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EFFECT OF CEREBELLECTOMY ON A STRYCHNINE FOCUS IN THE CEREBRAL CORTEX

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KEY WORDS: cerebellum; strychnine; epileptic activity.

In order to inhibit epileptic activity and also to cut short other neuropathological syndromes characterized by hyperactivity of pathological systems [1], a factor of great importance is activation of physiological antisystems, which are the functional opposite of structures involved in the pathological process [2, 3]. A component of the antiepileptic system is the cerebellum, activation of which can lead to the suppression of epileptic discharges in the cerebral cortex [6]. However, data on the effect of electrical stimulation of the cerebellum on epileptogenesis are ambiguous [4, 7, 8].

The aim of the investigation described below was accordingly to study the effect of cerebellectomy on the duration of existence of an epileptogenic focus, which reflects in a general manner the character of participation of the cerebellum in the epileptization of the brain.

EXPERIMENTAL METHOD

Acute experiments were carried out on 12 cats weighing 2.5-3.5 kg. Under ether anesthesia tracheotomy was performed, and the skin and subcutaneous cellular tissue was divided by a midline incision from the nasal bones to the occiput. The cranial bones were trephined in the frontal and occipital regions to provide access to the sensomotor areas of the neocortex and the ipsilateral surface of the cerebellum. After the dura had been opened an epileptic focus was created in the posterior sigmoid gyrus by application of a piece of filter paper (2 mm^2) soaked in 0.1% strychnine nitrate solution. The piece of paper with strychnine was removed in all cases 1 min after development of seizure potentials. The life of the foci was measured from the time of appearance of the first spike to disappearance of the last spike. After two or three such determinations the cerebellum was aspirated under visual control. Another strychnine focus was then created in the same way 40-60 min after aspiration of the cerebellum.

Cortical potentials were recorded by a monopolar method on the 4-ÉÉG-3 ink-writing electroencephalograph, the reference electrode being fixed in the nasal bones. The results described in this paper were obtained in experiments in which completeness of aspiration of the cerebellum was verified anatomically at autopsy. The experimental results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Seizure discharges were observed to appear 6 min after application of strychnine to the cortex of the sigmoid gyrus. During the next 5-8 min the amplitude of the potentials increased to 1.5-2.5 mV. The frequency of spike generation during this period was 10-40 spikes/min. The amplitude–frequency characteristic curves of the seizure discharges remained unchanged for 5-10 min after the discharges had reached their maximal amplitude, after which the level of seizure activity of the focus declined gradually and disappeared completely. The mean life of the foci was 22.7 ± 2.6 min (Table 1).

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TABLE 1. Effect of Aspiration of Cerebellum on Amplitude–Frequency Characteristics of Epileptogenic Foci (M ± m)

Experimental conditions	Latent period of epileptogenic discharges, min	Time taken to reach maximal amplitude of seizure discharges, min	Amplitude of potentials, mV	Total duration of existence of epileptogenic foci, min
Before aspiration of cerebellum	5,30±0,15	5,80±0,32	1,90±0,09	22,7±2,6
After aspiration of cerebellum	3,20±0,26	3,50±0,27	2,27±0,08	43,7±4,8
P	<0,01	<0,01	<0,01	<0,01

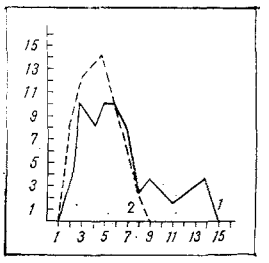

Fig. 1. Changes in duration of interspike interval after cerebellectomy: 1) before aspiration of cerebellum; 2) after aspiration of cerebellum. Abscissa, duration of interspike intervals (in sec); ordinate, number of interspike intervals.

After cerebellectomy strychnine potentials appeared 2-4.5 min after application of the epileptogen. The increase in amplitude of the potentials up to 1.8-2.7 mV lasted 2-5 min. Histographic estimation of interspike intervals revealed displacement of the mode toward shorter intervals than in the corresponding period before aspiration of the cerebellum (Fig. 1). Seizure potentials of unchanged amplitude were recorded for 20-25 min after reaching maximal amplitude, after which the amplitude and frequency of the discharges gradually declined and they disappeared completely. The mean life of the foci after aspiration of the cerebellum also was considerably shortened.

