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МАТЕРИАЛЫ КОНФЕРЕНЦИИ И ШКОЛЫ

MECHANISM OF ANANDAMIDE ACTION ON SPONTANEOUS ACETYLCHOLINE RELEASE IN MOUSE MOTOR SYNAPSES

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Murine skeletal muscle cells are able to produce and to release endocannabinoids. The retrograde action of this substances on motor synapses is still not thoroughly enough studied. The aim of this work was to describe the acute effects of the endocannabinoid anandamide (AEA) on the parameters of miniature end plate potentials (MEPPs) of the mice diaphragm and to unveil the mechanisms of its action.

Experiments were conducted on isolated neuromuscular preparations of mice diaphragms with use of the standard microelectrode technique of intracellular potential registration.

We found that on the second hour of application AEA (30 μM) causes an increase in MEPP frequency with a parallel decrease in MEPP amplitude and shortening of its decay time. The AEA-induced change of MEPP frequency is prevented by the CB1-receptor inverse agonist AM-251 (1 μM) and PKAinhibitor H-89 (1 μM) but is unaffected by PLC inhibition by U73122 (5 μM). The decrease in MEPP amplitude caused by AEA does not depend on muscle fiber membrane resistance or PLC activity but is prevented by blocking of either CB1-receptors or PKA. Shortening of MEPP decay time is mediated by CB1-receptor activation and depends on PLC but not PKA activity. MEPP decay time is usually considered as a postsynaptic parameter while changes in MEPP frequency occur on the presynaptic level. Therefore, AEA seems to activate both pre- and postsynaptic CB1-receptors in the neuromuscular junction.

Thus, we found acute effects of AEA on three different MEPP parameters (frequency, amplitude, and decay time) in mice motor synapses. As it seems, this pre- and postsynaptic effects of AEA are based on different intracellular signaling ways in muscle fibers and nerve terminals, albeit starting from CB1-receptors.

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