frequency of 4.0 sec^{-1}. A closely similar picture was observed in the left heart, although the nonlinearity of correlation in this case was rather higher ($y = 0.16$) than in the right heart ($y = 0.09-0.11$).

It can be concluded from the results given above that close correlation between contractility of the atria (as reflected in tension) and the hemodynamic activity of the ventricles (according to the maximal value of pressure developed) over a wide range of variations of interspike intervals is the basis for construction of the control loop for the artificial heart on the basis of information on atrial contraction.

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CHANGES IN AMPHETAMINE STEREOTYPY IN CATS AFTER ELECTRICAL STIMULATION OF THE CAUDATE NUCLEUS

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Two types of behavioral changes arise in cats after repetitive low-frequency stimulation of the head of the caudate nucleus in cats. Behavioral inhibition is more frequently triggered from the dorsomedial zone of the head, whereas activation phenomena precede depression during stimulation of the ventrolateral zone. The assortment and pattern of stereotyped movements following injection of the minimal effective dose of amphetamine vary in different ways against the background of these changes. After stimulation of the dorsomedial zones of the nucleus stereotypy is first disorganized and then weakened, whereas caudate activation is associated with strengthening of stereotypy.

KEY WORDS: amphetamine stereotypy; caudate nucleus; late behavioral changes

An important place in the organization of amphetamine stereotypy of behavior, used as an experimental model in psychopathology, is ascribed to functional insufficiency of the caudate nucleus [1]. One of the neurophysiological facts confirming the validity of this opinion is the sudden abolition of stereotyped movements on electrical stimulation of that structure [4]. However, it is claimed that the stable behavioral changes which persist for a long time after the end of stimulation are much closer to the indices of natural brain function than the phasic responses arising actually during stimulation [6].

It was therefore decided to study the effect of delayed caudate phenomena on the manifestation of stereotypy.

EXPERIMENTAL METHOD

Ten cats of both sexes, weighing 2.2-3.4 kg, took part in 74 experiments. In the preliminary stage under pentobarbital anesthesia bipolar stimulating electrodes were inserted into different parts of the caudate nucleus and adjacent brain structures. In two animals steel needles also were inserted into various parts of the cortex

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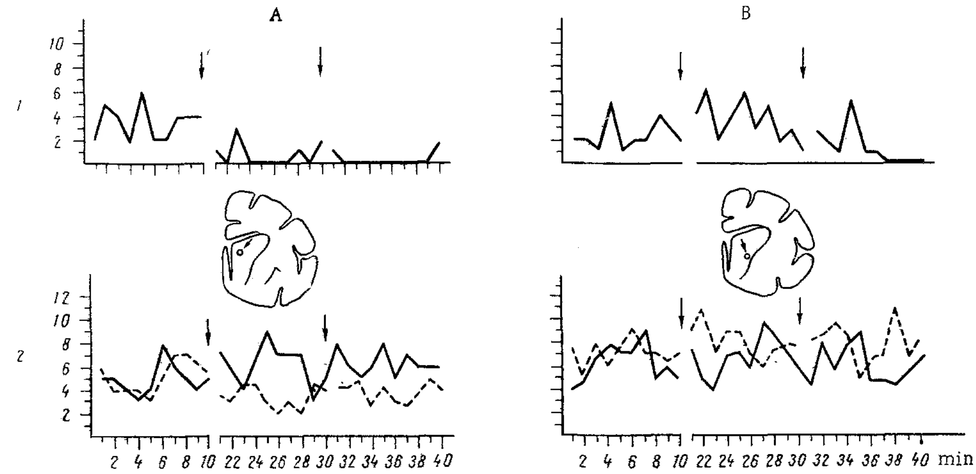

Fig. 1. Changes in spontaneous activity of cats and activity induced by amphetamine after stimulation of caudate nucleus. 1) Changes of spontaneous behavior after repeated stimulation (time indicated by arrow) of dorsomedial (A, cat No. 48), and ventrolateral (B, cat No. 47) zones of caudate nucleus. Here and in Fig. 2, location of electrodes indicated by arrows on schemes of frontal brain sections; 2) the same, against the background of amphetamine stereotypy (20 min after injection of 0.5 mg/kg amphetamine). Continuous lines: initial pattern of stereotypy; broken line; the same after stimulation of nucleus. Each trace represents mean of five experiments. Abscissa: time (in min); ordinate; number of head movements.

