3. N. S. Kositsyn and M. M. Svinov, Byull. Éksp. Biol. Med., No. 5, 486 (1990).
4. V. S. Rusinov, O. M. Grindel', and N. N. Bragina, Structure and Function of the Archipaleocortex [in Russian], Moscow (1968), pp. 359-370.
6. M. Marin-Padilla, Cerebral Cortex, Vol. 1, New York (1984), p. 200.
7. G. M. Shepherd, The Synaptic Organization of the Brain, New York (1979).

SEX DIFFERENCES IN RESERVE CAPACITY OF THE RAT PITUITARY-ADRENOCORTICAL SYSTEM

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UDC 612.433+612.453/.06:613.863/-055.1/.2

KEY WORDS: sex differences, stress, corticosterone, reserve capacity, dynamics

The writers showed previously that sensitivity and mobility of adaptive systems is higher in females than in males in situations of short emotional stresses [1]. An important property of adaptive mechanisms is their reserve capacity, on which not only the intensity of responses to stress but also the velocity of recovery processes [3, 9] and, consequently, the readiness of the individual to respond adequately to new and unforeseen stress [13], depends. This quality, because of the abundance of stress situations in present-day human life, assumes particular significance.

The aim of the investigation was to study the dynamics of responses in female and male albino rats to complex emotional stress and sensitivity to additional stress at different times of the stress and poststress periods.

EXPERIMENTAL METHOD

Experiments were carried out on 370 animals. Complex emotional stress consisted of a combination of immobilization for 60 min in a constriction cage, vibration on a shaker, loud dissonant music, and a flashing light. The corticosterone levels in the adrenals and blood plasma, collected at decapitation of the rats 10 and 60 min after the beginning of stress, and again 20, 40, 120, 180, and 240 min after its end, were determined fluorometrically. Additional stress consisted of strict immobilization for 10 min, applied 60 min after the beginning of the basic stress, and again 40, 120, 180, and 240 min after its end. Analysis of the results included calculation of the coefficient of variation and Student's test [7]. Vaginal smears taken after decapitation were studied in the females.

EXPERIMENTAL RESULTS

Calculations of the coefficients of variation revealed homogeneity of the groups of animals relative to reactivity to stress, in groups both of males and females, irrespective of their stage of the sex cycle. Just as in our previous experiments [1], sensitivity of the females to stress was higher than that of the males. The corticosterone concentration in the adrenals (Fig. 1a) and plasma (Fig. 1b) in females 10 min after the beginning of stress showed an increase of 3.3 and 4.7 times respectively, and it was maintained at about the same level until the end of stress. In the males, 10 min after the beginning of stress, the concentration of the hormone in the adrenals (Fig. 2a) and plasma (Fig. 2b) was increased by 2.5 and 2.9 times, but by the 60th minute of stress, although the corticosterone level in the plasma remained high, in the adrenals it fell to basic values and was 3.5 times less

Department of Biochemistry and Biophysics, N. G. Chernyshevskii Saratov University. (Presented by Academician of the Academy of Medical Sciences of the USSR N. V. Sudakov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 348-350, April, 1991. Original article submitted September 5, 1990.

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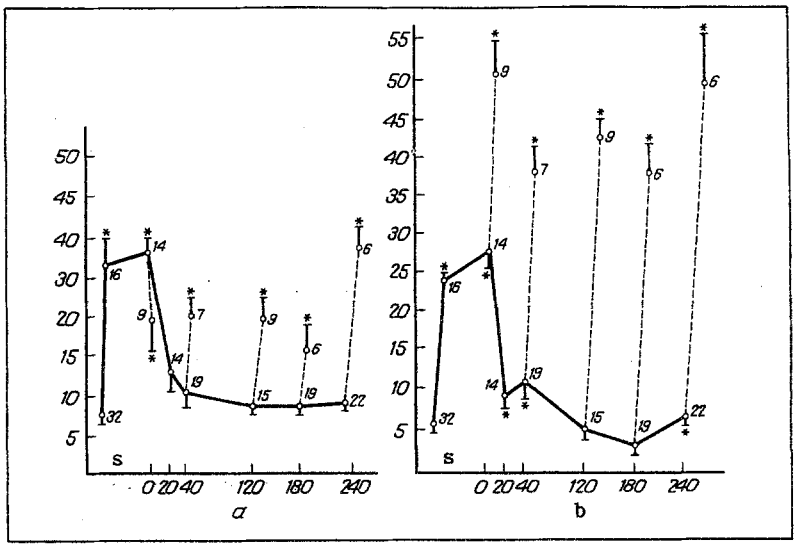

