

ROLE OF ANTERIOR COMMISSURE IN THE FORMATION OF MIRROR FOCUS DURING EXPERIMENTAL TEMPORAL LOBE EPILEPSY

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Abstract

In this study the role of anterior commissure was explained in the formation of secondary mirror focus during experimental temporal lobe epilepsy. The experiments were conducted on 12 adult male rabbits. Metallic cobalt powder was implanted unilaterally into basal amygdala as an epileptogenic agent. For the EEG recording bipolar electrodes of insulated nichrome wire were implanted into basal, medial and cortical amygdala, dorsal hippocampus, cortex and ventromedial hypothalamus. For each rabbit 2 recording sessions were held with a 15-channels electroencephalograph. First session was held on the 5th day after cobalt implantation (before the anterior commissure coagulation). Second session was held on the 2nd, 7th, 14th, 22nd and 27th day after anterior commissure coagulation. On the basis of results obtained it was concluded that the electrolytic destruction of only interamygdaloid anatomical connections does not arrest but delays the secondary focus formation (JPMA 30:244, 1980).

Introduction

Epilepsy is a chronic cerebral disease of varying a etiology. It is characterized by repeated fits occurring as a result of excessive neuronal discharges accompanied by various clinical and paraclinical symptoms. The investigations of this disease carry clinical as well as biological significance. Having a very low epileptic threshold amygdaloid complex plays an important role in the initiation of temporal lobe epilepsy (Nakao, 1967). The morphological information available about the connections of amygdala with other cerebral formations (Lammers, 1972; Leonard and Scott, 1971) serves as an important basis for the analysis of mechanisms influencing the duration and provocation of epileptic seizures in the case of temporal lobe epilepsy. It has been suggested that the experimentally induced forms of epilepsy in animals do not principally differ from the seizure activity observed in human patients (Gastaut et al., 1953). Various methods of local chemical actions on the cerebral tissues have been worked out to obtain experimental models of epileptic focus. Metallic cobalt powder is widely used as epileptogenic agent in various animals (Kopeloff, 1960; Mutani, 1967; Purpura, 1972; Shaikh, 1978).

The formation of secondary epileptic foci is accomplished through interamygdaloid pathways and amygdaloid connections with hypothalamus. The fibers of anterior commissure connect the amygdalae of both cerebral hemispheres. It was suggested that the amygdaloid fibers entering the anterior commissure take their origin from the basolateral group of amygdaloid nuclei (Jeserich, 1945). In the present study role of anterior commissure was studied in the formation of secondary mirror focus. It is a fact that the mirror foci are formed where close anatomical and functional connections exist between the cerebral structures involved. For amygdala these connections or pathways are practically unexplored.

Material and Methods

The experiments were conducted on twelve adult male rabbits weighing 1.5 to 2 kgs. Metallic cobalt powder with prior sterilization at 150°C was used as epileptogenic agent. Cobalt powder (8-10 mg) was unilaterally and chronically implanted into basal amygdaloid nucleus of the right hemisphere by means of a glass cannula (diameter-1 mm). Then bipolar electrodes of insulated nichrome wire (diameter-0.4 mm) were implanted bilaterally into basal amygdaloid nucleus, dorsal hippocampus, cortex (visual region) and unilaterally into (contralateral hemisphere to cobalt implantation) medial and cortical nuclei of amygdala and ventromedial hypothalamic nucleus. The coordinates of these structures were determined according to the stereotaxic atlas of Marshall and Fifkova (Bures et al., 1962). While working on the stereotaxic apparatus each animal was narcotized by Nembutal (40 mg/kg of body weight).

For five days after cobalt implantation primary focus formation was noticed. During this period favourable conditions are formed for the preconvulsive state in the contralateral amygdala (Shaikh, 1978). On fifth day anterior commissure was electrolytically destructed in the hemisphere with cobalt application. For the unilateral electrocoagulation of anterior commissure its rostral parts were chosen where it runs as a compact bundle of fibers (Van Alphen, 1969). For electrocoagulation an electric current of 5 mA was used.

