mutants. Remarkably, the mutants demonstrated strong and greater than controls interest to the exploration of the novel object after the stimulus onset but not in the end of the test. In the three-chamber social test, mutants spent more time near the cage with stimulus animal than controls. No differences in EEG during the exploration of social and non-social stimuli were revealed in this test in both groups. Thus, joint EEG-behavioral phenotyping in freely moving animals gives us more pieces of evidence of impairment of brain functions then behavior tests alone.

Keywords: NRXN1, synaptopathy, EEG, behaviour

MOLECULAR AND CELLULAR MECHANISMS OF TEMPERATURE RECEPTION BY PRIMARY AFFERENTS

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Primary afferent neurons (PANs) provide an organism interface with the environment by conveying to the CNS information about temperature, mechanical and other challenges. Temperature perception is of interest as the underlying mechanisms remain largely unknown because of restrictions of biomedical experiments. Computer models provide a complementary tool to overcome some restrictions. We combined experimental and simulation studies to disclose biophysical mechanisms, by which thermosensitive PANs convert temperatures into generator potentials and the action potential (AP) firing. Progress in molecular biology allowed expressing ion channels of targeted type and precise measuring their activation functions (e. g. Mtrp), current-voltage relations (IVs) etc. In this way, thermosensitive TRP-channels (thermoTRPs) were characterized as specialized temperature sensors. Experimental studies of concerted functioning of thermoTRPs and other channels populating PANs receptor zone (RZ) is hampered by the object size and existence of non-specific temperature effects on the equilibrium potentials Er and activation/inactivation rates characteristic of all types of channels. We demonstrate relative roles of different temperature-dependent mechanisms on examples of heat- and cold-activated thermoTRPs and voltage-gated channels present in PANs operating in different temperature ranges. We developed models of thermoTRPs (based on data obtained on HEK293 cells expressing human cold and menthol receptor TRPM8) and PANs equipped with the ion channels characteristic of the prototype Aδ- and C-afferents. The responses were evoked by step and ramp temperature stimuli. Effects of non-specific (Er and activation/inactivation rates) and specific (Mtrp) temperature-dependent properties were decomposed. Effect of Er was minor. That of rates was noticeable. The most prominent were effects of Mtrp that was represented by different models: linear two-state (Voets et al., 2004) and multiple-states (Fernandez et al., 2011) and allosteric (Latorre et al., 2007).

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