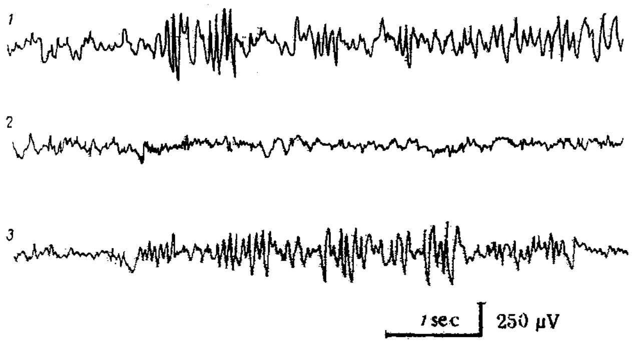

Fig. 2. Effect of repeated stimulation of caudate nucleus on EEG of sensomotor cortex of cat receiving amphetamine. 1) slow-wave EEG accompaniment of caudate depression (4th stimulation of nucleus); 2) typical desynchronization of EEG in cat with stereotyped behavior (40 min after injection of 0.5 mg/kg amphetamine); 3) appearance of synchronized rhythm in cat with stereotyped behavior after repeated stimulation of nucleus (40 min after injection of amphetamine). Results of different experiments on same animal (cat No. 51).

in order to record the EEG. Spontaneous behavior of the cats and the character of responses to test stimuli (a rustling sound, raising the hand, food, and so on) were assessed visually, photographically, and cyclographically. Stable behavioral changes were produced by long (2.5 min), repeated (every 10-20 min, up to 5 or 6 times in the course of the experiment) low-frequency (two pulses/sec, 0.5 msec) brain stimulation. Amphetamine (in doses of 0.1-3 mg/kg) was injected intraperitoneally. The experiments were carried out at intervals of a few days. The results of the main experiments were compared with those of various control determinations (prolonged recording of spontaneous behavior, assessment of evoked responses in the animal, effects of amphetamine alone, affects of injections of physiological saline on spontaneous and evoked behavior).

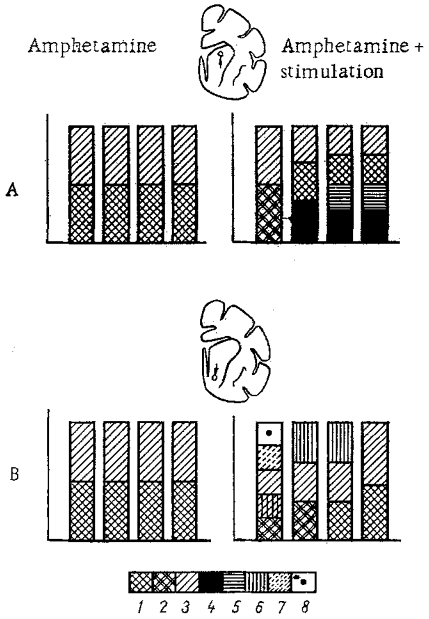

Fig. 3. Qualitative structure of amphetamine stereotypy in cats before and after stimulation of various zones of caudate nucleus. A) stimulation of dorsal zone of head (cat No. 27) leads to appearance of syncopal manifestations and transient depression of motor automatisms; B) addition of stepping movements to pattern of stereotypy after stimulation of ventral zone of nucleus (cat No. 28). Effects of second brain stimulation 30 min after injection of 0.5 mg/kg amphetamine shown in both cases. 1) Grooming outwardly resembling natural; 2) compulsive grooming, from which animal could be distracted only with difficulty; 3) head turning; 4) "Freezing" on the spot; 5) lying on the floor with cessation of all stereotyped movements; 6) stepping movements around the chamber; 7) vocal reaction; 8) gaze concentrated on one point.