For each rabbit two recording sessions were held with 15-channels electroencephalograph. First session was held on 5th day after cobalt implantation (before anterior commissure coagulation). Second session was held on 2nd, 7th, 14th, 22nd and 27th day after anterior commissure coagulation. Before starting each experiment the rabbit was unanesthetized and immobilized on a wooden board. As ventromedial hypothalamus is known to have a seizure provocative influence in intact animals (Shaikh, 1978; Sheblanov, 1975), its stimulation was carried out in every experiment after anterior commissure destruction. Ventromedial hypothalamus was stimulated on the contralateral side to the primary focus where amygdalo-hypo-thalamic connections were intact.

At the end of each experiment localization of electrode endings was determined. For this purpose a constant current of 1 mA was passed through the electrodes for 10 to 15 seconds. Then animals were sacrificed under deep Nembutal anesthesia and their brains were fixed in 10% formaline solution. After fixation brains were serially sectioned (70-86 µm thick) on the freezing microtome.

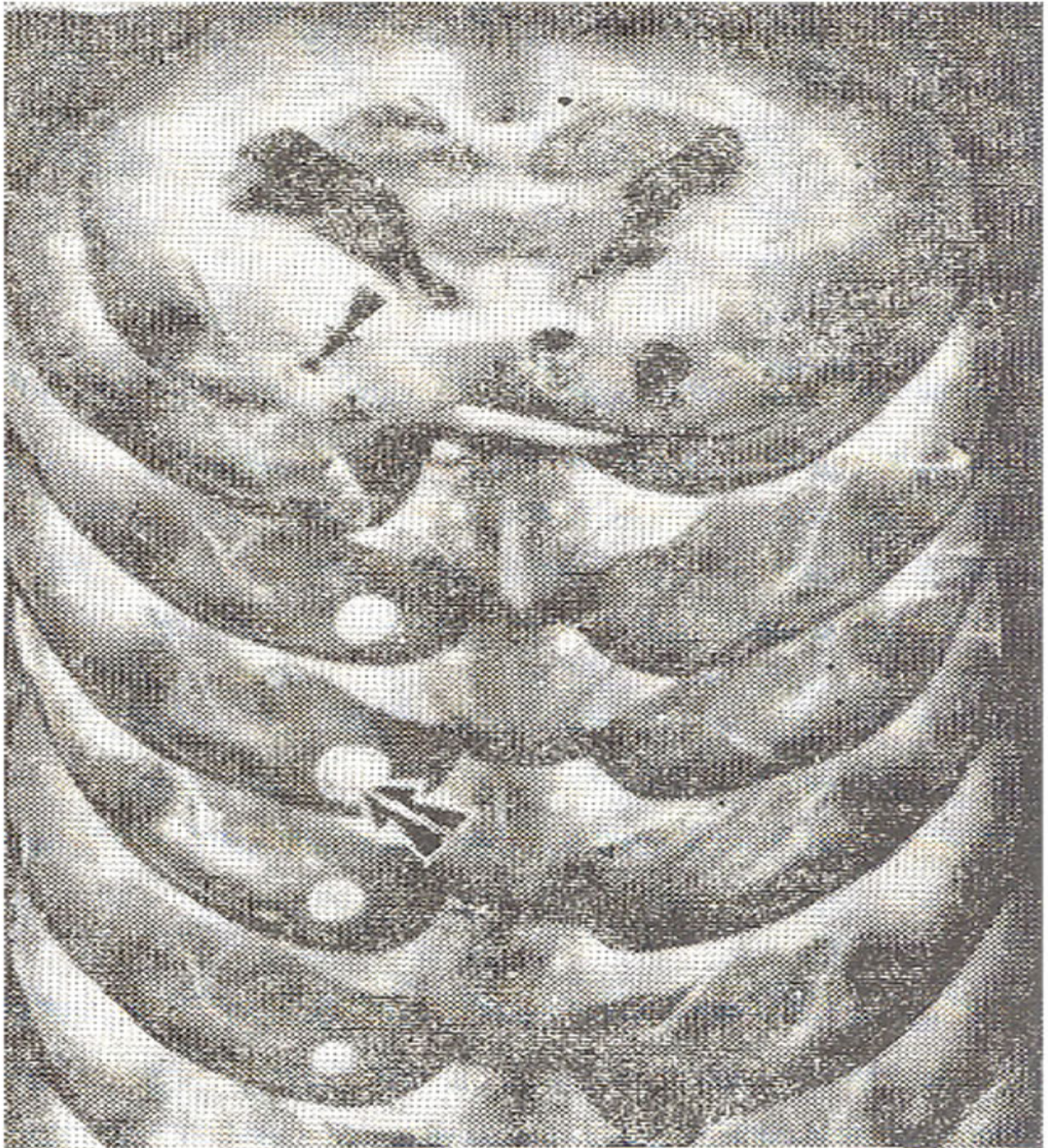


Fig. 1. Brain sections showing electrocoagulation of anterior commissure (single arrow) and cobalt localization in the basal nucleus of right amygdala (double arrow).

Fig. 1 shows the morphological control of cobalt localization and electrocoagulation of anterior commissure.

Observations and Results

After the electrolytic destruction of anterior commissure it was observed that on the 2nd day the mirror focus spikes became more frequent in the background activity. Towards 7th day some generalized seizures appeared. After two weeks in these animals intense nonmotor seizures, were recorded. Towards 27th day frequent seizures were recorded in the EEG and after their cessation the spike activity continued in the secondary focus and disappeared from the primary focus.

