CREATION OF HYPERACTIVE DETERMINANT DISPATCH STATIONS IN THE CAUDATE NUCLEUS IN EXPERIMENTAL NEUROPATHOLOGICAL SYNDROMES CAUSED BY TETANUS TOXIN

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Generators of pathologically enhanced excitation, playing the role of "hyperactive determinant dispatch stations" (DDS) were created with the aid of tetanus toxin, which disturbs various types of inhibition in rats, in the rostral part of both caudate nuclei. The formation of these DDS generators in the structures specified led to the formation of stereotypes, impulsive seizure movements, and catalepsy.

KEY WORDS: caudate nucleus; "determinant dispatch station"; generator of pathologically enhanced excitation; stereotypes; impulsive seizure movements; catalepsy; tetanus toxin.

Previous investigations [3-7, 9, 10] concerned with the study of the principle of the determinant dispatch station (DDS) showed that, after local disturbance of inhibition in various structures of the spinal cord and brain, corresponding neuropathological syndromes can be induced (pain syndrome of spinal origin, phantom pain syndrome, trigeminal and thalamic pain syndromes, vestibulopathy, and photogenic epilepsy). It was accordingly postulated that the formation of hyperactive DDS, based on generators of pathologically enhanced excitation [2, 8], is one of the most general mechanisms common to several neuropathological syndromes.

This paper gives details of the experimental production of neuropathological syndromes accompanying the creation of hyperactive DDS (generators of pathologically enhanced excitation) in the rostral part of both nuclei.

EXPERIMENTAL METHOD

Experiments were carried out on 70 noninbred male albino rats weighing 200-250 g. As in the previous investigations, the hyperactive DDS generators were created by the use of tetanus toxin (TT), which disturbs inhibitory processes [1, 11, 12]. Purified TT was injected in a dose of 3-5 MLD for rats (volume $0.2 \cdot 10^{-4}$-$0.5 \cdot 10^{-4}$ ml) as a single microinjection from glass micropipets (tip diameter 20-50 μ) into the rostral part of the caudate nuclei corresponding to stereotoxic coordinates AP−2.0, L 2.5, H 4.5 [13]. The preparatory operation and injection of TT were performed under hexobarbital anesthesia (100 mg/kg intraperitoneally). To prevent the spread of TT by the blood, 0.03 i.u. antitoxin was injected intramuscularly. Animals (10 rats) receiving an injection of inactivated TT served as the control. The presence of catalepsy was determined by the usual tests. After injection of TT all the animals were kept in individual cages measuring 25 × 25 × 25 cm.

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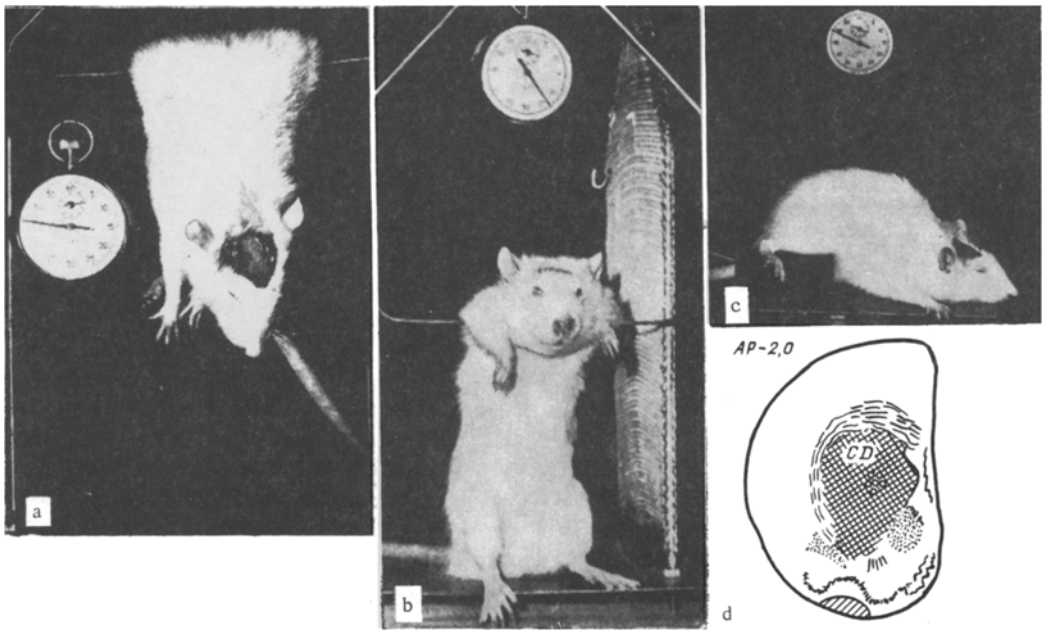

Fig. 1. Manifestations of experimental catalepsy after tetanus toxin injection. Special tests demonstrating the presence of plastic tone in cataleptic rats: a) hanging on a horizontal rod; b) standing by a horizontal rod; c) awkward position of hind limb; d) scheme of frontal section through rat brain passing through head of caudate nucleus (CD) taken from Fifkova and Marsala's atlas [13]. Region of head of caudate nucleus is shaded. Circles mark region of microinjections of TT.

