Experimental Model of the Process of Narcotics Addiction in Cats Based on Feeding Motivation

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Cocaine addiction is reproduced in cats on the basis of feeding motivation. Pure milk or milk with cocaine is used as reinforcement in the operant food-procuring behavior. Milk with cocaine induces specific changes in the food-procuring behavior. Cats are shown to differ in their individual sensitivity to cocaine. *Per os* intake of cocaine affects rather the processes of decision-making than the organizationof motor acts.

Key Words: *operant food-procuring behavior; cocaine*

The study of neurophysiological and neurochemical mechanisms underlying narcotic addiction is often complicated by the problem of inducing dependence in animals under conditions of their natural behavior. Numerous experimental data obtained on animals with artificial or forced administration of narcotics provide no way of deducing the dynamics of the development and physiological basis of natural addiction in animals [1]. On the other hand, the hypothesis of the formation of narcotic, drug, and alcohol addiction on the neurophysiological basis of biological motivations [2,3] allows for direct analyzis of the natural mechanisms of addiction.

In the present study we attempted to develop an experimental model of cocaine addiction in cats on the basis of natural food requirements.

MATERIALS AND METHODS

The experiments were performed in a specially equipped chamber with a pedal and a food dish. The cats pressed the pedal and received food reinforcement (3 ml milk). The method of conditioning the cyclic operant food-procuring behavior was described previously at length [5]. On the basis of the cyclic food-procuring behavior the animals were trained in the conditioned operant food-procuring behavior. An acoustic stimulus (1000 Hz, 40 dB) served as the signal, produced by an acoustic generator. Pressing the pedal against the background of the conditioned signal was reinforced by milk, while pressing the pedal without the signal was not reinforced.

The experiments were performed on 3 mongrel mature domestic cats. A concentration of cocaine in milk acceptable for *per os* intake by cats was determined.

The cats were offered 2-ml milk samples containing 0.1-1.0 mg/kg cocaine. In some cases the cats lapped up milk with 1.0 mg/kg cocaine, but they refused such milk when the period of food deprivation was reduced. Taking into account the amount of milk consumed, we chose a cocaine concentration of 0.5 mg/kg. The animals received 8-10 mg cocaine over the experiment, i.e., 2-3 mg/kg body weight. These doses did not lead to marked behavioral changes.

Effects of a toxic dose were observed when the animal received 26 mg/kg cocaine with milk. Milk

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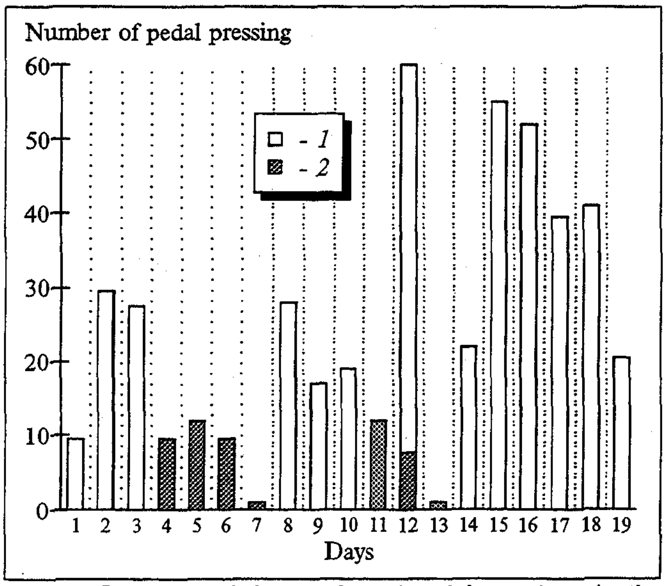

Fig. 1. Dynamics of the number of pedal pressings in the operant food–procuring behavior of a cat reinforced with cocaine–laced milk (*1*) and pure milk (*2*).

