ROLE OF ADRENERGIC STRUCTURES OF THE CNS IN CHANGES IN FUNCTION OF THE HYPOTHALAMIC-PITUITARY-ADRENAL SYSTEM DURING EXOGENOUS HYPERTHERMIA

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Subcutaneous injection of chlorpromazine into rats leads to a smaller rise of body temperature and a higher concentration of corticotropin-releasing factor in the hypothalamus and of ACTH in the pituitary during exogenous hyperthermia. The ascorbic acid concentration in the adrenals falls just as in hyperthermic animals without chlorpromazine. The weight of the adrenal is not significantly changed. It is concluded that central adrenergic structures play a part in the regulation of the synthesis or secretion of corticotropin-releasing factor.

KEY WORDS: *adrenergic structures; hypothalamic-pituitary-adrenal system; corticotropin-releasing factor; exogenous hyperthermia.*

Adrenergic structures of the CNS play a part in the production and liberation of the hypothalamic-releasing factors [13, 14], which liberate the pituitary tropic hormones and subsequently activate the function of the adrenal cortex [1, 3, 7, 10, 12]. The adrenals are known to play an important role in adaptation to harmful factors.

To determine the role and place of the adrenergic structures of the CNS in the changes in the function of the hypothalamic-pituitary-adrenal system (HPAS) during hyperthermia, the development and course of the hyperthermia and the changes in the hypothalamus, pituitary, and adrenals were studied after preliminary administration of chlorpromazine.

EXPERIMENTAL METHOD

Hyperthermia was induced in rats (150-200 g) in a hot chamber with an air temperature at 50-51°C. The development of hyperthermia was assessed from changes in the rectal temperature (TREM-1 electrothermometer). The hyperthermia was stopped when the animals developed heatstroke (convulsions). For the next hour, the rats were kept at a temperature of 18-20°C. Adrenergic structures of the CNS were blocked by subcutaneous injection of chlorpromazine in a dose of 10 mg/kg. The ascorbic acid (AA) concentration in the adrenals [15], the ACTH content in the pituitary [11], and the corticotropin-releasing activity of the hypothalamus [4, 6, 7] were determined in the animals.

EXPERIMENTAL RESULTS

The results obtained with the intact rats (Table 1) corresponded exactly to those in the literature [1, 4, 6, 8, 9].

A fall in the body temperature (on average by 2.6°C) in the AA content in the adrenals (by 26%) and in the content of corticotropin-releasing factor (CRF) in the hypothalamus (by 50%) was found 45-60 min after administration of chlorpromazine to the animals; the ACTH content in the pituitary was unchanged and the weight of the adrenals was increased by 37.5%. Other workers have obtained similar results [1, 2, 5, 9].

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TABLE 1. Effect of Chlorpromazine on Function of the HPAS during Exogenous Hyperthermia (M ± m)

Nature of experiment	Body temperature, °C	Corticotropin-releasing activity of hypothalamus, mg% AA	ACTH in pituitary, milliunits	Adrenals	
				weight, mg	AA, mg %
Control (n = 10)	37,3±0,21	125±2,3	11,7±1,34	18,4±0,50	427±8
Chlorpromazine (10 mg/kg) (n = 9)	34,7±0,19	64±4,7	10,1±1,47	22,0±0,80	318±17
P	<0,001	<0,001	>0,1	<0,01	<0,001
Hyperthermia for 15-20 min (n = 10)	40,6±0,26	85±5,8	5,4±0,92	16,0±1,20	382±18
P	<0,01	<0,001	<0,01	<0,05	<0,02
Heatstroke:					
surviving rats (n = 9)	41,8±0,13	43±3,9	2,4±0,26	14,0±1,40	261±21
P	<0,001	<0,001	<0,001	<0,01	<0,001
dying rats (n = 7)	41,8±0,08	66±3,1	4,3±0,66	16,0±2,30	331±28
P	<0,001	<0,001	<0,001	>0,1	<0,01
Hyperthermia for 15-20 min after chlorpromazine (n=10)	38,9±0,09	134±5,3	9,1±0,96	16,0±1,90	341±25
P	<0,001	>0,1	>0,1	>0,1	<0,01
P_1	<0,001	<0,001	<0,02	>0,1	>0,1
Heatstroke after chlorpromazine:					
surviving rats (n = 7)	39,0±0,16	127±5,5	7,9±0,95	15,0±1,70	278±25
P	<0,001	>0,1	<0,01	>0,05	<0,001
P_1	<0,001	<0,001	<0,001	>0,1	>0,1
dying rats (n = 10)	39,3±0,11	110±4,6	8,0±0,81	15,0±1,90	331±26
P	<0,001	<0,01	<0,05	>0,05	<0,01
P_1	<0,05	<0,001	<0,01	>0,1	>0,1

