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BRIEF COMMUNICATION

Interaction of Arena Size with Different Measures of Amphetamine Effects

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COLE, S. O. *Interaction of arena size with different measures of amphetamine effects.* PHARMAC. BIOCHEM. BEHAV. 7(2) 181–184, 1977. – The effects of d-amphetamine (0.0, 0.5, 1.0, 2.0 mg/kg) on feeding and activity of male Holtzman rats were investigated in 3 different size test arenas. Differences in the size of arenas significantly altered the drug's effect on ambulatory activity, but not on feeding or rearing. Also, differences in the size of arenas significantly altered the interrelationship (correlation) of amphetamine's effects on feeding and ambulatory activity, but not the interrelationship of the drug's effects on feeding and rearing. These findings suggest that test arena size differentially influences different general measures of amphetamine effects as well as differentially affecting the interrelationship of amphetamine effects. The importance of the interrelationship (correlation) data to the potential incompatability of the drug's effects is briefly considered.

d-Amphetamine Anorexia Ambulatory activity Rearing Feeding activity interrelationship

WHILE THE feeding-depressant and motor-stimulating effects of amphetamine are well documented [2, 3, 4], the importance of experimental conditions to the measurement of these effects remains unclear.

In order to determine the importance of apparatus differences to the measurement of drug-induced changes in behavior, the present study investigates the effects of amphetamine on food consumption, rearing, and ambulatory activity in three different size test arenas. The specific objectives of the study are: (1) to determine the importance of arena size to the general effects of amphetamine on feeding and activity; and (2) to determine the importance of arena size to the interrelationship (correlation) of amphetamine-induced changes in feeding and activity. The second of these objectives assesses the potential for amphetamine's depression of feeding being due to the drug's incompatible (competing) hypermotility action, a view that has been proposed by Carlton [1] and by Lyon and Robbins [5].

METHOD

Animals and Apparatus

Thirty adult, male Holtzman rats (300–450 g) were used. They were housed individually under standard laboratory conditions and, except when otherwise specified in the procedure, had ad lib access to Purina laboratory chow and water in the home cage.

Three different size test arenas, constructed of plywood, were used. The small arena (S) was 20 × 20 cm and permitted very limited locomotion. The medium size arena (M) was 40 × 40 cm, and the large arena (L) was 80 × 80 cm. With the use of floor markings the M arena was divided into 4 squares and the L arena divided into 16 squares, with each square equal in area to the total area of the S arena. The walls of all three arenas were a uniform 30 cm in height. A plastic food cup, firmly attached at floor level to the middle of a common wall of each arena, permitted free access to food. Fluorescent lighting directly above the testing area provided uniform illumination of the arenas.

Procedure

Initially, the 30 animals were assigned randomly to one of the three test arenas. Following such assignment, the 10 animals in each arena were administered two 30-min adaptation sessions following 24 hr food deprivation, separated by three days. During adaptation sessions, the animals were permitted to eat freely 45 mg precision food pellets placed in the food cup.

All animals, in their respective arenas, were then administered four 30-min drug test sessions (0.0, 0.5, 1.0, 2.0 mg/kg, IP d-amphetamine SO_4 in 1 ml/kg 0.9% NaCl) following 24 hr food deprivation, with the order of drug dose randomly assigned to the animals over sessions. Three to five days separated each of the drug test sessions. Food consumption was measured by placing 300 precisions pellets in the food cup at the beginning of the test, counting the number remaining at the end of the test, and taking the difference (corrected for spillage) as the number of pellets eaten. In the S arena, activity was measured only in terms of the number of discrete rearings (regardless of duration), as the apparatus confined the animals to the area

