Levetiracetam and piracetam provide inhibitory action on epileptiform discharges in CA-1 field of mice hippocampal slices.

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Epilepsy is one of the most common serious neurological disorders affecting, approximately 1% of the world population. Despite of the great variety of antiepileptic drugs, they are effective in only about 60 to 80% of epileptic patients. Knowledge of epileptogenesis and the mechanisms of action of anticonvulsants will help to elaborate the right strategy of the therapeutic treatment of this disease and syntheses of new antiepileptic drugs.

The aim of this work was to investigate the effects of piracetam and its derivative, new antiepileptic drug levetiracetam (UCB LO59) on epileptic discharges of pyramidal neurons in hippocampus. *In vitro* bicuculline model of epilepsy was used. Extracellular recording of field potentials, evoked by Schaffer-collateral stimulation in hippocampal area CA-1 of mice slices was performed to determine the fine mechanisms of action of levetiracetam and piracetam.

The amplitude of orthodromic field population spike (pop-spike) markedly increases and repetitive population spikes appeared in the later portion of the response after bath application of bicuculline methiodide (20-40μM). Bath application of piracetam (20, 60μM), levetiracetam (10, 40μM) or arterenol (noradrenaline analogue, 10, 30μM) induced the slow onset of depresses of first pop-spike and marked reduction of the second pop-spike. Compare to the baseline duration of the multiple discharges was decrease 4-5 times during 30min washout period. Arterenol has a dose-dependent effect and depresses of second pop-spike amplitude induced by 30μM of drug was 2 times stronger then with 10μM. Inhibition of second pop-spike induced by piracetam 20μM and levetiracetam 10μM was already maximal. The same concentration of piracetam and levetiracetam had no effect on basal synaptic transmission in normal ACSF.

Further experiments showed that inhibition of multiple discharges of pop-spikes evoked by arterenol are mediated mainly by activation of α-adrenoreceptors since the selective α-adrenomimetic cirasolin (3μM) mimicked the action of arterenol. A potent β2-agonist procaterol (10μM) even slightly increases the first pop-spike and had no significant effect on amplitude and duration of multiple discharges.

An involvement of adrenergic mechanism in inhibitory effect of piracetam was tested by application of piracetam and arterenol together. The results were same as after application piracetam or arterenol alone, so piracetam could work throughout release of noradrenaline from the adrenergic terminals. Depression of multiple discharges by levetiracetam (40μM) was probably not mediated by activation of adrenergic system, at least β1 and α-adrenoreceptors are not involved, since antagonists of these receptors - betaxolol (10μM) or prazosin (10μM), were not blocked the effect of levetiracetam. Thus, piracetam and levetiracetam could inhibit epileptic activity by activation different mechanisms.

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