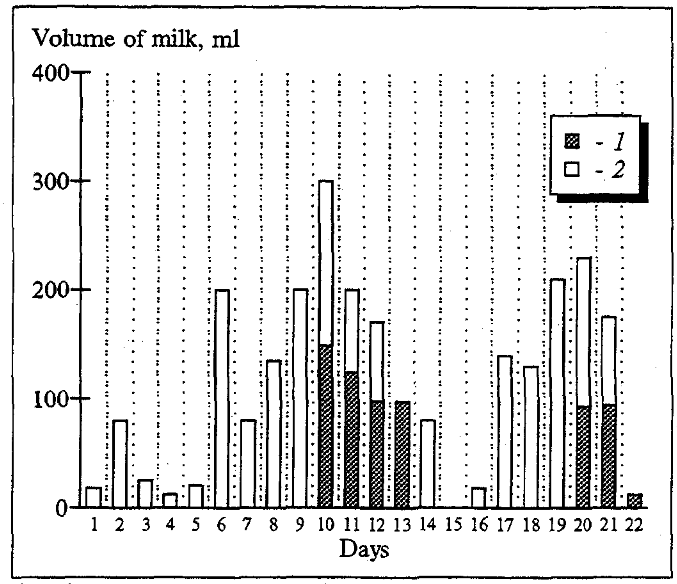

Fig. 2. Milk consumption in the operant food–procuring behavior of a cat reinforced with cocaine–laced milk (*1*) and pure milk (*2*).Volume of milk, ml; Days

thus laced with cocaine was offered ad libitum. Lapping ceased 23 min after beginning, the animal become torpid and exhibited passive defensive behavior and after 27 min mydriasis was observed. Thereafter we observed abundant salivation together with a single regurgitation and rigidity of the fore and hind paw muscles, which were followed 12-25 sec later by 3-10-sec hyperpnea with open mouth and subsequent seizures. This clinical picture is consistent with published data [4].

RESULTS

The effect of *per os* administration of cocaine on behavior was studied after acquisition and retention of the operant activity by the animals, which was judged from stabilization of the coefficient of variation of the intervals between pedal pressings within 25-30%. Administration of cocaine in a dose of 0.5 mg/liter revealed individual differences in the operant behavior of the animals. One cat sharply reduced the number of pedal pressings after cocaine intake. After termination of the food-procuring activity the cat walked around the chamber, rubbed against the walls, and purred. The cocaine solution was used during 6 days of the experiment, after which in control experiments the cat was given pure milk during 3 days. This resulted in an increased number of pedal pressings, but after repeated administration of cocaine the number dropped again (Fig. 1). In one case after the cat refused to press the pedal and lap milk with cocaine, it was offered pure milk, after which the cat performed 54 pressings, which considerably surpassed the usual number. Thus, the use of pure milk as reinforcement resulted in its increased consumption

TABLE 1. Dynamics of Specific Reaction after Intake of Milk with Cocaine in the Operant Food–Procuring Behavior

Reaction	Dose, mg					
	80	60	40	40	40	40
"Freezing" on pedal	9'	8'	20'	7'	8'	11'
Licking of dish	9'	11'	14'	7'	8'	9'
Mydriasis	40'	–	37'	28'	9'	11'
Rotation about vertical axis	3.5 h	–	–	–	1.3 h	–
Defensive reaction, spitting	40'	20'	37'	38'	9'	33'
Vomiting	2 h	22'	42'	–	1h 11'	–
End of aggressive manifestations	24 h	4h	–	–	–	–
Miosis	48 h					

Note. A dash denotes the absence of data.

and stimulated the operant food-procuring activity of the animal.

In contrast to the first cat, the second animal actively pressed the pedal and did not refuse milk with cocaine, and so after it had received the dose, the cat was offered pure milk. The total volume of consumed milk increased in comparison with the background level (Fig. 2). The mean duration of behavioral acts increased from 13.9 to 25.5 sec, and 50-sec intervals between pressings were noted (Fig. 3). Some specific behavioral features were observed: lapping ceased 7-14 min after beginning, the cat stopped pressing the pedal and, sitting on it, started to lick the dish; then licking ceased and the animal "froze" on the pedal. Its pupils dilated, and this was followed by passive defensive behavior: the cat spat and laid back its ears in response to the approach of experimenter's hand, and retreated to the back of the chamber; however, it hardly tracked movements of the hand within 10-15 cm from its face but did follow with the eyes the movement of objects 1.0-1.5 m away (Fig. 4). After the first administration of cocaine in a dose of 80 mg, i.e., approximately 20 mg/kg, after 3.5 hours we observed rotation about the vertical axis during 4 hours. The specific reactions produced by lower doses of cocaine were less pronounced, especially the passive defensive behavior and rotation about the vertical axis, however, the pupils dilated as before.

