ACTION OF CATECHOLAMINES ON THE HYPOTHALMO-HYPOPHYSEO-ADRENAL SYSTEM IN RATS

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UDC 615.357.452.015.4 : [612.432 + 612.826.4 + 612.45

If catecholamines are administered to animals previously receiving dexamethasone or reserpine, they act directly on the hypothalamo-hypophyseal system, and they are thus essential to the activation of this system. Noradrenalin is more active with respect to its action on the hypothalamo-hypophyseal system.

The role of the biogenic amines, especially catecholamines, in regulation of the hypophyseo-adrenocortical system is at present under extensive discussion [1, 2, 4, 5, 7, 9, 10]. Investigations using reserpine, a compound which exhausts the reserves of biogenic amines, have led to the hypothesis that catecholamines play an active role in the hypothalamic regulation of the adrenocorticotropic function of the pituitary gland [5, 8, 10, 11].

In the writers' opinion, investigations in which catecholamines are given after the preliminary administration of reserpine and against the background of blocking of the hypothalamo-hypophyseal system by dexamethasone could constitute an important link in the chain of evidence of the direct participation of catecholamines in hypothalamic regulation of the adrenocorticotropic function of the pituitary. At the same time these experiments would also identify which group of monoamines is responsible for the reserpine effect.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 180-200 g were sacrificed 7 min after intravenous injection of the preparations in order to determine the corticosterone level in the adrenals, and again 2.5 min later to determine ACTH in the circulating blood. The corticosterone concentration was determined fluorometrically by the method of Guillemin et al. [6], and ACTH by the Vernikos-Danellis biological method in Rozental's modification [3]. The various types of experiments are described in the text.

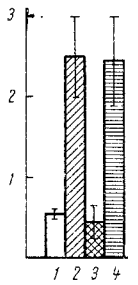

Fig. 1. ACTH level in circulating blood of animals receiving intramuscular injection of physiological saline 24 h before experiment (1); in animals receiving intravenous injection of physiological saline 24 h after previous intramuscular injection of physiological saline (2); in animals receiving intravenous injection of physiological saline 24 h after intramuscular injection of 2 mg/kg reserpine (3); after intravenous injection of noradrenalin (1 mg) into animals 24 h after intramuscular injection of 2 mg/kg reserpine (4) (M±m).

Laboratory of Physiology of the Endocrine System, Institute of Experimental Endocrinology and Hormone Chemistry, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Yudaev.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 72, No. 9, pp. 16-19, September, 1971. Original article submitted December 8, 1970.

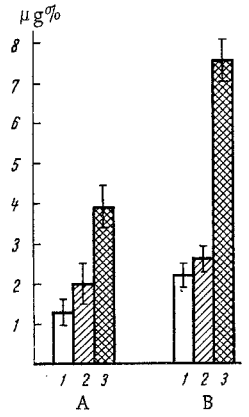

Fig. 2

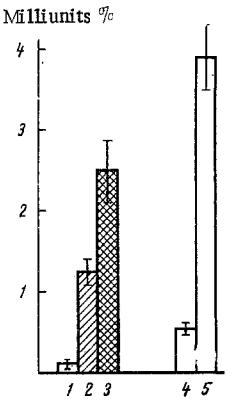

Fig. 3

Fig. 2. Effect of physiological saline (1), 0.5 mg (A) and 1 mg (B) adrenalin (2), and noradrenalin (3) on corticosterone concentration in adrenals of animals receiving dexamethasone 4 h before the experiment in a dose of 600 μg per rat (M±m).

Fig. 3. ACTH level in circulating blood (M±m) after injection of physiological saline (1), adrenalin (2), and noradrenalin (3) into animals receiving preliminary injection of dexamethasone (600 μg per rat) 4 h previously, and ACTH level in blood after surgical trauma (5) to animals receiving injection of physiological saline 24 h beforehand (4).

EXPERIMENTAL RESULTS

Injection of 0.2 ml physiological saline into the jugular vein 24 h after an intramuscular injection of reserpine in a dose of 2 mg/kg body weight caused no response of the hypothalamo–hypophyseo–adrenal system. The same injection of physiological saline 24 h after intramuscular injection of 2 ml of physiological saline, however, gave a distinct pituitary response in the form of ACTH liberation; consequently, this procedure acts as a stressor.

If animals whose catecholamine reserves had previously been exhausted by injection of reserpine were given an injection, not of physiological saline, but of noradrenalin in a dose of 1000 μg per rate into the jugular vein, ACTH was liberated from the pituitary (Fig. 1).

When physiological saline was injected into the jugular vein of animals which had received an intramuscular injection of 600 μg dexamethasone 4 h previously, complete blocking of the pituitary–adrenocortical system to stress was found (Fig. 2, 3).

In addition, dexamethasone in the dose used selectively reduced the noradrenalin concentration in the hypothalamus from 0.837 to 0.492 μg/g.

Injection of adrenalin in doses of 500 and 1000 μg into animals after a preliminary injection of dexamethasone caused virtually no change in the corticosterone concentration in the adrenals (Fig. 2), whereas injection of noradrenalin in the same doses gave rise to a distinct response: an increase in the corticosterone level of 2.8 times after a dose of 500 μg, and by 3.6 times after a dose of 1000 μg, compared with the control (Fig. 2). However, in this method of testing, the activation of the hypophyseo–adrenocortical system could still be attributed to the direct action of catecholamines on the adrenals. To rule out this possibility, in the next series of experiments the ACTH level was investigated directly in the circulating blood. In these experiments the results of injection of only a single large dose of catecholamines (1000 μg) were analyzed, for as the results of the previous tests showed, this dose gives the maximal effect.

When physiological saline was injected 4 h after a previous injection of dexamethasone, the ACTH concentration in the circulating blood was minimal. Injection of catecholamines evoked a definite pituitary response: the ACTH level in the circulating blood was increased by 8.8 times for injection of adrenalin and by 17.5 times after injection of noradrenalin (Fig. 3).

Comparison of the extent of the increase in the ACTH concentration in the circulating blood in response to injection of catecholamines after the dexamethasone block, on the one hand, and in the action of surgical trauma (laparotomy 24 h after intramuscular injection of physiological saline), on the other hand, showed that adrenalin gave virtually the same increase in ACTH as trauma, while after injection of noradrenalin the increase in the ACTH concentration was almost 2.5 times greater (Fig. 2).

Consequently, catecholamines have a direct action on the hypothalamo–hypophyseal system, abolishing the dexamethasone block, and they are evidently an essential component for the activation of this system. Noradrenalin, it must be noted, is more active in this respect.

The results thus indicate that in the hypothalamo–hypophyseal system the adrenergic structures constitute the essential component without which activation of this system in response to extreme situations would be impossible.

Since dexamethasone lowers the noradrenalin reserves in the hypothalamus, and in the case of blocking of the hypothalamo–hypophyseal system by dexamethasone and of exhaustion of its catecholamine reserves by reserpine the pituitary does not respond to stressors and ACTH is liberated only after injection of catecholamines into such animals, it can be postulated that adrenergic structures of the hypothalamus participate in the mechanism of the dexamethasone block to the hypothalamo–hypophyseal system.

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