The length of life of foci when produced consecutively was investigated in another series of experiments. A new focus of epileptic activity was formed in the same zone of the cortex 15-20 min after disappearance of activity in an earlier focus. The mean life of the successive foci was 22.8 ± 2.6, 23.6 ± 2.7, and 23.4 ± 3.2 min. Comparison of these figures with the results of experiments with a single focus showed no statistically significant increase in the life of the epileptic foci when produced consecutively.

The investigations thus showed that cerebellectomy leads to an increase in the life of epileptogenic foci produced in the cerebral cortex of cats by strychnine. The effect observed was not attributable to an increase in epileptic activity as a result of repeated strychninization, for the enhancement which occurred during consecutive creation of epileptic foci was statistically significantly less than the facilitation observed after cerebellectomy. These results are in agreement with those of investigations showing activation of a penicillin focus in the cat neocortex after aspiration of the paleocerebellar structures of the cerebellum [4], and the lengthening of the life of penicillin foci in the rat brain after removal of the cerebellum [5].

The antiepileptic role of the cerebellum is also confirmed by shortening of the latent period of the spikes and of the time taken for them to reach maximal amplitude, by an increase in their amplitude, and by a tendency for the frequency of seizure potential generation to rise.

Dow [6] also observed an increase in amplitude of cobalt seizure discharges in rats during cooling of the cerebellum. Meanwhile, Hablitz [8] found no increase in the level of seizure activity after removal of the cerebellum in rats. The contradiction between these findings may perhaps be explained by the fact that in order to produce an effect of increased amplitude and discharge frequency, foci with relatively low seizure activity which could be increased during weakening of antiepileptic influences on the epileptic focus must be created. In the present experiments the conditions of strychinization of the neocortex described above satisfied this demand, so that facilitation of generation of epileptic discharges could be revealed after aspiration of the cerebellum.

It is an interesting fact that the final resultant of efferent influences from the cerebellar nuclei, which facilitate epileptogenesis [7, 9], and of the cerebellar cortex, which inhibits epileptic activity [4, 6, 9], is antiepileptic. These results confirm those obtained by Walter et al. [10], who found increased excitability of the cerebral cortex in monkeys as a result of absence of the cerebellum.

The invariable discovery of potentiation of activity of the epileptic focus and the lengthening of its life after removal of the cerebellum indicate the importance of the study of natural pathways and mechanisms of activation of cerebellar antiepileptic structures. The results of this investigation on the whole are evidence that the cerebellum is an important component of the antiepileptic system of the brain and they confirm Kryzhanovskii's views [1] on the role of antisystems in depression of activity and in the prevention of formation of pathological systems.

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INHIBITION OF IMPRINTING BY BLOOD SERUM FROM SCHIZOPHRENICS

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At the present stage of the study of the pathogenesis of schizophrenia many workers [1, 4-8] have postulated the existence of toxic substances in such patients, whose effect on their brain is responsible for the mental disturbances. The chemical nature and sources of these abnormal metabolites are not yet known. Several hypotheses have been put forward, according to which the principal role in the pathogenesis of schizophrenia is played by disturbance of metabolism and functions of biogenic amines — the neurotransmitters of the brain [2, 4, 13, 15].

Much experimental evidence has now been obtained, on various biological objects, that the blood and CSF of schizophrenic patients has a toxic action [3, 5]. The object of this investigation was to study the effect of schizophrenic blood serum on the earliest form of learning and iconic long-term memory, namely imprinting, in chickens.

The essence of the imprinting phenomenon is that a special "attraction" arises in young birds or infants to the first moving object which they see after birth, and they will follow such an object everywhere. However, this is not the only possible form of manifestation of imprinting [9, 11, 12].

EXPERIMENTAL METHOD

Experiments were carried out on 62 White Leghorn chicks. The eggs were incubated at 37-38°C. A few hours before hatching, the eggs were wrapped in separate cardboard boxes so that after hatching imprinting in the chickens by each other would not take place. Imprint-

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