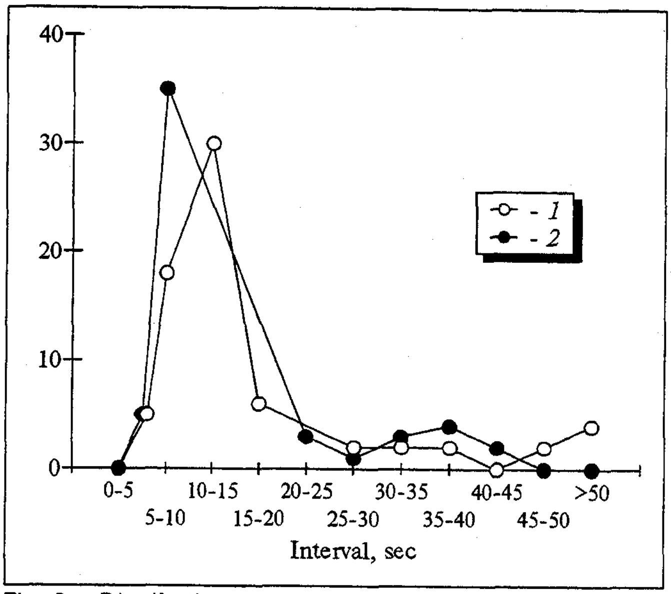

Fig. 3. Distribution histograms of percentage of intervals between pedal pressings in the operant food-procuring behavior of a cat reinforced with cocaine-laced milk (*1*) and pure milk (*2*).