Fig. 1. Dynamics of corticosterone concentration in adrenals (a) and plasma (b) in females during basic (continuous line) and additional (broken line) stress. S) stress. Abscissa, time (in min); ordinate, corticosterone concentration in adrenals (in μg/g) and in blood plasma (in μg%). Asterisk indicates significant shift relative to control ($p < 0.05 - 0.001$). Number of animals given in parentheses.

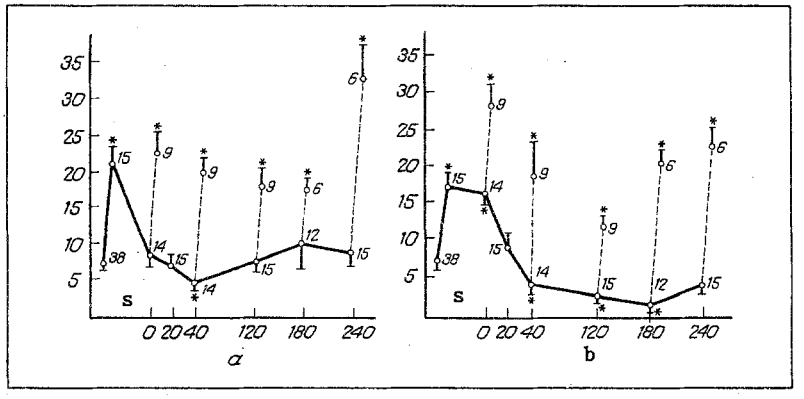

Fig. 2. Dynamics of corticosterone concentration in adrenals (a) and plasma (b) in males during basic (continuous line) and additional (broken line) stress. Legend as to Fig. 1.

than in females at this period. Thus, whereas in females increased sensitivity to emotional stress was combined with ability to maintain a high level of steroid production throughout stress, in males the initially depressed response to stress was accompanied by inhibition of steroid production which continued until the end of exposure to stress.

The recovery period also followed a different course in females and males. In females the hormone level returned to its initial value in the adrenals (Fig. 1a) after 20 min, but in the plasma (Fig. 1b) not until 120 min after the end of stress. The recovery processes in the females followed a smooth course without any disturbance of steroid homeostasis, for the corticosterone levels did not fall significantly below normal. The increase in the corticosterone concentration in the plasma 240 min after the end of stress evidently reflected the ability of the pituitary adrenocortical system to "join" the natural circadian rhythm of its activity with an increase in the hormone level (up to 13.3 $\pm$ 1.2 μg, according to our data) characteristic of the second half of the day.

In males the recovery period was accompanied by prolonged suppression of steroid production. The hormone concentration in the adrenals (Fig. 2a) 40 min after the end of exposure to stress was only half the basal level, and did not return to normal until the 120th minute of the poststress period. In the plasma (Fig. 2b) the corticosterone concentration 40, 120, and 180 min after the end of stress was 73, 39, and 17% of normal respectively, and after 240 min its level was returned approximately to the characteristic values for the first half of the day. Inertia of recovery processes in males with the characteristic deep depres-

sion of steroid production carries with it the risk of "expulsion" from the natural biorhythms, i.e., a condition of desynchronization develops, initiating pathological changes [9]. Prolonged suppression of steroid homeostasis, moreover, is accompanied by immunodepression [11].

