CHANGES IN THE ELECTRICAL ACTIVITY OF THE CORTICAL MOTOR ANALYZER IN WHITE RATS DURING A REFLEX EPILEPTIFORM ATTACK

V. M. Vasilyeva

From the Laboratory of the Pathophysiology of Higher Nervous Activity (Head - Doctor of Biological Sciences, L. V. Krushinsky) of the Chair of the Physiology of Higher Nervous Activity (Head - Corresponding Member of the Academy of Pedagogical Sciences of the USSR Professor L. G. Voronin) of the Faculty of Soil Biology of the M. V. Lomonosov Moscow State University

(Received March 5, 1956. Submitted by Active Member of the Academy of Medical Sciences of the USSR, P. K. Anokhin)

At the present time there is a considerable number of quite varied methods of obtaining pathological conditions in animals which reproduce the various forms of epilepsy fairly exactly in their external manifestations. During the last years, one more model of epileptiform attacks, which arises in a certain percentage of white mice and rats in response to strong stimulation by sound [1, 3], has attracted the attention of investigators. The advantage of this model is that convulsive attacks arise with only stimulation by means of sound, without preliminary action on the system by other epileptogenic agents.

The problem before the present investigation was the study of the nervous mechanism of the reflex epileptiform attacks in white rats, in particular, it was desired to discover stimulation of what areas of the brain causes various stages of this pathological motor reaction. In order to solve the problems which were set up, a method of registering the bioelectric processes of the brain was used.

Convincing information about the roles of various areas of the brain in the development of the motor reactions which develop in white mice and rats with strong sonic stimulation is almost absent from the literature. Two unsuccessful attempts [Lindsley, Finger and Henry [6], Griffiths [5]] to register the electric potentials in the brain of rats during the attacks have been described. On the admission of the authors themselves, the analysis of the data obtained is hampered by the distortion of the EEG by artifacts from the vigorous movements of the animals during the epileptiform reaction. More successful in this respect is the work of Ya. Buresh [4], who in a critical experiment, led off the electrical potentials from the cortex and hypothalamus of rats during generalized motor excitation and convulsive attack. In his experiments, the rat was tied to a special apparatus by three limbs and the head. Such fixation brought about inhibition of the reaction of the experimental animals in response to sonic stimulus, and, in order to reproduce it, it was necessary to increase the sensitivity of the animals to the sonic stimulus, which was achieved by the administration of subconvulsive doses of cardiazole. However, such a method of sensibilization lowers the value of the investigation, since the cardiazole causes considerable EEG changes. In addition, cardiazole alone is a potent epileptogenic agent, so its administration can change the nature of the attacks themselves.

In the present work, the following concrete problems were set up:

1. To discover the basic conditions necessary to obtain reflex epileptiform reactions in white rats, fixed in the position requisite for the undistorted registration of an electroencephalogram.

2. To trace the changes in the electrical activity of the cortical motor analyzer during the development of the pathological condition with the form of general motor excitation, clonic and tonic spasms, arising in rats on the action of a sonic stimulus.

3. On the basis of the changes in the electrical activity of the cortical motor analyzer to determine the nature of the functional changes in the activity of this area of the brain and to discover the possible role of the cerebral cortex in the development of various stages of the pathological motor reactions.

EXPERIMENTAL METHODS

In solving the first problem, we began with the data of L. V. Krushinsky, L. N. Molodkina and I. A. Kitsovskaya [2] that the conditions favorable for the development of reflex epileptiform reactions are an increased excitability of the nervous system and a weakening of the inhibitory process, which can be achieved by the removal of the parathyroid glands. Therefore, we used parathyroidectomy with the aim of increasing the sensitivity of the rats to sonic stimulus. Parathyroidectomy proved to be sufficient for the necessary increase in the nervous "epileptic readiness" of the rat. The system of partially fastening the rat which we worked out consisted of fastening the head rigidly until it was almost immobilized even during quite vigorous movements by the animal and in tying the body lightly to the bottom of the chamber. The limbs remained completely free, so that it was possible to observe almost all the stages of the epileptiform reaction. These conditions made it possible to obtain systematically several tens of attacks on each animal in the course of 3-5 months.

In order to study the electrical activity of the cortical motor analyzer, a method involving extradural leads for the electrical potentials in a continuing experiment was worked out with the help of implanted electrodes. This method represented a modification of A. B. Kogan's methods of implanting electrodes.

