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SUPPLEMENTARY MATERIALS

The Biochemical Model of the Synapse in Turpaev's Studies

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Supplementary file S31

DIFFERENT RESPONSES OF PREMOTOR INTERNEURONS OF NAIVE AND LEARNED SNAILS TO APPLICATIONS OF SEROTONIN AND SEROTONIN RECEPTORS ANTAGONIST METHIOTHEPIN

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There is a large number of studies that demonstrate the necessity of serotonin (5-HT) for the defensive reflex conditioning in mollusks. The concept about the important role of extrasynaptic transmission of 5-HT in the mechanisms of memory in mollusks is recently developing. The modulatory neurons of the pedal ganglion of the terrestrial snails are responsible for those modulations. Besides to the well-known role of 5-HT as a mediator in synaptic transmission, it has been shown that it can perform integrative functions during its release into the extracellular milieu. Long-term studies led prof. D.A. Sakharov to the opinion that the dynamic fluctuations of the neuroactive molecules (primarily 5-HT in mollusks) in the local intercellular milieu determine the physiological properties and receptor profile of individual neurons. It is also shown that a significant amount of 5-HT can be released into the non-synaptic milieu during long-term synaptic activity. One of the sites of 5-HT exposure may be non-synaptic 5-HT receptors.

Therefore we studied the reaction of serotonin receptors in premotor interneurons LPa3 and RPa3 of terrestrial snail on the application of 5-HT and methiothepin (MET), which is an antagonist of the serotonin receptor of first type. The defensive conditioned reflex to tap on the shell was developed. Next, the reactions of the neurons LPa3 and RPa3 on the application (during 30 min) of 5-HT; 5-hydroxytryptophan (5-HTP), a precursor of the synthesis of serotonin, and MET; all at a concentrations of $4x10^{-5}$ M/l were investigated. The changes of membrane (Vm) and threshold (Vt) potentials were recorded. It was found that 5-HT or 5-HTP applications cause a significant decrease in Vm of intact and learned snails, but don't cause any changes in Vt of intact snails. However, they cause increase of Vt in trained snails. MET in the control group leads to a decrease in Vm of neurons LPa3 and RPa3 and its increase to the initial level after subsequent application of serotonin. In trained animals, MET also results in a decrease in Vm, but subsequent application of serotonin don't change Vm. Results demonstrate that responsiveness of premotor interneurons to extracellularly applied 5-HT, 5-HTP and MET changes after associative training. It can be assumed that training leads to changes in the state of the serotonin system.

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