CATECHOLAMINES AND RENIN ACTIVITY OF BLOOD PLASMA OF KOLETSKY RATS DURING EMOTIONAL STRESS

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So-called natural models, namely, lines of rats with a high arterial blood pressure (BP), are of great interest from the standpoint of the study of neurohumoral mechanisms maintaining self-regulation of cardiovascular functions during emotional stress. An extensive literature is devoted to the spontaneously hypertensive line, rats of which develop stable hypertension during postnatal development. The Koletsky line [2], bred by crossing rats of the spontaneously hypertensive and Sprague–Dawley lines, has received less study. The Koletsky line contains a population of hypertensive rats of the ordinary size and obese rats.

This paper gives data on BP and plasma catecholamines (CA) levels and plasma renin activity (PRA) in control rats and in hypertensive and obese Koletsky rats during immobilization, with corresponding data for Wistar rats for comparison.

EXPERIMENTAL METHOD

Experiments were carried out on nine male Wistar rats and on nine hypertensive and two obese Koletsky rats; seven obese Koletsky rats did not survive the operation of introduction of a catheter.

On the day before the experiment a polyethylene catheter was introduced into the caudal artery of the rats for direct measurement of BP and for blood sampling [1]. Next morning a control blood sample (0.6 ml) was taken and the initial BP measured. The rats were then immobilized with the limbs and head securely fixed [3]. Blood samples were taken after 20 and 120 min of immobilization; BP was measured after 60 and 120 min of immobilization. The rats were decapitated after 120 min of immobilization. PRA was determined radioimmunologically using the REN Kit from Sorin (Italy); the plasma adrenalin and noradrenalin concentrations were measured by a radioenzymic method [5, 6].

EXPERIMENTAL RESULTS

BP in the control, hypertensive, and obese Koletsky rats was significantly higher than in Wistar rats (Fig. 1A). The dynamics of BP during immobilization in Koletsky rats differed in principle from that in Wistar rats: In Koletsky rats BP fell during emotional stress whereas in Wistar rats it was higher after 1 h of immobilization but then returned to its initial level.

Individual analysis of the dynamics of BP in the rats (Fig. 1B, C, D) demonstrates more clearly than analysis of mean values the differences between Wistar and Koletsky rats. In most hypertensive Koletsky rats BP fell sharply during immobilization. In two rats (Nos. 12 and 34) a fall in BP was observed only after 2 h of immobilization, and only in rat No. 13 did the curve of changes in BP resemble that for Wistar rats.

In obese Koletsky rats the dynamics of BP during immobilization showed the same tendency

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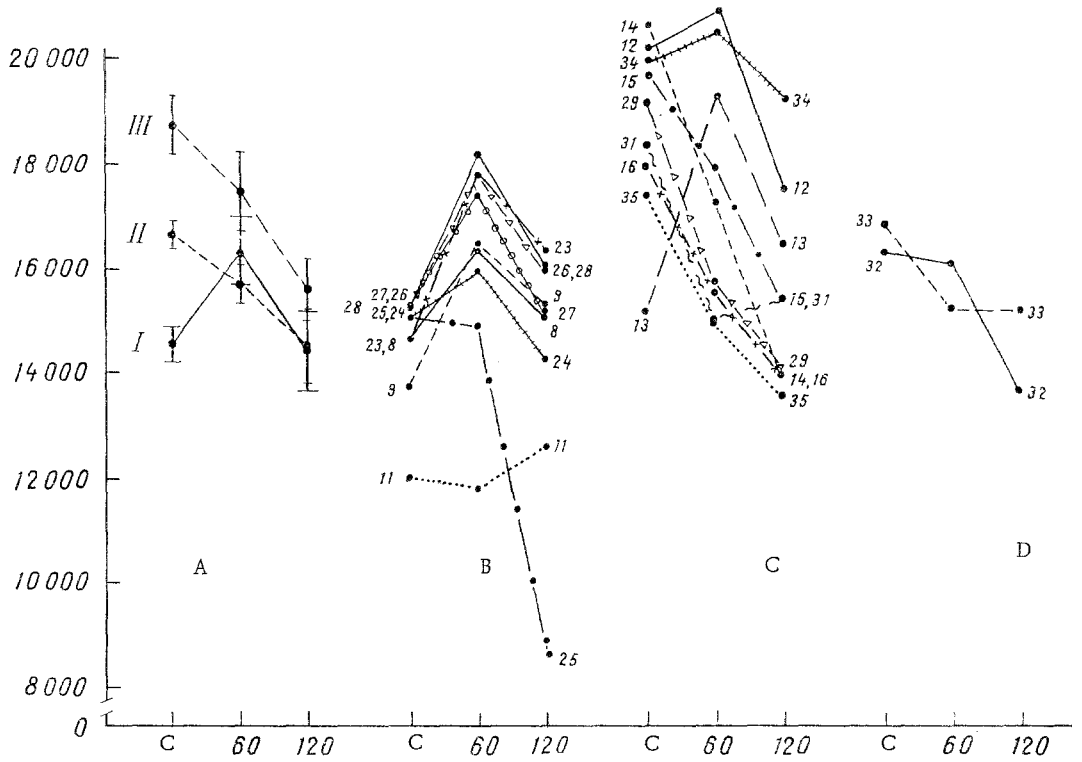

