Journal of Life Sciences & Biomedicine, vol. 5(78), No 1, p. 26-30 (2023)

Electrophysiological study of effects of basolateral Amygdala on the function of visual system structures

Ulduz Hashimova, Khuraman Miryusifova*, Arzu Allahverdiyeva, Nigar Huseynova, Kamala Javadova, Elmira Panakhova

Academician Abdulla Garayev Institute of Physiology, Ministry of Science and Education of the Republic of Azerbaijan, 78 Sharifzadeh Str., AZ1100, Baku, Azerbaijan

***For correspondence:** miryusifovaxuraman@mail.ru*

Received: February 15, 2023; Received in revised form: March 13, 2023; Accepted: March 30, 2023

Epilepsy is one of the most spread neurodegenerative diseases. This disease occurs in people of all ages from infancy to old age and can have lethal effects as well. The present work explores the electrical activity in the visual system structures, specifically in the visual cortex, lateral geniculate body, colliculus superior and retina in penicillin-induced amygdala epilepsy. Experiments were carried out on awake, non-anesthetized immobilized rabbits. The development dynamics of epileptic activity were observed in all visual system structures. Electroencephalogram and analysis of evoked potentials in the studied structures reaffirm the idea of direct connections between the visual cortex and the amygdala. This is evidenced by the generation of short-latency responses in the visual cortex and other visual system structures. For the first time, under the conditions of experimental epilepsy, it was shown that the epileptic activity is spread along the centrifugal pathways from the basolateral amygdala to neuronal elements of the primary visual cortex, lateral geniculate body, colliculus superior and ganglionic layer of the retina.

***Keywords:** Electroencephalogram, amygdala epilepsy, visual cortex, lateral geniculate body, superior colliculus*

INTRODUCTION

According to the latest statistics epilepsy occurs in only 1% of the world's population, but due to its specific gravity ranks third among neurological diseases and shows a clear upward trend in recent years. Affecting more than 70 million people worldwide is one of the most common serious brain diseases (Thijs et al., 2019). Despite the progress made in the study of this problem, the study of epileptogenesis in new aspects on the one side, and the creation and use of technologies, on the other side require a more precise study with the new achievements of fundamental sciences. Recently, the basolateral amygdala function attracts the attention of a significant number of researchers (Panakhova et al., 2022; Mahmood et al., 2023).

In literary sources, there are different systematics of epilepsy. However, the most interesting is the systematics created due to the localization of the focus in the brain. So, the most widespread is its temporal form, which at this time, the pathological focus develops in the temporal structures (hippocampus, amygdala) belonging to the limbic system of the brain (Falco-Walter, 2020; Pitkanen et al., 1998). These structures are involved in the regulation of various behavioral and cognitive processes; in pathological conditions, especially during the onset of epileptic activity regulation of the functioning mechanisms of this system is disturbed. The basolateral amygdala (BLA) has an important role in the initiation and propagation of epileptic seizures. Correlates of cognitive functions of the brain as known that there are rhythmic processes in different frequency ranges. During epileptogenesis, the rhythmic activity of the brain is disturbed.

Under the influence of harmful factors, foci

Available online 30 June 2023

of convulsive activity can occur as a result of morphological and functional changes in the brain. Activity synchrony may increase for some regions, for others, it may decrease. Thus, during epileptogenesis, dysfunction of the rhythmic activity of the brain occurs. At present time to understand the mechanisms of epileptogenesis and to study the brain's activity in the general and epileptic processes the most convenient method is the use of electroencephalogram (EEG) analysis. EEG allows the evaluation of the activity in different parts of the brain, as well as obtaining certain information about epileptic activity (Koutroumanidis et al., 2017).

MATERIALS AND METHODS

In the experiments, we used adult rabbits of the "chinchilla" breed weighing 2.5-3 kg. Animals raised in a vivarium were kept in special cells with free access to food and water before and after the research. Before starting research kept in a dark chamber for 7-10 minutes, so that the photosensitivity levels of the photoreceptors are the same.

Electrodes were placed on structures (colliculus superior - CS, lateral geniculate body-LGD, visual cortex-VC, basolateral amygdala-BLA) according to the coordinates of the stereotaxis atlas (Blinkov et al., 1973). The diameter of used electrodes for cortical structures was 0.5 mm, for subcortical structures - 0.1-0.15 mm. ERG from the retina was recorded using contact lenses.

Registration of electrical activity brain structures was carried out with a multichannel encephalography "Neuron-Spectrum-5". The retina photostimulation was carried out using a flash lamp of a photostimulator located at a 25-30 cm distance from the animal eye. An experimental model of epilepsy was created by injecting penicillin sodium (300 U in 10 µl of distilled water) through a cannula placed in a BLA.

