EFFECT OF PAROXYSMAL AND PREPAROXYSMAL COMPONENTS OF THE AUDIOGENIC SEIZURE ON CONSOLIDATION OF TEMPORARY CONNECTIONS

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Comparison of audiogenic seizures of varied severity in rats revealed the amnesic action of the paroxysmal phases of the audiogenic seizures on the consolidation of temporary connections and on short-term memory (but not long term). Audiogenic seizures without behavioral paroxysms disturbed it hardly at all. The results confirm data obtained by the writers previously on differences between the nature of the paroxysmal and preparoxysmal phases of motor activity in audiogenic seizures in rats. The preparoxysmal phase is regarded simply as a unique "motor aura" of the seizure, containing no paroxysmal components.
KEY WORDS: audiogenic seizure; preparoxysmal motor excitation; consolidation of temporary connections; short-term memory; amnesia.

A distinguishing feature of the audiogenic epileptiform reaction arising in certain mammals (rats, mice, rabbits, and guinea pigs) is the presence of violent preparoxysmal motor excitation, which some workers [6, 8, 10, 12] consider to be a response of flight from an excessively strong stimulus, whereas the subsequent convulsions are a manifestation of neurosis arising because of inability to avoid this stimulus in the closed chamber. Other workers [2, 9, 11, 13] regard the whole seizure as a pathological reaction of epileptoid character.

The writers showed previously that rats taught to run out of the chamber where the acoustic stimulation was applied, or familiar with the location of a hole in the wall of the chamber, take advantage of the opportunity to leave it during the preparoxysmal excitation [4], thus demonstrating that this avoidance reaction includes a defensive component. The problem of the presence of paroxysmal brain discharges in this phase is less clear [3].

Since paroxysmal brain activity is an effective amnesic factor even in the absence of behavioral paroxysms [1], in the investigation described below the effect of audiogenic seizures with and without a behavioral paroxysmal phase on the consolidation of temporary connections was compared. The action of audiogenic seizures was studied for comparison on conditioned, natural, and unconditioned food reflexes.

EXPERIMENTAL METHOD

Experiments were carried out on 83 rats of the Krushinskii–Molodkina strain, susceptible to audiogenic seizures (the ringing of a bell with an intensity of 112 dB). The intensity of the seizure was assessed in points by Krushinskii's scheme [3]: motor excitation, flight – 1 point; clonic convulsions – 2-3 points; tonic convulsions – 4 points.

In the experiments of series I the rats were taught to run away from the small dark chamber of an apparatus consisting of two chambers [7]. After 5 min to investigate the apparatus, the rats were placed in the small chamber and subjected for 1 min to unescapable painful electric shocks, and 20 sec later the animals were transferred to the chamber for acoustic stimulation and the bell started to ring. The rats were again allowed to investigate the apparatus 24 h later. The length of the stay in the small chamber during the first

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session of investigation (t_1) and 24 h later (T_1) was recorded.

In the experiments of series II the same rats were placed at the beginning of a corridor with their tails toward the entrance, which was then closed, and they were allowed to investigate the corridor until they reached the open exit from it into the acoustic stimulation chamber. The corridor measuring 40 × 10 × 12 cm sloped upward at an angle of 15° in the direction of movement of the rat. An avoidance reflex to nociceptive electrical stimulation was then produced in the rats by applying electric shocks to them until they escaped into the chamber for acoustic stimulation. The integrity of the avoidance reflex was tested after 24 h. The time taken to escape in the first combination (T_2) and 24 h later (t_2) was recorded.

In both series of experiments the control animals (18 rats) were trained and then subjected to a non-epileptogenic tone (4 kHz, 40 dB). The coefficient of amnesia was calculated from the temporal indices recorded in the two series, by the equation: $K = 100\ [1 - (T - t)/T]$, or $K = 100\ t/T$, where K is the reciprocal of the rate of formation of a reflex of escaping from the dark chamber or avoiding stimulation in the corridor, the values of which range from 0 to 100.

In series III six rats were taught a reflex to place [5], by reinforcing running only in one direction (to the right or left), and another six rats were taught responses of alternation of the locations of food reinforcement (in three rats the order of alternation was right–left–right; in the other three rats it was left–right–left), using an experimental technique with a screen [3] as suggested for the study of extrapolation reflexes. After the animal had drunk some of the milk in the feeding bowl through a slit in the middle of the screen the bowl was moved to the side of the screen, and in order to obtain the reinforcement the rat had to go around the screen on the appropriate side. The formation of the alternation reflex was tested by altering the order of alternation of the sides (for example, right–left–left–right, instead of right–left–right). After the consolidation of these reflexes, the effect of audiogenic seizures on them was studied.

