CHANGES IN A COMPLEX ADAPTIVE REFLEX IN DOGS CAUSED BY LSD-25

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Disturbances of a complex conditioned avoidance reflex caused by lysergic acid diethylamide (LSD-25) were studied in experiments on dogs. The disturbance began with the appearance of multiple responses between stimuli, reproducing a defensive movement. During the action of large doses of LSD-25, the conditioned-reflex movement to a distant acoustic stimulus was last to disappear and first to reappear, exhibiting greater stability than the unconditioned response to pain. The hypothesis is put forward that de-inhibition mechanisms participate in the hallucinogenic action of the drug.

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Despite the numerous experimental and clinical investigations of the action of lysergic acid diethylamide (LSD-25), complex forms of adaptive behavior of higher animals have been used in very few studies. I consider that the use of such experimental models would be most appropriate for comparing data obtained on animals with the results of self-observations and observations on human subjects receiving the drug.

EXPERIMENTAL METHOD AND RESULTS

The method of production of a complex defensive conditioned reflex, proposed originally by G. P. Zelenyi and modified by G. V. Skipin, was used in this investigation.

The results of the experiment showed that small doses of LSD-25, when given to animals in a state of generalized excitation, evoke responses in the interval between stimuli (interval responses) not present in the background. In the case of the dog Radzh (Fig. 1), a small dose (0.06 mg/kg body weight) gave rise to interval responses in the following order: Interval elevations of the forelimb first appeared, resembling in their form the adaptive response to the conditioned stimulus (Fig. 1B), next, the interval flexion of the forelimb was joined by interval elevations of the hind limb (C), and finally, the interval elevations of the forelimb disappeared whereas the movements of the hind limb continued for some time (D). The response to the conditioned stimulus remained normal under these circumstances.

Large doses (0.1-0.3 mg/kg) led to a transient appearance of interval responses of the forelimb 5-8 min after injection, followed by inhibition of conditioned motor responses. The action of LSD-25 began with disturbance of the tonic form of elevation of the forelimb. The dog had difficulty in holding its limb at the level of breaking the contact and received an electrical stimulus (Fig. 2B). The conditioned response to the ringing of a bell continued for a little longer.

In another experiment of the same dog restoration of reflex activity began with the appearance of a conditioned (!) response to the bell, but not with the unconditioned response of the hind limb to the action of electrical stimulation (Fig. 2C).

Small doses (0.05 mg/kg) given to the dog Ryzhik strengthened the interval flexion of the forelimb. At the same time, interval responses of the hind limb appeared. Large doses (0.1-0.2 mg/kg), as in the case of the dog Radzh, at first disturbed the conditioned response of the forelimb to electrical stimulation while the conditioned response to acoustic stimulation remained, and later inhibited the whole conditioned-reflex act. No elevation of the hind limb to electrical stimulation took place.

The animals' general behavior after injection of LSD-25 was very characteristic: they became restless, alert, looked around them continually, examined something on the floor persistently, barked and howled whenever the bell was switched on. After the end of the experiment, when released from the straps,

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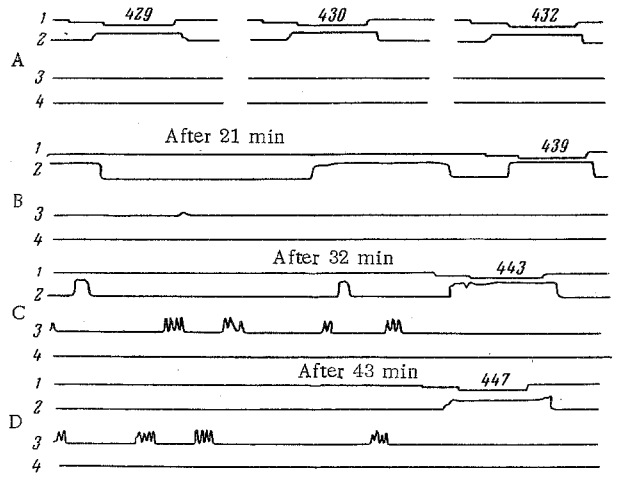

Fig. 1. A) Conditioned reflexes of the dog Radzh before injection of LSD-25; B) appearance of interval responses of the forelimb 21 min after injection of LSD-25 in dose of 0.06 mg/kg; C) interval responses of foure- and hind limbs; D) disappearance of interval responses of forelimb; 1) marker of acoustic stimulus and time of closed circuit; 2) trace of movements of forelimb; 3) trace of movements of hind limb; 4) marker of electrodermal stimulation. The numbers denote the serial number of presentation of the conditioned stimulus.

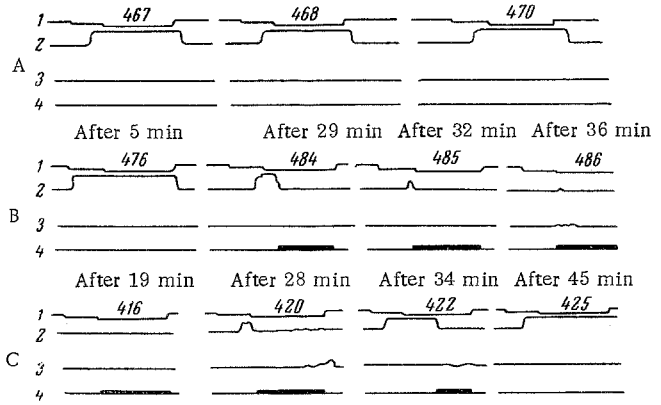

Fig. 2. A) Conditioned reflex of the dog Radzh before injection of LSD-25; B) stability of conditioned-reflex elevation of forelimb to acoustic stimulation after injection of LSD-25 in dose of 0.1 mg/kg; C) restoration of conditioned-reflex elevation of forelimb to acoustic stimulus. Remainder of legend as in Fig. 1.

the animals pressed themselves against the base of the frame and could not jump onto the floor. Outside the room they still exhibited a well-marked orienting response; in darkness they became cautious and slow to respond, and their movements were ataxic. Excitable dogs, with an aggressive tendency, showed an active defensive response.

In the course of disturbance of the complex avoidance reflex, attention was directed to two facts: the appearance of interval responses of the forelimb and the high stability of the motor response to a distant conditioned stimulus.

The onset of interval responses is evidently due to the de-inhibitory action of the drug, more especially because the whole symptom-complex produced by LSD-25 fits in well with the concept of disturbance of inhibitory processes. According to several authors, the de-inhibitory action of this drug is based on its ability to excite the adrenergic structures of the brain [3]. However, the de-inhibitory effect may also be due to blocking of serotonin structures [4]. Data have recently been published indicating that LSD-25 blocks the inhibitory influence of the hippocampus on the reticular formation of the brain stem [8], and the increase in sensory sensitivity in the limbic structures [6]. De-inhibition of orienting behavior is highly characteristic of LSD-25 [7]. It may be supposed that the above-mentioned physiological mechanisms participate in the hallucinogenic action of the drug, the basis of which is activation of neural traces which are "foreign" to the real experimental situation [5].

The evidence of high stability of the response to a distant conditioned stimulus which we obtained, and the whole dynamics of inhibition of motor activity, in which the conditioned component of the complex motor reflex disappears last and is restored first, are in conflict with data obtained by other authors [1, 2]. Possibly, the stability of the responses is based on specific features of the protective flexion of the forelimb, functioning without electrical stimulation. Absence of a response to electrical stimulation was due, in all probability, to low susceptibility to stimulation caused by inadequacy of the protective inhibitory mechanisms.

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