So far as the investigations of serum enzyme activity are concerned (Table 2) short-term crushing of the soft tissues preceded by administration of adrenalin to the rats led to a marked increase in activity of DNase, acid phosphatase, and aryl sulfatase; the degree of elevation of activity of all the enzymes was similar (activity was more than doubled compared with the control). With an increase in the period of crushing to 30 min activity of the acid DNase and phosphatase in the blood fell considerably (to 121 and 166% of the intact control, respectively), whereas aryl sulfatase activity remained at its previous level. With a further increase in the period of crushing of the soft tissues the dynamics of changes in the activity of these enzymes in the blood differed. DNase activity reached almost the control level after 1 and 1.5 h of crushing (113% of the control), but rose sharply again after crushing for 2 h (to 212%) and remained close to this level until the end of the investigation, when it fell again to 133%. Activity of aryl sulfatases A and B fell to 146% of the intact control during crushing of the tissues for 1.5 to 3 h, and then rose again after 3.5 h, to reach a maximum (258%) at the end of the experiment. Blood acid phosphatase activity remained high throughout the experiment and reached its highest peak 3.5-4 h after application of the forceps (258% of the control). Unlike the other two enzymes, blood acid RNase activity of rats traumatized after injection of adrenalin not only was not increased but, on the contrary, it was reduced by 21% below the control level after short-term crushing and remained somewhat reduced (by 10-15%) throughout the experiment, but returned to the control level at the end of the investigation.

The experiments thus showed that parenteral injection of adrenalin before infliction of trauma on animals does not cause any qualitative changes in the response of the liver lysosomes to trauma. This response was manifested as quantitative changes — activation of the lysosomal hydrolases studied and disturbance of stability with release of the enzymes into the cytoplasm of the hepatocytes, and from them into the systemic circulation.

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EFFECT OF ELECTRICAL STIMULATION OF THE DENTATE NUCLEUS ON CORTICAL EPILEPTIC FOCI

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Suppression of neuropathological syndromes on activation of corresponding brain structures is highly relevant to the understanding of activity both of pathological systems, which

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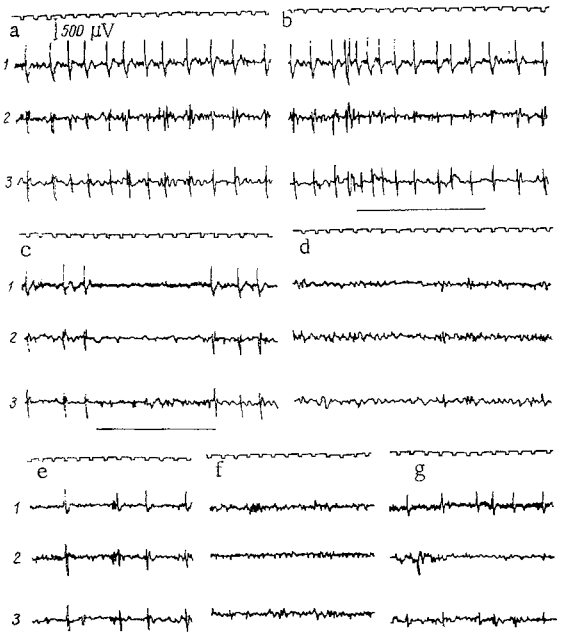