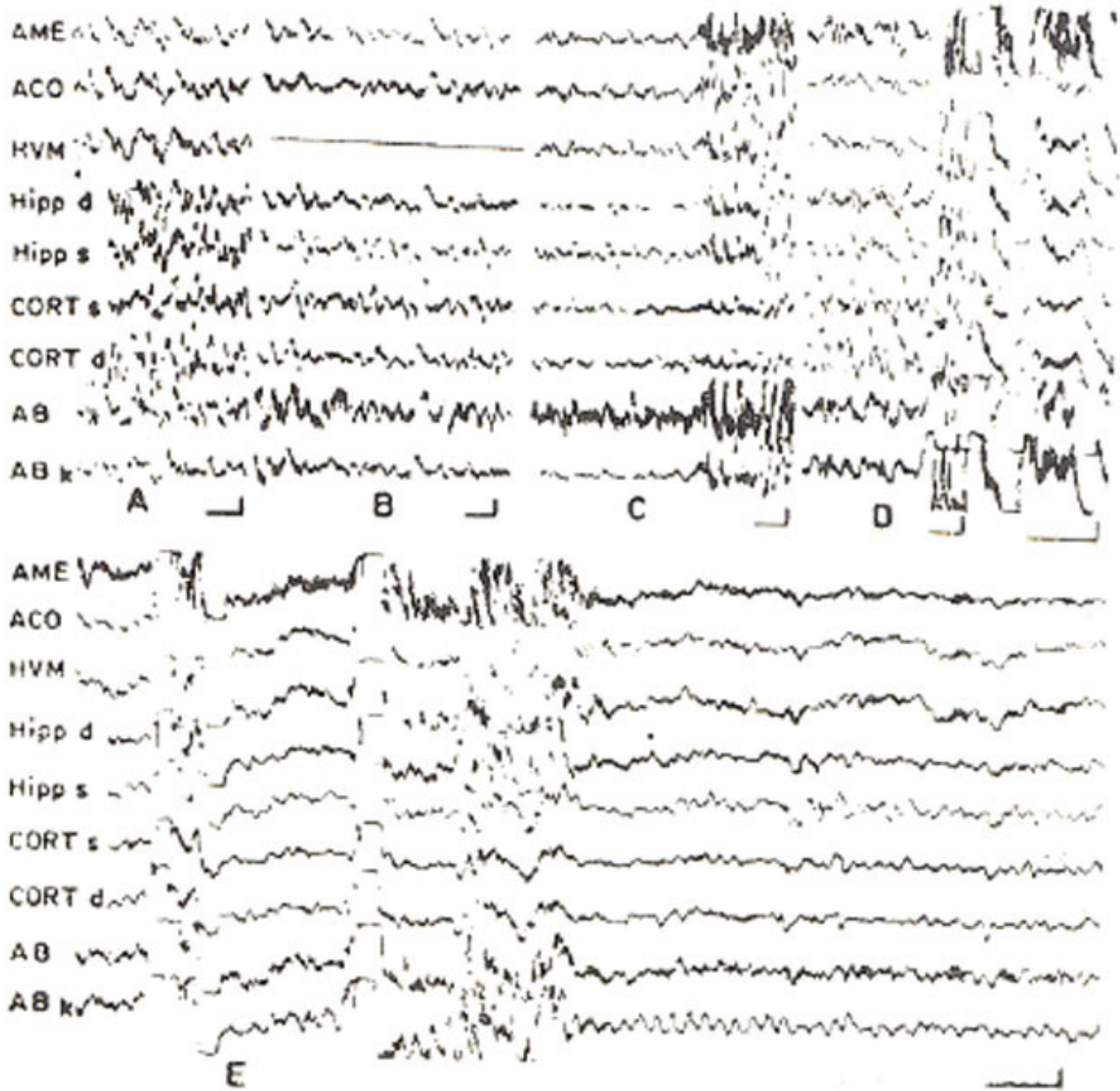


Fig. 2. Epileptic activity in the rabbit brain after unilateral application of coablt in thr right basal amygdala (ABK) at various periods before and after the commissural destruction.

Fig. 2 shows the changes in the epileptiform activity during 27 days after anterior commissure

destruction and 32 days after cobalt application in the right hemisphere amygdala. Before the electrolytic destruction of anterior commissure (after cobalt implantation) generalized pathological activity was recorded (Fig. 2-A). The epileptic spikes were not prominent in the contralateral basal amygdaloid nucleus (AB). On the second day after electrocoagulation of anterior commissure (7 days after cobalt application) frequent spikes were observed in the contralateral basal amygdaloid nucleus (mirror focus). Spike activity was also taken up by the cortical amygdaloid nucleus (ACO) on the mirror focus side (Figl 2-B). On the 14th and 22nd day after commissure destruction (Fig. 2-C, 2-D) spikes became intensive in the mirror focus and initiated the generalized spontaneous seizures in almost all the structures recorded. As it can be seen in Fig. 2-E, on the 27th day after commissure destruction prolonged seizure discharges were recorded in all the structures giving sufficient after discharges. After the cessation of epileptic seizures the spike activity continued