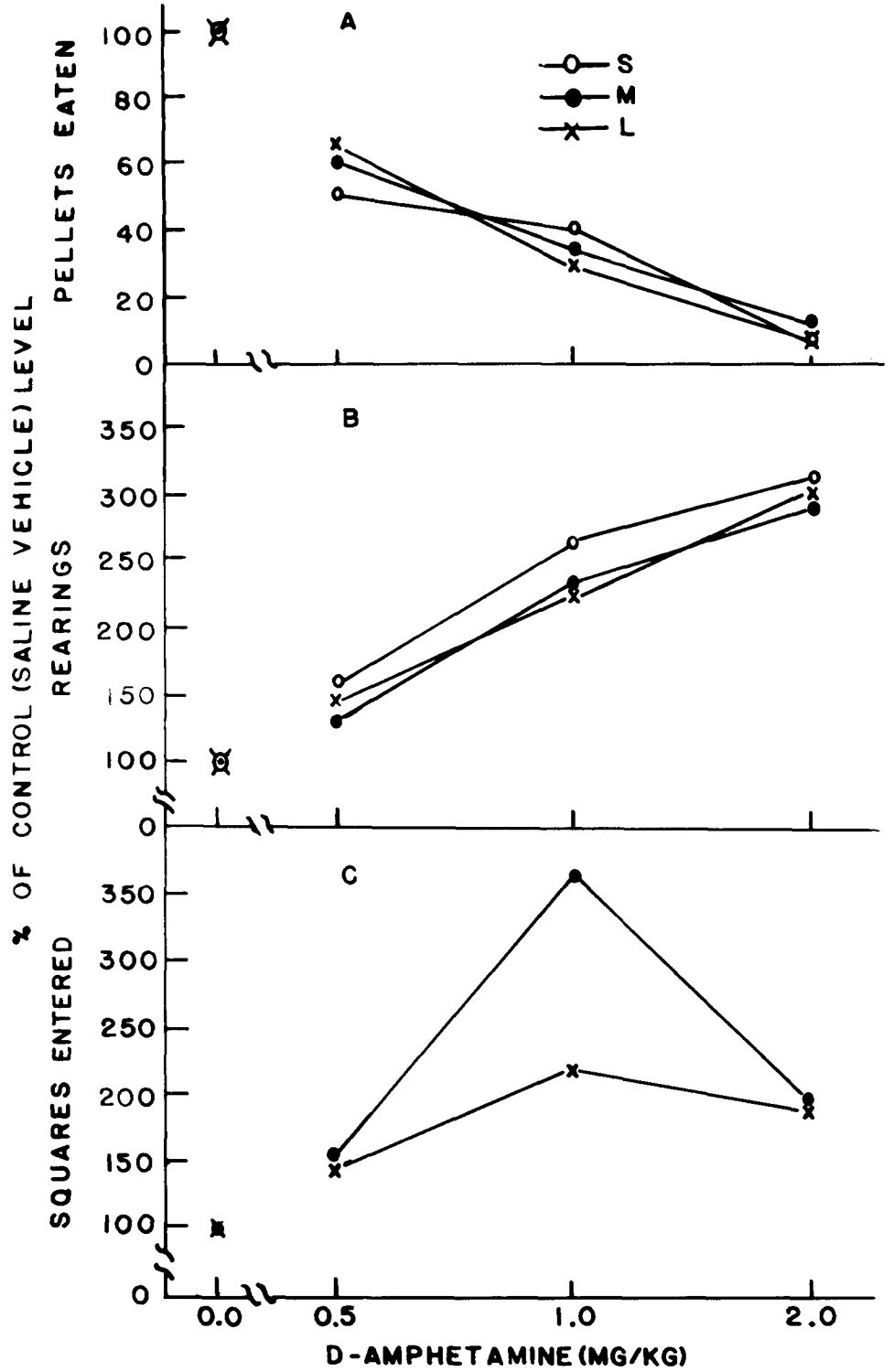

FIG. 1. Mean number of pellets eaten (panel A), mean number of discrete rearings (panel B), and mean number of squares entered (panel C) by animals in small (S), medium (M), and large (L) test arenas under different d-amphetamine dose conditions. Drug doses were assigned randomly to animals over four 30-min test sessions, and values are expressed as percentage of control (saline vehicle) level.

of a single square. In the M and L arenas, activity was measured both in terms of the number of discrete rearings and number of squares entered. Hand counters were used to record activity data, and the interjudge reliability of the three recorders of activity was high (r = .964).

The testing procedure for any one animal was as follows. The animal, after having been food deprived for 24 hr, was removed from the home cage, weighed, and injected with

the appropriate dose of d-amphetamine. Thirty min later, the animal was placed in the appropriate arena, in front of and facing the food cup, to begin the 30-min test session. Upon completion of the session, the animal was returned immediately to the home cage to await the next session.

RESULTS

The effect of the different doses of d-amphetamine on food consumption, rearings, and squares entered by animals in the different arenas is summarized in Fig. 1. Because baseline differences (0.0 mg/kg dose) in the number of squares entered by the animals in the M and L arenas were present (mean values in M arena were 51.20, 79.80, 186.50, 99.60 and in L arena were 153.90, 230.60, 323.00, 297.00 for 0.0, 0.5, 1.0, 2.0 mg/kg doses, respectively), all data in Fig. 1 are expressed and statistically analyzed (ANOVA) as percentage of control (saline vehicle) level.

