THE ROLE OF CENTRAL MUSCARINIC CHOLINORECEPTORS IN THE MECHANISM OF HYPOTHERMIC ACTION OF ANGIOTENSIN-II

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Most known neurotransmitters are shown to be involved in the central mechanisms of thermoregulation. Many researchers have paid attention to the role of cholinergic system of the brain since cholinergic synapses are known to be widely distributed in the central nervous system. The centrally acting cholinomimetic drugs have been reported to potentiate the heat loss processes and to induce a decrease in body temperature [2,3]. Centrally applied muscarinic cholinoblockers restrict heat loss and facilitate a body temperature rise upon overheating of animals [2].

Along with the central neurotransmitter system implicated in processes that may lead to hypothermia, of large interest are the mechanisms that involve some peptides whose central action is also accompanied by decreases in body temperature [1]. In particular, during fever and overheating the hypothalamic area shows changes in the activity of the renin-angiotensin system (RAS), and angiotensin-II (A-II) was found to have a distinct hypothermic and antipyretic action [5].

Analysis of these data raises a question of interaction between the cholinoreactive mechanisms and RAS in neural events capable of decreasing body temperature. In the present work we assumed that neurochemical mechanisms including RAS activation may be realized through the central cholinoreactive systems. The aim of the study was to ascertain the involvement of M-cholinoreceptors in the mechanism of hypothermic action of A-II.

MATERIALS AND METHODS

Experiments were performed in unanesthetized white rats weighing 160-180 g. To change the activity of the central cholinoreactive

systems and RAS, the M-cholinoblocker metamizyl and A-II were used. Aqueous solutions of the drugs prepared with apyrogenic distilled water were injected to the right lateral ventricle (icv) through pre-implanted chemotrodes in a volume 5 μl not earlier than 7 days after the operation. The experiments were conducted at ambient temperature 20-22 °C. The animals were divided to 4 groups:

(1) distilled water, icv + (in 15 min) distilled water, icv, (n=8)
(2) distilled water, icv + (in 15 min) metamizyl, icv, (n=8)
(3) distilled water, icv + (in 15 min) A-II, icv, (n=10)
(4) metamizyl, icv + (in 15 min) A-II, icv, (n=10)

The body temperature was measured with an electrothermometer 3 cm deep in the rectum. The measurements were taken at 15 min after the first injection and every 15 min within an hour after the second injection.

Results and Discussion

The control experiment (group 1) showed that distilled water in a volume 5 μl did not significantly influence the body temperature. In another series of the control tests (group 2) with centrally applied metamizyl in a dose 100 μg per animal the rectal temperature tended to increase with a maximum at 45 min after application of the blocker (by 0.34 °C higher than in group 1).

Central A-II in a dose 10 μg per animal (group 3) lowered the body temperature by 1.26 and 0.74 °C in 15 and 30 min, respectively ($P<0.001$). In the main experimental series (group 4) when A-II in the same dose was injected 15 min after icv administration of metamizyl the hypothermic effect of the neuropeptide was absent.

The results, like the evidence from the other authors [1,2,3,5], may be considered as that the RAS and central cholinoreactive systems are involved in the regulation of heat loss processes. It appears impossible yet to particularize brain structures that may be the site of this interrelation. However, the data obtained suggest that the neurochemical mechanisms contributing to the control of heat loss processes and involving RAS may realize their influences through the central M-cholinoreactive systems.

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