particularly in the mirror focus basal nucleus and also in the medial (AME) and cortical (ACQ) amygdaloid nuclei of the same hemisphere. Activity of last two nuclei synchronized with that of basal nucleus (mirror focus) even after the seizures were over.

Fig 2A. On the 5th day after cobalt application (before commissural lesion). Generalized pathological activity.

Pig, 2B. On. the 2nd day after commissural destruction (After 7 days of cobalt action). In the contralateral basal amygdala frequent spikes are prominent.

Fig. 2C. On the 14th day after commissural lesion. Spikes from the mirror focus initiate spontaneous generalized seizures.

Fig. 2D. On the 22nd day after commissural destruction. During interictal periods left medial amygdala shows intensive spikes.

Fig. 2E. On the 27th day after commissural destruction prolonged seizures can be observed with after discharges. After the seizures are over spikes continue in the left medial amygdala, mirror focus basal amygdala and orticalc nucleus of left amygdala.

Abbriviations: AME-left medial nucleus of amygdala; ACO-left cortical nucleus of amygdala; HUM-ventromedial hypothalamic nucleus; Hipp d-right dorsal hippocampus; Hipp s-left dorals hippocampus; Cort s-left visual cortex; Cort d-right visual cortex; AB-left basal neucleus of amygdala; ABK-right basal nucleus of amygdala with cobalt. Calibration; 100 uv. 1 second.

