Effect of Adrenocorticotropic Hormone and Calcitrine on the Lung Surfactant System by Action on Lateral Hypothalamus and Amygdala

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It is shown on rats that cobalt activation of the hyperactivity focus in the lateral hypothalamic area causes a decrease of the phospholipid and cholesterol content and a reduced blood supply in the lungs but an increase of these factors in the basolateral amygdala area. Intracranial microinjection of adrenocorticotropic hormone, combined administration of adrenocorticotropic hormone + calcitrine, and administration of calcitrine alone cause a marked increase of the alveolar phospholipid content and normalize blood filling for action on the lateral hypothalamic area. Action on the basolateral amygdala induces an increase of the phospholipid and cholesterol concentration and augmentation of lung blood supply, but to a lesser degree. The role of peptidergic mechanisms in the realization of hypothalamic and amygdala influences on lung surfactant and hemodynamics is described.

Key Words: *surfactant; blood supply of lungs; lateral hypothalamus; basolateral amygdala; regulation*

One of the current trends in the study of the biological role of peptides is investigation of their influence on the regulatory processes in the functioning of the visceral organs. Neuroendocrine cells secreting peptides such as calcitonin, bombesin, and others have been discovered in human lung tissue, their number depending on age and on the presence of respiratory diseases [10,13]. Peptide hormones may perform neurotransmitter and trophic regulatory functions in the respiratory system, having an influence on the smooth muscle system of the respiratory pathways and blood vessels by altering the respiratory and blood flows and also ephithelial secretion [8]. At the same time, the role of neuropeptides in maintaining surfactant metabolism and functions has been little investigated. A normalizing influence of some regulatory neuropeptides (for example, substance P, adrenocorticotropic hormone - ACTH) on the lung surfactant system under hypofunctional conditions has been shown.

The aim of the present study was to investigate the influence of the peptide hormones ACTH and calcitrine on surfactant and lung blood filling by activation of the vegetoendocrine regulatory centers of the limbic systems.

MATERIALS AND METHODS

Taking into account our previous data concerning the multifunctional action of brain structures on alveolar phospholipids [5,6], we activated lateral hypothalamic area (LHA) structures in laboratory animals by local implantation of 1 mg dispersed cobalt according to stereotaxic coordinates [4]. In another group of laboratory animals cobalt implantation caused activation of the basolateral area of the amygdaloid complex (BAC). Some animals

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received ACTH (1 μg) in the analogous contralateral structure or hypodermal calcitrine (1 U) injections simultaneously with intracranial cobalt implantation. Ten experimental series comprising 106 rats were carried out. Also carried out were left-side cobalt implantation in LHA (8 rats) and BAC (10), against the background of hypodermal calcitrine injection (8 and 7, respectively), cobalt influence in conjunction with ACTH implantation in the contralateral area of LHA (7) or BAC (6), and intracranial cobalt and ACTH influence in the same localization against the background of hypodermal calcitrine injection (7 and 6, respectively). Eleven animals received calcitrine only. The control group included 36 rats.

The hemoglobin content in blood and lung tissue homogenates was studied on the 10th day after the beginning of treatment. Lung blood filling was estimated taking into account the total weight of the lungs and the indexes described above [1,12]. Phospholipid and cholesterol ratio and concentrations were estimated in bronchoalveolar flushes [3].

RESULTS

Ten-day influence of implanted cobalt on LHA caused a marked decrease of lung filling, and of the phospholipid and cholesterol content ($p<0.05$) in the bronchoalveolar flushes. At the same time, local cobalt action on BAC caused a slight increase of the alveolar lipid concentration, especially of cholesterol, against the background of decreased hemoglobin content and lung blood supply ($p<0.05$) (Table 1).

Contralateral (in relation to brain-implanted cobalt localization) ACTH injection caused a sharp increase of the alveolar phospholipid content ($p<0.05$) for action on LHA and a less marked increase of the cholesterol and phospholipid concentrations in bronchoalveolar flushes for analogous action on BAC. Normalization of lung blood filling occurred in both groups.

Local intracranial cobalt injection into LHA against the background of calcitrine injection caused a marked phospholipid increase in flushes and lung blood filling normalization. The same action on BAC caused an increase of lipids, especially of cholesterol. The low level of blood filling remained unchanged. Calcitrine injection without action on the brain caused a reliable increase of the phospholipid concentration in the bronchoalveolar flushes.

Cobalt on the left and ACTH on the right in combined action on brain structures against the background of hypodermal calcitrine injection in the animals with hypothalamic localization of intracranial influences caused a phospholipid concentration increase in the bronchoalveolar flushes and normalization of lung blood filling. The same action on animals with amygdaloid localization caused a rise of the alveolar lipid level, especially of cholesterol, along with a low level of lung blood filling (Table 1).

Comparison of the results obtained from calcitrine experiments showed that almost all animals to a various degree exhibited a marked increase of the surface-active lipid level in bronchoalveolar flushes independently of the localization of the cobalt-activated limbic structure. This index

TABLE 1. Lipid Content in Bronchoalveolar Flushes and Lung Blood Filling in Rats with Lateral LHA and BAC Cobalt Activation ($M \pm m$)

Indexes	Phospholipids, μmol/g lung tissue	Cholesterol, mmol/g of lung tissue	Lung blood filling, %
Control	61.92±9.00	19.04±3.72	4.31±0.37
Local cobalt implantation:			
LHA	13.86±4.14*	4.85±0.63*	2.18±0.18*
LHA along with:			
ACTH administration (contralaterally)	369.32±74.36*°	23.46±10.83	4.41±0.46°
calcitrine administration (hypodermally)	368.09±46.79*°	18.48±4.64°	3.24±0.91
ACTH and calcitrine	259.09±149.90	25.42±4.54°	3.55±0.99
BAC	85.62±18.73*°	57.87±9.11*°°	1.13±0.19*
BAC along with:			
ACTH administration (contralaterally)	90.70±18.31	48.04±5.10*	3.65±0.57
calcitrine administration (hypodermally)	75.64±12.44	40.08±4.20*	1.09±0.17*
ACTH and calcitrine	144.54±55.71	62.06±7.06*	2.21±0.3*°
Calcitrine	142.87±39.24*	24.22±4.04	4.98±1.54

Note. * — $p<0.05$ in comparison with control; ° — $p<0.05$ in comparison with brain cobalt activation; °° — $p<0.05$ in comparison with action on various brain structures.

remained unchanged only in animals administered preparation against the background of amygdaloid activation.

Action on the amygdala produced a marked cholesterol increase in flushes (cholesterol is a much less active surfactant).

The dynamic of lung blood filling against the background of calcitrine administration showed its normalizing action on the microcirculation in the lesser circulation of animals with activation of lateral hypothalamic structures and the absence of additional effects against the background of amygdala activation.

Calcitrine is known to be a hormonal preparation which regulates calcium and phosphorus metabolism. Its administration, like thyrocalcitonin, causes hypocalcemia. A recently discovered new regulatory peptide, calcitonin, is found in the epithelium of the respiratory pathways located near blood vessels and in lung afferent endings belonging to C fibers. This peptide is thought to initiate central reflexes and the release of biologically active compounds [8,9,11]. Taking into account these data, our results confirming the surfactant-stimulative activity of calcitrine are consistent with the data of other authors.

The effects of surfactant stimulation in animals by ACTH implantation in various limbic structures do not contradict the data on the adaptive influence of the hormone on physiological functions. It may be assumed that the observed marked augmentation of alveolar phospholipids resulting from combined ACTH-calcitrine application may be linked with activation of brain peptide processing because protease activity depends on the calcium concentration [3,9].

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