Thus the adaptive systems of females, which demonstrate "functional excessiveness" during stress [5], ensure a smooth return, without suppression of steroid production, to the physiological norm. In males the stress response is significantly weaker and is accompanied by prolonged suppression of steroid production in the relaxation period.

In females the adaptive systems are responsible for high reactivity to immobilization for 10 min both at the height of the basic stress reaction and in the recovery period. Moreover, stressor levels of plasma corticosterone reached 37.3 ± 3.8 — 51.1 ± 4.0 μg% (Fig. 1b), significantly higher than the corticosterone level during this kind of stress under ordinary conditions (21.6 ± 2.8 μg%). In males, additional stress also evoked responses (Fig. 2a, b). However, increased reactivity to additional stress was manifested only at the height of the basic stress reaction: the plasma corticosterone level rose to 27.5 ± 2.4 μg% (Fig. 2b), compared with 13.8 ± 2.2 μg under ordinary conditions. Increased sensitivity of females and males to additional stress at the height of the basic stress reaction revealed the common principles of working of the adaptive mechanisms: the reserve capacity of the adaptive systems and absence of their refractoriness. It is important to emphasize that at all times of testing of the reserve capacity, corticosterone levels in the plasma were 2-4 times higher in females during stress than in males.

Consequently, ability to respond to additional stress against the background of previous stress is preserved in both females and males, indicating that this effect is biologically meaningful. Suppression of steroid homeostasis in males in the poststress period is evidently a preventive measure, ensuring an adequate response to the new stimulus. In females a full and effective response to unforeseen stress does not require suppression of steroid production in the recovery period after previous stress.

Thus the dynamics of stress and poststress changes in the intensity of steroid production and of reactivity to additional stress is evidence of the increased reserve capacity of the adaptive systems of females compared with males. The validity of this conclusion is confirmed by the positive correlation between individual stress-reactivity and reserves of adaptive capacity, discovered within the same (male) sex [6, 12]. The data obtained provide an explanation for the more successful adaption of women to climatogeographic conditions in different regions [8], to production work conditions [4], and the more effective medical rehabilitation of women compared with men [2].

Considering the higher levels of catecholamines [14] and opioid peptides [15] in the brain in women compared with men, and the role of these substances in individual resistance to emotional stress [10], it can be tentatively suggested that sex differences and individual differences in stress reactivity are produced, at least in part, by common mechanisms.

LITERATURE CITED

1. T. G. Anishchenko, S. N. Burshina, and L. N. Shorina, Stress and Immunity [in Russian], Leningrad (1989), p. 220.
2. V. N. Vasil'ev and V. S. Chugunov, Sympathico-Adrenal Activity in Various Human Functional States [in Russian], Moscow (1985).
3. A. A. Viru, Hormonal Mechanisms of Adaptation and Training [in Russian], Leningrad (1981).
4. V. P. Kaznacheev, R. M. Baevskii, and A. P. Berseneva, Prenosologic Diagnosis in Mass Population Survey Practice [in Russian], Leningrad (1980).
5. M. G. Kolpakov and M. G. Polyak, Endocrine Mechanisms of Regulation of Adaptive Processes [in Russian], Novosibirsk (1975).
6. N. G. Lopatina, N. D. Shiryaeva, A. I. Vaido, and D. A. Kulagin, Ontogenetic and Genetic-Evolutionary Aspects of Neuroendocrine Regulation of Stress [in Russian], Novosibirsk (1988), p. 941.
7. I. V. Polyakov and N. S. Sokolova, Textbook of Practical Medical Statistics [in Russian], Leningrad (1975).
8. E. P. Sivkov, Ecologo-Physiological Problems in Adaption [in Russian], Moscow (1988), p. 208.
9. S. I. Stepanova, Biorhythmologic Aspects of the Adaptation Problem [in Russian], Moscow (1986).
10. K. V. Sudakov, Patol. Fiziol., No. 1, 3 (1989).
11. I. D. Surkina, E. P. Gotovtseva, L. V. Kostina, et al., The Problem of Evaluation and Prediction of Functional States of the Individual in Applied Physiology [in Russian], Frunze (1988), p. 251.
12. A. A. Filaretov, Yu. G. Balashov, A. I. Bogdanov, et al., Ontogenetic and Genetic-Evolutionary Aspects of Neuroendocrine Regulation of Stress [in Russian], Novosibirsk (1988), p. 181.
13. A. Armario, J. Hidalgo, and M. Giralf, Neuroendocrinology, **47**, No. 3, 263 (1988).