Fig. 1. Dynamics of BP in Wistar and Koletsky rats in control test and during immobilization. A) Mean value (I — Wistar rats; II — obese Koletsky rats; III — hypertensive Koletsky rats). B) Individual curves of changes in BP during immobilization of Wistar rats. Numbers (in this and subsequent figures) correspond to identification numbers of rats on records. C) The same for hypertensive Koletsky rats. D) The same for obese Koletsky rats. Abscissa, duration of immobilization (in min), C) control; ordinate, BP (in Pa).

as that for hypertensive Koletsky rats, but the range of the changes was smaller.

The plasma adrenalin level in the control was similar in both Koletsky and Wistar rats, and its changes during the first 20 min of immobilization also were similar (Fig. 2A). However, by the end of the second hour of immobilization the adrenalin concentration was raised in the obese rats.

Individual changes in the adrenalin level during immobilization (Fig. 2B, C, D) also were similar in the rats of all groups, but among the Koletsky rats there were some (Nos. 16, 29, 31, and 32) in which the adrenalin level was higher than in the Wistar rats.

The noradrenalin level in the control was significantly higher for obese than for hypertensive Koletsky rats (Fig. 3A). After 2 h of immobilization the noradrenalin level differed significantly in the Wistar and Koletsky rats and also in the two populations of Koletsky rats.

The dynamics of individual changes in noradrenalin during immobilization differed significantly in the Wistar and Koletsky rats (Fig. 3B, C, D). Only in Wistar rats Nos. 8, 9, and 27 was the plasma noradrenalin level after 2 h of immobilization similar to that characteristically observed in most Koletsky rats.

Changes in the noradrenalin level in Koletsky rat No. 13 were similar in their course to those in Wistar rats. It will be noted that, with respect to BP and plasma adrenalin levels and to their changes in the course of immobilization rat No. 13 also showed the greatest similarity to Wistar rats (see Figs. 1 and 2).

In the control, PRA in hypertensive Koletsky rats was significantly higher than in the Wistar rats (Fig. 4A). After 20 min of immobilization the difference still remained — in Koletsky rats PRA rose by a greater degree during the first minute of immobilization than in Wistar rats. During the next period of immobilization (20-120 min) a sharp increase in

