that factors inducing reduction and destabilization of a pathological (epileptic) system may prove useful from the therapeutic point of view, by facilitating the suppression of the pathological system by natural mechanisms of recovery.

LITERATURE CITED

1. G. N. Kryzhanovskii, Zh. Nevropatol. Psikhiatr., No. 11, 1730 (1976).
2. G. N. Kryzhanovskii, Vestn. Akad. Med. Nauk SSSR, No. 7, 37 (1979).
3. G. N. Kryzhanovskii, General Pathology of the Nervous System [in Russian], Moscow (1980).
4. G. N. Kryzhanovskii, R. F. Makul'kin, and A. A. Shandra, Byull. Éksp. Biol. Med., No. 1, 5 (1977).
5. G. N. Kryzhanovskii, R. F. Makul'kin, and A. A. Shandra, Zh. Nevropatol. Psikhiatr., No. 4, 547 (1978).
6. V. M. Okudzhava, Basic Neurophysiological Mechanisms of Epileptic Activity [in Russian], Tbilisi (1969).
7. M. Demetrescu and M. Demetrescu, Electroencephalogr. Clin. Neurophysiol., 14, 37 (1962).
8. T. Reinoso-Suarez, Topographischer Hirnatlas der Katze, Darmstadt (1961).

ROLE OF MONOAMINES IN RESTORATION OF CNS FUNCTION AFTER EXPERIMENTAL INJURY TO THE FRONTAL CORTEX

G. A. Romanova, N. L. Vekshina, and A. M. Sovetov

UDC 616.831.31-001.092.9-093:577.175.823

KEY WORDS: monoamines; extirpation; compensation; serotonin; noradrenalin; 5-hydroxytryptophan.

The problem of recovery of disturbed functions after organic and functional injuries to the CNS is still an important one for experimental neuropathology and also for clinical neurosurgery. It can be firmly accepted that one of the causes of many pathological states of the CNS is a disturbance of the functions of mediator systems [1-4, 6, 7].

However, there have been few studies of changes in the concentrations of neurohumoral factors during the development of pathological and compensatory processes in the CNS [5, 8, 9]. Changes in the concentrations of monoamines in the brain have been described in pathological states, but the mechanism of participation of physiologically active substances in repair processes in the CNS remains unexplained. Yet the importance of this problem from both the theoretical and the practical points of view will be obvious.

The aim of this investigation was to study the role of serotonin (5-HT) and noradrenalin (NA) in the mechanisms of recovery in the CNS after experimental injury to the cortex of the frontal lobes.

EXPERIMENTAL METHOD

Experiments were carried out on 20 male abino rats weighing 180-200 g under chronic conditions. Conditioned motor food reflexes with two-way reinforcement to photic and acoustic stimuli were formed in the animals. Conditioned reflexes were considered to have been formed if 90-100% of correct responses were obtained on three successive days. When conditioning was complete in the rats of the experimental group, the frontal cortex was removed bilaterally. Intact animals, in which the same stereotype of conditioned reflexes was formed served as the control. The experimental rats in the stage of recovery of the original level of conditioned reflexes (14-20 days after the operation) and control animals were decapitated. The brain was removed and frozen in liquid nitrogen. The concentrations

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' Eksperimental'noi Biologii i Meditsiny, Vol. 90, No. 11, pp. 536-538, November, 1980. Original article submitted December 19, 1979.

0007-4888/80/9011-1500$07.50

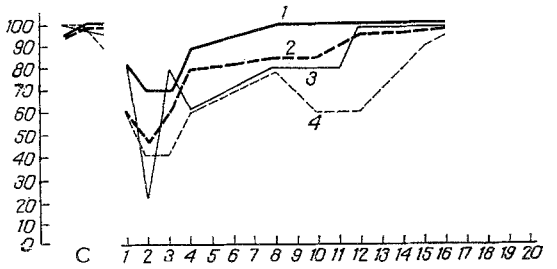

Fig. 1. Level of conditioned reflexes in rats after extirpation of frontal cortex. C) Level of reflexes before operation. Changes in conditioned reflexes to photic (1) and acoustic (2) stimuli in rats after extirpation of frontal cortex, with daily administration of 5-HTP to rats after operation and in animals not receiving 5-HTP after the same operation, also to photic (3) and acoustic (4) stimulation. Abscissa: days after extirpation of frontal cortex. Ordinate: level of conditioned reflexes, in % of preoperative period (100%).

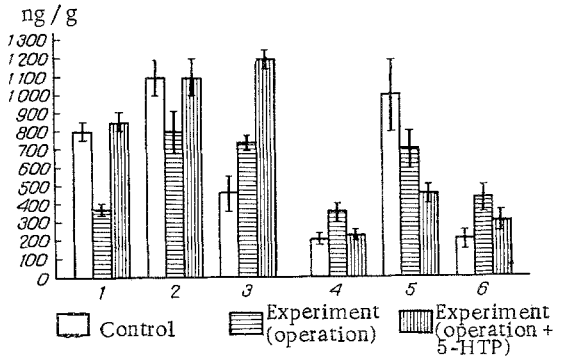

Fig. 2. Changes in monoamine concentration in brain structures of rats during recovery of conditioned reflexes after extirpation of frontal cortex. Serotonin (left) and noradrenalin (right) concentrations in cortex (1; 4), hypothalamus (2; 5), and brain stem (3; 6) of rats, in ng/g wet weight of brain tissue.

of 5-HT and NA were determined spectrofluorometrically [10] in the cerebral cortex, hypothalamus, and brain stem. The results of the biochemical tests were subjected to statistical analysis by Student's t-test.

