ROLE OF THE FRONTAL LOBES IN HYPOTHALAMIC AUTOSTIMULATION IN RATS

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Injury to the frontal lobes in rats abolishes autostimulation in a chamber equipped with a pedal, during the first few days after the operation, but depresses autostimulation by a much lesser degree in a chamber on a wheel, in which volleys of stimuli accompany rotation of the wheel by the running rat.

The effects of exclusion of local regions of the brain [1, 6], of pharmacological agents [4], and of other factors on autostimulation (AS), are usually judged from changes in the frequency of pressing upon a pedal, when each pressure is accompanied by the sending of a volley of stimuli of definite duration to the brain. The effects discovered may be due to the action of the test factor not only on the intimate mechanisms of AS, but also on the animal's motor activity. This complication is a particularly real one in the case of exclusion of certain parts of the brain. In such cases it is desirable to use an AS method based on different types of motor activity.

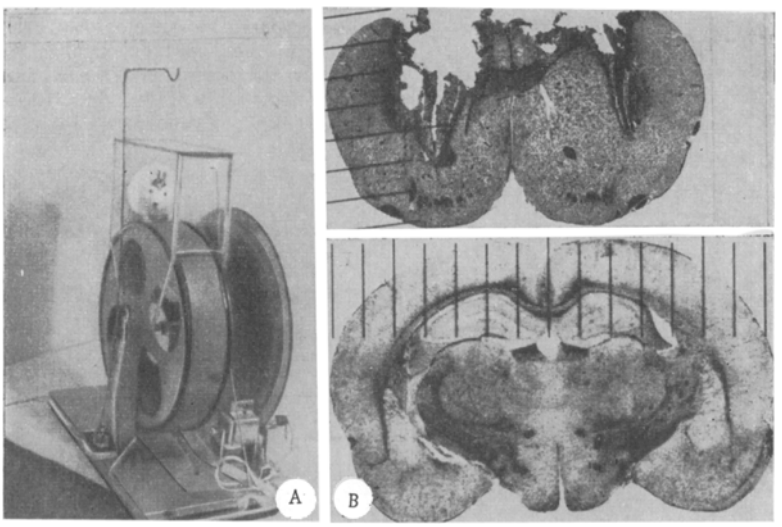

Fig. 1. General appearance of apparatus for autostimulation in chamber on wheel (A) and frontal sections through the brain (B) on rat No. 10 in the region of injury to the cerebral hemispheres (above) and through the location of the tips of the stimulating bipolar electrode in the lateral hypothalamic region (below).

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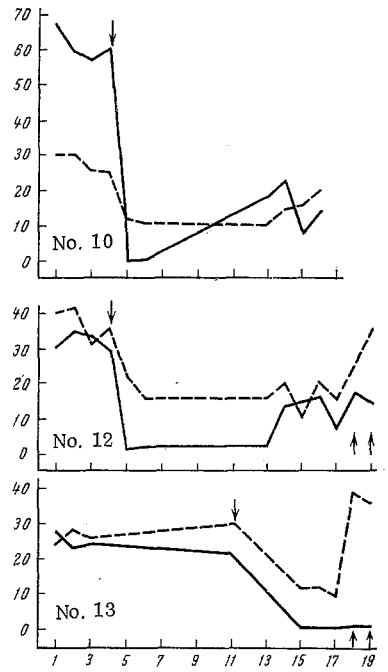

Fig. 2. Autostimulation in chamber with pedal (continuous line) and in chamber on wheel (broken line). Arrow pointing downward denotes day of injury to frontal lobes. Strength of current for rat No. 10, 70 μA in all tests, for rat No. 12, 90 μA, but in last two tests (shown by arrows pointing upward) 120 μA; for rat No. 13, 50 μA, but in last two tests (shown by arrows pointing upward) 90 μA. Abscissa, successive days; ordinate, mean number of volleys of stimuli per minute in successive tests.

In the present investigation the effect of injury to the frontal lobes was studied in two experimental situations: a usual situation, in which AS was connected with pressure on a pedal, and on the basis of locomotion, i.e., motor activity of which even a mesencephalic rat is capable [7]. In the first case, stimulation of the lateral hypothalamus was produced by pressure on the pedal, in the second case by rotation of the wheel by the rat running on it.

EXPERIMENTAL METHOD

Under nembutal anesthesia, bipolar electrodes (two nichrome wires, each 90 μ in diameter, insulated except at their tips), were implanted into albino rats weighing 200-250 g in accordance with the coordinates [3]: A 4.0-4.5, L 1.2-1.5, H (−2)-(−3). The experiments began on the 5th-7th day after implantation of the electrodes. The pedal measuring 20-40 mm was in the center of one wall of the chamber measuring 35 × 40 × 35 cm, and 2 cm above the floor. Transmission of a volley of impulses (duration 0.7 msec, frequency 40/sec) began if the pedal was pressed upon with a force of not less than 20 g for 0.4 sec, if the rat did not release the pedal sooner. The number of pressures on the pedal per minute was recorded for 14 min. Observation were then made on the same rat for 11 min during AS on the basis of locomotion. For this purpose the animal was placed in a transparent plastic chamber measuring 20 × 10 × 12 cm, the base of which consisted of the surface of an easily rotated wheel 30 cm in diameter (Fig. 1A). When the rat ran, it set the wheel in motion, and after every half-turn the rat received a volley of stimuli 0.4 sec in duration. Usually training took place during the first experiment. The number of turns of the wheel was recorded every minute. The strength of the current used in both versions of AS was the same for each rat.

