ROLE OF PSYCHOTROPIC EFFECTS OF NICOTINE IN HABITUATION TO IT IN RATS

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When the causes of development of drug addictions are analyzed consideration must be paid not only to predisposition to this pathology, but also to the intrinsic phamacologic effects of the drugs inducing it [2]. For instance, when predisposition of animals to the development of experimental alcoholism was studied it was shown that an alcoholic motivation exists *ab initio* only in a certain proportion of animals, characterized by a low adaptive potential, and this evidently provides the basis for the positive emotional effects and the spectrum of behavioral activity in these individuals [1, 5, 6].

The aim of this investigation was to study the tendency of animals differing in adaptive potential toward the development of nicotine addiction, and also to study the pharmacologic effects of nicotine by means of behavioral methods.

EXPERIMENTAL METHOD

Experiments were carried out on 126 noninbred male albino rats weighing 200-250 g and 320 noninbred male albino mice weighing 18-22 g.

In the experiments of series I the strength of nicotine motivation was studied in animals with different adaptive potential, which was evaluated in relation to the intensity of the depressive-like (DLS) arising in a situation of unavoidable swimming for 600 sec [2]. According to data in the literature [3], the intensity of DLS is proportional to the total time of immobilization (TTI), when the rat swims passively in the vertical posture, leaning slightly forward. Rats with TTI of under 100 sec (90.2 $\pm$ 6.8 sec) were classified as highly active, those with TTI over 240 sec (258.3 $\pm$ 10.67 sec) as relatively inactive.

Nicotine motivation in the rats was assessed by placing the animals in individual cages measuring 40 $\times$ 12 $\times$ 15 cm, equipped with a feeding bowl and two graduated drinking bowls — one with water, the other with a 0.005% solution of nicotine. The quantitiy of liquid drunk was measured daily for 10 days.

In the experiments of series II the effect of nicotine in doses of 0.05 and 0.1 mg/kg was estimated after a single intraperitoneal injection on the intensity of DLS in rats. For this purpose 30 highly active and 30 relatively inactive rats were chosen and divided into three groups. Each group consisted of 10 highly active and 10 relatively inactive animals. After 24 h rats of the first and second groups were given an intraperitoneal injection of nicotine in doses of 0.05 and 0.1 mg/kg respectively. Animals of group 3 were given an injection of physiological saline. The animals were retested 30 min after the injection under conditions of unavoidable swimming.

In the experiments of series III the effect of a single intraperitoneal injection of nicotine on the ability of the rats to compete, under conditions of zoosocial conflict in a tank of water in which there was a dry platform, sufficiently large for only one animal, was studied by the method in [4]. The number of attempts made by each animal to knock its partner from the dry platform and the effectiveness of the knocking attempts (EKA) were recorded:

$$\text{EKA} = \frac{\text{Number of time knocking off was successful}}{\text{Total number of attempts at knocking off}}$$

Nicotine was injected into the "subordinate" individual 30 min before the beginning of retesting, after an interval of 24 h.

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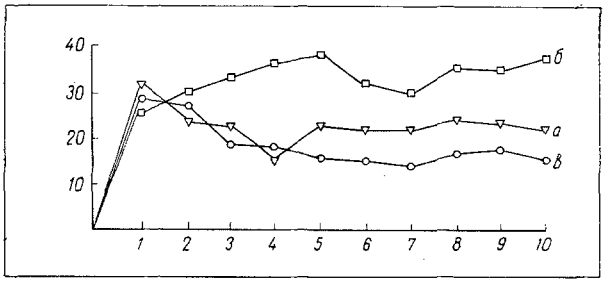

Fig. 1. Consumption of 0.005% nicotine solution by rats. Abscissa, time of experiment (in days); ordinate, volume of nicotine solution consumed (in ml/kg body weight); a) intact rats, b) highly active rats, c) relatively inactive rats.

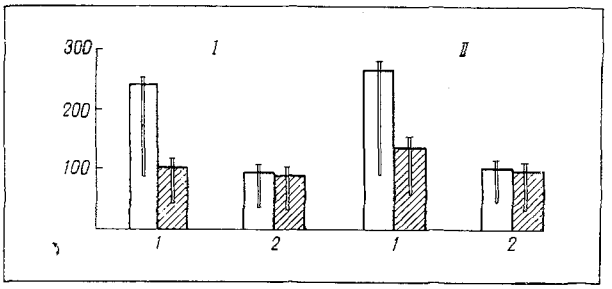

Fig. 2. Effect of nicotine in doses of 0.05 mg/kg (I) and 0.1 mg/kg (II) on duration of immobilization of rats. Ordinate, time (in sec). 1) relatively inactive rats, 2) highly active rats. Unshaded columns — background, shaded — experiment.

