ADRENOCORTICAL FUNCTION DURING TRAUMATIC SHOCK IN RATS AFTER REMOVAL OR DEAFFERENTATION OF THE HYPOTHALAMUS

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UDC 616.831.41-089.87-06:617-001.36-092.9-07:616.453-008.6-072.7

The 11-hydroxycorticosteroid (11-HCS) concentration was determined in the blood plasma of rats undergoing a mock operation, and rats with an intact, extirpated, or deafferented medio-basal hypothalamus (MBH), during traumatic shock. No significant differences were found in the basal 11-HCS level in the rats of the different groups. Removal of MBH led to a decrease in weight of the adrenal and pituitary glands, whereas deafferentation of MBH led to an increase in weight of the adrenals. The 11-HCS level in rats with complete deafferentation of MBH was significantly higher than in the animals undergoing the mock operation when both were in a state of traumatic shock.

KEY WORDS: corticosterone; shock; hypothalamus.

Activation of hypothalamic centers controlling ACTH secretion is determined during stress by both nervous and humoral factors [7, 9].

To analyze their comparative roles changes in the blood corticosterone concentration were studied during shock in rats after extirpation and also after total and partial deafferentation of the medio-basal part of the hypothalamus.

EXPERIMENTAL METHOD

Experiments were carried out on 108 male albino rats weighing 180-320 g. Complete and partial (of the anterior portion only) deafferentation of the medio basal hypothalamus (MBH) was carried out 5-6 weeks before the production of shock under deep ether anesthesia by the method of Halasz and Pupp [8]. In some animals MBH was removed by means of a knife with a special blade [5]. Intact animals and animals undergoing a mock operation, during which the skull was trephined and the longitudinal sinus destroyed but without injury to the hypothalamus, served as the control. Adrenocortical activity was estimated from the 11-hydroxycorticosteroid (11-HCS) level in the blood plasma, measured by a fluorometric method [4]. Some of the animals of each group were decapitated before shock was produced in order to determine the basal 11-HCS level. Traumatic shock was produced by Cannon's method. Samples of 1 ml blood were taken from the femoral artery immediately after fixation of the animals to the frame and dissection of the vessels, and also at different stages of shock. The dynamics of shock were assessed from the arterial blood pressure. After death of the rats the pituitary and adrenal glands were weighed and completeness of deafferentation or removal of MBH was verified histologically.

EXPERIMENTAL RESULTS AND DISCUSSION

Removal or complete isolation of MBH has been shown [2, 6] to lead to hyperphagia and to a sharp increase in body weight. In the present experiments a considerable gain in body weight (twice the control level) was observed only after extirpation of the hypothalamus.

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(Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 7, pp. 785-787, July, 1976. Original article submitted November 24, 1975.

TABLE 1. Plasma 11-HCS Concentration and Weight of Endocrine Glands in Rats with Different Injuries to the Hypothalamic Region during Traumatic Shock (M ± m)

Animals	11-HCS level (in μg %)					Weight of endocrine glands (mg/100 g body weight)	
	basal	after fixation of animals and dissection of vessels	in different phases of traumatic shock: beginning of torpid phase (stabilization)	in different phases of traumatic shock: end of torpid phase	in different phases of traumatic shock: terminal phase	pituitary	adrenals
Control (with intact MBH)	9,1±1,41 (20)	46,3±1,44 (18)	45,7±1,56 (15)	48,3±2,70 (11)	48,6±2,83 (7)	2,7±0,09 (18)	13,2±0,39 (18)
Undergoing mock operation	8,1±1,65 (10)	45,0±3,58 (14)	39,4±3,73 (13)	45,8±5,75 (7)	44,8±3,02 (7)	3,0±0,17 (14)	12,3±0,37 (14)
With MBH removed	8,5±2,63 (4)	33,9±4,83 (15)	40,2±8,51 (11)	41,3±4,52 (9)	45,9±7,73 (13)	2,3±0,16 (19)	11,1±0,69 (19)
P						<0,01	
P_1		=0,01				<0,05	<0,01
With total deafferentation of MBH	13,3±5,41 (5)	55,5±3,72 (7)	58,0±6,59 (7)	75,9±8,0 (5)	60,2±13,82 (4)	2,6±0,14 (12)	15,8±0,83 (12)
P							<0,01
P_1		=0,05	=0,02	<0,01			<0,01
With total deafferentation of MBH	5,7±0,95 (6)	48,8±5,32 (8)	41,2±5,32 (6)	54,2±5,25 (7)	60,4±14,20 (3)	2,7±0,20 (8)	12,8±0,81 (8)

Legend. Number of animals given in parentheses; P) significance of differences compared with animals undergoing mock operation; P_1) the same compared with control animals.