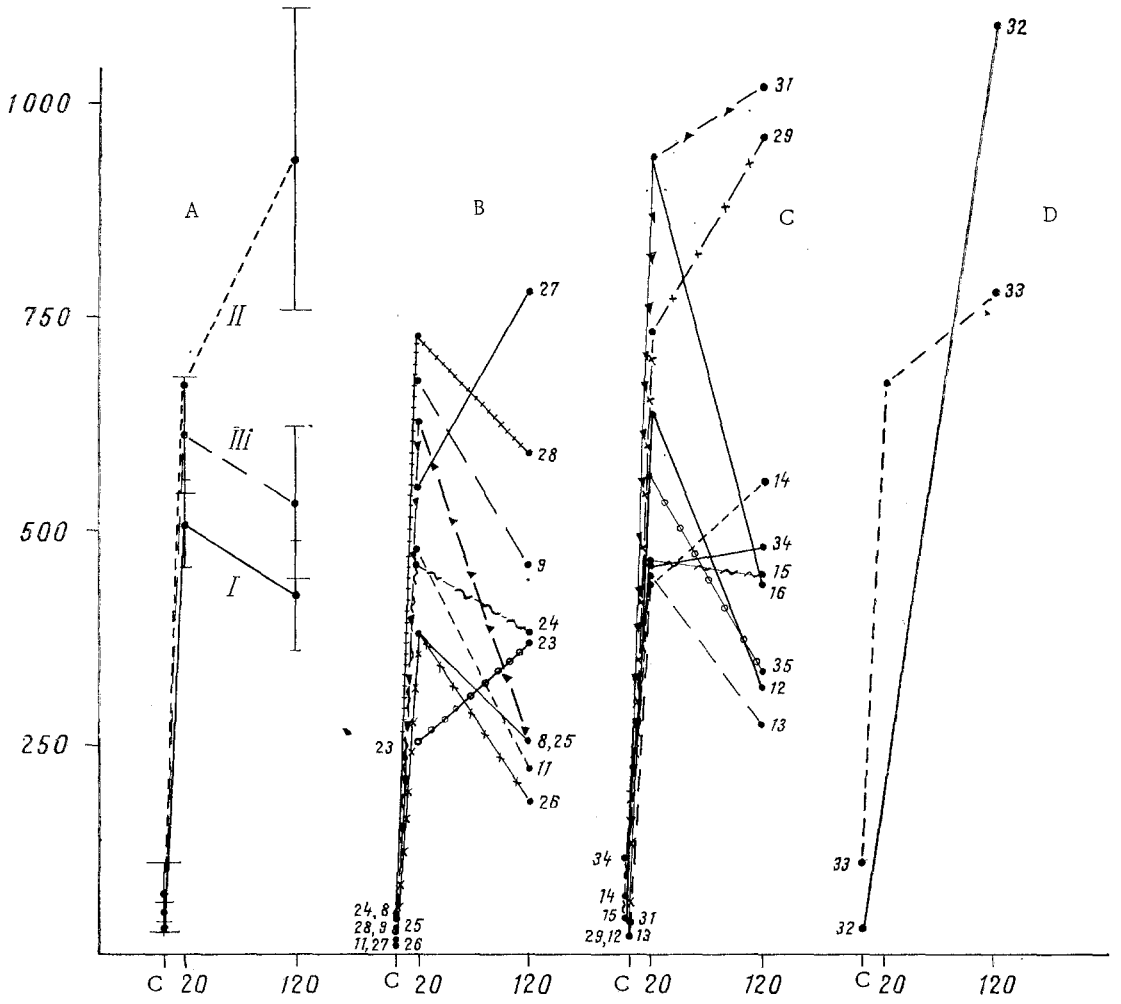

Fig. 2. Changes in plasma adrenalin level of Wistar and Koletsky rats during immobilization. Ordinate, plasma adrenalin level (in pg/ml). Remainder of legend as to Fig. 1.

PRA was observed in the Wistar rats, but in the Koletsky rats it remained virtually the same as after 20 min of immobilization.

The individual graphs (Fig. 4B, C, D) show that the sharp rise in PRA in the Wistar rats between the 20th and 120th minutes of immobilization was due mainly to a sharp increase in PRA in two rats (Nos. 25 and 26). Rat No. 25 died — its BP fell sharply toward the 120th minute of immobilization (Fig. 1B).

The BP level was thus significantly higher in control Koletsky rats than in Wistar rats. The initial PRA also differed significantly in these rats (it was significantly higher in hypertensive Koletsky than in Wistar rats). Conversely, the initial adrenalin concentration was similar in Wistar and Koletsky rats. Significant differences between Wistar rats and obese Koletsky rats also were found with respect to the control noradrenalin level.

The dynamics of all parameters studied during immobilization also differed significantly in Wistar and Koletsky rats. The character of the changes in BP differed in principle. During the first minutes of immobilization significant differences between Wistar and Koletsky rats were found only in the case of PRA: The increase in PRA was less in Wistar than in Koletsky rats. Later during immobilization differences also were found in the plasma CA level, especially of noradrenalin.

