EFFECT OF PSYCHOTROPIC DRUGS ON SELF-STIMULATION

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Amphetamine and cocaine have been shown to facilitate septal self-stimulation. Morphine, imipramine, benactyzine, meprobamate, diazepam, chlordiazepoxide, phenobarbital, and DLK-25, in small doses do not affect, but in large doses inhibit this reaction. It is suggested that amphetamine and cocaine have a direct activating effect on the positive reinforcement system of the septum. The ineffectiveness of the other drugs is explained by the absence of a nervous substrate for negative reinforcement at the septal level. Comparative analysis of the effect of psychotropic drugs on septal and hypothalamic self-stimulation leads to the conclusion that the activating effect of psychtropic drugs on the positive reinforcement system depends on their action on the emotiogenic structures of the brain and not on structures responsible for the formation of motivations.

KEY WORDS: *septum; self-stimulation; psychotropic drugs.*

The neurophysiological properties of the structures of positive emotions formed during electrical stimulation of the hypothalamus and septum may be responsible for differences in the sensitivity to the action of psychotropic drugs [5, 8]. Some special features of the effect of these drugs on positive emotiogenic structures at the hypothalamic level were discovered in a previous investigation [3].

This paper describes the study of the effect of drugs on the structures responsible for positive emotions formed during electrical stimulation of the septum.

EXPERIMENTAL METHOD

Experiments were carried out on 48 male albino rats weighing 250-300 g, with monopolar nichrome electrodes 25 μ in diameter, implanted bilaterally into the septal region of the nucleus of the diagonal bundle of the septum in accordance with the coordinates of De Groot's atlas of the brain [6]: A 8.5 mm, L 0.7 mm, H 8 mm. The operation was performed under pentobarbital anesthesia (40 mg/kg, intraperitoneally). Seven days after the operation the animals were taught to press on a pedal to obtain brain stimulation by sinusoidal pulses (0.02 sec, 50 Hz). After determination of the threshold of self-stimulation the strength of the stimulating current was gradually increased by 20 μA. The frequency of self-stimulation was recorded for 5 min. Rats taught self-stimulation in the experimental chamber endeavored to obtain brain stimulation and succeeded in pressing the pedal up to 50 times in the course of 5 min, even if the pressure was not followed by brain stimulation. Consequently, the maximal current at which the frequency of self-stimulation did not exceed 50 was taken as subthreshold, and the current at which the intensity of the self-stimulation response exceeded 100 but did not exceed 200 self-stimulations was taken as the threshold. The effect of amphetamine, cocaine, caffeine, morphine, imipramine, phenobarbital, DLK-25, benactyzine, meprobamate, diazepam, and chlordiazepoxide was studied. The drugs were in-

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TABLE 1. Effect of Psychotropic Drugs on Indices of Self-Stimulation

Drug	Dose, mg/kg	Threshold of self-stimulation	Number of self-stimulations
Amphetamine	0,5	↓13	↑10
	1	↓16	↑18
	2	↓11	↑9
Cocaine	5	↓8	↑12
	10	↓14	↑20
	25	↓7	↑15
Caffeine	15	0	↑9*
	30	↓5	↑12
	45	0	↑6*
Imipramine	2—5	0	↑4*
	10	↑12	↓10
Morphine	3—6	0	↑5*
	10	↑6	↓14
Benactyzine	1—6	0	↑6*
	12	↑5	↓12
DLK-25	0,05	0	0
	0,1	0	↑4*
	0,3	↑6	↓9
Phenobarbital	5	0	0
	10	0	↑8*
	20	↑5	↓7*
Diazepam	1	0	↑6*
	2	↑9	↓7*
	4	↑16	↓13
Chlordiaz-epoxide	3	0	↑9*
	6	0	↓5*
	12	↑7	↓19
Meprobamate	10	0	↑10*
	20	0	↓6*
	40	0	↓15

Legend. 1) Numbers give mean values of changes in indices of self-stimulation in percentage of initial values. 2) Arrows pointing downward and upward indicate decrease and increase of index of self-stimulation, respectively. 3) Asterisk indicates that results are not statistically significant ($P > 0.05$).

jected intraperitoneally 30-40 min before the experiments in doses used most frequently in experiments to study the effect of these drugs on behavioral responses. After determination of the mean indices of the frequency of self-stimulation in response to currents of different strengths, by the method of least squares [4], curves showing how the frequency of self-stimulation depended on the strength of the current were plotted. At the end of the experiments the location of the electrodes in the brain was verified histologically.

EXPERIMENTAL RESULTS AND DISCUSSION

The threshold strengths of current for the self-stimulation response in individual animals varied from 10 to 30 μA. An increase in the strength of the current led to an increase in the frequency of self-stimulation, which was maximal at 50-90 μA, namely from 400 to 800. A further increase in the strength of the current did not affect the frequency of self-stimulation. When the current was 140-180 μA, during self-stimulation the rats began to have convulsions, which interrupted the self-stimulation response.

