EFFECT OF PHARMACOLOGICAL BLOCKADE OF VARIOUS COMPONENTS OF THE HYPOTHALAMIC – PITUITARY – ADRENAL SYSTEM AND ITS FUNCTION IN ACUTE ANEMIC ANOXIA

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The response of the hypothalamic–pituitary–adrenal system to acute anoxia induced after pharmacological blockade of the various components of that system was studied in experiments on male rats. Acute anoxia was shown to reduce the corticotropin-releasing activity of hypothalamic extracts, the ACTH content in the adenohypophysis, and the AC concentration in the adrenals. The degree of functional activity of this system plays an important role in the development of the resistance of the body to anoxia. The most important stage of activation of this system is the secretion of corticotropin-releasing factor by the hypothalamus.

KEY WORDS: anemic anoxia; hypothalamic–pituitary–adrenal system.

Modern views on the role of the endocrine system in the chain of response reactions of the organism to anoxia have been formed comparatively recently [2, 9]. The resistance of animals to oxygen deficiency is reduced after removal of the adrenals [2, 9, 18] and injection of corticosteroids increases resistance to acute anoxia [17]. The functional state of the pituitary gland in oxygen deficiency has been studied in only a few investigations [8, 9, 15]. No direct data on the state of the function of all components of the hypothalamic–pituitary system in acute anoxia could be found in the accessible literature.

The functional state of this system was accordingly investigated in a lethal form of anemic anoxia.

EXPERIMENTAL METHOD

Experiments were carried out on 228 male rats weighing 150-200 g, 142 of which were used for biological testing of corticotropin-releasing factor (CRF) and ACTH. Anemic anoxia was produced by injecting the animals subcutaneously with a 3% solution of sodium nitrite, a compound producing methemoglobin, in a dose of 12-15 mg/100 g body weight [10]. The degree of anoxia was assessed from the blood methemoglobin level [3, 4]. Functional activity of the adrenal cortex was estimated from the ascorbic acid concentration in the gland [16]. The ACTH level in the pituitary was tested on recipient rats [12]. The CRF content in the hypothalamus also was tested [5, 13].

Pituitary function was blocked by prednisolone in a dose of 6 μg/100 g body weight [12] and hypothalamic function by administration of chlorpromazine, morphine, and pentobarbital [13].

EXPERIMENTAL RESULTS AND DISCUSSION

The results of determination (Table 1) of the CR activity of the hypothalamus, the ACTH level in the adenohypophysis, and the ascorbic acid (AA) level in the adrenals of the control rats agreed with data in the literature [5, 6, 11, 12, 15] After administration of sodium nitrite to the animals the highest concentration of methemoglobin in the blood was observed after 40-50 min. The CRF content in the hypothalamus (CR

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TABLE 1. CR Activity of Hypothalamic Extracts, ACTH Content in Adenohypothesis, and AA Content in Adrenals of Rats in Lethal Form of Anemic Anoxia (M ± m)

Parameter studied	Control (50)	Lethal hypoxia (50)	P
Blood methemoglobin (in %)	4,36±0,08	53±0,54	<0,001
Hypothalamic CRF, in mg % decrease of AA in recipients	132±2,7	77±2,0	<0,001
Pituitary ACTH, in i. u./100 μg acetone-treated pituitary tissue	7,2±0,55	4,1±0,48	<0,001
Adrenal AA (in mg %)	410±4,55	329±4,44	<0,001

TABLE 2. Effect of Pharmacological Blocking of Components of Hypothalamic–Pituitary–Adrenal System on its Function in Acute Anemic Anoxia (M ± m)

Experimental conditions		Duration of experiment (in min)	Blood methemoglobin concentration (in %)	P	Hypothalamic CRF in mg % decrease of AA in recipients	P	Pituitary ACTH (in i. u./100 μg acetone-treated tissue)	P	Adrenal AA (in mg %)	P
Blockade of hypothalamus and pituitary and injection of physiological saline	7	37	4,35±0,08		No decrease		No decrease		385±5	
Lethal anoxia + blockade of hypothalamus and pituitary	10	37±1,43	44±0,39	<0,001	» »		» »		370±10	>0,1
Blockade of hypothalamus and injection of physiological saline	7	42	4,35±0,08		» »		8,5±0,6		392±6	
Lethal anoxia + blockade of hypothalamus	10	42±2,17	54±1.8	<0,001	» »		10,0±1,5	>0,2	323±7	<0,001
Blockade of pituitary and injection of physiological saline	7	41	4,2±0,11		37±4		No decrease		389±6	
Lethal anoxia + blockade of pituitary	10	41±1,7	46±0,7	<0,001	22±3	<0,001	0,4±0,14		285±11	<0,001

activity) was then 48% below the control level. The ACTH concentration in the adenohypophysis (by 43%) and the AA concentration in the adrenals (by 20%) were considerably reduced. The results as regards ACTH and AA are in agreement with those obtained by other workers [1, 7, 14]. No reports on the CRF content in the hypothalamus in acute anoxia could be found in the accessible literature.

In the next experiment (Table 2) the functional state of the hypothalamic–pituitary–adrenal system was studied during lethal anoxia produced in conjunction with blocking of the various components of that system. Control animals were injected with physiological saline in addition to the corresponding block. It is evident that an adequate block of the components of the hypothalamic–pituitary system was obtained, as shown by the absence of a decrease in AA concentration in the right adrenal of recipient rats after receiving an injection of extract of the blocked organ.

In conjunction with combined blocking of the hypothalamus and pituitary, anoxia did not cause a decrease in the AA concentration in the adrenals; these animals, moreover, died 8 min sooner ($P < 0.001$) than animals receiving sodium nitrite without the pharmacological block, although their blood methemoglobin concentration was lower. This indicates the important role of the hypothalamic–pituitary–adrenal system in the resistance of the animal to anoxia.

After blockade of the hypothalamus alone, acute anoxia caused a small but statistically significant decrease in the AA concentration in the adrenals, accompanied by a high ACTH concentration in the pituitary. Pharmacological blocking of the hypothalamus in animals with anoxia evidently disturbed the liberation of ACTH but did not completely block it, as shown by the decrease in the AA concentration in the adrenals.

If only the adrenocorticotropic function of the pituitary was blocked in animals with anoxia, the AA concentration in the adrenals fell considerably and the CRF activity in the hypothalamus was reduced at the same time. This last phenomenon could be due to liberation of CRF into the general circulation [19].

The changes observed in the function of the hypothalamic–pituitary–adrenals system are evidence that its role in protective and adaptive responses to acute anoxia is effected through the hypothalamus by an increase in the secretion of CRF.

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