Legend. P) Significance of differences between data for control and experimental animals; P_1) ditto between data for rats receiving and not receiving chlorpromazine.

The body temperature in the rats exposed to hyperthermia for 15-20 min (until the appearance of motor excitation) rose by 3.3°C and the AA concentration in their adrenals was 10% below normal; the weight of the adrenals was the same as initially. The content of CRF in the hypothalamus was reduced by 33% and that of ACTH in the pituitary by 53% compared with initially.

The body temperature of the rats at the time of heatstroke was on average 4.5°C higher than initially. During the next hour, when the animals were kept at room temperature, the rectal temperature of the surviving rats returned to normal and the content of AA in their adrenals, CRF in their hypothalami, and ACTH in their pituitaries continued to fall.

In some animals, which died within an hour after development of heat convulsions and termination of hyperthermia, a further rise of the rectal temperature by 0.2-0.4°C was observed; in the others it fell below the initial level. The content of AA in the adrenals, CRF in the hypothalami, and ACTA in the pituitaries of the dying rats, although lower than in the intact animals (by 22.4, 46.4, and 63.2%, respectively), was nevertheless higher than in the surviving animals.

The functional activity of the HPAS is thus increased in animals during exogenous hyperthermia.

In the next series of experiments, the rats were exposed to hyperthermia after preliminary (60 min beforehand) administration of chlorpromazine. In these animals, unlike those not receiving chlorpromazine, motor excitation did not arise before 15-20 min of hyperthermia. Their body temperature was raised on average by only 1.6°C compared with its initial level. The AA content in the adrenals was 20% lower than in rats not receiving chlorpromazine, whereas the level of CRF in the hypothalamus and of ACTH in the pituitary was considerably higher than in rats exposed to hyperthermia without chlorpromazine.

In the animals in which hyperthermia (after chlorpromazine administration) was terminated at the time of heat convulsions and which survived for 1 h at room temperature, the mean body temperature was only 1.7°C above its initial level, whereas in the corresponding experiments without chlorpromazine it was raised by 4.5°C. The AA level in the adrenals and their weight were not significantly different from their values in the corresponding experiments without chlorpromazine. The content of CRF in the hypothalamus and of ACTH in the

pituitary, on the other hand, was much higher than in animals exposed to hyperthermia without chlorpromazine.

In the animals that died during the first hour after hyperthermia induced after chlorpromazine administration, the body temperature also was raised less than in the corresponding rats in which hyperthermia was induced without chlorpromazine. If the already lowered temperature recorded in the rats receiving chlorpromazine without induction of hyperthermia was taken as the initial level for this group, the increase in temperature in the animals dying after hyperthermia was the same in the experiments with or without chlorpromazine. However, to judge from the absolute values of the body temperature, hyperthermia in the animals receiving chlorpromazine nevertheless ran its course at a lower level.

Among the indices describing the state of the HPAS in these animals the higher content of CRF in the hypothalamus and of ACTH in the pituitary than in rats dying after hypothermia and not receiving chlorpromazine must be noted, although the amount by which these indices were higher was less than in the rats which survived.

Central adrenergic structures thus evidently participate in the regulation of the synthesis or secretion of hypothalamic CRF.

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