The alimentary and social instrumental performance in dogs is suppressed by various doses of amphetamine

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Abstract. Amphetamine was administrated intramuscularly 20-25 min before each experimental session in doses of: 0.2 mg/kg, 0.5 mg/kg and 1.0 mg/kg. Each dose was applied twice and preceded by a regular experimental sessions without any treatment. An instrumental performance consisted of alimentary-social differentiation of two tones reinforced either by food or by sensory-social reward (petting by the experimenter). Amphetamine produced dose dependent decrease of the instrumental performance of both alimentary and social responses. This decrease was however not equal regarding both reactions. The dose of 1 mg/kg produced deep, statistically significant deterioration of alimentary as well as social responses. After the administration of the dose of 0.5 mg/kg the decrease of alimentary responses was equal to that produced by 1 mg/kg, whereas social responses were less deteriorated. After the dose of 0.2 mg/kg the reduction of alimentary responses was smaller than produced by 0.5 mg/kg but still more pronounced than in the case of socially reinforced reactions. The results confirm our previous data that amphetamine suppresses positively motivated instrumental performance in dogs. The results also show that amphetamine-evoked suppression is dose dependent and that it is different for alimentary and social responses. This might indicate that the positive reward system is not homogenous but consists of some subsystems related to different kinds of reward. It is concluded that the suppressing effect of amphetamine is due to the inhibitory effect on motivation, but not on purely instrumental mechanisms nor on hedonic processes.

Key words: amphetamine, instrumental performance, alimentary reward, social reward, dogs
INTRODUCTION

Amphetamine was considered by many authors to be an activator of the reward system. This assumption was based on data of Stein (1964) and Stein and Wise (1969) showing that amphetamine produced an increase of the rate of self-stimulation in rats. The authors attributed the positive role of amphetamine in reward mechanisms to its adrenergic effect. Similar opinion concerning the role of noradrenaline as a transmitter of the reward mechanisms was presented by Cytawa and Trojniar (1979), and Cytawa and Jurkowlaniec (1978) as well as by other investigators. The original hypothesis that the positive role of amphetamine in the reward system is due to the release of noradrenaline was replaced by the dopamine theory of reward (Wise 1982). Amphetamine is an agonist of both noradrenaline and dopamine. The data of Hernandez and Hoebel (1988) on stimulation of the hypothalamic (LH) feeding zone, strongly suggest the important role of dopamine in hedonic processes related to food. The experiments of Hernandez et al. (1987) gave the evidence that amphetamine produces the release of dopamine into the nucleus accumbens. Hoebel et al. (1983) also showed that rats will bar-press in order to self-inject amphetamine into the nucleus accumbens. Intravenous self-injection of amphetamine was reported by Risner (1975) also on dogs.

All these experiments and several others which have shown the stimulatory effect of amphetamine on operant behavior (see Wise 1982) seem to prove the positive role of amphetamine in reward mechanisms as well as in motivation.

On the other hand, various other authors have shown that amphetamine may also produce a suppressing effect. At first the inhibitory effect of amphetamine was observed in feeding. Amphetamine has been used in human clinic for the treatment of obesity as it produces anorexia. Then, its suppressing effect on food intake and other behaviors was also demonstrated in the experiments performed on various species (Blundell and Latham 1978, Thompson and Moerschbaecher 1980, Colle and Wise 1988, Zagrodzka and Jurkowski 1988, Motles et al. 1989, Saito et al. 1991 and others). Also our previous experiments showed that amphetamine produced suppressing effect on instrumental response in dogs (Fonberg et al. 1983, Kostarczyk and Fonberg, 1988).

The differential effect of amphetamine may be attributed to application of different doses of amphetamine (see Blundell and Latham 1978, Colle and Wise 1988, Wolgin et al. 1988, Motles et al. 1989). For example Colle and Wise (1988) found that small doses of amphetamine (0.125 mg/kg, 0.25 mg/kg i.p.) facilitated eating evoked by the stimulation of hypothalamic feeding area, whereas high doses (1.0 mg/kg, 2.0 mg/kg i.p.) produced the opposite effect. The authors assumed that either noradrenergic or dopaminergic mechanisms may be susceptible to different concentrations of amphetamine. Dopamine may play facilitory role, whereas noradrenaline is supposed to be inhibitory.

In the present paper we applied three different doses of amphetamine in order to verify the hypothesis that different doses produce a different or even opposite effect on positively reinforced performance. Most authors in their investigations had been using food reward. We studied the effect of different doses of amphetamine on instrumental responses reinforced by two different rewards - alimentary and social.