For checking electrodes at the end of each experiment animals were preliminarily coagulated, then embolized with air, the brain was removed from the skull and placed in a 10% formalin solution, after making frontal incisions.

RESULTS AND DISCUSSION

Electrophysiological research was carried out in several stages. First, background activity was recorded in the studied structures of animals (EEG, EP-evoked potential) (Fig. 1.)

The results obtained revealed that a high degree of correlation between the activity of the studied structures in healthy animals indicates their close functional relationship. This is confirmed by the available information about the presence of anatomical relationships between them. At the next stage of research, penicillin is injected into the amygdala through a cannula placed in it. After the registration of the brain electrical activity of the animal, it was placed in a sound and lightproof chamber.

As a result of the research, it was found that the introduction of penicillin led to the development of prolonged epileptic activity. In 15-20 minutes after the injection, epileptiform discharges are observed in all structures (Fig. 2). The epileptiform activity involves all brain structures. Then the duration of the attacks is lengthened.

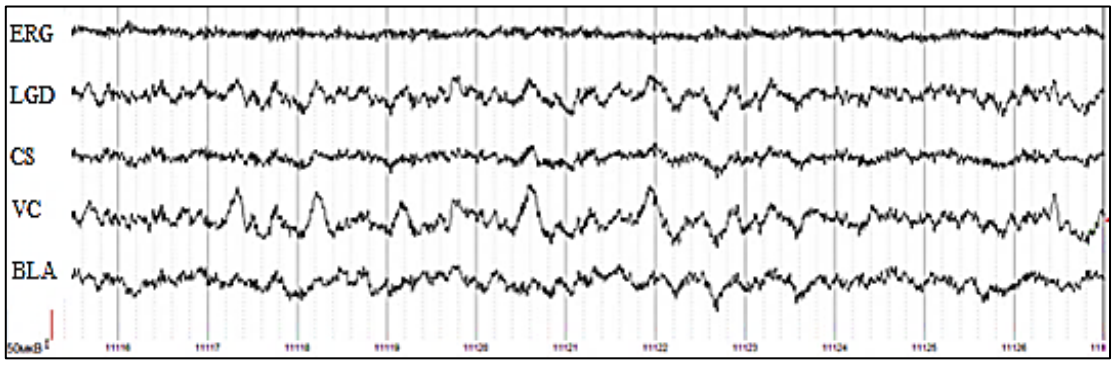
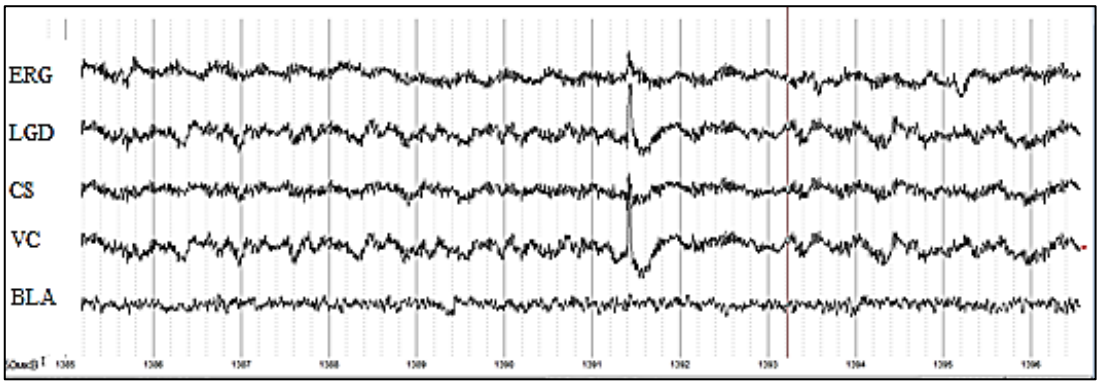
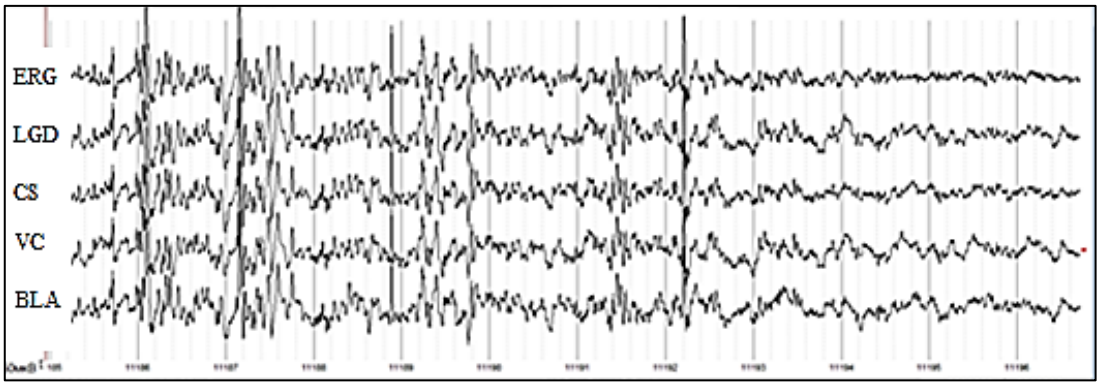


Fig. 1. Background activity of the visual analyzer structures and the amygdala (CS, LGD, VC, BLA)



A - The first single spike was registered on the recording



B - Epileptic activity spreading to all visual structures

Fig. 2. Amygdala epileptogenesis.

