

# EFFECT OF ADRENALECTOMY ON CIRCULATION OF NORADRENALIN IN THE RAT BRAIN AND HEART

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Adrenalectomy potentiates the action of disulfiram and nialamide on the catecholamine content in the heart. No such effect is observed after demedullation of the adrenals.

Numerous connections exist between adrenocortical hormones and biogenic amines, and they have been studied at different levels: from biosynthesis to regulation of the activity of nerve centers of the corresponding systems [2, 5, 7]. It has recently been shown that the activity of adrenergic structures can be estimated on the basis of the velocity of circulation, i.e., the amount of the decrease in content of amines after blocking of their synthesis or their accumulation after administration of monoamine oxidase inhibitors [11].

This paper describes the results of an investigation of the velocity of circulation of noradrenalin in the rat brain and heart after adrenalectomy and after adrenal demedullation.

## EXPERIMENTAL METHOD

Experiments were carried out on 30 male albino rats. Bilateral adrenalectomy was performed in one stage 5-6 days before the experiment. Completeness of removal of the adrenals was verified at autopsy and by the fall in level of 11-hydroxycorticosteroids in the circulating blood plasma of the rats (normal level  $30 \pm 1.2 \mu\text{g}\%$ , after adrenalectomy  $5.9 \pm 1.7 \mu\text{g}\%$ ). Catecholamine biosynthesis was blocked by the use of disulfiram (teturam) in a dose of 150-200 mg/kg, intraperitoneally, in 1% starch gel 3 h before sacrifice. This compound is a powerful inhibitor of dopamine- $\beta$ -oxidase [11]. The monoamine oxidase inhibitor nialamide (nethalide) was injected subcutaneously in a dose of 20 mg/kg 24 h before the experiment. The noradrenalin content in the brain and heart was determined by Osinskaya's trihydroxyindole method [3], using a modified ÉF-3M fluorometer [4].

## EXPERIMENTAL RESULTS

Adrenalectomy had no effect on the noradrenalin content in the brain and heart (Table 1), in agreement with data in the literature [6, 9]. Administration of disulfiram reduced the content of mediator by 54% in both organs of pseudoadrenalectomized animals. Nialamide produced no statistically significant increase in the noradrenalin level in these animals, by contrast to the response of intact rats [11], and this result could possibly be attributed to the effect of trauma. Adrenalectomy sharply potentiated the action of both agents on the heart. After administration of disulfiram the noradrenalin content fell by 88%, while after administration of nialamide it increased by 87%.

Isolated demedullation of the adrenals did not potentiate the effect of disulfiram on the heart. Whereas in the pseudoadrenalectomized animals this compound caused a decrease in the noradrenalin concentration from  $0.76 \pm 0.16$  to  $0.38 \pm 0.01 \mu\text{g/g}$ , the decrease in demedullated rats was from  $0.73 \pm 0.09$  to  $0.50 \pm$

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TABLE 1. Effect of Disulfiram and Nialamide on Noradrenalin Content ( $\mu\text{g/g}$ ) in Rat Brain and Heart ( $\bar{x} \pm S\bar{x}$ )

Group of animals	Control	Disulfiram	P	Nialamide	P
Heart					
Pseudoadrenalectomized	$0.72 \pm 0.05$	$0.33 \pm 0.06$	$<0.01$	$0.87 \pm 0.12$	$>0.1$
Adrenalectomized	$0.75 \pm 0.14$	$0.09 \pm 0.02$	$<0.01$	$1.41 \pm 0.08$	$<0.01$
P	$>0.5$	$<0.01$		$<0.01$	
Brain					
Pseudoadrenalectomized	$0.48 \pm 0.08$	$0.22 \pm 0.04$	$<0.02$	$0.54 \pm 0.03$	$>0.1$
Adrenalectomized	$0.43 \pm 0.08$	$0.18 \pm 0.02$	$<0.01$	$0.70 \pm 0.14$	$>0.1$
P	$>0.5$	$>0.1$		$>0.1$	

0.05  $\mu\text{g/g}$ . The results of the adrenal demedullation experiments demonstrate that acceleration of the noradrenalin circulation, discovered in adrenalectomized rats, was due to removal of the adrenal cortex.

In experiments in which labeled noradrenalin was injected into the cerebral ventricles after adrenalectomy, only a very slight increase in the rate of circulation of mediator in the brain was obtained [9]. The results now obtained are in agreement with those previously obtained on hypophysectomized animals [10], in which the elimination of labeled noradrenalin from the heart was accelerated.

Interaction between corticosteroids and catecholamines at the tissue level may take place, at least partially, through an adenyl cyclase mechanism. Corticosteroids create a definite concentration of electrolytes in the region of the cell membrane which promotes the reaction between catecholamines and the receptors [1, 8]. In the absence of corticosteroids (after adrenalectomy or hypophysectomy), activity of the sympathetic innervation is modified.

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