EXPERIMENTAL RESULTS

Stereotypy evoked by low threshold doses of amphetamine for that state was used as the test object. As a rule stereotypy of this sort is easier to simulate by various measures than behavioral disorders after high doses of the drug. Usually 0.5-1 mg/kg of amphetamine was injected for this purpose, after which most cats developed stereotypy consisting of turning the head from side to side, sniffing, stepping from one paw to another, and licking the fur monotonously (grooming). Against the background of this stereotypy, repeated electrical stimulation of the caudate nucleus was carried out.

The writers' previous observations [5] show that the nucleus is the source of two types of behavioral response which sometimes last for tens of minutes after the end of high-frequency stimulation. A more widespread phenomenon is depression of the animals, outwardly resembling natural sleep: The cats cease their locomotion, lie on the floor with their eyes closed, and respond apathetically to test stimuli (caudate depression). Certain points can be distinguished in the nucleus to stimulation of which the animals respond by activation phenomena, consisting of more frequent movements of the head from side to side and grooming. In repeated experiments the degree of this activation usually decreases and behavioral depression can easily arise in its place.

In a low dose (0.1-0.25 mg/kg), too small to induce the stereotypy, amphetamine weakened the formation of caudate depression and, on the other hand, facilitated the appearance of activation changes. That is why, against the background of a dose of amphetamine large enough to produce the stereotypy, the previous pattern of behavioral depression was not obtained even during repeated stimulation of the nucleus. However, an appreciable change was found in the character of stereotyped behavior: The pattern and assortment of automatic movements and their intensity and stability change. Although these changes varied substantially with time from one experiment to another and in different animals (making analysis of the results as a whole more difficult), certain general principles could nevertheless be detected.

The first consequence of interaction between behavioral disorders caused by amphetamine and behavioral shifts triggered by stimulation of the nucleus was weakening of the stereotypy. This passed through a phase of disorganization of motor automatisms. After the first one or two brain stimulations the head turnings assumed the form of sweeping, wide-amplitude movements, usually toward the side opposite to the stimulated side of the nucleus. Monotonous grooming in a certain location (licking the side, the tail, or the anus) was replaced by extremely chaotic cleaning movements, with frequent changes of location, and formalized up to the limit.

Distinct features of restriction of stereotypy appeared after 3-5 stimulations of the caudate nucleus (Fig. 1A). The number of stereotyped head turnings was reduced, they took place more slowly, and were interrupted by frequent pauses, during which the animals' gaze was concentrated on one point. For a short time (30-40 sec) the animal could lie on the floor with its eyes closed. All movements disappeared at such times. The clearest depression of stereotypy took place when caudate depression reached a maximum in the control (2-7 min after the stimulating current was stopped). In some experiments (25-30% of all cases) repeated stimulation of the nucleus hastened the end of amphetamine stereotypy. Normal behavior was restored on average 10-15 min earlier than in the control determinations.

Besides the purely external features described above, two other indices gave evidence of weakening of stereotypy. The response of the animals to various tests (the introduction of indifferent and adequate visual stimuli into the chamber, stroking, threatening with an object) during the period of maximal limitation of motor automatisms indicated that their behavior had become less adequate. The cats followed the object shown to them longer and responded more eagerly to stroking. Weakening of the stereotype also was shown by the EEG data. Whereas amphetamine, in the doses used, caused persistent desynchronization of the electrocorticogram, during the period of artificially evoked depression of stereotyped movements, the pauses and fixation of the gaze corresponded to rhythmic synchronization of sensomotor cortical electrical activity. When the animals lay on the floor, assuming for a short time the typical posture of caudate depression, its EEG-accompaniment was recorded in the form of spindle-shaped discharges (Fig. 2).