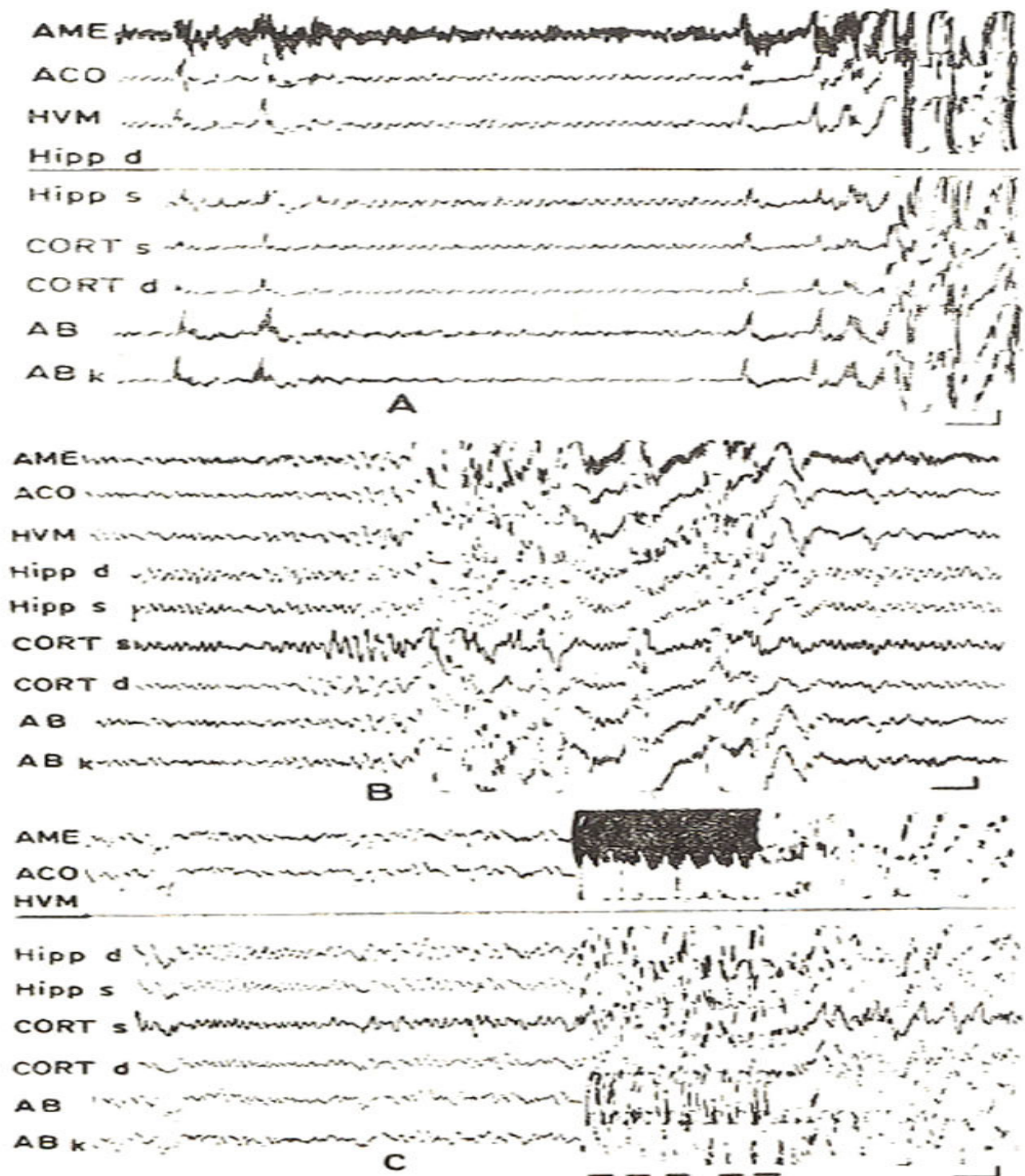


Fig. 3. Dynamics of changes in the epileptiform activity after chronic destruction of anterior commissure and ventromedial hypothalamic stimulations.

Fig. 3-A. 7 days after the commissural destruction (12 days after cobalt action). Stimulation of ventromedial hypothalamus gives rise to frequent spikes in the left medial amygdala which later on lead to generalized seizures.