After four experiments, in which neither the frequency of pressing on the pedal nor the speed of running along the wheel deviated systematically toward either side, frontal lobotomy was performed. For this purpose, through a series of burr-holes drilled 1-2 mm anteriorly to the bregma under ether anesthesia, anodic electrolysis with a current of 20 mA was carried out for a few seconds along each track.

The surviving animals were tested repeatedly (at least five tests) in both experimental situations. The tests were continued so long as the electrode block remained in situ. Then, after fixation in 10% formalin solution, frontal sections of the brain, 40 μ in thickness, were cut on a freezing microtome through the location of the electrode tips and at the level of the frontal lobotomy. The unstained sections were photographed under a magnification of 8 times. The end of the electrode was located in the lateral hypothalamic region, while the site of the lobotomy was in the frontal plane A 8-9.5 passing through the head of the caudate nucleus, and it affected not only the gray matter and the subjacent white matter of the cortex, but also the caudate nucleus to a degree which differed from one rat to another (Fig. 1B).

EXPERIMENTAL RESULTS AND DISCUSSION

If the animal carried out AS in the chamber with the pedal, it did so almost always in the chamber on the wheel also, provided that the stimuli did not evoke direct motor responses (turning of the head or trunk, lifting the paw, and so on). The presence of motor responses interfered with running on the wheel or even made AS impossible under these conditions.

During AS in the chamber on the wheel the rat regularly ran for short periods, interrupted by stops. With the usual strengths of current applied (from 50 to 90 μA for different animals), the duration of the runs was 10-30 sec and of the stops 1-5 sec. During consecutive minute intervals of the same test the number

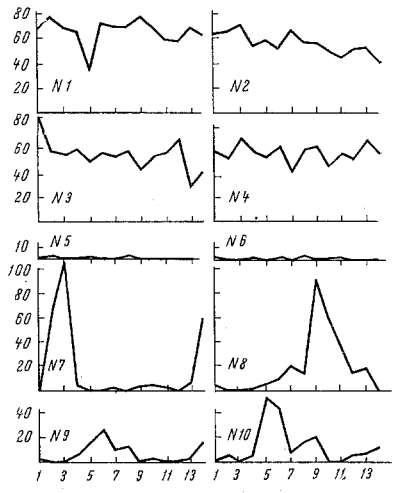

Fig. 3. Number of volleys of stimuli during each minute of autostimulation (ordinate) in chamber with pedal in tests before (rats Nos. 1-4) and after (rats Nos. 5-10) injury to frontal lobes. Abscissa, successive minutes of test.

of turns of the wheel varied in the same way as the number of pressures in the chamber with the pedal; the coefficient of variations was 0.05-0.15.

With an increase in strength of the current both the speed of running and the mean velocity of rotation of the wheel were increased. With the same strength of current, both the character of the run and its mean speed were quite constant from one experiment to another. The maximum deviations of the running speed from the mean value for four tests (on different days) were 11-16%, i.e., not more than the maximum deviations of the frequency of pressing on the pedal from the mean for four tests on these same rats, namely, 10-17%. During AA in the chamber with the pedal, rats Nos. 12 and 13 received approximately the same number of volleys of stimuli per minute as in the chamber on the wheel, while rat No. 10 received more (Fig. 2). In the absence of stimuli, the rats performed 0-1 rotation of the wheel per minute and 0-2 pressures on the pedal per minute. A break of several days in the tests had no appreciable effect on the AS in any of its versions (Fig. 2, animal No. 13).

In the first 7-9 days after frontal lobotomy all three rats practically never pressed the pedal, but performed AS in the chamber on the wheel, although the speed of running at this time was only about half that before the operation (Fig. 2). On subsequent days, two rats exhibited AS in the chamber with the pedal also. However, the method of pressing on the pedal was significantly altered. Whenever the number of pressures exceeded 7-10/min, the rat did not press with its paw, as before lobotomy, but seized the pedal with its teeth, held it with its head, and thus achieved a high frequency of opening and closing of the contact. The number of pressures on consecutive minutes under these conditions was very unstable (Fig. 3). The third rat (No. 13) likewise did not reproduce AS in the chamber with the pedal despite repeated attempts at training by application of a stronger current; meanwhile AS in the chamber on the wheel was activated by an increase in strength of the current (Fig. 2).

Whereas the results of injury to the frontal lobes were evaluated purely on the basis of changes in AS in the chamber with the pedal, it could be assumed that the operation would disturb the mechanisms of AS at least temporarily. This was the conclusion reached by Bures et al. [2] and Olds [4] on the basis of their experiments in which the cortex was blocked by spreading depression. In the case of acute blocking of the cortex of a whole hemisphere, significant depression of hypothalamic activity evidently must have taken place. However, injury to the frontal lobes caused only a decrease in the frequency of AS in the chamber on the wheel on those very days after the operation when AS was virtually absent in the chamber with the pedal.

Injury to the frontal lobes evidently disturbed not so much the mechanisms of AS as the ability of the animal to perform movements: movement of pressing on the pedal was affected much more severely than locomotion. Brief periods of frequent pressures on the pedal, sometimes observed with rats after operation, were due to frequent biting of the pedal, i.e., to a movement for which, like locomotion, the rostral portions of the brain are not essential. The lobotomized rat could press on the pedal sporadically with its paw, but found it difficult to perform this movement systematically in the experiment with AS. Since under these circumstances AS on the basis of locomotion was only slightly affected, it can be concluded that, while injury to the frontal lobes significantly interferes with the use of pressure on the pedal for its production, it only slightly affects the basic mechanisms of AS. Autostimulation in the chamber with the pedal can also recover 9-10 days after the operation, just as after destruction of the preoptic region, the mamillo-thalamic tract, or the ventral part of the rostral division of the mesencephalon [1].

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