For the firing patterns decisive were: (1) the thermoTRP “working” temperature range; (2) contrast or blurred borders of the latter; (3) fixed or varied maximum opening probability and shift of the half-activation potential.

Keywords: primary afferent neurons, firing patterns, temperature reception, TRP-channels, computer modeling

SUPPRESSION OF BURSTING ACTIVITY OF THE HIPPOCAMPAL GRANULAR NEURON BY THE HYPOTHERMAL DEACTIVATION OF TRP-CHANNELS: A MODEL STUDY

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Bursting discharges of the action potentials (APs) of neurons are characteristic of the epileptiform activity of the brain, reflected in the EEG as episodes of the "burst-suppression" type. To suppress drug-resistant epileptic foci the therapeutic hypothermia (controlled decrease in body temperature) is increasingly being used, the mechanisms of therapeutic effect of which are largely unknown. One of the possible mechanisms has been investigated by us on the model of the granule neuron (GN) of the dentate gyrus of the hippocampus. This neuron is the first link in the tri-synaptic chain of the hippocampus, the brain region, where sources of epileptiform activity are often localized. A feature of the model neuron was the inclusion of the TRP-type temperature-sensitive channels in its somatodendritic membrane, along with other prototype-inherent ion channels. Such TRP-channels are expressed in the GN and conduct a depolarizing current. Tonic synaptic excitation uniformly distributed over dendrites resulted in the generation of periodic bursting AP discharges at a temperature of 37 °C (normothermy). When the temperature was lowered to 36, 34, 32 and 30 °C (corresponding to the boundaries of weak, moderate, moderately deep and deep therapeutic hypothermia), the pattern patterns were degraded and transformed into a low-frequency sequence of single APs. Characteristically, at these temperatures, the depolarizing current of the TRP channels was deactivated. The decrease in the amplitude, duration and frequency of repetition of the "burst-suppression" episodes, characteristic of the EEG of newborn children with hypoxic-ischemic CNS lesions, corresponded to the degradation of the bursting activity of the model GN under conditions of moderate hypothermia used at the clinic (34 ° C). On the basis of a comparison of these observations, it can be assumed that hypothermic suppression of the hippocampal neuronal bursting by deactivation of thermo-sensitive TRP channels can be one of the mechanisms of the therapeutic effect of hypothermia.

Keywords: granule neuron, TRP-channels, excitability, epileptiform EEG, therapeutic hypothermia, models