Data on the effect of afferentation and extirpation of MBH on the basal corticosterone level in rats are contradictory [3, 6, 10]. The results of the present experiments (Table 1) showed that the initial 11-HCS level in the animals undergoing the operations was virtually the same as in the control rats.

Shock followed a similar course in the animals of all groups. The only point worth noting was that rats with partial deafferentation of MBH had the shortest survival period (2.5 h), compared with 3.5-4.5 h for the other two groups.

Fixation of the rats to the frame and dissection of the vessels, which usually took 20-30 min, caused a sharp increase in the plasma corticosterone level in the animals of all groups. However, the increase was least marked in rats after removal of MBH and most marked in rats with total deafferentation of the hypothalamus. The difference in the response of the animals after operation to stress can tentatively be attributed to changes in the functional state of their pituitary–adrenal system. This view is confirmed indirectly by the change in weight of the adrenal and pituitary glands in the rats after extirpation and complete deafferentation of MBH. Akmaev et al. [1] have shown that hypertrophy of the adrenals in rats with complete isolation of the hypothalamus is accompanied by increased functional activity of the cells of the zona fasciculata of the cortex.

The blood level of the hormone in the rats of the different groups under observation after fixation was maintained until death of the animals; the 11-HCS concentration in animals with total deafferentation of the hypothalamus was much higher than in animals undergoing the mock operation at nearly all stages of traumatic shock.

The results indicate that activation of brain centers controlling ACTH secretion during shock is virtually independent of the morphological intergrity of the nervous connections of the hypothalamus and is dependent chiefly on humoral influences.

Several workers [7, 9] nowadays distinguish between "systemic" stimulators of the function of the pituitary–adrenal system, with humoral action (histamine, insulin, a combination of biologically active substances liberated in response to mechanical trauma, etc.) and "neurogenic" stimulators (vibration, noise, light), which act on afferent neurons.

On the basis of these views it can be postulated that a combination of immobilization with dissection of the vessels after injection of procaine is an adequate stimulus for the hypothalamus when deprived of its nervous connections with surrounding brain regions. This activation was subsequently maintained by trauma to the limb, and after the development of shock, by changes in the humoral background (acidosis, hypoxemia, increased concentration of mediators and metabolic products in the blood) typical of traumatic shock.

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PATHOGENESIS OF THE LOW CARDIAC OUTPUT SYNDROME IN POSTRESUSCITATION STATES

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UDC 616-036.882-08-036.8-7:616.12-008.1-092-07

Acute hypervolemia induced in experiments on dogs by infusion of dextran, did not produce decompensation of the circulation in animals whose cardiac output was sharply depressed in the postresuscitation period after circulatory arrest lasting 15 min. The increase in the venous return and change in the conditions of the peripheral circulation as a result of dextran administration temporarily increased the central venous pressure, caused a lasting increase in the arterial pressure, cardiac output, stroke volume, work of the left ventricle, and total oxygen consumption by the body, and lowered the peripheral vascular resistance. In model experiments on dogs subjected to isolated compression ischemia of the brain for 20 min, a low cardiac output syndrome also developed.

KEY WORDS: hypoxia; postresuscitation period; cardiac output; hemodynamics.

In the postresuscitation period after various types of terminal state, similar phasic changes in the central hemodynamics have been found [6, 7, 11]. The period of hyperperfusion, at a time of extremely intensive work of the heart at the beginning of resuscitation, is gradually replaced after 2-3 h by the onset of a low cardiac output syndrome which may continue for up to 24 h. Among the factors responsible for its development injury to the myocardium as a result of hypoxia and toxemia and a decrease in the absolute circulating blood volume may be distinguished [4, 5, 12]. However, there is as yet no general agreement regarding the nature and functional significance of this phenomenon.

The two objects of this investigation were as follows: first, to investigate the functional reserves of the cardiovascular system in the period of maximal depression of the cardiac output during resuscitation after circulatory arrest in vivo, and second, to determine the role of disturbances of neurohumoral regulation in the development of the low cardiac output syndrome after resuscitation.

EXPERIMENTAL METHOD

Two groups of experiments were carried out on 17 anesthetized (pantopon 4-6 mg/kg, pentobarbital 8-10

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(Presented by Academician of the Academy of Medical Sciences of the USSR N. A. Fedorov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 82, No. 7, pp. 787-789, July, 1976. Original article submitted November 5, 1975.