Effect of Oxidative Stress on the Structure of Glutamate Receptors and Membranes in Neural Cells

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Amino acid residues such as cysteine, methionine, tyrosine, histidine and tryptophan, as well as the carboxyl group in the structure of phospholipid membranes are most likely to undergo changes as a result of oxidative stress in the structure of the NMDA glutamate receptor [1], [2], [3]. In this work, the modeling of the network activity of neurons with damaged glutamate receptors and POPC (1-palmitoyl-2-(9'-oxo-nonaoyl)-gycero-3-phosphocholine) lipid membranes was carried out in two stages. At the first stage, 100 ns molecular dynamics modeling of NMDA receptors containing modified amino acid residues was carried out. Based on a comparative analysis of the dynamics of the ion channel radii of the damaged and native forms of molecular systems, the ratio of receptor conductances $g = G/G_b$ was determined, where G is the ion channel conductance of the damaged system receptor, G_b is the ion channel conductance of the native system.

In the second stage, the local potential of the neuronal population and the power spectrum of the EEG signal were calculated using the NEURON program for the model [4], where the necessary parameters of the receptor ion channel were changed in accordance with the obtained data on the conductivity of the receptor ion channels. The ionic current of the glutamate receptor in the neural network model is represented as:

$$I_{\mathrm{NMDA}} = G_{\mathrm{NMDA}} P(V_{\mathrm{pre}})(V - V_e)/(1 + [\mathrm{Mg}^{2+}] \exp(-qV)/K_d), \quad (3)$$

where G_{NMDA} is the maximum conductance of the NMDA receptor for a certain type of ion, $P(V_{\mathrm{pre}})$ is the probability of channel opening depending on the presynaptic potential and the macroscopic kinetics of the receptor states, V is the postsynaptic membrane potential with equilibrium voltage V_e, q is a phenomenological constant reflecting electrochemical properties [5], K_d is the dissociation constant [6], $[\mathrm{Mg}^{2+}]$ is a magnesium binding parameter.

In the course of the present study, the values of collective rhythms (theta and gamma) of the hippocampal neural network were determined during oxidative modification of the system and changes in the local potential of the neural population of the model were revealed depending on the localization of damage in the structures of the receptor and phospholipid membrane.

References

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