Fig. 1

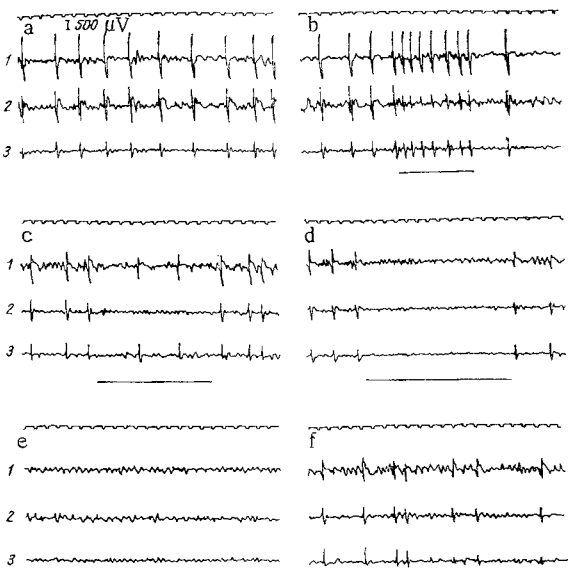

Fig. 2

Fig. 1. Effect of ES of DN on a relatively weak epileptic focus in anterior sigmoid gyrus, focus of induced seizure activity in the hemisphere contralateral to the stimulated nucleus, and on a "mirror" epileptic focus. a) 12 min after application of penicillin solution (16,000 Units/ml) to zone 1, after appearance of discharges in zones 1, 2, and 3 the penicillin was removed; b) decrease in amplitude of conducted discharges in zone 2 during ES of DN 6 min after end of penicillin application to zone 1 (first session of ES); c) suppression of epileptic discharges in zones 1, 2, and 3 during repeated ES of DN 5 min after beginning of ES of DN (third session of ES); d) 50 sec after c — absence of epileptic activity; e) recovery of epileptic activity in foci 30 sec after d; f) complete suppression of epileptic activity after next, fifth, ES of DN, recording made 1 min after end of ES; g) 7 min after electrical coagulation of DN (9 min after end of last ES). 1) Anterior sigmoid gyrus, 2) posterior sigmoid gyrus, 3) "mirror" focus. Parameters of ES: 300 Hz, 0.25 msec, 3.5 V. Time marker 1 sec, calibration 500 μV.

Fig. 2. Effect of ES of DN on a powerful epileptic focus in anterior sigmoid gyrus, focus of induced seizure activity in hemisphere contralateral relative to stimulated DN, and on a "mirror" epileptic focus. a) 9 min after application of penicillin solution (40,000 Units/ml) to zone 1, after appearance of discharges in zones 1, 2, and 3 penicillin was removed; b) increase in frequency of discharge generation in zones 1, 2, and 3 and decrease in discharge amplitude in zone 2 during ES (first session of ES, 5 min after end of penicillin application); c) reduction in amplitude and frequency of discharges in zones 1 and 3 and suppression in zone 2 during repeated ES of DN (fifth session of ES, 16 min after end of penicillin application); d) suppression of epileptic discharges in zones 1, 2, and 3 during ES of DN (seventh session of ES, 21 min after end of penicillin application); e) complete suppression of discharges in all zones after ninth session of ES of DN, 25 min after end of penicillin application; f) 6 min after electrical coagulation of DN. Remainder of legend as to Fig. 1.

lie at the basis of neuropathological syndromes, and of physiological antisystems responsible for the effects of suppression of these syndromes and leading to a state of relative functional homeostasis [1]. According to some workers [12, 13] electrical stimulation (ES) of the dentate nucleus in the cerebellum inhibits epileptic activity in the cerebral cortex. Meanwhile a twofold influence — both inhibitory and activating — of the dentate nucleus on epileptic activity has been described during ES [6].

In the investigation described below effects of ES of the dentate nucleus (DN) of the cerebellum on ipsilateral and contralateral foci of epileptic activity in the cerebral cortex were studied.

EXPERIMENTAL METHOD

Acute and chronic experiments were carried out on 21 cats. Under ether anesthesia bipolar electrodes were implanted in DN in accordance with coordinates taken from the atlas [14], after which the cranial bones in the vault of the skull were trephined to provide access to different parts of the frontal and parietotemporal zones of the neocortex of both hemispheres. The experiments began 1.5-2 h after the end of administration of ether. The animals were immobilized (D-tubocurarine, 0.12-0.28 mg/kg) and artificially ventilated. A single epileptic focus was created by application of a piece of filter paper measuring 2 × 2 mm, soaked in a solution of the sodium salt of benzyl penicillin (16,000 and 40,000 Units/ml) to the anterior, posterior, and middle sigmoid, coronal and orbital gyri, and also in different zones of the lateral, ectosylvian, and suprasylvian gyri. Potentials were derived by a monopolar technique, the reference electrode was secured to the nasal bones, and the active electrodes were cotton threads soaked in Ringer's solution. Potentials were recorded on a 4-ÉÉG-3 ink-writing electroencephalograph. ES of DN was carried out by means of an ÉSU-1 electrostimulator, with series of square pulses (0.25-0.5 msec, 100-300 Hz, 2-7 V), in sessions 5-10 sec in duration, with an interval of 2-3 min between sessions. The position of the electrodes was verified histologically. The results were subjected to statistical analysis and differences between the experimental and control groups were assessed by nonparametric tests [5].

