ANALYSIS OF THE PHASE OF PREPAROXYSMAL MOTOR EXCITATION DURING AUDIOGENIC FITS IN RATS

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To study whether the preparoxysmal motor excitation accompanying audiogenic fits in rats is a response of avoidance of the accoustic stimulus or a distinctive phase of the fit itself, the frequency of running away during this phase through a hole in the cage wall was compared for rats unfamiliar and familiar with the position of the hole and also for rats with a developed defensive response of running through this hole to the action of a nonepileptogenic stimulus. Running away took place in 17, 67, and 96.3% of cases, respectively. These results indicate the presence of two components in the first phase of the fit: pathological audiogenic excitation (comparable with the motor aura in epileptics) and a defensive response of active avoidance of the epileptogenic stimulus.

KEY WORDS: audiogenic fits; preparoxysmal excitation; avoidance response.

Audiogenic epileptiform fits in rats, mice, and rabbits differ from all other forms of epilepsy in the manifestations of motor excitation (jumping, running), preceding the paroxysms, that are regarded either as a response of flight and active avoidance of an excessively strong stimulus [5, 6, 11, 13] or as one phase of a reflex response of pathological character [1, 9, 12, 14].

To investigate this problem the possibility of appearance of defensive motor responses was studied during preparoxysmal excitation in rats before and after appropriate training.

EXPERIMENTAL METHOD

Two groups of rats of the Krushinskii–Molodkina breed, subject to audiogenic fits, were used; the fits were induced by a bell (112 dB). The conventional stimulus was a pure tone (4 kHz, 40 dB) and the unconditioned stimulus pulses of alternating current (10 V) applied through the floor of the cage. The transparent plastic cage, measuring 44 × 28 × 46 cm, had a hole 3.5 cm in diameter in one wall, 8 cm from the floor.

In the experiments of series I the behavior of the rats in the chamber with the hole open and in the absence of stimulation was studied for 3 min (10 rats); in series II behavior was studied during the application of a nonepileptogenic tone (3 min) with the hole covered by means of a movable screen to which a rubber balloon connected pneumatically with a Marey's capsule was fixed; in this way the movements of the rat hitting the closed hole could be recorded on a kymograph. The tests were repeated three times. The experiments of series III were carried out to study whether the response of running to the hole (open or closed in such a way that the rat could open it by hitting it) was present to the sound of a bell in the same rats and in 20 fresh rats. In series IV a conditioned reflex of active avoidance of painful electrical stimulation, in the form of running from the cage through the covered hole in response to the action of the pure tone, was produced in nine rats. In series V the presence of the avoidance response during preparoxysmal motor excitation evoked by the ringing of a bell was tested in the same nine rats. This test was repeated twice at an interval of 24 h; if the rat ran away before the beginning of excitation in the second experiment, it was replaced in the cage.

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EXPERIMENTAL RESULTS AND DISCUSSION

Rats placed for the first time in a cage with the hole open exhibited an orienting response (they sniffed and tapped the floor and the wall of the cage, the edges of the hole, and poked their head into the hole), but did not leave the cage. If the hole was covered by a shutter and a nonepileptogenic tone applied (experiments of series II) the rats hit the shutter before and after its action (on the average for 3 min, 16 and 19 blows, respectively, in the first experiment, 4 and 12 in the second, 4 and 16 in the third). During the action of the epileptogenic bell, in 36 experiments (nine rats) there were 24 cases of running away during motor excitation (67%), but in 40 experiments with the 20 fresh rats there were only seven cases (17.5%; $P < 0.001$). There was no difference in the number of runnings to the open or covered hold. Consequently, rats previously familiarized with the position of the hole could make use of this experience during motor excitation also. The fresh rats probably discovered the hole by chance during running and jumping.

Rats with a developed defensive avoidance reflex to the action of the tone ran away in response to the bell in 96.3% of cases ($P < 0.001$). In some cases they ran away before the general motor excitation began (during the latent period). These rats were immediately replaced in the cage, when they ran away like the rest at the beginning of the phase of motor excitation, except that their latent period was significantly lengthened. Only in three cases did the animals run away after 4, 5 and 18 sec of motor excitation.

Rats with a developed defensive reflex of running away in response to a pure tone thus ran away in nearly every case in response to the action of a bell and under these circumstances they did not develop fits. In the experiments of Plotnikoff [13] untrained mice ran away in 70-80% of cases, and 10% of animals developed fits (74% in the control); on this basis Plotnikoff regards audiogenic excitation as similar to "flight from a harmful stimulus." However, the results of these experiments can also be explained by chance discovery of the hole by the mice. There is evidence that defensive conditioned reflexes can be manifested during the latent period of the fit [7]. The present experiments showed that conditioned and unconditioned defensive reflexes can appear not only before, but also during the phase of motor excitation. The fact that the frequency of the avoidance responses depends on the degree of familiarity of the animals with the escape hole and on their preliminary training indicates that in these cases the rats did not find the hole accidentally but aimed for it deliberately.

Nevertheless, there are grounds for considering that the phase of preparoxysmal motor excitation is an active and purposive attempt by the animals to escape from the chamber. Running and jumping by the rats during this period are evidently involuntary movements, although the animals remained capable of perceiving stimuli and responding adequately to them, as well as of directing their locomotion to some degree. Evidence of the automatic and pathological character of the entire audiogenic fit is available; the hereditary mechanism of the fit and the constancy of its components (latent period, character, and duration of the phases) in inbred animals [2]; the manifestation of spontaneous fits of running and seizures in rats kept on a diet deficient in magnesium [2]; the reproduction of such fits by electrical stimulation of the auditory subcortical nuclei [4]. The possibility of inducing fits and an increase in sensitivity to acoustic stimulation by convulsant poisons and of preventing fits by anticonvulsants. A similar motor excitation can also be observed during repeated acoustic stimulation immediately after the fit [3] and in the postparoxysmal "aggression," when there are clear signs of uncontrollable automatic actions. In the preparoxysmal phase, on the other hand, at least at its beginning the animal can still coordinate its movements and make use of individually acquired experience. This phase can therefore be compared with the preparoxysmal motor aura in epileptics [15], during which the person can actually prevent the onset of the fit by taking suitable measures.

Although audiogenic motor excitation is evidently not in itself flight from a stimulus, it is a background for the manifestation of a "true" defensive response, which during training acquires an increasingly adaptive character toward the concrete situation. Since audiogenic motor excitation and the defensive avoidance response were manifested in these experiments both together and separately, they are evidently based on different mechanisms. It has been shown [8, 10, 16] that destruction of the inferior colliculi (by contrast with other nuclei of the auditory pathway) prevents the running fit while preserving the preceding motor and autonomic components of the unconditioned and conditioned defensive responses to sound. It is claimed [16] that these responses are connected with the extralemniscal pathways and the flight response with colliculofugal pathways.

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