The statistical analysis of the results was carried out by assessing the significance of the difference between sample means by Fisher's criterion.

EXPERIMENTAL RESULTS

In experiments in which the rats were trained to escape from the dark chamber the coefficient of amnesia in the control was 8.5 ± 1.8. If the rats did not give an epileptiform response to the ring of the ball (0 points) or responded only by running (1 point), the corresponding values of K did not differ significantly from the control (9.0 ± 3.3 and 15.8 ± 6.9, respectively; $P > 0.05$). If seizures of varied intensity developed (2, 3, and 4 points), the values of K were significantly higher than the control, namely 59.1 ± 4.2 and 89.8 ± 4.5 compared with 30.2 ± 8.3 ($P < 0.05$). In the experiments to study avoidance of nociceptive electrical stimulation by leaving the corridor, in the absence of a response to the ringing of the bell and in the presence of motor excitation the values of K did not differ from the control (control 17.0 ± 4.0; 0 points 17.6 ± 3.8; 1 point 21.6 ± 3.3; $P > 0.05$).

Consequently, neither the ringing of the bell itself nor the flight evoked by it caused a disturbance of short-term memory or of the consolidation of temporary connections. Amnesia appeared only after paroxysmal components of the seizure; tonic convulsions (4 points) were accompanied by a more severe amnesic effect than clonic (2 or 3 points).

After epileptiform seizures the conditioned and unconditioned reflexes previously formed were suppressed (moving around the chamber, unconditioned and natural food reflexes, conditioned reflex to place, and the response to alternation of the reinforcement sides). These reflexes recovered after the seizure in the following order: unconditioned food reflex (after 34.0 ± 2.9 min), natural food reflex (85.1 ± 2.6 min), conditioned reflex to place (98.2 ± 3.5 min), and reflex to alternation of the reinforcement sides (106.1 ± 3.8 min).

Consequently, the epileptiform seizure does not disturb the traces of long-term memory, although the manifestation of inborn and acquired reflexes is temporarily suppressed.

The results show that the audiogenic seizure selectively disturbs short-term memory and the process of consolidation of temporary connections, but this takes place, however, only if it includes behavioral paroxysmal phenomena. The violent motor excitation does not affect consolidation of temporary connections and, consequently, it evidently does not contain cerebral paroxysmal components. However, in the writers' opinion [4], it does not itself constitute flight from the acoustic stimulus. Meanwhile the fact that previously acquired skills, enabling the animal to avoid an audiogenic seizure [4], can be carried out during the phase of motor excitation reflects the similarity between this phase and the preparoxysmal motor aura in patients with epilepsy.

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MECHANISM OF DISTURBANCE OF INHIBITORY ELECTROGENESIS IN SPINAL α-MOTONEURONS IN EXPERIMENTAL LOCAL BOTULINUS POISONING

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The character of changes in postsynaptic inhibition in spinal α-motoneurons of cats was studied in the course of experimental local botulinus poisoning. At the beginning of development of the local paralytic syndrome a marked decrease in the amplitude of the reciprocal, and a smaller decrease in amplitude of the polysynaptic IPSPs was observed. On the appearance of total paralysis of the muscles from botulinus poisoning the reciprocal and polysynaptic IPSPs were inhibited even more, but they never disappeared completely and were never converted into depolarization potentials. During the development of the IPSP the synaptic permeability of the motneurons as a rule was reduced.

KEY WORDS: botulinus poisoning; spinal motoneurons; inhibitory postsynaptic potential.

Some workers regard botulinus toxin (BT) as a purely peripheral blocking agent [4, 5]. However, loss of the spinal reflexes and mono- and polysynaptic ventral root potentials of the spinal cord and a decrease in the excitability of the somatic membrane of α-motoneurons always precede the development of the transmission block in the myoneural synapses. This is evidence that the primary disturbance of activity of the centers is connected with the development of the paralytic syndrome [1, 2]. It is still uncertain to what extent the depression of excitability of the nerve cells at the various stages of botulinus poisoning is connected with a change in

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