EXPERIMENTAL RESULTS

In the experiments of series I (15 experiments) the effect of stimulation and destruction of DN on activity of the epileptic focus and induced seizure discharges in the cortex of the ipsi- and contralateral hemispheres was investigated. Potentials with an amplitude of 400-800 μV, reaching a value of 1.0-1.5 mV during the next 5-8 min, appeared 6-10 min after application of penicillin solution (16,000 Units/ml) to the anterior sigmoid gyrus. The frequency of discharge generation was 15-35/min. Potentials of induced seizure activity were recorded at the same time in the posterior sigmoid gyrus of the ipsilateral and anterior sigmoid gyrus of the contralateral hemisphere relative to the stimulated DN (Fig. 1a). Their amplitude was 100-200 and 150-350 μV, respectively. Stable seizure activity was identified for 7-12 min, and for the next 3-5 min the amplitude and frequency of the discharges decreased and they disappeared. The duration of the focus was 15-25 min.

ES of DN (contralateral relative to the primary epileptic focus) in the stage of stable seizure activity in the focus (6 min after the end of penicillin application) led to a decrease in amplitude of the discharges in the ipsilateral focus of induced seizure activity (Fig. 1b, zone 2). The frequency of generation of seizure discharges during the period of ES was substantially unchanged. After cessation of ES, the amplitude was restored in zone 2. After one or two sessions of ES a decrease in amplitude to 500-900 μV and in the frequency of the seizure discharges in the zone of the primary focus to 10-25/min was observed. During this period, during ES discharges were completely suppressed in all foci (Fig. 1c). After the end of ES the epileptic discharges were restored. In seven of the 10 experiments after the end of ES and a brief period (20-30 sec) of recovery of the epileptic discharges, a second spontaneous complete or considerable inhibition of the seizure potentials was observed in all zones of the cortex, lasting from 20 sec to 1-1.5 min (Fig. 1d). Seizure activity was then restored again in the foci (Fig. 1e). After 4-6 sessions, ES of EN caused complete inhibition of seizure discharges in the foci, which continued even after the end of ES (Fig. 1f). The duration of the seizure focus during ES was 10-15 min ($P < 0.001$). Electrical coagulation of DN in the stage of complete disappearance or of a marked decrease in amplitude of the epileptic discharges after ES led to the appearance of epileptic potentials up to 800 μV in amplitude in the zone of the primary focus (Fig. 1g); activity of this kind was recorded for a further 5-10 min. ES of DN ipsilateral to the primary focus under similar conditions had a weaker action in these experiments on epileptic activity: In six of the seven experiments only a small reduction in frequency of seizure potentials generated was observed in the period between ES to 15-30/min ($P < 0.05$), with no change in amplitude of the seizure discharges.

In the experiments (11) of series II effects of ES of DN on a single epileptic focus in the anterior sigmoid gyrus, a focus of induced seizure activity in the posterior sigmoid gyrus of the contralateral hemisphere and a focus of induced seizure activity in the anterior sigmoid gyrus of the ipsilateral hemisphere relative to the stimulated nucleus, created by application of penicillin solution in higher concentration (40,000 Units/ml), were investigated. Seizure discharges with an amplitude of 500-900 μV, which reached an amplitude of between 2 and 3 mV during the next 4-7 min, appeared 4-8 min after application of penicillin to the an-

terior sigmoid gyrus. The frequency of discharge generation under these circumstances was 20-40/min (Fig. 2a). The amplitude of discharges in foci of induced seizure activity in the ipsilateral and contralateral hemisphere was 1.2-2.0 and 0.5-0.8 mV, respectively. Stable seizure activity was recorded for 12-20 min, and for the next 6-8 min a decrease was observed in the amplitude and frequency of the discharges followed by their disappearance. The duration of the focus was 25-35 min. ES of DN contralateral to the primary focus in the stage of stable seizure activity (5 min after the end of penicillin application) led to an increase in the frequency of discharge generation in all foci during ES (Fig. 2b). In the ipsilateral induced focus (zone 2) the amplitude of the seizure potentials fell from 2.0 to 0.5 mV (Fig. 2c). After the end of ES the amplitude of the discharges recovered and the frequency of their generation was 10-40/min. After 4-6 sessions of ES from the beginning of stimulation a decrease in amplitude of the discharges in the primary focus was observed to 1.7-2.0 mV. In ipsilateral and contralateral foci of conducted seizure discharges (zones 2 and 3) potentials of about equal amplitude (1.0-1.2 mV) and with a generation frequency of 15-30/min were recorded during this period. ES of DN against this background led to a decrease in amplitude of the discharges in the primary focus to 1.3-1.6 mV and also to complete suppression of discharges in the focus of induced activity ipsilateral relative to the primary focus (Fig. 2c, zone 2). The amplitude of discharges in the focus of induced activity (zone 3) contralateral to the primary focus was unchanged during ES. After the end of ES the amplitude and frequency of discharge generation were restored. During further ES procedures (usually 2-3 sessions) the amplitude of discharges of the primary focus fell to 1.2-1.5 mV. ES of DN against this background caused complete suppression of discharges in all zones during the period of ES (Fig. 2d). After the end of ES discharges were restored in all foci. After another 1-3 sessions complete suppression of discharges was observed in all foci (Fig. 2e). On subsequent observation (5-20 min) spontaneous recovery of discharges in the foci was not observed. Electrical coagulation of the region of DN under these conditions caused recovery of seizure potentials in all foci (Fig. 2f). The duration of existence of the focus under these experimental conditions was 20-27 min, i.e., it was 5-8 min shorter than the duration of the focus without ES ($P < 0.05$).