EXPERIMENTAL RESULTS AND DISCUSSION

Injection of TT into the rostral part of the head of both caudate nuclei led to the formation of stereotypes, impulsive seizure movements, and catalepsy. These phenomena were not observed in the animals of the control group after injection of inactivated TT.

1. Stereotypes. Features of stereotyped behavior appeared in nearly all the animals 12-18 h after injection of TT. Most rats developed a motor stereotype: a short run from the corner of the cage, followed by a rapid return to the previous place and the original posture. Later, this form of stereotype was accompanied with great constancy by repeated rearing movements, by clambering up the wall of the cage, and moving along it. Another less common form of stereotyped behavior consisted of consecutive short runs with stops, digging holes in each corner of the cage, and then piling up shavings in one quarter of the cage. These forms of stereotypes were accompanied by simpler elements of stereotyped behavior, in the form of minor movements of the forelimbs and head resembling the monotonous performance of simple behavioral reactions (an inquisitive movement of the head, sniffing at the walls of the cage, biting movements, and so on). Normal behavioral responses, the taking of food and water, and sleep were all upset to some extent. As a rule the stereotypes diminished and disappeared 24-32 h after the injection of TT.

2. Impulsive seizure movements. In most animals tic like up and down movements (jerks) of the head appeared 22-24 h after the injection of TT. The frequency of the jerks varied in the same animal. Intervals between them varied from 3-4 sec to 30 min. The intensity of the jerks also was inconstant: They varied from trivial twitches of the head to throwing the head backward. In some cases the jerks changed into convulsions, which ended in hyperextension of the head, sitting up on the hind limbs, and waving the forlimbs in front of the face. Some animals developed convulsions without jerks. The duration of the convulsions varied from 3-5 to 40-55 sec. Often they were accompanied by trampling and circular movements on the hind limbs, or the animal would step backward. The severest convulsions terminated with the animal falling on its back, after which it rapidly resumed its normal posture. After the end of the convulsion, the tone of the trunk muscles was increased, so that the animal adopted a humpbacked posture with, less frequently, flexion of the head and extension of the forelimbs.

3. Catalepsy. Injection of TT into the rostral part of the caudate nuclei led to the formation of a cataleptic syndrome in all the experimental animals. The development of plastic tone took place in three

phases. In the first phase (12-18 h after injection of TT) there was a selective increase in tone of the tail. If the tail was put in an artificial position, this was kept for several minutes, even while the animal moved about. In the second phase (18-36 h) the increase of plastic tone was manifested in the animal's becoming completely motionless. This effect was paroxysmal in character. The postures in which the animal stopped dead were apparently stages of a locomotor act. In the third phase (from 36 h to 4-5 days) the increase in plastic tone led to frank status catalepticus (Fig. 1). If put into an artificial position the animal would remain in it for a long time. It would stay more than 30 sec hanging by its forelimbs. All the specific tests for catalepsy were present: an awkward position of the limbs, standing up by a horizontal rod, hanging on a net, and so on. The animals would remain in these positions for 10-20 min or more. The response to nociceptive stimulation (pinching the tail) remained intact and the animal regained its normal posture if turned over onto its back.

These results show that microinjection of TT into the rostral part of both caudate nuclei leads to the development of a symptom-complex, in the course of which various neuropathological syndromes can be distinguished, either in an isolated form or in overlapping succession. For example, the first phases of manifestation of plastic tone could be observed while stereotyped reactions and impulsive seizure movements were still present, and complete status catalepticus in the rats was interrupted by single jerks. Various automatic disorders also were noted: ptosis, lacrimation, secretion of nasal mucus, and salivation. During the first day after injection of TT hyperesthesia was present to touching the vibrissae and the lateral surfaces of the body, and to pinching the tail. The hyperesthesia was later followed by hypoesthesia.

On the basis of these results, together with those of previous investigations, certain conclusions can be drawn.

As was shown previously, a population of neurons in which inhibitory connections are disturbed becomes a generator of pathologically enhanced excitation [2, 8], which plays the role of a hyperactive DDS, capable of inducing a corresponding neuropathological syndrome, depending on the system in which the DDS arises. The neuropathological syndromes described in this paper are the result of the creation of hyperactive DDS (generators of pathologically enhanced excitation) in systems of neurons in the rostral part of the caudate nuclei.

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