# EFFECT OF ELECTRICAL STIMULATION OF THE DENTATE NUCLEUS ON MULTIFOCAL EPILEPTIC COMPLEXES IN THE CEREBRAL CORTEX

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Electrical stimulation (ES) of the dentate nucleus has been shown [4] to inhibit interictal epileptic discharges in single foci of epileptic activity created in the cerebral cortex by local application of penicillin. The intensity of the effects of ES was found to depend on the level of epileptic activity in the focus. The object of the present investigation was to study the effect of ES of the dentate nucleus on a multifocal epileptic complex, which is a model of a special kind of pathological system [1] which arises as a result of the influence of a determinant focus on foci with comparatively low initial activity [2]. The individual parts of such a system are functionally dissimilar and they behave differently in response to factors leading to their destabilization [1, 3].

## EXPERIMENTAL METHOD

Acute experiments were carried out on 11 cats. Under ether anesthesia bipolar electrodes were introduced into the dentate nucleus, using coordinates from the atlas [6], after which the calvaria was trephined to give access to the various parts of the frontal region of the neocortex of both hemispheres. Experiments began 1.5-2 h after administration of ether ceased. The animals were immobilized (D-tubocurarine, 0.12-0.28 mg/kg) and artifically ventilated. Scattered foci of epileptic activity were created by application of a piece of filter paper, measuring 2 × 2 mm, soaked in a solution of the sodium salt of benzylpenicillin (16,000 Units/ml) to different parts of the anterior and posterior sigmoid gyri and the coronal gyrus. A focus of powerful epileptic activity, playing the role of determinant, was created in the middle sigmoid or orbital gyrus by application of penicillin solution in a concentration of 40,000 Units/ml. Potentials were derived by a monopolar technique and the reference electrode was secured in the nasal bones. The active electrodes were cotton threads soaked in Ringer's solution. Potentials were recorded on a 4-EEG-3 ink-writing electroencephalograph. ES of the dentate nucleus was carried out with an ESU-1 electrostimulator, by series of square pulses (0.25-0.5 msec, 100-300 Hz, 2-7 V), in sessions 5-10 sec in duration, separated by intervals of 2-3 min. The location of the electrodes was verified histologically. The results were subjected to statistical analysis and differences between the experimental and control group were assessed by nonparametric tests [7].

## EXPERIMENTAL RESULTS

Application of the concentrated penicillin solution to zone 1 and of the relatively weaker solutions to zones 2, 3, and 4 created an epileptic complex, by the technique described previously [2], consisting of four foci (Fig. 1a). The frequency of discharge generation in the foci was 30-45/min, and the amplitude of the discharges was 1.5-2.0 mV in the dependent foci and 2.5-3.0 mV in the determinant focus. Control experiments (seven observations) showed that the epileptic complex thus formed generated synchronized seizure discharges for a period of 35-45 min, but during the next 15-20 min the amplitude and frequency of discharges in the foci decreased, and in the dependent foci the discharges disappeared completely (disintegration of the complex). If ES was applied during stable epileptic activity (5 min after the end of penicillin application to all zones) it caused an increase in discharge frequency to 60-70/min. The discharge frequency in the foci was restored (Fig. 1b). After 25-35 min (10-15 sessions of ES) outside the period of ES there was a gradual decrease of

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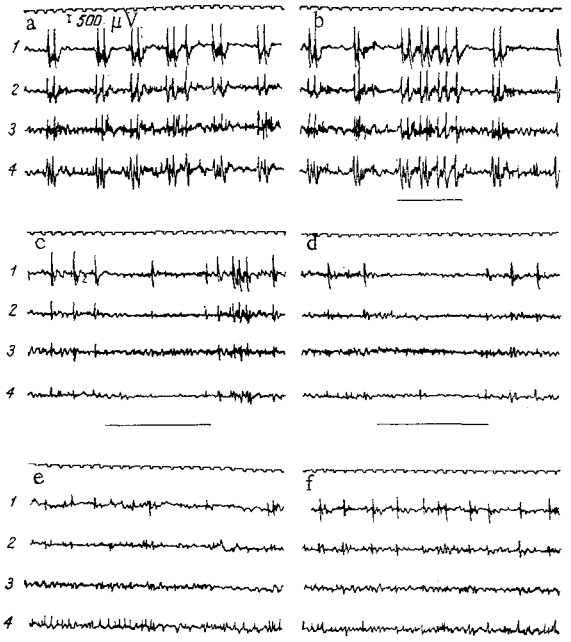