For this purpose, two trepanned openings, separated from each other by 2 mm, were drilled in the skull bone above the motor zone of the cerebral cortex under local anesthesia with the help of a dental drill. In all cases, the dura mater remained unharmed. The electrodes were introduced through the trepanned opening and were placed on the dura mater. The electrodes were silver disks, equal in diameter to the trepanned opening, and 0.25-0.50 mm in thickness, to which the wire leads were soldered. The silver disks and wire leads were carefully isolated with bakelite lacquer (in order to avoid recording the muscular potentials). Before implantation, a small area, 1-1.5 mm^2 in area, was cleaned on the lower contact surface of the disk. The fixation of the electrodes to the skull bones was carried out with dental phosphate cement. The junction of the electrodes with the apparatus were made with serfiny leads with a silver contact surface. The leading off of the electrical potentials was bipolar in all cases. Registration of the potentials was carried out by a 4-channel amplifier of biological currents with an ink recorder. During the experiment, the rat was placed in a shielded chamber 20 × 25 × 60 cm in size, in the rear of which was a source of sound in the form of a telephone bell. In order to avoid recording the electromagnetic waves from the bell, all the wires and the bell were carefully shielded and grounded. The reported data were obtained in 97 experiments on 4 rats with permanently implanted electrodes.

EXPERIMENTAL RESULTS

In Fig. 1 are shown the most frequently observed changes in the electrical activity of the cortical motor analyzer during the time the sonic stimulus acted. 7.5 seconds after the bell was turned on, the motor reaction of the rat appeared in the form of disorganized movements of the extremities, body and tail (stage of general motor excitation). In this stage, some strengthening of the quick fluctuations is observed in the EEG. The stage of motor excitation changes almost instantaneously at the 24th second of the bell's action to general clonic spasms (clonic stage). At the moment the clonic spasms appear, a group of rapid fluctuations in the form of a "volley" of impulses with a frequency of not less than 75 per second (75 waves per second is the limit of the frequencies which the apparatus with ink recording can reproduce without distortion). Then the rhythmic electrical activity changes sharply, in spite of the fact that the clonic spasms still continue for a considerable time, and acquires the aspect of alpha-like waves, which in their turn, are gradually replaced by delta-rhythm. While delta-rhythm predominates in the motor area of the cerebral cortex, the clonic spasms are replaced by tonic spasms (tonic stage), followed by a slackening of all the muscles (stage of complete areflexia). The delta-rhythm remains approximately until the rat returns to its original condition.

In Fig. 2 there is shown another variant EEG of the cortical motor analyzer, recorded under the same conditions, but it is encountered considerably less frequently. In this case the epileptiform reaction occurs somewhat faster, and there are some differences in the nature of the changes in electrical activity as compared with the first case. The motor excitation which arises at the 5th second of the bell's action, less than two seconds later changes into clonic spasms, very quickly replaced by a prolonged (about 19 seconds) tonic

spasm, after which the rat falls into a nearly comatose state. During the motor excitation in this case, a noticeable increase in the rapid waves is not observed, while the slow waves, 3-4 per second, reach 7-8 per second and acquire a more regular outline. The rapid waves at the beginning of the clonic spasms are considerably smaller in amplitude and do not change to alpha-like waves at once. The alpha-like waves appear only 5, 7 seconds after the clonic spasms changed into tonic spasms and change into delta-activity, as in the first case, when the tonic spasm ends, and the rat falls into a comatose state.

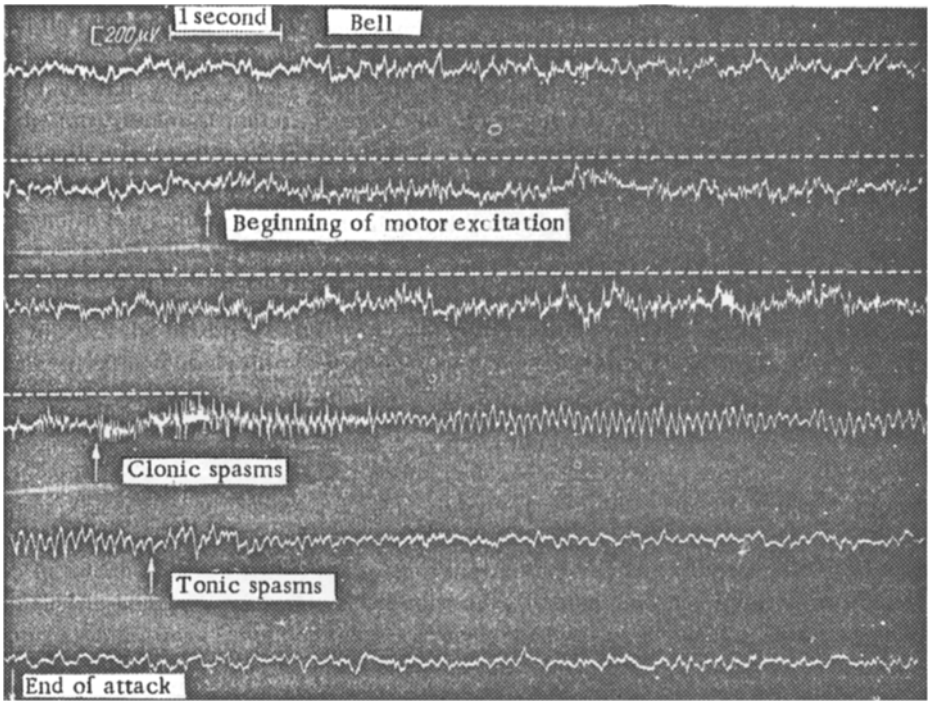

Fig. 1 Electrical activity of the cortical motor analyzer of a white rat during a reflex epileptiform attack, caused by strong sonic stimulus (Experiment on Jan. 9, 1954).

