# Functioning of Hypophysial Adrenocortical System in Rats Selected by the Threshold of Sensitivity to Electrical Current

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An enhancement of stress reactivity of the hypophysial-adrenocortical system in response to emotional and physical influence was shown in rats with a low threshold of sensitivity to electrical current. This phenomenon was observed as a rise in the maximum level of blood corticosterone and acceleration of stressor hormonal response. In the high-threshold rats a decrease in sensitivity of the hypophysial adrenocortical system to the feedback signals was observed.

**Key Words:** *hypophysial adrenocortical system; stress reactivity; corticosterone; line rats*

Animal experiments confirm that basic properties of the nervous system are determined genetically [6]. Selection according to the excitability threshold of the nerve-muscle apparatus [2] show that not only behavioral characteristics, but also reactivity to stress and ability to adapt to the environment depend on the excitability of the nervous system [1,9,10]. These findings support the hypothesis that the divergence of these properties is determined predominantly by hypophysial-adrenocortical system (HACS). There are data indicating that neuron excitability depends on corticosteroids [13]. We studied functional state of HACS in rats, in which not only the peripheral subdivision of nervous system [2], but also its central structures, the midbrain reticular formation in particular [5], had different threshold of excitability [2].

## MATERIALS AND METHODS

The study was carried out on 120 male Wistar rats weighing 350±25 g, which were genetically selected according to the threshold of sensitivity of the tibial nerve to electrical current. Selection was performed from two independent autobred populations: the high sensitivity LT-1 and LT-2 rats (low threshold: first selection program — 34th generation and the second selection program — 24th generation) and low sensitivity HT-1 and HT-2 rats (high threshold: the first and second selection programs of the same generations). The rats were grown and maintained on the standard diet at the Laboratory of Genetics of Highest Nervous System (I.P. Pavlov Institute of Physiology).

Basal state of HACS was evaluated by plasma content of corticosterone (CS) at rest. Blood samples were taken from the caudal vein at 4 p.m. Stress response of HACS was estimated by the maximum rise in blood CS. Several types of stressor stimulation were used. Emotional stress caused by new environment was estimated by measuring blood CS after a 30 min vein (I series). In the 2nd series, the rats were stimulated transcutaneously with electrical current (0.5 mA, 50 Hz, maximum duration 15 sec) which was applied 15 times to the floor of a 20×20×13 cm chamber. Blood was taken from the caudal vein 1, 3, and 24 h after stimulation.

The sensitivity of HACS to feedback signals was determined in a 2-day dexamethasone test [4].Two

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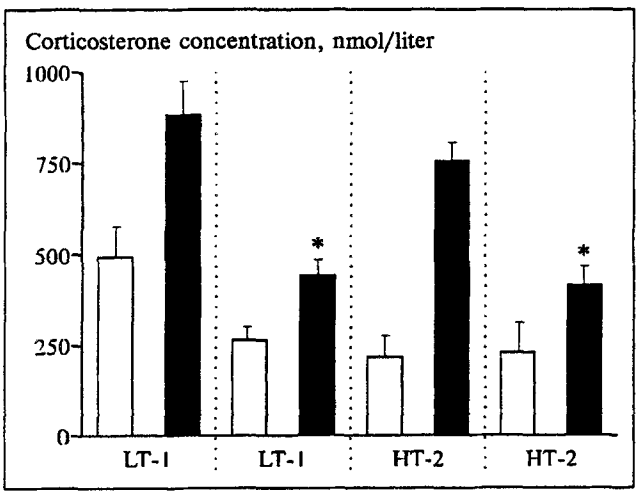


Fig. 1. Plasma corticosterone in the line rats placed in new environment. Light bars refer to intact, the solid ones to stressor rats. Here and in Fig. 2: *$p<0.05$ in comparison with the rats of another line.

rats were in a chamber. On the 1st day, the rats were injected intraperitoneally with 1 ml 0.9% NaCl at 10:00. Blood from the caudal vein was collected from nonnarcotized rats at 4 p.m. (basal state of HACS). Blood was taken again after 30 min (stress state of HACS). On day 2, the rats were injected intraperitoneally with dexamethasone sodium phosphate (Galenika), and blood was taken at 10:00. Thus, on day 2 the basal and stress state of HACS were evaluated after injection of dexamethasone.

Inhibition of basal function of the system was studied with 10 mg/kg dexamethasone, while a dose of 20 μg/kg was used to study inhibition of stress function. Blood level of CS was determined by radioimmune assay [7]. Data on the CS content were analyzed using Wilcoxon's nonparametric *U* test.

## RESULTS

Only LT-1 rats had significantly higher basal level of CS (Table 1).