METHODS

Subjects

Experiments were performed on five mongrel dogs housed in individual cages 2 x 2.5 m and fed once a day ad lib. on cereal soup with meat and vegetables.

Instrumental training

Dogs were trained to differentiation of two tones reinforced by two different rewards, i.e. either by food or by sensory-social contact. The tone of 500 Hz and the tone of 1,000 Hz were applied as condi-
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Amphetamine-suppressed signals (CSi) in random order and their duration was 10 s in every trial. The tone of 1,000 Hz was used as CS for the instrumental response reinforced by food and the tone of 500 Hz as CS for the instrumental response reinforced by social reward. Both tones were of the same intensity. The instrumental response consisted of lifting the proper leg and putting it on the food tray during 10 s of CS presentation, and the adequate reward was administered immediately after such performance. Thus, the reinforcement was dependent on the performance. Alimentary reward consisted of mashed cooked meat mixed with bread powder, supplied in the automatically moving bowls on the food tray, in the amount of 50 grams per each bowl. The social reward consisted of petting the dog by the experimenter (stroking, i.e., "overpassing the hand gently" on the head and back). Experimental sessions were performed five days a week. During one experimental session CSi for alimentary and social responses were presented five times each, intermixed at random. Intertrial intervals also varied randomly, ranging between 1 and 2 min (for details see Fonberg 1992).

Amphetamine treatment

Amphetamine (Psychedrinum-Polfa) was injected intramuscularly in doses of: 0.2 mg/kg, 0.5 mg/kg and 1.0 mg/kg about 20-25 min before experimental sessions, by a person other than the experimenter. Higher doses were not used in order to avoid the anorexic effect. Amphetamine was applied six times (twice each dose) and the sequence of the particular doses was random. Sessions with amphetamine were separated by sessions without drug application and their number was also random (ranging from 2 to 6). Experimental sessions were run 5 days a week.

Statistical analysis

The Wilcoxon signed ranks test (Conover 1971) was used to compare the mean number of social and

Fig. 1. The effect of different doses of amphetamine (0.2 mg/kg, 0.5 mg/kg and 1.0 mg/kg) on instrumental performance in dogs. Bars represent the mean number of alimentary and social responses in percent related to the performance without the drug. Black bars, the alimentary reactions; hatched bars, the social reactions; *, statistically significant difference (P<0.01) in relation to the performance without amphetamine.
alimentary reactions before and after the administration of each particular dose of amphetamine.

RESULTS

Figure 1 illustrates the effect of amphetamine on alimentary and socially reinforced responses. Amphetamine produced a suppressing effect on both kinds of behaviors. This effect, however, was much greater in the alimentary responses. Each dose of amphetamine (0.2 mg/kg, 0.5 mg/kg and 1.0 mg/kg) produced a statistically significant deterioration of instrumental responses rewarded by food ($P<0.01$ for all three doses). A comparison of the mean number of responses after the doses of 0.2 mg/kg and 0.5 mg/kg showed that the dose of 0.5 mg/kg produced a deeper effect than the dose of 0.2 mg/kg ($P<0.05$). The effect of the dose of 1.0 mg/kg was similar to the effect of the dose of 0.5 mg/kg. The influence of amphetamine on social reactions was much smaller than on alimentary ones. Only the dose of 1.0 mg/kg caused statistically significant ($P<0.01$) deterioration of responses. The dose of 0.5 mg/kg produced slightly significant ($P<0.10$) effect and the decrease of performance produced by the dose of 0.2 mg/kg was not statistically significant.

During an experimental session the dogs were standing quiet and they discriminated tones well. Although the number of responses decreased after amphetamine, the dogs gave adequate responses to proper stimuli. Before and after experimental sessions the dogs were very lively and revealed increase of friendly attitude toward the experimenter (jumping on, licking his hands, etc.). Stereotyped behavior was not observed.

DISCUSSION

Our experiment has shown that the suppressive effect of amphetamine was evident for all doses and relevant to dose. A higher dose produced stronger suppressive effect. Several authors showed that low doses may cause different or even opposite effect than high doses. High doses may suppress feeding or various other behaviors as well as particular components of behavior, whereas low doses may in contrast augment the response or have no effect (Blundell and Latham 1978, Colle and Wise 1988, Wolgin et al. 1988, Evans and Vaccarino 1990, Motles et al. 1991, Saito et al. 1991).