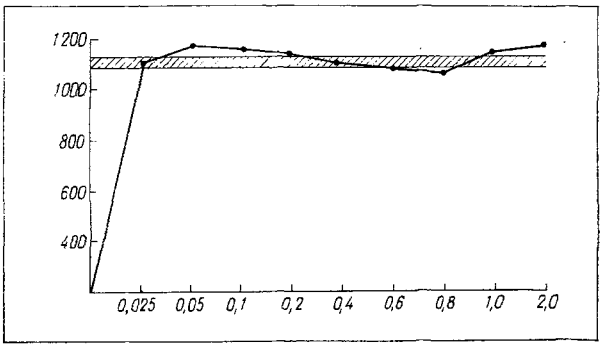

Fig. 3. Effect of nicotine in different does on motor activity in mice. Abscissa, dose of nicotine (in mg/kg body weight); ordinate, motor activity of mice. Horizontal band represents control.

In the experiments of series IV the effect of nicotine in doses of 0.025, 0.05, 0.1, 0.2, 0.4, 0.6, 0.8, 1.0 and 2.0 mg/kg on motor activity of albino mice was studied in an "Animax" actometer. Nicotine solution was injected intraperitoneally into all the mice, divided into groups with 10 mice in each group, and 30 min after the injection they were placed in the actometer for 10 min. The experiments were carried out from noon until 1 p.m.

The results were subjected to statistical analysis by the nonparametric difference test

[8]; the significance of difference between the fractions was estimated by Fisher's method [7].

EXPERIMENTAL RESULTS

Consumption of the 0.005% nicotine solution by relatively inactive animals (36.5 ± 9.8 ml/kg) was almost twice that of the highly active animals (14.5 ± 6.24 ml/kg). These differences became statistically significant by the 3rd day of testing, and remained so until the end of the experiment (Fig. 1). In the relatively inactive animals, characterized by marked predisposition to the development of experimental alcoholism [3], ability to develop a craving for nicotine was high. It follows from Burov's concept [2] that the development of drug addiction may be based on a positive emotiotropic effect of the drug giving rise to this pathology, the action of nicotine on behavior of the rats was studied. Nicotine was found to reduce the intensity of DLS substantially in relatively inactive animals (to the greatest degree by a dose of 0.05 mg/kg), but had virtually no effect on the behavior of highly active rats (Fig. 2).

To study the effect of nicotine on the ability of the animal to compete, 24 pairs of rats with established relationships of dominance and subordination were selected. These animals were divided into three groups (8 pairs in each group). Nicotine was injected into the "subordinate" animals of the first two groups in doses of 0.05 and 0.1 ml/kg. Into rats of the third group (control) 0.15 ml of physiological saline was injected. Under these circumstances injection of 0.05 mg/kg of nicotine caused a marked increase in ELS of the "subordinate" rat, and in most cases (6 of 8 cases) a change of dominant individual took place (Fig. 3). Injection of 0.1 mg/kg of nicotine into the "subordinate" individual also increased its ELS, but a change of dominance took place in only 4 of 8 cases.

When the effect of nicotine, over a wide range of doses, was studied on the motor activity of mice no significant effect of any kind was observed.

It can thus be concluded that nicotine has a specifically activating action on animals with low adaptive potential, and which differs from the action of psychostimulants by the fact that it is evidently due to their marked addiction for nicotine.

The experiments are evidence that some individual of the male population of noninbred albino rats have a marked predisposition to develop addiction to nicotine. It is an interesting fact that this pathology develops in animals with low adaptive potential and occupying lower ranks of the zoosocial hierarchy. Such individuals usually have high sensitivity to stress factors and a marked tendency toward the development of experimental alcoholism, based on the normalizing effect of ethanol on the emotional sphere and behavior of these individuals [1, 6]. The results of this investigation are thus evidence that habituation to nicotine and to alcohol possesses common causes.

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