14. A. Siddique and D. Gilmore, Acta Endocrinol. (Copenhagen), **118**, 483 (1988).
15. S. L. Wardlow, Endocrinology, **119**, No. 1, 19 (1986).

EFFECT OF PN 200-110 ON PENICILLIN-INDUCED EPILEPTIC ACTIVITY IN THE RAT CEREBRAL CORTEX

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UDC 616.831.31-009.12-02:615.334]-092.9-092-02:615.22:547.822.1

KEY WORDS: Ca^{2+} antagonists, PN 200-110, focal epileptic activity, penicillin

Since entry of Ca^{2+} into the neuron plays an important role in the mechanisms of hyperactivation of neurons and the genesis of epileptic activity (EA) [7, 8, 13], interest in Ca-channel blockers as possible antiepileptic agents has increased [4, 9-11].

The aim of this investigation was to study the effect of one such blocker, namely PN 200-110 (the preparation was generously provided for testing by the firm of "Sandoz," Switzerland), a substance belonging to the 1,4-dihydropyridine class, on activity of a penicillin-induced epileptic focus in the cerebral cortex of unanesthetized, unrestrained animals.

EXPERIMENTAL METHOD

Experiments were carried out on 65 male Wistar rats weighing 250-300 g. Under hexobarbital anesthesia (150 mg/kg, intraperitoneally) and local procaine anesthesia, 24 h before the experiment a burr-hole measuring 2 × 4 mm was drilled in the animal's skull above the sensomotor cortex of the left cerebral hemisphere, the dura was removed from that part, and monopolar cortical silver electrodes were applied to record electrical activity (electrocorticogram — ECoG). The reference electrode was inserted into the nasal bones. The external leads of the electrodes were fixed to the surface of the skull with "Noracryl" dental paste and a capsule was formed around the burr-hole. To prevent exposed parts of the brain from drying the capsule was filled with physiological saline and covered above by a waterproof film which was fixed around the edges with Noracryl. Next day, to create foci of EA the film was removed from the capsule and filter paper soaked with a solution of the sodium salt of benzyl penicillin in a concentration of 20,000 IU/ml was applied to the exposed area of the cortex. The ECoG was recorded on an EEG8S electroencephalograph (Hungary) from two unrestrained animals with foci of EA simultaneously: one animal had been given PN 200-110, the other the solvent, dimethyl sulfoxide (DMSO). The solution of PN 200-110 was made up immediately before injection in a dark room illuminated with red light.

There were three series of experiments. In the experiments of Series I the preparation was injected intraperitoneally in a dose of 2 mg/kg against a background of stable EA in the focus (25-35 min after penicillin application). In the experiments of Series II the preparation also was injected intraperitoneally in a dose of 5 mg/kg, 25 min before penicillin application. The control animals received DMSO in the same volume (0.1 ml) under similar experimental conditions. In the experiments of Series III the preparation was injected into the cerebral ventricles in a dose of 1 and 10 nmoles in 2 μl of a 50% solution of DMSO. The injection was given by means of a steel cannula (concentric configuration, external diameter 0.82 mm), implanted into the lateral ventricle, taking coordinates from the atlas [12], 20 min before penicillin application. The control animals received 50% DMSO solution in the same volume. The location of the cannula was verified after each experiment.

Research Institute of General Pathology and Pathological Physiology, Academy of Medical Sciences of the USSR, Moscow. Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 111, No. 4, pp. 351-353, April, 1991. Original article submitted September 7, 1990.