In our experiment the positive excitatory effect of amphetamine on instrumental performance was never observed even with the lowest dose of 0.2 mg/kg. The dogs were generally excited before and after the experimental sessions, but during the session they stand quiet. In spite of that instrumental performance decreased. It should be stressed that the effect was not identical in respect to alimentary and social responses. Highly statistically significant effect of amphetamine on alimentary responses was observed already with the dose of 0.2 mg/kg, whereas on social responses highly statistically significant effect was produced only by 1 mg/kg. The dose of 0.5 mg/kg produced only slightly significant effect and the decrease produced by 0.2 mg/kg was not significant. The discrepancy between the effects of amphetamine on alimentary and social performance may speak for that the positive reward system is not homologous. It is possible that its subsystems are more or less sensitive either to dopamine or to noradrenaline.

Colle and Wise (1988) suggested that different effects of various doses of amphetamine may be caused by a different degree of release of noradrenaline or dopamine and that the inhibitory effect on feeding may be due to adrenergic mechanisms, whereas the facilitory effect due to dopamine. In our experiment, however, all used doses produced a deterioration of the instrumental performance of both alimentary and social responses. Although the suppressive effect of amphetamine on social reactions was smaller than on alimentary ones, it was still evident (Fig. 1). In the case of social responses as their suppression could not be due to anorexia so it is rather not mediated by noradrenergic mechanisms. On the other hand, the performance of both social and alimentary reactions could not be also attributed to dopaminergic mechanisms as the stimu-
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Amphetamine suppresses instrumental performance and reward seems to be well documented (see Wise 1982).

Therefore, it should be taken into account that the inhibitory effect of amphetamine may be due to the release of serotonin. A significant increase of serotonin has been reported in rats after hypothalamic infusion of amphetamine (Parada et al. 1988). The other possibility is that the inhibitory effect of AMPH might result from DA/5-HT interactions (Romaniuk et al. 1989, Kuczenski and Segal 1991, Motles et al. 1991).

The different degree of suppression by amphetamine of social and alimentary responses demonstrates that this drug does not affect purely instrumental mechanisms. In this last case instrumental performance reinforced by food and social reward should be equally affected. From our previous works (Fonberg et al. 1983, Kostarczyk and Fonberg 1988, Fonberg and Kraszewski 1990) it follows that hedonic processes (need for petting and preference for palatable food) are not affected by amphetamine either. Kostarczyk and Fonberg (1988) showed that the need for petting evaluated by the time of petting the dog by experimenter which was regulated by the dog itself, increased during amphetamine treatment. Therefore, it might be concluded that the positive value of the social-sensory reward was not inhibited and, what follows, that hedonic processes were not suppressed but even augmented. The same conclusion may be drawn from the paper of Fonberg and Kraszewski (1990), who showed that heart rate characteristics which had been evidenced by Kostarczyk and Fonberg (1982) to be a denominator of the hedonic state, is not changed by amphetamine. According to Kostarczyk and Fonberg (1982) the heart rate increase during the initial phase of eating is dependent on the food palatability. The most palatable food produces the greatest increase of heart rate. Under amphetamine treatment the differences of heart rate increase related to food palatability are even more evident (Fonberg and Kraszewski 1990). These data speak for that hedonic processes are not suppressed but enhanced.

If amphetamine does not impair either the motor mechanism of instrumental performance, as such, or the hedonic processes it remains to consider the effect of amphetamine on motivation (see also Wolgin et al. 1988). The decrease of alimentary and social responses may be due to impairment of the mechanisms of motivation to perform, whereas hedonic processes and purely instrumental mechanisms remain intact. Such conclusion is in disagreement with suggestions of many authors who postulated the positive role of amphetamine in motivation. Those authors, however, used mostly the procedure of bar-pressing by rats. Increase of such rhythmic performance may be due to general motor excitement and stereotypic behavior. Also, the often used procedure of self-injection of amphetamine either into the brain (Stein 1964, Stein and Wise 1969, Hoebel et al. 1983) or intravenously (Risner 1975) may suggest the analogy to drug addicts who use amphetamine as a narcotic. They report the state of well being, euphoria, pleasure (hedonic processes augmented) but are motivated mostly to seek for another portion of drug and self-inject, similarly as rats and dogs in the above cited experiments. Although due to the increased arousal they may appear very active they are not motivated to live tasks which need great effort to accomplish them. This suggests that the mechanisms of reward and motivation may be separated. Drug-seeking response is based on hedonic processes of the reward mechanisms which seem to be independent and may be even opposite to the drive mechanisms (see also Konorski 1967).

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