The results of these experiments thus showed that ES of DN leads to inhibition of epileptiform activity evoked in the cerebral cortex by application of penicillin in a relatively low concentration. This result is in agreement with those of investigations [12] which demonstrated the development of inhibition in a weak penicillin epileptogenic focus in the cat neocortex during ES of DN. Antiepileptic effects arising during activation of DN also are confirmed by restoration of seizure activity, suppressed by ES, after electrical coagulation of DN. This effect also was observed in experiments with stimulation and coagulation of the caudal reticular nucleus of the pons [2].

Inhibition of epileptic activity mainly in the hemisphere contralateral to the stimulated DN can be explained by predominance of connections of DN with the neocortex of the opposite hemisphere [15]. This fact also explains the greater reduction in induced discharges in the hemisphere contralateral to the stimulated nucleus compared with the reduction in amplitude of discharges in the "mirror" focus. The lesser degree of depression of discharges in the "mirror" focus may perhaps also be connected with the stronger influence of the determinant focus on it than of the ipsilateral focus of induced seizure activity.

It is an interesting fact that inhibition of epileptic activity in a focus of weak seizure activity was preserved after the end of ES of DN. Similar changes were found in a model of penicillin foci during ES of the caudal part of the vermis of the cerebellum [4] and also in a model of generalized penicillin convulsions during stimulation of the cortex of the cerebellar vermis [10]. The similar character of the effects of stimulation of the cortex and nuclei of the cerebellum on epileptic discharges contradicts data on inhibition of neurons of the cerebellar nuclei during activation of Purkinje cells [9]. In this connection it should be pointed out that during the period of stimulation of the cerebellar cortex activation of neurons of the nuclei and inhibition of spike discharges of Purkinje cells were noted [7, 8]. The results of the present experiments also demonstrate the possibility of a leading role of cerebellar nuclei in the development of poststimulation inhibition of epileptic activity.

In the present experiments enhancement of seizure activity was observed in a powerful epileptic focus created by application of concentrated penicillin solution during the period of ES of DN. Meanwhile, ES of DN has an inhibitory effect on epileptic activity in a weak seizure focus. A relationship of this kind between the effect of stimulation and the level of epileptic activity in the foci also was observed during stimulation of the posterior hypothalamus [11] and of the thalamic nuclei [16]. These findings can be explained on the grounds that during ES of DN two types of efferent influences arise — inhibitory and excitatory, as

has been described in other models (the principle of the dual functional burst) [1]. Just as in cases of generators of pathologically enhanced excitation (GPEE) formed during a disturbance of inhibitory control in other CNS structures [1], the character of changes arising in epileptide cortical structures receiving the burst depends on the degree of disturbance of inhibition and of lowering of the thresholds of excitability in these structures. If a sufficient degree of effectiveness of inhibitory neurons is preserved in the epileptic focus, the incoming impulsation during stimulation of DN activates these neurons and causes suppression of the focus. During a considerable disturbance of inhibition and lowering of the thresholds of excitability of the neurons in the focus, however, impulsation from DN may cause increased activity of the epileptic focus. Support for this mechanism is given by the fact that ES of DN causes inhibition of activity in the zone where secondary conducted activity, induced by the determinant focus, was recorded, i.e., where inhibitory mechanisms were preserved. With a fall in the intensity of epileptic activity (with the course of time and during continued sessions of ES), however, i.e., during restoration of the inhibitory mechanisms, ES of DN suppresses epileptic activity.

The results thus indicate the great importance of the dentate nucleus of the cerebellum as part of the antiepileptic system of the brain in suppression of epileptic activity in the neocortex.

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DYNAMICS OF BLOOD TYROSINE LEVEL IN ADRENALECTOMIZED AND INTACT RATS EXPOSED TO STRESS

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The reserve powers of the adrenal cortex in clinical practice are usually estimated by studying changes in the blood and (or) urinary levels of corticosteroid hormones after admin-

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