Penicillin caused the appearance of generalized spikes in all visual structures, accompanied by massive myoclonic convulsions. Sometimes there were epileptic seizures, which quickly turned into myoclonic convulsions. Such changes in the EEG were recorded within 3-4 hours. Within an hour, the convulsions reach their peak, after which certain dynamics of epileptiform waves are formed. So, over time the attacks begin to alternate.

In our research, we recorded ERQ from the retina as well as EP from the cortical and subcortical structures.

At this time, reactions to light are formed both in the retina and in the amygdala. This fact confirms that the centrifugal pathway continues from the retina to the amygdala.

The number of alternating epileptic seizures begins to decrease and the activity stops 2.5 hours after the injection of the penicillin into the amygdala. In addition, during epileptogenesis in the amygdala spontaneous responses are generated, that extend to the retina (Fig. 3). These responses in the amygdala resembled EP, although no external stimulus was used.

Registration of EEG from several brain structures allows you to study the time sequence of the involvement of the studied structures in the pathological process. EEG analysis showed that epileptic activity first occurs in the amygdala, then in the VC, CS, and LGD and also affects retinal activity. Most likely, manifestations of such a sequence of activity distribution between structures are associated with the presence of unilateral and bilateral morphofunctional relationships between these structures. The duration of experimental amygdalar epilepsy caused by the administration of penicillin into the amygdala was 3-3.5 hours.

In electrophysiological research along with the EEG, we also recorded EP and ERG (Fig. 4).

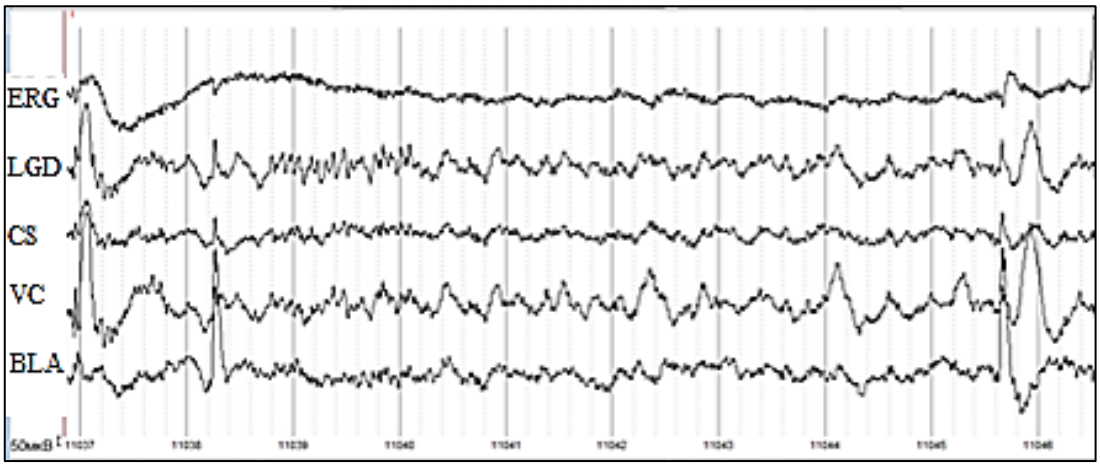


Fig. 3. Spontaneous activity originating in the amygdala and spreading to other structures.

