7. F. Z. Meerson, M. V. Shimkovich, and V. A. Khorunzhii, Byull. Éksp. Biol. Med., No. 3, 272 (1980).
8. V. Yu. Ostrovskii, Éksp. Khir., No. 4, 62 (1972).
9. O. Desiderato and M. Testa, Physiol. Behav., 16, 67 (1976).
10. E. H. Sonnenblick, Am. J. Physiol., 202, 931 (1962).

EFFECT OF ELECTRICAL STIMULATION OF NUCLEUS CAUDALIS RETICULARIS PONTIS ON FOCI OF EPILEPTIC ACTIVITY IN THE CORTEX

G. N. Kryzhanovskii,* R. F. Makul'kin, A. A. Shandra, and B. A. Lobasyuk

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KEY WORDS: epileptic focus; epileptic complex; pathological system; antiepileptic system; "antisystem"; neocortex; nucleus caudalis reticularis pontis.

Stimulation of nucleus caudalis reticularis pontis (NCRP) has been shown to depress epileptic activity [6, 7]. To elucidate the special nature of this effect it was decided to study it in the presence of different forms of epileptic activity in the cerebral cortex: a single epileptic focus and a complex of foci of epileptic activity [4, 5], constituting a unique form of pathological system [2, 3], which arises under the influence of a hyperactive determinant structure [1-3] or determinant epileptic focus [4].

EXPERIMENTAL METHOD

Acute experiments were carried out on cats. Under ether anesthesia bipolar constantan electrodes, 120 μ in diameter with interpolar distance of 0.5 mm, were inserted into NCRP, and a monopolar electrode 250 mm in diameter was inserted into the central periaqueductal gray matter in accordance with coordinates of a stereotaxic atlas [7, 8]. The central periaqueductal gray matter was destroyed by coagulation (2-4 mA, 15-20 sec). The eye was then drained and the bones of the calvaria and orbit were removed, to provide wide access to different parts of the frontal region of the neocortex of one hemisphere. Scattered foci of epileptic activity were created by application of a piece of filter paper (2 mm^2) soaked in 0.1-0.5% strychnine nitrate solution. Foci of this sort were created in different parts of the coronal and anterior, posterior, and middle sigmoid gyri. A focus of more powerful epileptic activity was created in the orbital or coronal gyrus by application of a 1-3% solution or a crystal of strychnine. After the appearance of the foci the application of strychnine ended and the filter paper with strychnine was removed. Potentials were derived by a monopolar technique; the reference electrode was fixed in the nasal bones, and cotton threads soaked in Ringer's solution served as active electrodes. Potentials were recorded on the 4-ÉÉG-3 ink-writing electroencephalograph. Electrical stimulation (ES) of NCRP was carried out with series of square pulses (0.5 msec, 220 Hz, 3-5 V), in sessions 10-20 sec in duration, separated by intervals of 2 min. The locations of the electrode tip in the subcortical structures were determined histologically.

EXPERIMENTAL RESULTS

In the experiments of series I the effect of stimulation and destruction of NCRP on activity of a single epileptic focus was studied. An epileptic focus (Fig. 1A) was created in the cortex of the posterior sigmoid gyrus with the aid of a 1% solution of strychnine (Fig. 1A). ES of NCRP was shown to completely suppress epileptic discharges in the focus;

*Corresponding Member, Academy of Medical Sciences of the USSR.

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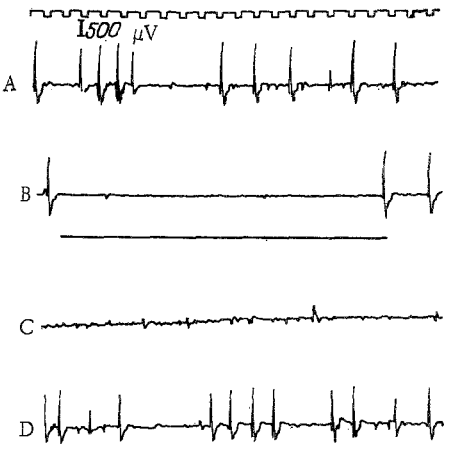

Fig. 1. Effect of stimulation and coagulation of NCRP on a cortical epileptic focus. A) Epileptic discharges in posterior sigmoid gyrus after application of 1% strychnine solution; B) inhibition of discharges during ES of NCRP; period of ES indicated by horizontal line; C) electrical activity in cortex of posterior sigmoid gyrus after 12 sessions of ES; D) restoration of epileptic discharges 3 min after electrical coagulation of NCRP (5 mA, duration 2 min). Here and in Figs. 2 and 3, signal calibration 500 μV, time marker 1 sec.

after discontinuation of ES epileptic activity was restored (Fig. 1B). Total inhibition of epileptic activity in the focus was produced after 10-12 sessions of stimulation and it was not restored even after ES had ended (Fig. 1C). Electrical coagulation of the region of NCRP under these conditions led to recovery of the epileptic discharges in the focus (Fig. 1D). These experiments showed that ES of the nucleus completely suppresses epileptic activity of a single focus and that this effect is connected with activation of the nucleus and not with weakening of the action of strychnine, for after coagulation of the nucleus epileptic activity in the focus reappeared.

