EFFECT OF HYPOTHALAMIC STIMULATION ON THE KININOGEN DYNAMICS IN THE BLOOD SERUM OF RABBITS DURING SENSITIZATION AND ANAPHYLACTIC SHOCK

G. K. Vasil'eva, E. P. Frolov, N. V. Shatilova, and M. I. Undritsov

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In rabbits exposed to prolonged stimulation of the lateral hypothalamus the kininogen concentration in the blood serum in the early stages of sensitization not only was not increased, as it was in the control animals but, on the contrary, it was reduced. On reinjection of the antigen the experimental rabbits either did not develop anaphylactic shock or it was mild in severity, and the kininogen level was unchanged or fell only slightly. In the control animals with anaphylactic shock the sharp drop of arterial pressure was accompanied by a marked decrease in the blood kininogen concentration.

A decrease in the blood kininogen concentration can be due to its conversion into bradykinin [15, 18-20, 22, 24], which plays a role in the pathogenesis of allergic reactions. An increase in the blood kininogen concentration was discovered previously by the writers during sensitization, with a sharp fall in its level during the development of anaphylactic shock in rabbits [10]. The hypothalamus is also known to influence the formation of immunoallergic reactivity [1-6, 9, 12, 13, 16, 17, 23]. In particular, stimulation of the periventricular system of the hypothalamus (mainly the medial periventricular structures) has been shown to stimulate, while stimulation of the lateral portions of this system inhibits the formation of the response of the body to an antigenic stimulus, as shown by an increase (decrease) in the intensity of antibody formation, and by an increase (decrease) in the intensity of anaphylactic shock in response to the reacting injection [11]. It has accordingly been postulated that changes in the severity of the course of anaphylactic shock in animals undergoing hypothalamic stimulation are connected with changes not only in antibody formation, but also in the kininogen level during sensitization and during anaphylactic shock.

The experiments described below were carried out to test this hypothesis.

EXPERIMENTAL METHOD

Male rabbits weighing 3 kg were used. The animals were sensitized by subcutaneous injection of type A streptococcal cytoplasmic antigens [8]. Anaphylactic shock was induced on the 21st day of sensitization. The severity of the shock was judged from the degree of lowering of the blood pressure.

One week before the experiment nichrome bipolar stimulating electrodes were inserted into the lateral portions of the hypothalamus of the rabbits, taking bearings from the appropriate coordinates [21]. The hypothalamus was stimulated by volleys of pulses (2-6 V, 3-5 msec, interval between volleys 0.3-0.5 sec) for 20-30 min daily for 15-20 days, starting 1-2 days before sensitization. The amplitude of stimulation

O. V. Kuusinen Petrozavodsk University. Research Laboratory of Experimental Immunobiology, Academy of Medical Sciences of the USSR, Moscow. Allergologic Research Laboratory, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR N. N. Zhukov-Verezhnikov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 76, No. 8, pp. 28-30, August, 1973. Original article submitted September 27, 1972.

TABLE 1. Dynamics of Kininogen Concentration during Sensitization and Shock in Rabbits Undergoing Chronic Stimulation of the Lateral Hypothalamus

Statistical index	Kininogen concentration (in μg bradykinin/ml)				
	before sensitization	during sensitization			after reinjection of antigen
		7th day	14th day	21st day	
n	5	5	4	4	4
$M \pm m$	6,0±0,7	6,5±0,74	6,0±0,39	3,8±0,44	3,5±0,2

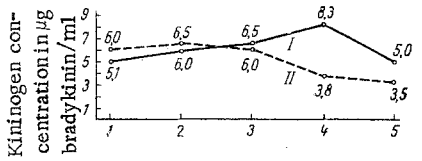

Fig. 1. Dynamics of kininogen in rabbits during sensitization and shock while exposed to chronic hypothalamic stimulation: I) mean values of kininogen concentration in control rabbits; II) in rabbits with hypothalamic stimulation; 1) initial value; 2) on 7th day of sensitization; 3) on the 14th day of sensitization; 4) on 21st day of sensitization; 5) after reinjection of antigen.

was chosen so as to induce positive behavioral responses in the animals (food excitation or, in special conditions, autostimulation). The blood serum kininogen concentration was determined before and 7, 14, and 21 days after sensitization and after the reacting injection of the antigen [7, 14].

EXPERIMENTAL RESULTS

By contrast with the dynamics of the kininogen concentration in the control animals, in which an increase was observed during sensitization [10], in the rabbits sensitized during stimulation of the lateral hypothalamus the kininogen concentration not only did not increase, but on the 14th and 21st days of the experiment it actually decreased ($P < 0.01$) (Table 1).

Unlike the controls, the experimental animals either did not develop anaphylactic shock or it ran a mild course. Injection of the reacting dose of antigen (2 ml intravenously) did not cause the arterial pressure to fall at all in two rabbits, while in another two rabbits it fell only slightly – by 18 and 20 mm.

It is interesting to note that in those rabbits which did not develop shock as such the kininogen level was unchanged from that observed before the reinjection of antigen. A mild form of shock was accompanied by a very slight decrease in the kininogen level – by 9.3 and 15.2%. The dynamics of kininogen during sensitization and anaphylactic shock in the control and experimental animals is shown in Fig. 1. In all these animals the electrodes were located in the region of the lateral hypothalamic zone (at the level P_1-P_2). In one experimental rabbit (not included in the table), just as in the control, sensitization was accompanied by an increase in the kininogen concentration (6.8 μg/ml on the 14th day; 8.5 μg/ml on the 21st day). On reinjection of the antigen, the animals developed severe anaphylactic shock with a sharp fall of blood pressure and a decrease in the kininogen concentration to 6.4 μg/ml. In this case the electrode tip was in the medial portion of the hypothalamus (on the boundary between the ventromedial and dorsomedial nuclei) and not in the lateral portion.

These results show that during hypothalamic stimulation the change in the degree of sensitization and in the severity of shock is connected not only with a disturbance of the intensity of the specific immunological processes, but also with changes in the kinin system.

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