After exposure to in new environment (series I) in LT-1 and LT-2 rats CS blood level was much higher than in HT-1 and HT-2 rats (Fig. 1). This finding may indicate not only a higher stress-reactivity of HACS in the high-threshold rats, but also its higher sensitivity to weak emotional stimulation. In the 2nd series (transcutaneous stimulation), the dynamics of stressor response corroborated the enhanced reactivity in LT-1 and LT-2 rats (Fig. 2). The maximum of CS secretion in LT rats was observed for 1, and for 3 h in HT rats. In addition, in LT rats high level of CS was maintained throughout the entire observation period, while in HT rats CS level decreased and did not differ from the original value on the next day.

With the use or high- and low-sensitive rats of two selection programs it was found that some features of HACS function, are common and some depend on the excitability of nervous system. It is unlikely that the increase in the basal CS level in LT-1 rats is caused by a decrease in the excitability threshold, because LT-2 rats did not differ by this characteristic from HT rats. From the same stress-reactivity and dynamics of HACS stressor response in the high-sensitive LT rats it can be concluded: 1) rats with a low excitability threshold of the nerve-muscle apparatus and midbrain reticular formation are characterized by higher stress-reactivity of HACS and by accelerated development of hormonal stress response; 2) the protracted hormonal stressor response in the high-threshold rats attests to attenuated sensitivity of HACS to feedback signals. More details on HACS inhibition via feedback mechanisms were obtained with the help of the dexamethasone test.

The dexamethasone test consists in determining changes in plasma CS level in response to the synthetic glucocorticoid dexamethasone. The test is negative if a certain dose of injected hormone decreases the basal CS level by more than 50%. We studied inhibition of basal and stressor HACS activities (Table 1). The differences were revealed only in the efficiency of inhibition of the HACS stressor activity. Injection of 20 μg/kg dexamethasone to HT rats led to an almost two-fold decrease in the stressor level

TABLE 1. Changes in Blood CS (nmol/liter) in after Injection of Dexamethasone (*M±m*)

| Line and number of rats | Basal CS level | | Stressor CS level | |
|---|---|---|---|---|
| | 1st day | 2nd day (dexamethasone, 10 μg/kg) | 1st day | 2nd day (dexamethasone, 20 μg/kg) |
| LT-1 (*n*=10) | 485±66.4* | 172±41.8** | 1028±112.6* | 834±71.3 |
| LT-2 (*n*=12) | 219±81.7 | 79±39.6** | 1075±157.6* | 723±156.5 |
| NT-1 (*n*=14) | 242±20.2 | 108±8.3** | 444±49.1 | 262.6±24.5** |
| NT-2 (*n*=14) | 265±22.5 | 121±14.9** | 545.5±82.8 | 312±29.4** |

Note. *$p<0.05$ compared in the HT rats; **the 1st day of testing.

of plasma CS, while LT rats the same dose of dexamethasone decreased the CS level only by 74%. The dexamethasone test showed that in HT rats subjected to stressor activation the sensitivity of HACS to the feedback signals is attenuated.

Enhanced stress-reactivity of HACS and accelerated development of hormonal stress response in high-sensitivity LT rats are probably related to decreased excitability threshold of the reticular formation, where general nonspecific activation is formed [12]. However, a decrease in of HACS sensitivity to feedback signals in high-sensitivity rats seems to be determined by the mechanisms that are independent on excitation. Some of these mechanisms may be involve the corticosteroid receptors in hypophysis and cerebral structures participating in the regulation of HACS activation [11]. Previously, we demonstrated the differences in cerebral content of CS-receptors in high- and low-sensitivity rats [3,8].

Our data point to important role of the nervous system excitability in the development of stress reaction of the organism to changes in environ mental.

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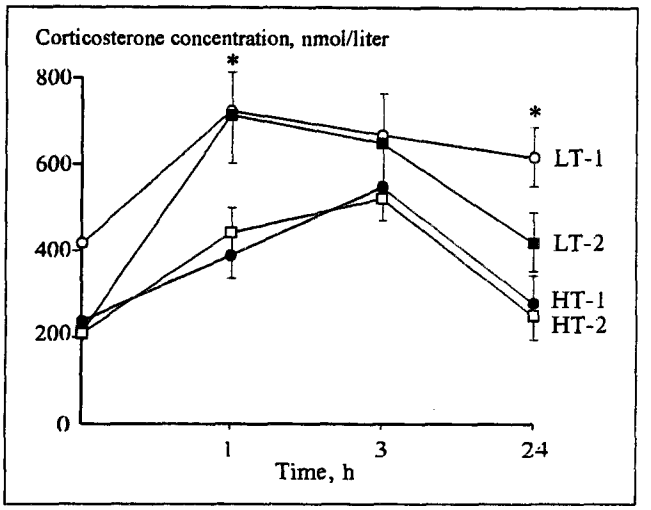


**Fig. 2.** Dynamics of plasma corticosterone in the line rats subjected to transcutaneous electric stimulation.

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