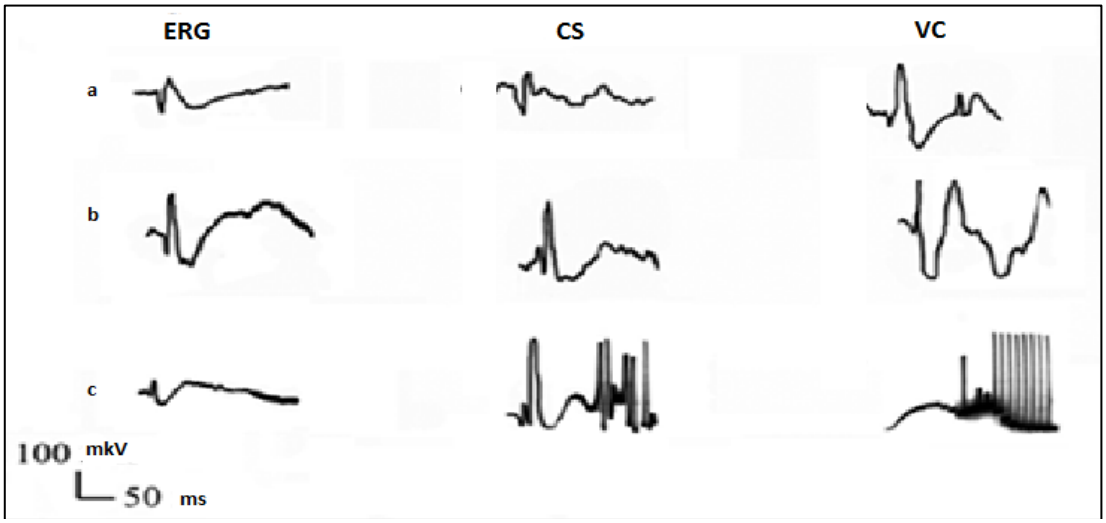


Fig. 4. Comparative analysis of spike characteristics of visual system structures: a-control, b-effect of penicillin instillation into the amygdala, the c-centrifugal spread of epileptiform activity to retina's distal elements.

After the instillation of penicillin into the amygdala, significant changes occur in the retina and visual cortex evoked potentials. From a clinical point of view, it is accompanied by a high level of arousal in the amygdala, the appearance of seizure activity, breath shortness and difficulty breathing. From an electrographic point of view, epileptic spike activity is recorded not only in the cerebral cortex EP and even on an electroretinogram. Interictal spikes, as an indicator of epileptic activity, occur first in the visual cortex, then after 10-12 ms are visible in the retina. There is a sharp increase in the amplitude parameters of the retina's c-wave, which is not involved in the transmission of information to the centers of vision. From the results obtained, it can be said that epileptic foci caused by penicillin in the amygdala have a stimulating effect on the central subcortical and peripheral parts of the visual system.

According to literature sources, it is known that discharges cause the death of GABAergic cells in the hippocampus, septum (up to 40%), amygdala (44-75%) and piriformis cortex (46%). (Cendes et al., 1993).

Changes in the brain structure activity of several begin to be synchronized during experimental epileptogenesis. The activity that begins in the amygdala extends to the brain's visual structures and the retina. The initiation of

paroxysmal activity in the amygdala confirms the information that, along with the hippocampus, it can be the center of epileptic genesis and cause convulsive activity due to the presence of a powerful glutamatergic system in it (Mc Namara, 1994).

Thus, in the studied structures, the processes of excitation begin to predominate over the processes of inhibition, which is expressed in an increase in the frequency of activity on the EEG. In addition, the death of GABA-ergic cells weakens the inhibitory control of pyramidal cell activity, projected into different parts of the basal brain, and contributes to the generalization of convulsive activity (Salamon et al., 2005).

Thus, the electrophysiological results obtained are evidence of a direct connection between the basolateral amygdala and the primary area of the visual cortex (area 17). This is evidenced by the appearance of epileptic discharges (ictal and interictal). First, epileptic spikes appeared in the visual cortex, then similar spikes (ictal and interictal) were observed in the retina. The first results were obtained indicating that under the conditions of creating experimental epilepsy, the fact of spread along the centrifugal pathways from the basolateral part of the amygdala to the neuronal elements of the VC, CS, LGD was revealed. American scientists J.L.Freese and D.G.Amaral using electron and confocal microscopes, investigate the synaptic organization of these projections by injecting anterograde tracers into the amygdaloid complex of Macacafascicularis monkeys and examining labeled boutons in areas TE and V1. The authors conclude from these observations that the amygdaloid complex (magnocellular part of the basal nucleus) provides excitatory input to areas TE and V1 that primarily influence spiny, probably pyramidal neurons in these cortices (Jennifer, 2006).

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Citation: Hashimova Ulduz, Miryusifova Khuraman, Allahverdiyeva Arzu, Huseynova Nigar, Javadova Kamala, Panakhova Elmira (2023) Electrophysiological study of effects of basolateral Amygdala on the function of visual system structures. *Journ. Life Sci. & Biomed.,* **78(1):** 26-30

U.Hashimova ORCHID: https://orcid.org/ 0000-0002-7740-0972
Kh. Miryusifova ORCHID: https://orcid.org/ 0000-0001-6529-3869
A. Allahverdiyeva ORCHID: https://orcid.org/ 0009-0001-0997-1116
N. Huseynova ORCHID: https://orcid.org/ 0009-0002-0095-3744
K. Javadova ORCHID: https://orcid.org/ 0009-0003-8437-4770
E. Panahova ORCHID: https://orcid.org/ 0009-0004-2103-7475