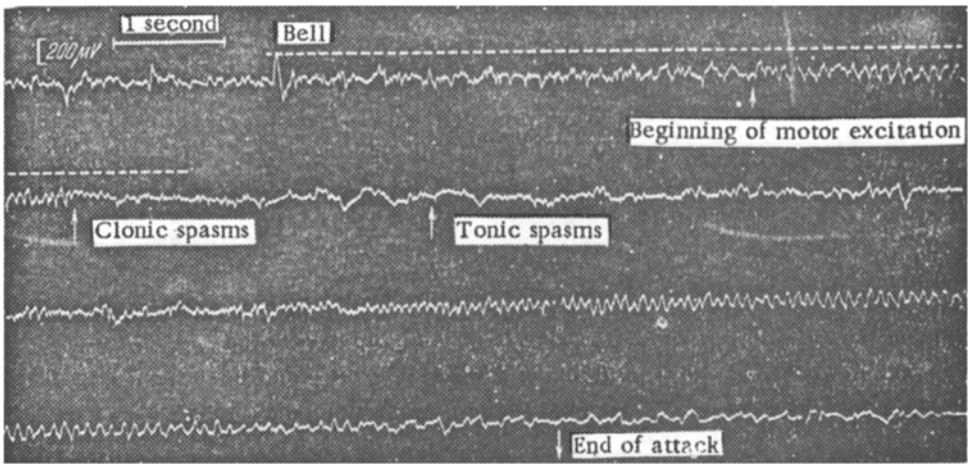

Fig. 2. Electrical activity of the cortical motor analyzer of a white rat during a reflex epileptiform attack, caused by a strong sonic stimulus (Experiment on April 4, 1954).

Thus, the above data regarding the changes in the electrical activity of the cortical motor analyzer in white rats during sonic stimulation causing an epileptiform reaction, show that distinct, regularly occurring changes in electrical activity corresponding to the various stages in the development of the pathological motor reaction, were observed in the cerebral cortex.

During the stage of motor excitation, in comparison with the original background, some generalized increase in the frequency of the rhythms was observed (in the first case, it was in the form of reinforcement of the rapid fluctuations; in the second, in the form of increasing the frequency of the slow waves from 3-4 per second to 7-8 per second), indicating that the excitation process in the cortex was strengthened. The group of rapid fluctuations (about 75 per second), which appeared at the beginning of the clonic spasms, indicated a sharp excitation of the cortex which occurred at this moment. This state of excitation is replaced in some cases after only 1-2 seconds, in other cases somewhat later, by a depression of the functional state, represented electrographically in the form of a sharp slowing of the rhythms (appearance of alpha-like and delta-like waves). The depressed functional state of the cortex remains throughout the entire remaining period of clonic spasms, and also throughout the entire stage of tonic spasms and in the post-attack period, which is typified by signs of areflexia and catelepsy.

The data which were obtained indicate that the cortical motor analyzer can hardly be considered responsible for all the stages of development of a given spasm attack. It can be supposed that the excitation of other areas of the brain, namely the subcortical motor areas, is responsible for the clonic and tonic stages of the attack.

SUMMARY

Elaboration of a special system of partial fixation in rats and their sensibilization to an acoustic epileptogenic stimulation after parathyroidectomy have enabled us to register bioelectrical processes of the brain in chronic conditions during all stages of audiogenic seizures.

On the basis of the data obtained we are enabled to hypothesize concerning the role of cerebral cortex in preconvulsive and convulsive stages of attack.

LITERATURE CITED

[1] L. V. Krushinsky, Uspekhi Sovremennoi Biology, 1949, vol. 28, issue 1 (4), pp. 108-133.

[2] L. V. Krushinsky, L. N. Molodkina and L. A. Kitsovskaya, Byull. Eksptl. Biol. i Med., 1950, vol. 30, issue 8.

[3] L. V. Krushinsky, Uspekhi Sovremennoi Biology, 1954, vol. 37, issue 1.

[4] Ya. Buresh, Experiments on the Electrophysiological Analysis of the Generalization of an Epileptic Fit, Chekhoslovatskaya fiziologiya, 1953, vol. 11 No. 4.

[5] W. Y. Griffiths, The Influence of Behavioral Factors on the Incidence of Audiogenic Seizures in Rats, J. Comp. and Physiol. Psychology, 1953, vol. 46, No. 2.

[6] D. Lindsley, W. Finger and C. E. Henry, Some Physiological Aspects of Audiogenic Seizures in Rats, J. Neurophysiol., 5, 3, 1942.