Fig. 1. Effect of ES of dentate nucleus on epileptic complex in cerebral cortex: a) 9 min after formation of stable epileptic complex by application of weak penicillin solution (16,000 Units/ml) to zones 2, 3, and 4 and of concentrated solution (40,000 Units/ml) to zone 1; b) increase in discharge frequency in all zones during period of ES of nucleus, 1 min after creation of epileptic complex (first session of ES); c) inhibition of discharges in zones 2, 3, and 4 during period of ES of nucleus 26 min after increase in discharge frequency (10th session of ES); d) 15 min after suppression of discharges in zones 2, 3, and 4 — inhibition of seizure discharges in zone 1 during period of ES (16th session of ES); 3) another 5 min later — inhibition of activity in all zones, continued after next session of ES, recording made 2.5 min after termination of ES; f) 7 min after electrocoagulation of nucleus. 1) Orbital gyrus, 2) anterior sigmoid, 3) middle sigmoid gyrus, 4) coronal gyrus. Parameters of ES: 300 Hz, 0.25 msec, 4 V. Time marker 1 sec, calibration 500 μV.

activity, followed by its disappearance, in one of the dependent foci of the complex. The amplitude of discharges was reduced in the determinant focus (2.0 mV) and in the dependent foci (1.0-1.4 mV), and the frequency of generation of epileptic potentials was reduced in the determinant focus (15-20/min) and also, consequently, in all foci of the complex. During ES in this period discharges in the dependent foci were depressed or even disappeared completely, and the amplitude of the potentials in the determinant focus was reduced (to 1.0 mV) and their frequency diminished (to 10-12/min; Fig. 1c). After termination of ES the amplitude and frequency of discharges in the foci were restored. After another 10-18 min (5-8 sessions of ES) the complex disintegrated: Epileptic activity disappeared in all the dependent foci; in the zone of the former determinant focus discharges with an amplitude of 1.0-1.5 mV and a frequency of 10-15/min were recorded (Fig. 1d). The life of the complex during ES of the dentate nucleus was 50-60 min, which did not differ statistically significantly from the control observations ($P > 0.05$). ES against this background led to total suppression of discharges in the zone of the previous determinant focus, and these were restored after termination of ES (Fig. 1d). After another 2 or 3 sessions of ES, outside the period of ES marked inhibition of epileptic discharges was observed in the zone of the former determinant focus, but these did not recover spontaneously (Fig. 1e, zone 1). Electrical coagulation of the nucleus led to restoration of seizure potentials in the zone of the determinant focus (Fig. 1f, zone 1), and these continued to be recorded for a further 10-15 min after coagulation; potentials of reduced amplitude, but synchronized with the determinant focus, also appeared in the dependent focus (zone 2).

The results of these experiments show that ES of the dentate nucleus of the cerebellum in a model of a multifocal epileptic complex gives rise to both facilitatory and inhibitory effects. Facilitatory effects were observed in the early stages of existence of the complex, when the level of its activity was high, and they were manifested as an increase in the amplitude and frequency of generation of epileptic discharges in the foci during the period of ES of the dentate nucleus. These results agree with those of previous investigations showing that these effects of ES of the caudal reticular nucleus of the pons [3], the cerebellar dentate nucleus [4], and the hypothalamus and reticular formation [5, 8], are dependent on the level of epileptic activity in the cortex. The increase in amplitude and frequency of potential generation during the period of ES of the dentate nucleus, incidentally, was observed in both determinant and dependent foci of the epileptic complex. Meanwhile, as previous investigations [4] showed, ES of the dentate nucleus, in experiments in which single epileptic foci were created, caused an increase in amplitude and frequency of discharges in a powerful epileptic focus, accompanied by simultaneous inhibition of discharges in foci of induced electrical activity. In experiments in which relatively weaker single epileptic foci were created, however, ES of the dentate nucleus caused suppression of epileptic activity in such foci throughout the period of ES, and considerably shortened their life [4]. The union of such scattered foci under the influence of a determinant focus into a single epileptic complex, which constitutes an epileptic system [1], thus significantly increases the resistance both of the single foci (components of the system) and of the system as a whole to inhibitory influences during the period of ES of the dentate nucleus.

In the later stages of existence of an epileptic complex, as the level of its activity falls (decrease in amplitude and frequency of epileptic discharges) and as the epileptic system is reduced (decrease in the number of foci) inhibitory effects of ES of the dentate nucleus were observed, as shown by suppression of epileptic discharges during the period of ES. Repeated sessions of ES of the dentate nucleus caused a relatively lasting effect of suppression of epileptic activity, which continued even after termination of ES. These experiments show that suppression of epileptic activity in the foci was connected with prolonged activation of the dentate nucleus, due to the appearance of an excitation generator in that structure, and not to cessation of the action of penicillin. Abolition of the excitation generator by electrical coagulation of the dentate nucleus caused epileptic activity in the foci to be restored.

On the whole the results of these experiments confirm Kryzhanovskii's views [1] on the role of "antisystems," and in this particular case the role of structures of the antiepileptic system, in the suppression of epileptic activity and prevention of the formation of pathological systems. The dentate nucleus of the cerebellum is an important component of such an antiepileptic system of the brain.

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