FUNCTIONAL STATE OF THE SYSTEM OF HEMOSTASIS AFTER ELECTROLYTIC INJURY TO THE MEDIAN EMINENCE OF THE HYPOTHALAMUS

V. P. Baluda, G. N. Sushkevich, N. A. Zhukova, and E. M. Parshkov

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Electrical coagulation of the rostral region of the median eminence of the hypothalamus in male Wistar rats weighing 190-200 g (plane A-5.2, depth of insertion of electrode 9.8 mm from the center of the sagittal sinus) led after 9 days to marked changes in the functional state of the system of hemostasis: an increase in the bleeding time, a decrease in activity of factor XIII, and a decrease in resistance of the vessel walls, which still continued 30-33 days after the operation. It is postulated that these changes in the system of hemostasis are due to disturbance of the transhypophyseal mechanism of neuroendocrine hypothalamic regulation. On the 9th day after electrical coagulation of the median eminence of the hypothalamus in rats the bleeding time was increased, and activity of factor XIII was reduced, and the resistance of the vessel walls was diminished.

Investigations have demonstrated the importance of adrenergic, cholinergic, and serotoninergic structures of the hypothalamus in the regulation of the blood clotting system [1-3]. Little information has been obtained on the mechanism of hypothalamic regulation of the system hemostasis [4] and it does not reflect the role of the humoral transhypophyseal influence of the hypothalamus in this process.

The object of the present investigation was to study the functional state of the system of hemostasis during a disturbance of hypothalamo-hypophyseal relations. This was achieved by electrolytic destruction of the median eminence, the site of transmission of neurohormones from the hypothalamus to the pituitary gland [5-7].

EXPERIMENTAL METHOD

Experiments were carried out on 72 sexually mature Wistar male rats weighing initially 190-200 g. Electrical coagulation of the median eminence was carried out under nembutal anesthesia on a stereotaxic apparatus in plane A-5.2 with the electrode inserted to a depth of 9.8 mm from the center of the sagittal sinus. The region of destruction was identified from the maps of de Groto [8]. To produce electrical coagulation a direct current of 1 mA was applied to the anodal electrode for 10 sec. Rats undergoing the same manipulations of insertion of the electrode, but without application of the current, were used as the control. To identify the zone of electrocal coagulation, frontal and sagittal sections through the hypothalamus, 7 μ in thickness and stained with paraldehyde-fuchsin by Gomori's method in Maiorova's modification [9], and also with gallocyanin by Einarson's method and with 0.1% toluidine blue solution, were studied histologically. To investigate the functional state of the system of hemostasis the following indices were determined: bleeding time [10], blood loss [11], resistance of the vessel walls by the method of Hecht and Nesterov (pressure 200 mm Hg, exposure 5 min), platelet count [12], plasma recalcification time and blood fibrinogen concentration

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TABLE 1. Functional State of the System of Hemostasis after Electrolytic Injury to the Hypothalamus in Rats (M±m)

Index	Time after mock operation (in days)			Time after destruction of median eminence (in days)		
	1	9	30—33	2	9	30—33
Bleeding time (in min)	2,9±0,4	2,1±0,2	2,7±0,2	2,9±0,3	3,0±0,3*	3,0±0,2
Blood loss (in 1×10⁻⁴ ml)	120±15	111±26	—	122±21	90±14	—
Resistance of vessel wall	0,6±0,3	0,6±0,2	0,5±0,1	0,7±0,2	1,2±0,3	1,4±0,2*
Platelets (thousands/mm³)	1 112±176	1 335±56	1 072±41	1 242±54	1 269±103	1 155±31
Plasma recalcification time (in sec)	517±71	443±25	430±41	447±29	402±39	431±36
Fibrinogen concentration (mg %)	306±23	318±22	301±12	420±27*	320±33	272±18
Activity of factor XIII (in sec)	55,0±5,9	58,0±5,7	56,0±7,7	56,0±5,9	38,0±4,3*	46,0±3,1
Thrombotest (degree)	4,2±0,8	3,9±2,4	4,1±0,3	4,0±0,3	4,0±0,3	3,5±0,2
Tolerance of fibrin clot to plasmin (in min)	137±9	129±9	124±10	138±6	121±9	111±6

* Significance of difference relative to results obtained in animals undergoing mock operation ($P > 0.05$).

Fig. 1. Frontal section through rat hypothalamus: a) median eminence of intact rat; b) collection of Gomori-positive neurosecretory material in median eminence 9 days after operation; c) formation of scar tissue and absence of neurosecretion in median eminence 30 days after operation. Gomori's paraldehyde-fuchsin, 56×.

[13], activity of factor XIII [14], thrombotest [15], and tolerance of the fibrin clot to plasmin [16]. The investigations were carried out on the 2nd, 9th, and 30th-33rd days after the operation.

EXPERIMENTAL RESULTS AND DISCUSSION

Morphological examinations of sections through the hypothalamus showed that the zones of electrical coagulation were mainly in the rostral region of the median eminence. A collection of a considerable quantity of neurosecretion was observed proximally to the focus of destruction 2 and 9 days after the operation, and after 1 month there was almost total resorption of the Gomori-positive substance from the median eminence. A glial scar was formed in the zone of destruction, modifying the normal structure of the median eminence (Fig. 1).

The functional state of the system of hemostasis two days after electrical coagulation of the median

eminence of the hypothalamus showed no significant change (Table 1). In the animals of the experimental group only the fibrinogen concentration was higher than in animals undergoing the mock operation.

On the 9th day the bleeding time in the rats with injury to their median eminence was 43% higher than in the rats undergoing the mock operation, while the activity of factor XIII and resistance of the vessel walls were 35 and 50% lower respectively. In the late stages after electrical coagulation of the median eminence (30-33 days) the resistance of the vessel wall still remained low.

Electrolytic destruction of the median eminence of the hypothalamus in rats thus gives rise to changes in the system of hemostasis characteristic of the state of an animal with a bleeding tendency. The severity of these changes depends on the time elapsing after the operation and is evidently determined by differences in the morphological and functional state of the hypothalamo-hypophyseo-adrenocortical system. In the early stages after electrolytic damage to the median eminence (2nd-9th days) the supply of neurohormones from the hypothalamus to the pituitary is blocked, as is shown by the accumulation of secretion proximally to the focus of destruction. According to data in the literature, ACTH synthesis is inhibited in animals during this period and adrenocortical function is depressed. Later the morphological and functional state of the hypophyseal-adrenal system returns to normal [17, 18]. As previous investigations by the present writers [19, 20] and others [21-23] have shown, during functional insufficiency of the pituitary and adrenals, a bleeding tendency develops. This state can be terminated by adminsistration of ACTH or glucocorticoids. The most marked changes in the system of hemostasis on the 9th day after damage to the median eminence evidently coincided with the depth of hypocorticism.

The results described above suggests that changes in the system of hemostasis in animals after electrical coagulation of the median eminence of the hypothalamus are due to functional insufficiency of the pituitary and adrenal cortex and arise as a result of a disturbance of the transhypophyseal mechanism of neuroendocrine hypothalamic regulation.

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