EFFECT OF STIMULATION AND BLOCKADE OF THE DOPAMINERGIC SYSTEM ON CHOICE OF BEHAVIOR STRATEGY BY RATS IN A SHUTTLE BOX

O. B. Butenko, R. N. Kordzadze, and G. G. Barsegyan

UDC 616.831-008.92/.93-02:613.863]-092.9-07

KEY WORDS: defensive behavior; dopaminergic system.

Research into the concrete neurochemical mechanisms of the brain during realization of behavioral reactions in various extremal situations has drawn attention to the important role of the dopaminergic systems of the brain in these processes It has been suggested that an important role in the choice of an adequate strategy is played by dopaminergic systems [4]. Several workers [2, 3, 6] have distinguished two strategies of behavior of rodents in a shuttle box – selective response to a conditioned stimulus or to nociceptive stimulation. It is accordingly important to study the effect both of activation of the dopaminergic system, due to systemic administration of Levodopa (Madopar), a dopamine precursor, and of hypofunction of this system, caused by administration of haloperidol, a specific blocker of dopaminergic receptors, on choice of behavior strategy.

The aim of this investigation was to study the role of the dopaminergic systems of the rat brain in a situation of choice of behavior strategy in a stress-inducing situation created in a shuttle box.

EXPERIMENTAL METHOD

Experiments were carried out on 49 male Wistar rats weighing 200-220 g. The experiments were conducted in a "Reflex-16" experimental system ("Columbus Instruments," USA). The system enables three stimuli to be used: photic, acoustic (presented 20 sec after the end of action of the photic stimulus), and nociceptive (foot-shock). The duration of each stimulus was 10 sec. Each experiment included 20 presentations, 60 sec in duration (interval between them 30 sec). To determine the type of chosen behavior strategy the latent period of response, the number of active and passive avoidances, and the number of responses to the conditioned stimulus and nociceptive stimulation were recorded. In the 1st stage of training the acoustic stimulus was significant: it was accompanied by an electric shock, i.e., a conditioned avoidance reflex to the acoustic stimulus was formed. The photic stimulus remained neutral. After 200 experiments the stereotype was changed by altering the significance of the stimulus, i.e., the photic stimulus became significant (2nd stage), and retraining took place, creating additional stress. In the 2nd stage of training the rats were given levodopa (100 mg/kg intraperitoneally 20 min before the experiment began) or haloperidol (1 mg/kg intramuscularly 10 min before the experiment began), and rats of the control group received 1 ml physiological saline. The significance of differences was assessed by Wilcoxon's test [1].

All-Union Mental Health Research Center, Russian Academy of Medical Sciences, Moscow. All-Union Research Center, Ministry of Health of Russia, Moscow. (Presented by Academician of the Russian Academy of Medical Sciences M. E. Vartanyan.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 12, pp. 573-574, December, 1992. Original article submitted May 12, 1992.

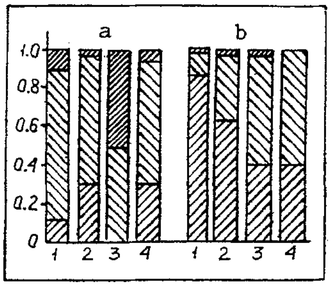

Fig. 1. Behavior of rats in response to a change in stimulus significance: a) strategy 1, b) strategy 2; oblique shading sloping to the right – conditioned reflex to light or sound, oblique shading sloping to the left – response to electric shock; close oblique shading sloping to the right – absence of change of meaning, close oblique shading sloping to the left – intertrial responses. 1) Last experiment with sound used as conditioned stimulus; 2) last experiment with light used as conditioned stimulus; 3) injection of levodopa; 4) injection of haloperidol.

EXPERIMENTAL RESULTS

In the 1st stage of training (the significant stimulus was acoustic) two basic behavior strategies of the rats were discovered (Fig. 1): type 1, when the animals reacted by running away immediately in response to the nociceptive stimulus (after a latent period of not more than 0.2 sec). There were 25 such rats. Passive defensive reactions were observed in this same group with a frequency of up to 9% of the total number of responses, when the animals sat in the corner of the compartment during the whole 10 sec of action of the current. Other rats ($n = 24$) responded to the conditioned acoustic stimulus (type 2 strategy). During training of these rats, a certain number of conditioned responses to time was observed (to the 90-sec interval), i.e., the rats crossed into the safe compartment a certain time (up to 10 sec) before the conditioned stimulus.

This specific nature of behavior was observed throughout the period of training, and, moreover, by the end of training the difference between the types of strategy was more marked than at the beginning, and in most rats responses of type 1 to the conditioned stimulus were not observed at all (although at the beginning of training they sometimes were present). We thus observed two behavior strategies, as described in [2, 3, 6].

A change in significance of the stimulus (from acoustic to photic) led to the appearance of many passive-defensive reactions and to an increase in the latent period of response to the nociceptive stimulus. In the course of training, a conditioned response to the photic stimulus was formed in the rats that responded to the conditioned acoustic stimulus (although the number of responses made by these rats directly to the electric shock increased). In the group of animals preferring the type 1 strategy, however, in some cases responses appeared to the conditioned photic stimulus.

An increase in the dopamine concentration led to a sharp and significant decrease in the number of conditioned responses to sound in animals with both strategies (Fig. 1) compared with intact rats; in rats which responded predominantly to nociceptive stimulation, there was a further sharp increase in the number of passive defensive reactions (up to 50%, $p < 0.05$). In the light of data on the role of the dopamine system in the development of various depressive symptoms, including those determining anxiety states [5], it can be tentatively suggested that excess of dopamine became a factor disturbing adaptation, by preventing the development of anxiety, a normal component of adaptation.

During blockade of the dopaminergic receptors, however, an effect could be seen only in rats preferring to respond to the conditioned stimulus: in these rats the number of conditioned responses to light decreased significantly whereas in rats with strategy 1 virtually no difference was observed compared with the control animals (Fig. 1).

Thus an increase in the dopamine concentration in the rat brain (as a result of injection of the dopamine precursor) led to similar changes in the behavior of animals with both types of strategy. Blockade of dopaminergic receptors, however, was reflected only in the behavior of animals with strategy 2, and the changes were similar to those observed in response to an increase in dopamine concentration In other words, animals responding predominantly to the conditioned stimulus were more sensitive to factors acting on the dopaminergic system, whatever the character of the changes taking place in it.

It can be tentatively suggested on the basis of the foregoing facts that dopaminergic systems have a modulating effect on the mechanism of realization of the behavior strategy. Participation of the dopaminergic system in the realization of the type of strategy evidently has specific features, and one of the systems involved in the realization of the type 2 strategy is evidently more sensitive to a change in functional activity of the dopaminergic system.

REFERENCES

1. V. Yu. Urbakh, Biometric Methods [in Russian], Moscow (1964).
2. G. Bignami, L. de Acetis, and G. L. Gatti, J. Pharmacol. Exp. Ther, **176**, 725 (1971).
3. H. Kuribara and S. Tadakoro, Pharmacol. Biochem. Behav., **11**, 203 (1979).
4. R. D. Oades, Neurosci. Behav. Res., **9**, 261 (1985).
5. N. R. Swerdlow and G. F. Koob, Brain Sci., **10**, 197 (1987).
6. S. Takaori, N. Yoda, and G . Mori, Jpn. J . Pharmacol., **19**, 587 (1969).