EFFECT OF PROLONGED CHRONIC STIMULATION OF POSITIVE EMOTIOGENIC HYPOTHALAMIC ZONES ON BLOOD LIPID AND ARTERIAL PRESSURE LEVELS

L. V. Simutenko, N. L. Yastrebtsova, N. G. Bogdanovich, and T. A. Leontovich

UDC 612.826.4-06:613.863[-08:]612.123+612.143

KEY WORDS: emotiogenic zones of the hypothalamus; blood lipids; arterial pressure.

Emotional-behavioral reactions, differing in biological quality (negative and positive), evoked by short-term hypothalamic stimulation, may be accompanied by opposite changes in autonomic components [1, 4, 9].

Experiments by the writers on dogs and rabbits have shown that short-term negative emotional-behavioral reactions with elements of aggression lead to a transient (up to 60 min) increase in the blood lipid concentration. Positive emotional-behavioral reactions and self-stimulation reactions, on the other hand, cause the blood lipid level to fall [6, 9]. It has also been shown that prolonged (for several months) stimulation of negative emotiogenic zones of the rabbit hypothalamus leads to the development of a lasting rise in the blood lipid level [8, 10] and arterial blood pressure [10].

The question arises whether prolonged chronic stimulation of positive emotiogenic hypothalamic zones can evoke a lasting fall in these parameters in animals kept on an ordinary diet or whether such stimulation may have an alleviating effect on the development of alimentary hypercholesteremia.

EXPERIMENTAL METHOD

Experiments were carried out on 20 male Chinchilla rabbits weighing 3-3.5 kg, divided into three groups: 1) experimental (10 rabbits), 2) control animals with implanted electrodes (five), and 3) control intact rabbits (five).

Electrodes were implanted into the positive emotiogenic zones of the hypothalamus by a trial and error method, using coordinates taken from a stereotaxic atlas [15]. The accuracy of implantation of the electrodes was verified by the appearance of a self-stimulation reaction and by subsequent determination of the location of the electrode tips.

Behavioral testing began 10 days after implantation of the electrodes. Prolonged stimulation of positive emotiogenic zones of the hypothalamus was carried out for 3 months, for 2 h daily with interruptions. The stimulation was intermittent, aperiodic, and was applied by means of an independent microstimulator, on freely behaving animals, just as in the case of stimulation of negative emotiogenic hypothalamic zones [10]. The stimulus used consisted of a series of square pulses 0.3 msec in duration, with a frequency of 50 Hz, and whose amplitude varied from 1.5 to 3 V.

For the first 2 months the rabbits were kept on an ordinary laboratory diet, but during the 3rd month all animals of the experimental and both control groups received cholesterol in a daily dose of 60 mg/kg body weight. Blood was taken from the animals every 10 days before they were fed. Cholesterol was determined by the method in [12] and triglycerides as in [13]. Before the beginning of chronic stimulation, the mean initial blood concentrations of cholesterol and triglycerides were calculated from the results of two to four determinations over a period of 1 month in all groups of animals. The arterial pressure was measured at intervals of 2-3 days in the carotid artery, exteriorized into a skin flap.

Research Institute of Pediatrics, Academy of Medical Sciences of the USSR. All-Union Cardiologic Scientific Center, Academy of Medical Sciences of the USSR. Brain Institute, Academy of Medical Sciences of the USSR, Moscow. (Presented by Academician of the Academy of Medical Sciences of the USSR M. Ya. Studenikin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 6, pp. 650-652, June, 1981. Original article submitted October 17, 1980.

 0007-4888/81/9106-0714$07.50

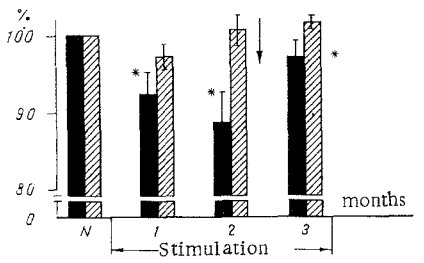

Fig. 1. Development of lasting fall of arterial pressure under the influence of prolonged chronic stimulation of positive emotiogenic hypothalamic zones in rabbits kept on an ordinary diet and elevation of its level during continued stimulation in rabbits fed cholesterol. Abscissa, time (in months); ordinate, arterial pressure (in % of initial value, taken as 100%). Black columns indicate experimental group, obliquely shaded columns control group of rabbits with implanted electrodes. *) $P < 0.01$ relative to initial level, taken as 100%. Arrow indicates injection of cholesterol.

EXPERIMENTAL RESULTS

Prolonged stimulation of positive emotiogenic hypothalamic zones for 2 months did not cause any lasting changes in the blood levels of endogenous cholesterol and triglycerides. Only in one rabbit of the experimental group was a lasting fall in the cholesterol level observed from 34 ± 8 to 19 ± 3.5 and from 20.3 ± 4.8 mg% after 1 and 2 months respectively.

Measurement of the arterial pressure showed that daily stimulation of positive emotiogenic zones caused a significant fall in its level in eight of 10 rabbits as early as after 1 month (on average for the group 107 ± 1.3 mm Hg, normal level 98 ± 2.1 mm Hg, after 2 months to 95 ± 3.4 mm Hg, i.e., a fall of 9%). The arterial pressure of some animals was reduced by as much as 23 mm Hg. In the control group of rabbits with implanted electrodes the arterial pressure fluctuated within normal limits (Fig. 1).

Prolonged chronic stimulation of positive emotiogenic hypothalamic zones in freely behaving animals thus did not cause lasting changes in the blood lipid level of the animals, as was observed during stimulation of negative emotiogenic zones under the same conditions [10], but it led to the development of lasting neurogenic hypotension.