In experiments of series II the effect of ES of NCRP on epileptic activity of a single focus and of a complex of foci was investigated. A single focus created by application of 1% strychnine solution to the middle sigmoid gyrus (zone 1) was completely suppressed during ES of NCRP (Fig. 2A). After this testing with ES two additional foci were created by application of a weaker (0.1%) solution of strychnine in zones 2 and 3. Under the influence of a more powerful determinant focus in zone 1 these foci joined with it to form a single epileptic complex with synchronized activity, the pattern of which was determined by the determinant focus (the process of formation of a complex and the role of the determinant focus were described in detail previously [4, 5]). Under these conditions ES of NCRP, with the same or with higher parameters of stimulation, did not change the amplitude-frequency characteristics of discharges in the foci (Fig. 2B). Meanwhile, sessions of stimulation had an inhibitory effect on the level of epileptic activity; this effect, moreover, was exhibited first in one of the dependent (usually that located farthest from the determinant) foci (in zone 3); when the decrease in amplitude and frequency of the discharges was sufficiently stable, ES evoked considerable or virtually total suppression of epileptic activity in that focus. At the same time activity also was reduced in the other dependent focus (zone 2) (Fig. 2C). With further application of ES (usually 10-15 sessions) activity disappeared in the focus in zone 3 and was considerably reduced in zone 2 (Fig. 2D). In this period ES of the nucleus led to total suppression of epileptic activity in all dependent foci (zones 2 and 3), but activity remained in the determinant focus (Fig. 2E). In the next stage ES suppressed activity in zone 1 (the former determinant focus) also (Fig. 2F).

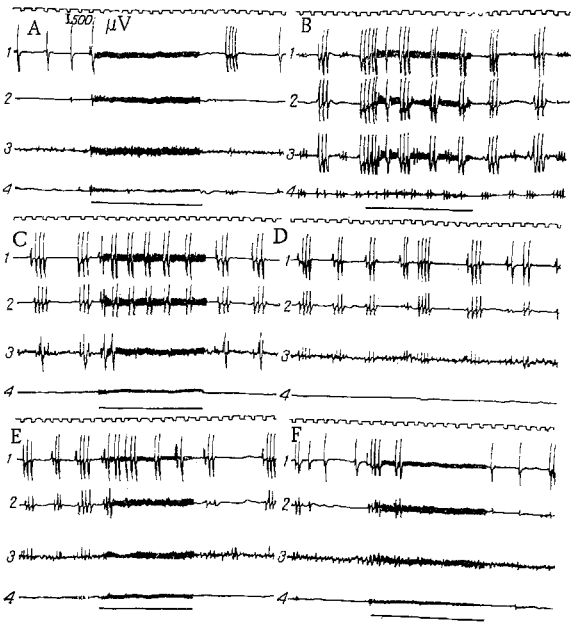

Fig. 2. Effect of ES of caudal nucleus on activity of a single focus and epileptic complex in the cerebral cortex. A) Focus of epileptic activity in zone 1 after application of 1% strychnine solution; inhibition of discharges during ES of nucleus; B) formation of epileptic complex from foci in zones 1, 2, and 3 after additional application of 0.1% strychnine solution to zones 2 and 3; ES of nucleus with the same parameters of stimulation does not lead to inhibition of any focus of the complex; C) reduction in amplitude of discharges in zone 3 and inhibition of activity in focus in zone 3 due to ES of nucleus after preliminary sessions of ES; D) 12 min after beginning of sessions of ES; E) inhibition of discharges in zone 2 in response to ES; F) paroxysmal discharges preserved in determinant focus (zone 1), but they are suppressed by ES. Here and in Fig. 3 zones correspond to: 1) middle, 2) anterior and 3) posterior sigmoid gyri, 4) coronal gyrus.

In the experiments of series III the role of the number of foci included in an epileptic complex in the suppression of its activity in response to ES was studied. By application of 1% strychnine solution to zone 1 and of 0.1% strychnine solution to zone 2 a complex consisting of two foci was created; during ES of NCRP both foci of the complex were suppressed (Fig. 3A). The creation of a complex of three foci by application of 0.1% strychnine solution to zones 3 and 4 rendered ES of NCRP ineffective; it did not suppress epileptic activity but merely reduced the frequency of the epileptic discharges in all foci of the complex (Fig. 3B, zones 1-3). Meanwhile the focus in zone 4, which was not a component of the epileptic complex and which generated asynchronous discharges independently, was completely suppressed during ES (Fig. 3B). Blocking the focus in zone 3 by local application of 6% pentobarbital solution to this zone (Fig. 3C), i.e., reduction of the complex to the two original foci, had the result that ES of NCRP under these conditions suppressed activity in both foci of the complex, and also in the focus in zone 4 (Fig. 3D).