In earlier experiments [3] to study the effect of psychotropic drugs on self-stimulation arising in response to electrical stimulation of the hypothalamus, the frequency of self-stimulation was shown to depend on the strength of the current and the relationship was expressed graphically as a parabola (Fig. 1, curve 1). The descending part of this curve (a decrease in the frequency of self-stimulation with an increase in the current) was interpreted as the result of opposition between the process of self-stimulation and the hypothalamic negative reinforcement system, as a result of its proximity to the system of positive reinforcement.

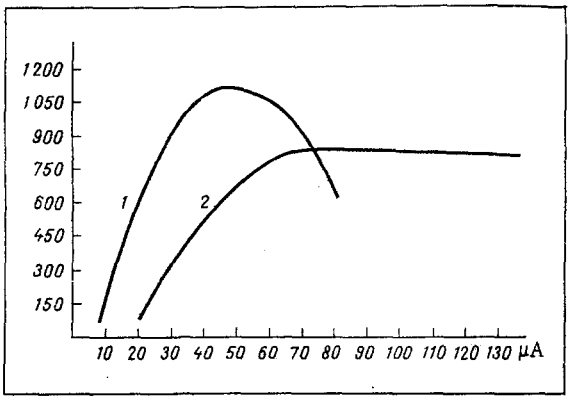

Fig. 1. Changes in intensity of self-stimulation depending on strength of stimulating current: 1) parabolic curve characteristic of self-stimulation response at the hypothalamic level; 2) hyperbolic curve describing self-stimulation at the septal level. Abscissa, strength of current (μA); ordinate, number of self-stimulations.

Curves characterizing the frequency of septal self-stimulation as a function of current strength obtained in the present experiments were hyperbolic in shape (Fig. 1, curve 2) and differed from the parabolic curves describing self-stimulation to electrical stimulation of the hypothalamus with respect to the criterion of an excess of one series over the other, and also the criterion of nonparallelism of the series. These differences between the curves were most marked after the frequency of self-stimulation reached its maximum: With a further increase in the strength of the current the self-stimulation response to electrical stimulation of the hypothalamus diminished sharply, whereas self-stimulation in response to septal stimulation remained virtually unchanged. This last fact suggests that self-stimulation arising in response to septal stimulation, unlike self-stimulation at the hypothalamic level, takes place without the participation of negative reinforcement structures. This hypothesis is confirmed by data in the literature indicating close and reciprocal relations between the hypothalamic systems of reward and punishment in rats [7], facilitation of self-stimulation at the hypothalamic level by psychotropic drugs with a depriming action on structures of negative reinforcement [1-3], and by the absence of data indicating that negative emotions can be induced by electrical stimulation of the septum.

Quantitative changes in the threshold of the self-stimulation response and in the number of self-stimulations against the background of psychotropic drugs are shown in Table 1. Of the drugs tested, only amphetamine and cocaine (maximal effect in doses of 1 and 10 mg/kg, respectively) and, to a lesser degree, caffeine had an activating effect on the self-stimulation reaction, lowering its threshold and increasing the number of self-stimulations in response to all strengths of current ($P < 0.05$).

The remaining substances in small doses had no effect on the self-stimulation response, but if the doses were increased they inhibited it.

The stimulant effect of amphetamine and cocaine could be attributed to the direct action of these drugs on the adrenergic structures of the positive reinforcement system, which reached the septum via the medial forebrain bundle [10]. Activation of the mechanisms of positive emotions by phenobarbital, DLK-25, benactyzine, meprobamate, diazepam, and chlordiazepoxide has been shown to be determined largely by their ability to exert a depriming action on the structures responsible for the formation of negative emotions, as is clearly manifested in the case of self-stimulation at the hypothalamic level [3]. As a result of this, the inability of the drugs listed above to activate self-stimulation arising in response to septal stimulation can probably be explained by the absence of a nervous substrate of negative emotions at the septal level. On this basis it can also be postulated that the euphoric action of these drugs, of which there is frequent evidence in the literature, is not the result (except in the case of amphetamine and cocaine) of their

activating effect on the system of positive emotions from the septum, but is connected with other systems of positive reinforcement, especially of the hypothalamus. Despite the closeness of the hypothalamic system of positive emotions to the systems of the basic biological motivations, the predominant effect of the drugs on the hypothalamic systems of positive reinforcement could hardly be explained by their action on the nervous mechanisms of motivations. This hypothesis is based on the fact that amphetamine and cocaine, which inhibit feeding and drinking motivations [9, 11], effectively facilitate self-stimulation through electrodes in the hypothalamis and septum, regardless of the relations of these structures to the nervous mechanisms of motivations, whereas neuroleptics, which as a rule depress the self-stimulation reaction irrespective of the structure from which it is obtained, like amphetamine have a marked anorexic action [11]. In addition, substances facilitating self-stimulation at the hypothalamic level, such as amphetamine, cocaine, caffeine, atropine, meprobamate, and phenobarbital, act in different directions on the level of feeding and drinking motivations, [9, 11].With these considerations in mind, it must evidently be concluded that the activating effect of psychotropic drugs on the positive reinforcement system is dependent more on their action on the emotiogenic structures of the brain than on structures responsible for the formation of motivation.

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