Continuation of stimulation after the rabbits had been transferred to an atherogenic diet not only did not delay the development of alimentary hypercholesteremia but, on the other hand, it led after only 10 days to a significant ($P < 0.05$) increase in its intensity compared with that observed in control animals of group 3; experiment 244 ± 21 mg%, control 126 ± 18.1 mg% (initial levels 32.4 ± 3.02 and 30.5 ± 5.2 mg% respectively).

A tendency was found for the arterial pressure to rise under these circumstances (Fig. 1). On average for the group it came close to the initial level (103 ± 2.4 mm Hg), and in two rabbits it actually exceeded it.

Histological verification of the location of the electrode tips showed that they lay along the whole diameter of the lateral hypothalamus at the level of the tuber cinereum. At autopsy on the animals hypertrophy of the adrenals with a considerable increase in their weight was found. In rabbits with implanted electrodes (groups 1 and 2) their weight was 1129 ± 15.9 and 888 ± 21.4 mg respectively, whereas in the control intact animals it was only 440 ± 25.5 mg. Microscopic investigation revealed foci of holocrine secretion, evidence of the functional strain on the gland. Prolonged stimulation of positive emotiogenic hypothalamic zones was thus not without its effects on the animal and led to changes in the activity of the hypothalamus–adrenals system. Evidence of activation of this system during positive emotional stimulation was also obtained by other workers [2, 3].

It is an interesting fact that prolonged stimulation of positive emotiogenic hypothalamic zones has the same effect against this functionally changed background of hypercholesteremia as stimulation of negative

zones. Potentiation of the alimentary hypercholestermia was found, as was also observed by other workers during stimulation of all zones of the hypothalamus, together with a rise in the arterial pressure. The latter effect may probably be due to changes in the reactivity of the morphologically and functionally changed blood vessels to neurogenic stimulation, with a tendency toward the appearance of constrictor effects [11].

The results provide an explanation for clinical observations which show that even positive emotions may give rise to attacks of angina or may lead to myocardial infarction in patients with coronary atherosclerosis [5, 7].

LITERATURE CITED

1. I. I. Vainshtein, in: Physiological Features Distinguishing Positive and Negative Emotional States [in Russian], Moscow (1972), pp. 11-32.
2. L. Levy, in: Emotional Stress [Russian translation], Leningrad (1970), pp. 225-233.
3. Yu. A. Makarenko, Fiziol. Cheloveka, 3, No. 4, 665 (1977).
4. K. Lishak, Data on Interaction between Self-Stimulation and Humoral Factors [in Russian], 5th Sechenov Lecture, Moscow (1974).
5. A. L. Myasnikov, Essential Hypertension and Atherosclerosis [in Russian], Moscow (1965).
6. L. V. Simutenko, N. L. Yastrebtsova, and T. A. Leontovich, Byull. Éksp. Biol. Med., No. 3, 211 (1979).
7. B. Folkow and E. O'Neill, The Circulation [Russian translation], Moscow (1976).
8. P. V. Khomulo, Byull. Éksp. Biol. Med., No. 11, 1294 (1976).
9. N. L. Yastrebtsova and L. V. Simutenko, Dokl. Akad. Nauk SSSR, 201, No. 4, 1001 (1971).
10. N. L. Yastrebtsova and L. V. Simutenko, Byull. Éksp. Biol. Med., No. 1, 20 (1976).
11. N. L. Yastrebtsova, I. P. Azizov, and V. P. Kulagina, in: Systemic Mechanisms of Emotional Reactions [in Russian], Moscow (1978), pp. 98-100.
12. L. L. Abell, B. B. Brodie, and F. E. Kendall, in: Standard Methods of Clinical Chemistry, Vol. 2, New York (1958), pp. 26-33.
13. L. A. Carlson, J. Atheroscler. Res., 3, 334 (1963).
14. C. G. Gunn, M. Friedman, and S. Byers, J. Clin. Invest., 39, 1963 (1972).
15. C. H. Sawyer, J. W. Everett, and J. D. Green, J. Comp. Neurol., 101, 801 (1954).

ROLE OF THE LUNGS IN REGULATION OF ACTIVITY OF THE KALLIKREIN – KININ SYSTEM IN IMMOBILIZATION STRESS

O. A. Gomazkov, N. V. Komissarova, and M. P. Gorizontova

UDC 613.863-02:612.766.2]-07:616
24-008.94:577.175.85 77.175.85

KEY WORDS: kallikrein–kinin system; immobilization stress; lungs.

Activation of the kallikrein–kinin system (KKS) in various pathophysiological situations is primarily compensatory in its role, regulating the state of the blood, the microcirculation, and the hemodynamics as a whole. The dynamics and degree of participation of kinins in these processes are determined by the ratio between activating (Hageman factor, kallikrein, etc.) or regulating (inhibitors, kininases) biochemical components of the system.

An important role in this regulation is played by the microcirculatory system of the lungs, the endothelium of which possesses powerful kinin-destroying activity [7]. Protease inhibitors with a marked anti-kallikrein action also have been isolated from the lungs. It is logical to suggest that not only factors limiting the effectiveness of the kinin system, but also those with the opposite effect, promoting it, may be localized in the pulmonary microvessels. This suggestion is more likely to be correct because the lungs are known

Laboratory of General Pathology and Experimental Therapy, Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 91, No. 6, pp. 652-654, June, 1981. Original article submitted August 26, 1980.

0007-4888/81/9106-0716$07.50