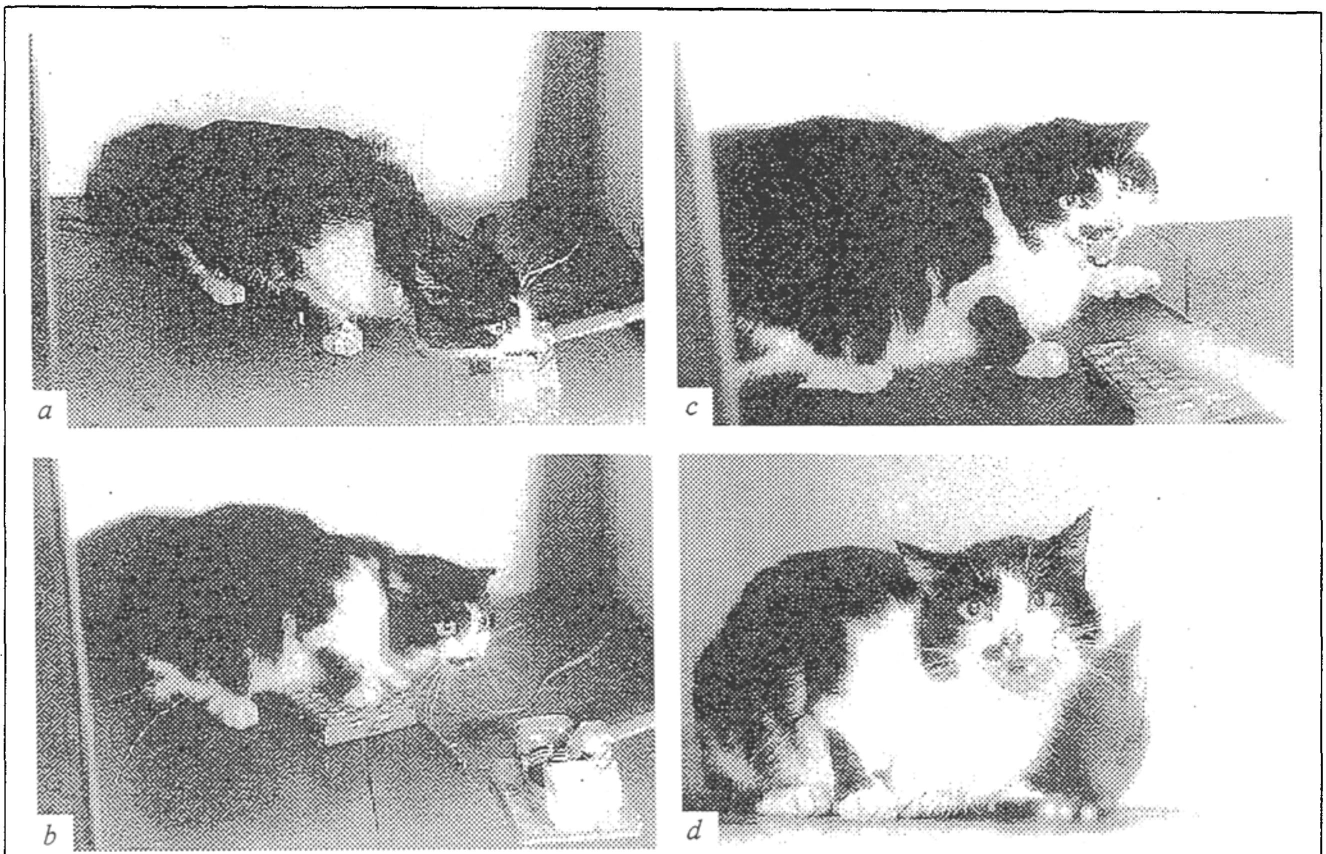

Fig. 4. Specific changes in behavioral pattern of cat after *per os* intake of cocaine-laced milk in operant food-procuring behavior. *a*) licking of the dish; *b*) "freezing" on the pedal; *c*) passive defensive reaction; *d*) fixation of gaze on distant objects.

