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The mode of neuropeptide action on thermoregulation.
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Summary

There is ample evidence in literature for effects of centrally applied neuropeptides on thermoregulation. Our method of intestinal cooling and heating in chronic experiments in rabbits makes it possible to reveal the mechanisms of thermoregulatory action of some neuropeptides.

It was shown that neurotensin raised to higher temperatures the thresholds of effector responses without affecting the central thermosensitivity. Similar changes are characteristic also of the early phase of endotoxin fever. The late phase of fever shown dissociation of warm and cold defense thresholds.

Bombesin diminished central thermosensitivity and simultaneously lowered activation thresholds of thermoregulatory effectors. Effect of bombesin on neuronal activity was investigated in a separate series of experiments in hypothalamic slices. It was found that bombesin not only activated warm- and cold-sensitive and thermoinsensitive neurons, but also altered nervous cell thermosensitivity, i. e. 7 of 12 thermoinsensitive neurons became warm-sensitive after bombesin administration, and 5 of 12 warm-sensitive neurons increased their warm-sensitivity. Thus, thermosensitivity is likely to be not the fixed property of single nervous cell, but is rather due to complex pattern of biochemical and temperature stimuli on the whole neuronal network.

It was also found that adrenocorticotropin (ACTH) did not influence thermoregulation in non-febrile rabbits, but produced the antipyretic effect during endotoxin fever. The mechanisms of the antipyretic action of ACTH are different at the early and late phases of fever: at the early phase the peptide reduces thermosensitivity (according to the cold thermogenesis response) as well as induces dissociation of warm and cold defense thresholds, thus transferring the first phase to the second, while at the late phase ACTH loweres thresholds of thermoregulatory effector responses without influencing thermosensitivity. It is suggested that ACTH is involved in the negative feed-back control of the febrile response.

The thermoregulatory action of another candidate for the role of endogenous antipyretic substance — arginine vasopressin — was examined as well. In our experiments vasopressin injected in the ventral septal area exerted no effect upon normal body temperature, and induced not antipyretic but hyperpyretic response to both intravenous endotoxin and intracentral prostaglandin E_2 injections. Pharmacological analysis using V_2-arginine vasopressin agonist (dDAVP) and V_1-antagonist ($d(CH_2)_5Tyr(Me)AVP$) showed that hyperpyretic and fever-prolonging effects of vasopressin may be mediated through the central receptors similar to peripheral receptors of V_2-subtype, though the antipyretic action is associated with V_1-receptors.

It is concluded that thermoregulatory effects of neuropeptides are structure-specific, as far as bombesin, neurotensin and ACTH were effective when applied to the medial preoptic area of anterior hypothalamus, but not to posterior hypothalamus. Another feature of neuropeptide effects is the dependence on the body temperature homeostasis

state. Thus, ACTH exerted different thermoregulatory action in nonfebrile animals, and in the early or in the late phase of endotoxin fever. It is possible also that even when applied to one structure and in similar conditions of thermoregulatory system functioning the peptide can influence temperature regulation in different manner depending on its dose and mode of administration. In our experiments arginine vasopressin acted as hyperpyretic agent when injected in ventral septal area of the rabbit during both lipopolysaccharide fever and prostaglandin hyperthermia, but it is known that this peptide acts in the same structure of the same species as antipyretic substance when applied by perfusion.

The above effects and mechanisms of peptide actions on thermoregulation make it possible to concretize the concepts of biochemical contribution to the central control of body temperature stability.

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