Fig. 3-B. On the 27 day after commissural destruction (32 days after cobalt alteration). Spontaneous

spike activity of the left medial nucleus is attenuated and becomes noticeable only in the interictal periods.

Fig. 3-C. The ventromedial hypothalamic stimulation (100 Hz, 10v; indicated by the dotted line) leads to generalized seizures. During interictal periods spikes become prominent in the left medial amygdala. After the seizures are over spikes remain prominent in the left medial amygdala and primary focus (AB_k).

Abbreviations and calibration same as in the Fig. 1.

After 7 days of anterior commissure destruction stimulation of ventromedial hypothalamic nucleus (HVM) on the contralateral side to the cobalt application lead to an intensive spike activity in the medial amygdaloid nucleus of the contralateral hemisphere. This spike activity initiated generalized seizures involving all the structures (Fig. 3-A). On 27th day after anterior commissure destruction the spike activity of medial nucleus was attenuated becoming prominent only in the interictal periods during the spontaneous seizures (Fig. 3-B) or seizures provoked by the stimulation of ventromedial hypothalamic nucleus (Fig. 3-C). After the seizures were over frequent spikes continued in the medial nucleus of the mirror focus side as well as in the primary focus (AB_K).

The control experiments have shown that damage to the interamygdaloid connections does not lead to the formation of epileptic foci.

On the basis of results obtained it was concluded that the destruction or damage to the interamygdaloid connections e.g. anterior commissure after the action of epileptogenic agent delays the development of mirror focus but does not prevent its formation.

Discussion

The electrophysiological investigations of clinical forms of epilepsy and its various experimental models on animals lead to an understanding of mechanisms concerning the occurrence and irradiation of epileptic seizures. These studies also provide an information about the cellular mechanisms determining the pathological rhythms of excitation which are conducive to the development of seizures. The results obtained can be explained on the basis of morphological information about the fiber contents of anterior commissure. Van Alphen (1969) reported that the posterior branch of anterior commissure (in rabbits) is projected onto the prepyriform cortex and anterior part of the lateral amygdaloid nucleus. Fibers of this part mainly arise from the prepyriform cortex.

The transection of any anatomical pathway within the limbic circuits means transection of bilateral connections e.g., it may lead to the degenerative changes retrograde as well as anterograde.

Experiments conducted on isolated cortex (Krnjevic et al., 1970) showed that the processes of deafferentation can be the source of neuronalepileptic activity and that the tendency to neuronal paroxysmal activity depends upon the extent of deafferentation. Our earlier experiments have shown that only deafferentation of amygdala does not play an important role in the cessation of mirror focus formation (Shaikh and Chep-urnov, 1977). -More important is the obstruction of inhibitory influences bilaterally conveyed through the amygdalo-hypothalamic neuronal circuits, interhemispheric and interamygdaloid connections. Destruction of anterior commissure leads to the disturbance of bilateral symmetry in the olfactory analyser and to the damage of connections between the nuclei of striopallidal system (putamen). So only polysynaptic connections through hypothalamic structures or through structures of temporal lobe cortex are left for the formation of secondary foci.

In this study it was observed that the medial and cortical amygdaloid nuclei became the main nuclei in which the epileptiform activity is formed secondarily and epileptic discharges are initiated from them. It was also noticed that the electrolytic destruction of only interamygdaloid anatomical connections does not arrest but delays the secondary focus formation. These results can be explained by the fact that destruction of anterior commissure equally traumatizes the axons of amygdaloid neurons of both the

hemispheres and contralateral projections from the olfactory bulbs also get destroyed. Consequently the partial deafferentation of the contralateral amygdaloid neurons may take part in the process of epileptic activity in these nuclei where primary and secondary fibers of olfactory system are degenerating. The data obtained by simultaneous recording of epileptic activity from various amygdaloid nuclei are in conformity with the anatomofunctional division of amygdala (Chepurnov et al., 1977; Koikegami, 1963; Ursin and Kaada, 1960). The stimulation of ventromedial hypothalamus in these experiments gave rise to the effect similar to those of intact animals-provocation of epileptic seizures (Shaikh, 1978; Sheblanov, 1975),

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