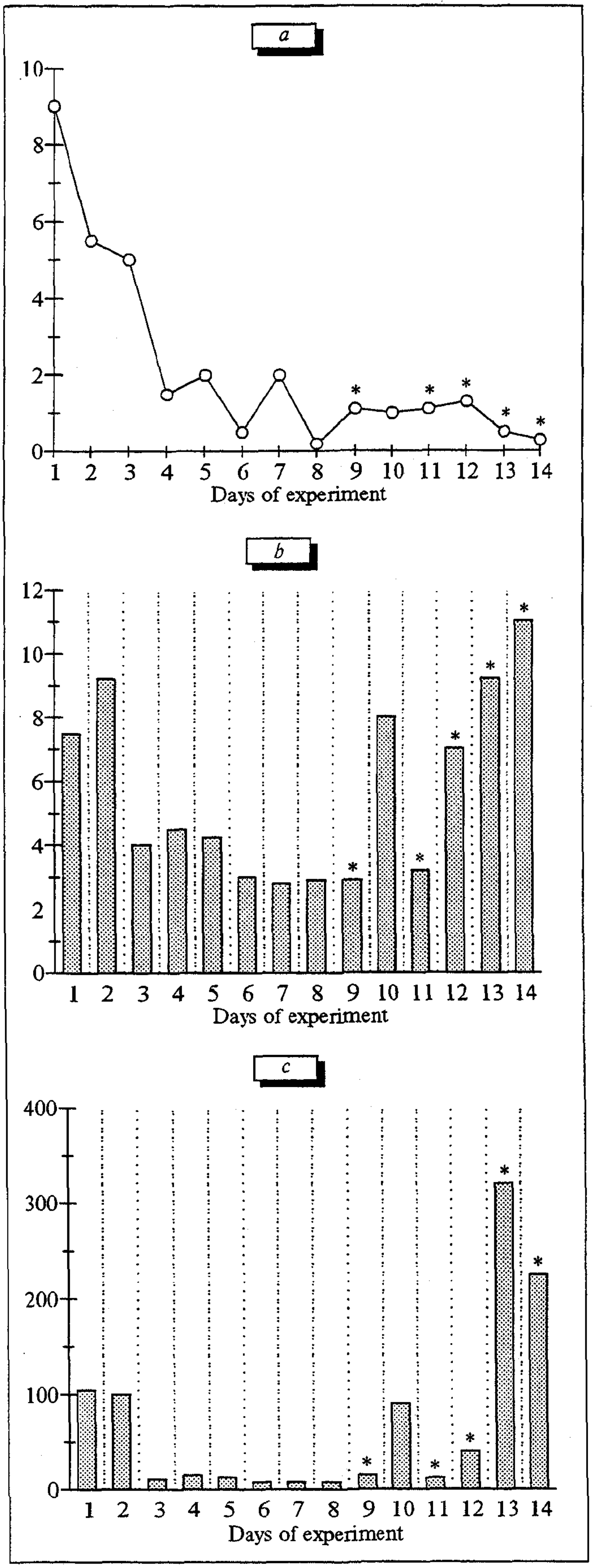

Fig. 5. Dynamics of behavioral parameters in the operant food–procuring behavior of a cat reinforced with with cocaine–laced milk (*1*) and pure milk (*2*). Ordinate: *a*) coefficient of efficiency of learning, arb.units; *b*) mean latency from acoustic stimulation to pressing the pedal, sec; *c*) coefficient of variations of latent periods, %. Asterisk signifies cocaine.

In the analysis of conditioned operant food-procuring behavior we used another criterion of retention - the coefficient of learning efficiency: the ratio of unreinforced to reinforced pressings of the pedal. The analysis of the learning dynamics revealed certain tendencies in the changes of this parameter. During the first few days of conditioned operant food-procuring behavior, all trained animals had a high coefficient of learning efficiency, but this decreased after 120-150 reinforced pressings of the pedal, i.e., after 4-5 days of the experiment, when the acoustic stimulus became a conditioned signal (Fig. 5, *a*).

The subsequent intake of milk with cocaine did not reliably change the coefficient of learning efficiency, this apparently being connected, first, with the strength of acquisition and, second, with the general cocaine-induced reduction of motor activity.

Analysis of the obtained data revealed a rather low informativeness of the chosen criterion of learning for evaluation of the degree of disintegration of the conditioned operant food-procuring behavior. In our further experiments we analyzed another parameter of the dynamics of acquisition of the conditioned operant food-procuring behavior, namely the latency of pedal pressing after the conditioned acoustic signal. Such a criterion could be used because perception of the acoustic stimulus was independent of its location in the cage and of the position of the cat's head vis-a-vis the sound source. During the first few days of the experiment the mean latency of pedal pressing for all animals ranged from 4 to 9 sec, but it reliably decreased and stabilized in the course of acquisition (p>95%). Intake of milk with cocaine prolonged the latency in a dose-dependent manner (Fig. 5, *b*). Cocaine intake also led to an increase of the coefficient of variation of pedal pressing latency after acoustic stimulation (Fig. 5, *c*).

The dynamics of latencies during one experimental day with the use of milk and milk with cocaine reinforcements demonstrated that cocaine is the factor prolonging the latency at the end of the experiment. Moreover, whereas the intake of milk with cocaine increased during the first day or two of the experiment, it decreased during the subsequent days, to the point of complete refusal of food on the part of one animal.

The observed lengthening of the latency of pedal pressing after the conditioned stimulus as well as the increase of the coefficient of variation of its duration may be assumed to be connected with the effect of cocaine on the CNS rather than with a decline of feeding motivation, since the presentation of milk without cocaine at the end of the experiment induced vigorous feeding behavior - enthusiastic lapping of the milk.

Our results demonstrated the possibility of achieving addiction in cats by giving cocaine in milk, the primary manifestation being prolonged food intake accompanied by operant activity. Furthermore, we concluded that cats show individual sensitivity to cocaine, as is seen in the specific sequence and expression of behavioral effects in each animal. The experiments also clearly demonstrated the cocaine-induced disintegration of complex behavior, which involves first of all neurophysiological mechanisms of the latest elements (according to time acquisition) of the newly developed behavior. Such a "young" neurophysiological mechanism in our experiments functioned during the time from the acoustic signal to the pressing of the pedal. This interval, according to Anokhin (1968), corresponds to the development of integrative processes connected with the mechanisms of afferent synthesis and decision-making.

The findings allow us to conclude that the effect of cocaine on the organism mainly involves this particular integration of excitations, while the mechanisms of motor activity are disturbed to a lesser extent.

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