Bearing in mind the observations of Kvetnansky et al. [4], who showed that during stress changes in the plasma adrenalin level are determined by the character of adrenal activity whereas changes in noradrenalin are determined by sympathetic nerve endings, it can be concluded that activity of the adrenal medulla and of the sympathetic division of the nervous

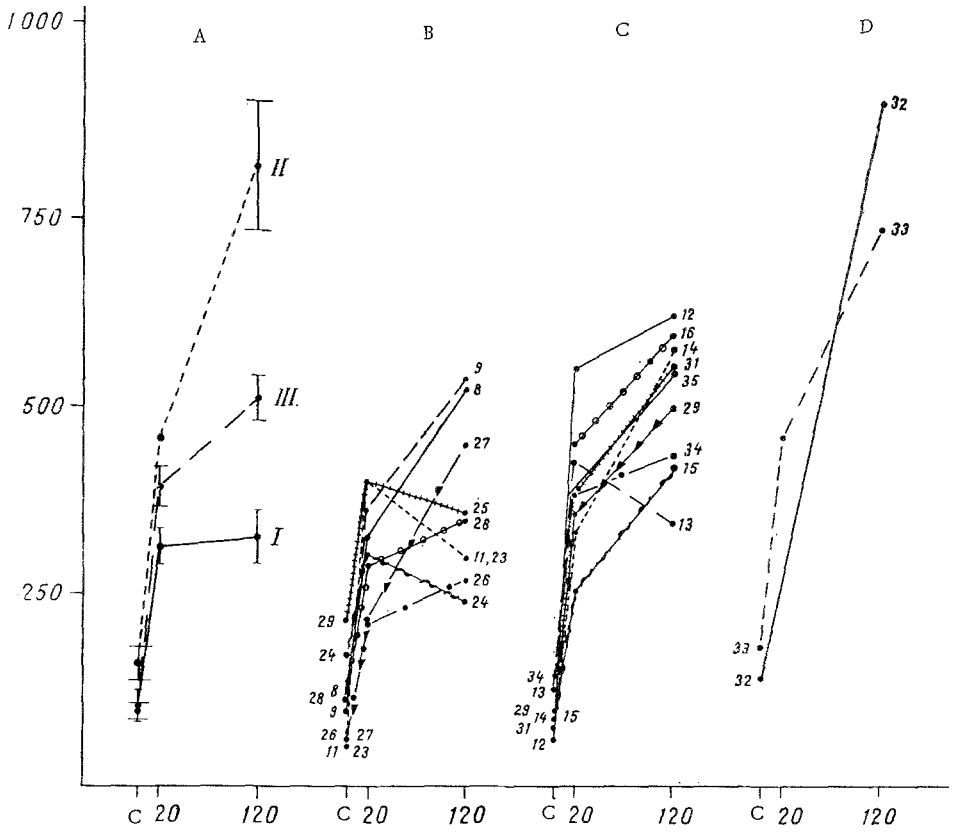

Fig. 3. Changes in plasma noradrenalin level during immobilization in Wistar and Koletsky rats. Ordinate, plasma noradrenalin level (in pg/ml). Remainder of legend as to Fig. 1.