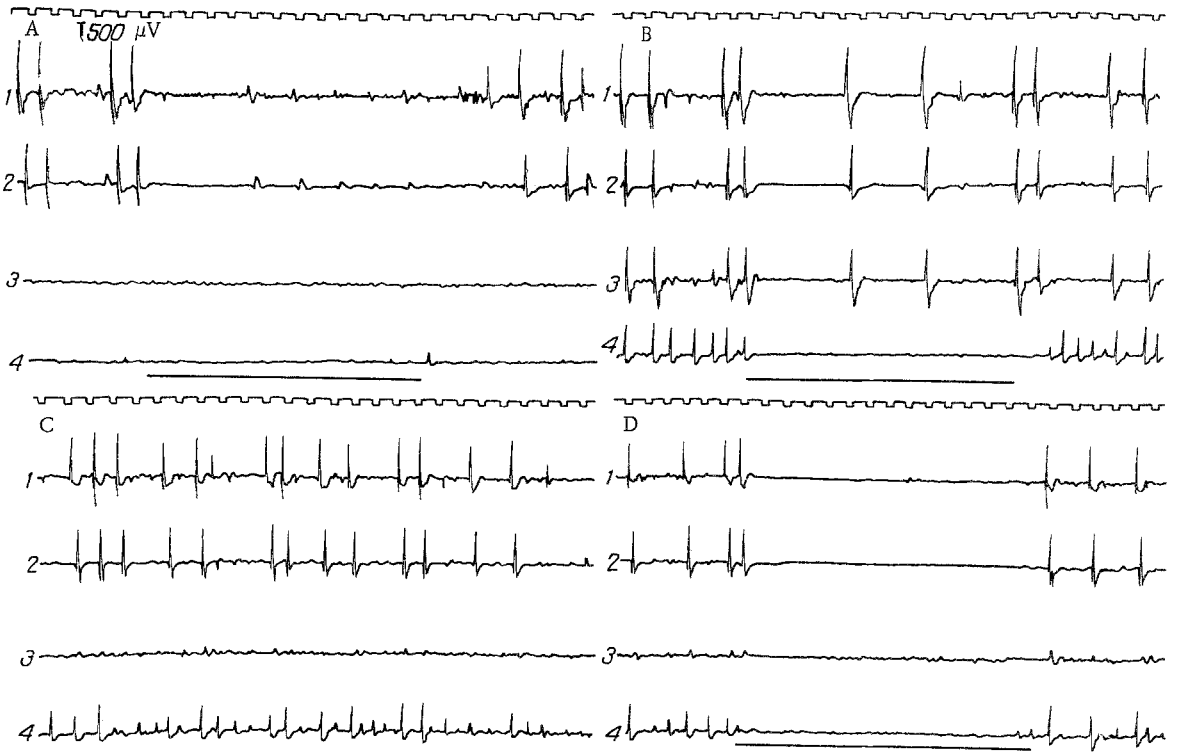

Fig. 3. Effect of ES of NCRP on epileptic foci within and without a complex. A) Suppression of epileptic discharges in a complex of two foci in zone 1 (application of 1% strychnine solution) and in zone 2 (application of 0.1% strychnine solution) during ES of caudal nucleus; B) suppression of epileptic activity in zone 4 (isolated focus) and reduction in discharge frequency in foci of complex (zones 1, 2, and 3) during ES of NCRP; C) blocking of epileptic focus in zone 3 by application of 6% pentobarbital solution (2 min after application); D) suppression of epileptic activity in foci of complex (zones 1 and 2) and in isolated focus (zone 4) during ES of caudal nucleus. Period of ES of NCRP indicated by horizontal line.

A number of conclusions can be drawn from the results of these experiments. They showed that ES of NCRP in fact suppresses epileptic activity in the cortex, in agreement with observations by other workers [6, 7]. It can be tentatively suggested that this nucleus is an important component of the "antiepileptic system" of the brain. After sufficiently long stimulation of NCRP (sessions of ES) a comparatively stable effect of suppression of epileptic activity arises, evidence of a state of prolonged activity of the nucleus, which suggests that an excitation generator [1-3], maintaining the activity of the nucleus, has arisen in it. Abolition of the generator by coagulation of the region of NCRP leads to resumption of epileptic activity in the cortex. The results of these experiments confirmed the view that "antisystems" play a role in the suppression of activity and in the prevention of formation of pathological systems.

At the same time, these investigations showed that the resistance of a single epileptic focus differs from that of a complex of epileptic foci. The complex is a pathological system [2, 3] which possesses new mechanisms of stabilization, and the more powerful the pathological system, the larger the number of structures it includes (the number of epileptic foci in the complex), the more resistant it is to inhibitory influences and, in particular, to inhibitory influences from the "antiepileptic system." Reduction of the pathological system weakens its resistance, and in that case influences of the "antisystem" become effective. It is interesting to note that reduction of a pathological system can be brought about both by direct intervention on it (removal of one or more foci) and by continuous activation of the "antisystem" (sessions of ES of NCRP).

The results of these experiments are interesting also from the practical point of view. They are evidence that destruction and suppression of a pathological epileptic system can be facilitated not only by eradication of the determinant structure (determinant focus), as was shown previously [4, 5], but also by reduction of the system through suppression of its components and destabilization of the system by activation of its "antisystem." This means

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

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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.

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