESTERASE FOR THE TREATMENT OF MYASTHENIA GRAVIS

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Acetylcholinesterase (AChE) inhibitors are widely used in medical practice for symptomatic treatment for Myasthenia Gravis (MG) and Alzheimer disease. However, all anti-AChE drugs suppresses the cholinesterase activity both in target-organs and organs where correction does not required. The lack of selectivity possess various side effects, such as diarrhea, excessive salivation, nausea, vomiting, stomach pain, bradycardia, arrhythmia and etc., mostly caused by hyperactivation of cholinoreceptors in vegetative nerve systems (mainly smooth muscles and myocardium). The drawbacks could be overcome by using inhibitors capable of inactivating AChE selectively in definite organs (skeletal muscles in case of MG) in doses ineffective with respect to smooth muscles and myocardium. Quite recently the evidences of the possibility of "muscles-specific" AChE inhibition have appeared when a new set of promising compounds, the alkylammonium derivatives of 6-methyluracil (ADEMS), have been synthesized and identified as inhibitors of AChE. Our results have shown that the synapses of locomotor muscles are more sensitive to the action of ADEMS as compared to synapses of smooth muscles or myocardium. Experimentally we confirmed that two selected compounds were able to remove symptoms of the muscle weakness in the animal model of myasthenia Gravis. These observations indicate that ADEMs can be perspective as AChE inhibitors for the treatment of MG lacking the majority of side effects on smooth muscles and myocardium. Acknowledgement: This study was supported by RFBR grant № 11-04-121026 RFBR grant № 11-04-01188-a, grant "Scientific school".

Keywords: acetylcholinesterase, myasthenia Gravis