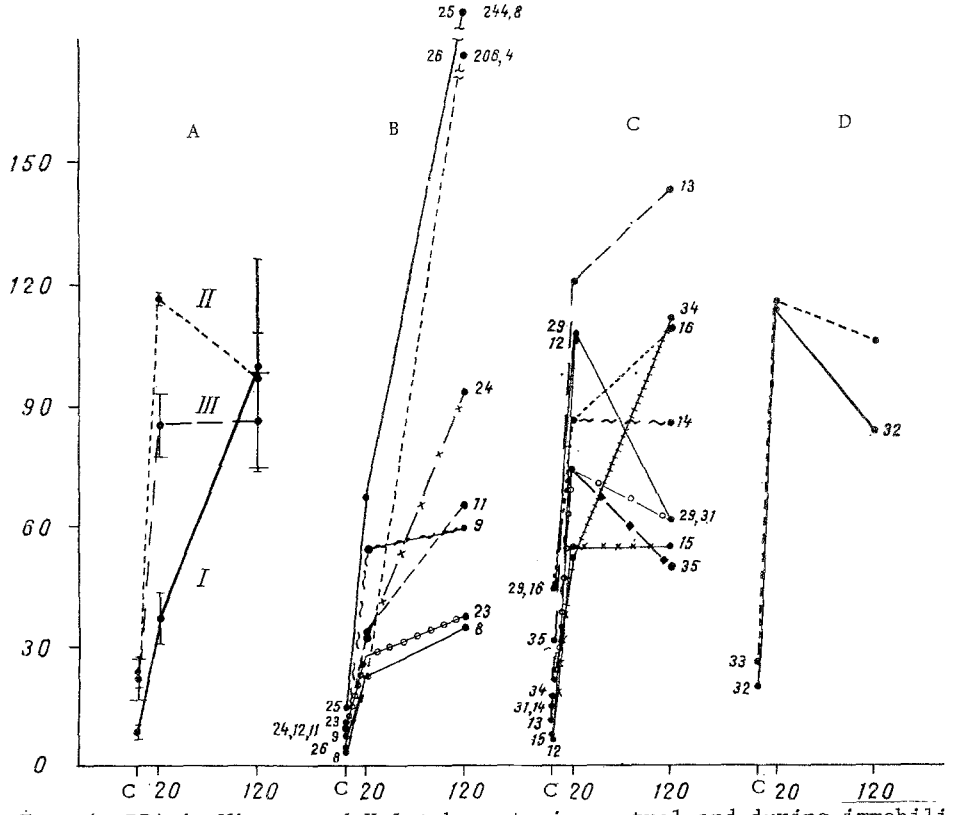

Fig. 4. PRA in Wistar and Koletsky rats in control and during immobilization. Ordinate, PRA (in mg/ml/h). Remainder of legend as to Fig. 1.

system, as well as activity of the renin-synthesizing structures, differs in Wistar and Koletsky rats under conditions of emotional stress.

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EFFECT OF L-DOPA ON THE DEVELOPMENT OF EXPERIMENTAL HYPERLIPIDEMIA AND ATHEROSCLEROSIS

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L-dopa, a precursor for catecholamine biosynthesis [2], is used in the combined treatment of Parkinson's disease [3, 7, 9]. There is information in the literature that this disease is often preceded by cerebrovascular atherosclerosis [4, 5].

It was therefore decided to study the effect of L-dopa on lipid metabolism and, in particular, on the development of experimental hyperlipidemia and atherosclerosis, and the investigation described below was undertaken for this purpose.

EXPERIMENTAL METHOD

Male albino rats (weighing 250-300 g), guinea pigs (weighing 250-300 g), and rabbits (weighing 2.5-3 kg) were used. Hyperlipidemia was induced in the rats by intraperitoneal injection of Triton WR-1339 in a dose of 225 mg/kg. L-dopa was injected twice, intraperitoneally, in a dose of 100 mg/kg, 24 h before and at the same time as the injection of Triton. Guinea pigs received cholesterol (CH) in a dose of 0.5 g/kg in sunflower oil by gastric tube daily for 25 days; L-dopa was given by the same method in a dose of 100 mg/kg. Atherosclerosis was induced in the rabbits by daily administration of 0.3 g/kg of CH in sunflower oil for 3 months. L-dopa was given perorally in a dose of 100 mg/kg. The acute toxicity of L-dopa was determined in experiments on mice. Peroral administration of L-dopa in a dose of 4 g/kg had no toxic action; LD_{50} by intraperitoneal injection was 2750 mg/kg body weight. Concentrations of total CH [11] and triglycerides (TG) [13] were determined in the blood and liver. The rabbits were killed by injection of air into the auricular vein; the aorta was isolated along its whole length and subjected to planimetry [1], after which its total CH content was determined.

EXPERIMENTAL RESULTS

The experiments on rats showed that during hyperlipidemia induced by Triton administration L-dopa reduced the increase in the CH level and, to a lesser degree, in the TG level in the blood (Fig. 1). After administration of CH to guinea pigs for 25 days, an increase in the serum CH and TG levels was observed. Combined administration of L-dopa and CH caused a marked hypolipidemic effect. In addition, under the influence of L-dopa a marked decrease in the TG concentration in the liver was noted, from 12.7 ± 1.1 to 6.25 ± 0.49 mg/g

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