Limitation of the intensity of the stereotypy was observed after repeated electrical stimulation not of the whole caudate nucleus, but predominantly of the dorsomedial zones of the head, i.e., in those regions where caudate depression can more easily be provoked (Fig. 1). Stimulation of the cortex above the nucleus or internal capsule gave no such effect. The ventrolateral region of the head was the source of behavioral changes of a different type. Control stimulation of this region of the nucleus without amphetamine led to a state predominantly of activation, marked by an increase in or stabilization of the number of head turnings and grooming movements. Under ordinary conditions as the animal became accustomed to the chamber the number of head turnings decreased gradually. It is not surprising, therefore, that against the background of amphetamine these behavioral shifts were potentiated. Repeated brain stimulation was accompanied by an increase in the frequency of head turnings and of grooming, resembling the ordinary stereotypy in its pattern, but more intensive (Fig. 1B). New forms of motor automatisms also could be provoked from the ventrolateral regions of the nucleus. In particular, both during stimulation and at various times after its end, "dressage" movements frequently appeared. The whole behavior of the animals acquired an emotional overlay, with elements of anxiety and restlessness. As a whole, against the background of behavioral shifts of different character and origin, the assortment of component elements of stereotypy was different (Fig. 3).

Stable behavioral states triggered by repeated stimulation of the caudate nucleus in cats can thus give rise to divergent effects of the manifestations of amphetamine stereotypy. This confirms the suggestion made previously, that the nucleus has a varied role in stereotyped behavior, and that such behavior may arise through disturbance of intracaudate relations [1].

It is reasonable to assume that on account of the same neurochemical mechanism, namely potentiation of nigrostriatal dopaminergic transmission, in the process of organization of amphetamine stereotypy the drug can block regions of the nucleus which exert an inhibitory effect on behavior and, at the same time, can stimulate zones which serve as the source of behavioral activation. The basis for this assumption is the existence of antagonistic zones in the nucleus, with opposite roles in the organization of rotatory movements, and topographically close to those described in this paper [2, 3], and also the probability of dissimilar (excitatory and inhibitory) synaptic roles of caudate dopamine [7].

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HYPERVENTILATION AND INHIBITORY SYNAPSES

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Injection of a subconvulsive dose of strychnine, which blocks inhibitory synapses, considerably potentiates the reflex activity of the respiratory muscles in response to sciatic nerve stimulation and inhalation of a hypercapnic mixture. Inhibitory synapses thus prevent excessive hypocapnia induced by hyperventilation.

KEY WORDS: strychnine; hyperventilation; hypercapnia.

Strychnine is a stimulator of respiration. Its action is due to blocking of inhibitory synapses [4]. However, it does not affect the vagal inhibitory reflex from the lungs [1-3]. It can be postulated that the mechanism of action of strychnine on the respiratory system depends on its disinhibitory action on motoneurons innervating the respiratory muscles. To analyze this question the effect of subconvulsive doses of strychnine (0.07 mg/kg) was studied on: 1) respiratory reflexes induced by stimulation of the central end of the divided sciatic nerve, and 2) activity of respiratory muscles induced by inhalation of a hypercapnic mixture.

EXPERIMENTAL METHOD

Experiments were carried out on 12 cats anesthetized with urethane (1.5-2.0 g/kg, intravenously). Recording electrodes were sutured to the sternal part of the diaphragm. The central ends of the divided sciatic nerve were stimulated with square pulses 0.5 msec in duration and with a frequency of 10 Hz. A gas mixture consisting of 6% CO_2 in air was used.

EXPERIMENTAL RESULTS

Before injection of strychnine the respiration rate was 24.5 ± 1.4 per minute. The threshold of the respiratory reflex (quickening of respiratory discharges of the diaphragm) was 20-30 V. When stimulation of the nerves ceased, respiration was immediately restored. Subconvulsive doses of strychnine caused a very slight increase in respiration rate (27.5 ± 2.1), and sometimes also an increase in the respiratory discharges of the diaphragm.

After injection of the subconsulsive dose of strychnine the threshold of the respiratory reflex was reduced by 75-80%. The respiration rate reached 36.0 ± 1.7 and remained at this level for 15 sec to 1 min after the end of nerve stimulation.

Inhalation of the hypercapnic mixture caused an increase in the depth and frequency of the respiratory discharges. After injection of strychnine, inhalation of the same gas mixture caused a sharper increase in the

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