EXPERIMENTAL RESULTS

The results showed that extirpation of the frontal cortex of the rats caused a decrease in the number of correct responses to both photic and acoustic stimuli; the decrease in the number of correct responses to the acoustic stimulus was greater than to switching on the light. Meanwhile the animals exhibited motor excitation, in the form of running from one feeding bowl to the other in the intervals between stimuli, and pendulum-like movements. On the days after the operation, recovery of the conditioned reflexes and of the animals' general behavior was observed. However, this process occurred in waves and the number of correct responses reached its initial level after 15-20 days.

Restoration of disturbed conditioned-reflex activity was studied in experimental animals of the other group against the background of daily (1 h before the beginning of the

experiment) injection of the serotonin precursor 5-hydroxytryptophan (5-HTP), in a dose of 15 mg/kg intraperitoneally. Comparison of the dynamics of changes in the conditioned reflexes of the animals of the two groups showed that administration of the 5-HT precursor to rats led to improvement of the course of recovery in the CNS. Against the background of 5-HTP administration, recovery of the original, preoperative level of the reflexes was complete by the 9th-10th days (Fig. 1). The animals no longer ran to the feeding bowl in the interval between stimuli and the pendulum-like movements ceased, i.e., normalization of higher nervous activity occurred sooner and was more stable in character.

Analysis of the 5-HT and NA concentrations in the brain at the stage of recovery of conditioned-reflex activity in the animals after operation showed that their concentrations in all brain structures studied (cerebral cortex, brain stem, hypothalamus) differed significantly from their concentration in the control animals. A marked fall in the 5-HT level (in the cortex to 44%) in animals after removal of the frontal cortex, and some increase in the NA concentration in the same brain structures except the hypothalamus, in which it had a tendency to fall, will be noted (Fig. 2).

Injection of 5-HTP into rats after extirpation of the frontal cortex led to an increase in the 5-HT concentration in all brain structures studied, which was most marked in the cortex, where it was more than doubled compared with the animals undergoing the operation and not receiving 5-HTP. The NA level was unchanged under the influence of 5-HTP and remained below the control in the hypothalamus and higher in the cortex and brain stem (Fig. 2). If the dynamics of the changes in conditioned-reflex activity in the rats after extirpation of the frontal cortex, as described above, is compared with the results of biochemical studies of the brain of these animals at the stage of completion of compensation and repair processes it can be concluded that the course of recovery is accompanied by marked shifts in the 5-HT and NA levels in these brain structures. It can be concluded from these facts that the increase in 5-HT concentration in these structures leads to the more rapid normalization of the disturbed brain functions and, in particular, the more rapid recovery of conditioned motor food reflexes.

Neurohumoral processes taking place at cortical and subcortical levels are among the important mechanisms of integrative brain activity. The role of neural mediators is particularly important in the case of disturbance of brain activity. The present experiments showed that the development of recovery of disturbed functions is improved by normalization of the concentrations of physiologically active substances in the corresponding zones of the brain. It must be emphasized that restoration of the normal monoamine concentrations in the brain structures helps to eliminate a defect or disturbance of function which has arisen. The results of these experiments suggests that the compensatory powers of the brain may be increased by the use of various physiologically active substances and pharmacological agents with an appropriated oriented action on brain metabolism of biogenic amines.

LITERATURE CITED

1. N. P. Bekhtereva (ed.), The Role of Deep Structures of the Human Brain in Mechanisms of Pathological Reactions [in Russian], Leningrad (1965).
2. N. P. Bekhtereva (ed.), Deep Structures of the Human Brain under Normal and Pathological Conditions [in Russian], Moscow–Leningrad (1966).
3. E. A. Gromova, in: Memory and Trace Processes [in Russian], Pushchino (1974), pp. 114-115.
4. E. A. Gromova, T. P. Semenova, O. N. Li, et al., Zh. Vyssh. Nerv. Deyat., No. 2, 261 (1979).
5. I. K. Kazakov, N. A. Rubanova, and T. V. Dergunova, Tr. Gork. Med. Inst., No. 77, 137 (1976).
6. N. K. Popova, E. V. Naumenko, and V. G. Kolpakov, Serotonin and Behavior [in Russian], Novosibirsk (1978).
7. W. B. Essman, in: Biology of Memory, Budapest (1971), p. 213.
8. R. G. Robinson, W. Y. Shoemaker, and F. E. Bloom, Nature, 255, 332 (1975).
9. R. G. Robinson, F. E. Bloom, and L. F. Battenberg, Brain Res., 132, 259 (1977).
10. B. Welsh and A. Welch, Anal. Biochem., 30, 161 (1969).