Analysis of food consumption data yielded a significant Drug dose effect, $F(2,54) = 80.39$, $p < 0.01$, only. Similarly, analysis of rearing data indicated a significant Drug dose effect, $F(2,54) = 21.33$, $p < 0.01$, but no other significant sources of variance. However, analysis of the number of squares entered by the animals indicated a significant Drug dose effect, $F(2,36) = 32.28$, $p < 0.01$, a significant Arena effect, $F(1,18) = 9.20$, $p < 0.01$, and a significant Drug dose × Arena Interaction, $F(2,36) = 10{,}58$, $p < 0.01$. Differences in the relative effectiveness of the 2.0 mg/kg dose in the M and L arenas were of major importance to the Drug dose × Arena Interaction. Half of the animals (5/10) in the M arena displayed periods of mild stereotypical behavior (immobility accompanied by head and shoulder bobbing) interspersed between periods of ambulation under the 2.0 mg/kg dose, which contributed to the relative reduction in the number of squares entered (t-test comparison of 1.0 and 2.0 mg/kg doses following ANOVA; $t = 2.40$, $df = 9$, $p < 0.05$). Although similar interspersed stereotypical episodes were also observed with three animals in the L arena under the 2.0 mg/kg dose, the occurrence was not of sufficient frequency or magnitude to produce a significant relative reduction in ambulation (t-test comparison of 1.0 and 2.0 mg/kg doses following ANOVA).

In order to determine the interrelationship of the effects of d-amphetamine on feeding and on rearing and squares entered in the different arenas, individual and group (pooled) drug-dose correlations of feeding with measures of activity were calculated. These results are summarized in Table 1. The group drug-dose correlations of feeding with rearing were significant ($p < 0.01$) in all three arenas. In contrast, the group drug-dose correlation of feeding with ambulatory activity (squares entered) in the M and L arenas was statistically significant ($p < 0.05$) only in the latter case. It is also of interest to note that, in general, the individual drug-dose correlations of feeding with ambulatory activity vary more markedly than those of feeding with rearing in the same arenas. This individual variation was due to the fact that, with those animals demonstrating stereotypical episodes under the 2.0 mg/kg dose, the drug-dose correlations of feeding with ambulatory activity were uniformly lower than was the case with animals who did not demonstrate such episodes.

DISCUSSION

The results of the present study indicate that arena size differentially influences the general effects of amphetamine on behavior. Differences in arena size did not significantly alter the dose-ordered depression of feeding by d-amphetamine or the dose-ordered increase in rearings produced by the drug. However, differences in the size of the M and L arenas did have a significant effect on drug-induced changes in ambulatory activity, as evidenced by the significant Arena effect and significant Arena × Drug dose Interaction. Thus, under the conditions of the present study, the importance of arena size to the measurement of amphetamine effects appears to depend specifically upon the behavior (ambulatory activity) that is identified.

The drug-dose correlation data also suggest that arena size differentially influences the interrelationship of amphetamine's effects on feeding and activity. While the group drug-dose correlations of feeding with rearing were significant in all three arenas, the group drug-dose correlation of feeding with ambulatory activity was significant in the L arena but not in the M arena. Differences in the frequency and magnitude of the stereotypical episodes observed with animals in the two arenas under the 2.0 mg/kg dose undoubtedly contributed to these differences in the correlation of feeding with ambulation. Due to such a confounding of ambulation and stereotypy, it is probably

TABLE 1

SUMMARY OF INDIVIDUAL AND GROUP (POOLED) DRUG DOSE CORRELATIONS OF FEEDING WITH REARING (r) AND WITH AMBULATORY ACTIVITY (a) IN SMALL (S), MEDIUM (M), AND LARGE (L) TEST ARENAS

		Individual Correlations										Group r
S	r	−.9983	−.9927	−.5877	−.7228	−.9622	−.8298	−.4982	−.8470	−.9254	−.9282	−.8292†
	a	—	—	—	—	—	—	—	—	—	—	—
M	r	−.8751	−.9158	−.7820	−.8270	−.9639	−.6828	−.7314	−.6221	−.5986	−.9335	−.7932†
	a	−.3700	−.9332	−.4008	−.9076	−.2616	−.5089	−.8201	−.5606	−.4207	−.6526	−.5836
L	r	−.7925	−.8770	−.7306	−.8711	−.6059	−.8060	−.8667	−.3007	−.9131	−.9927	−.7756†
	a	−.3098	−.7367	−.2512	−.5126	−.8573	−.2093	−.7168	−.8804	−.9428	−.9925	−.6409*

*0.05 level of significance ($df = 8$).
†0.01 level of significance ($df = 8$).

inappropriate to conclude that these correlation data represent a true assessment of differences in the interrelationship of ambulation and feeding. However, the interrelationship of such activity with feeding is, nevertheless, less stable with differences in the M and L arenas than is the interrelationship of rearing with feeding in the same arenas.

The present correlation data also have some relevance to the proposed view that amphetamine's depression of feeding is due mainly to the drug's hypermotility action which produces behavior that competes with feeding [1,5]. If one assumes that significant correlations reflect the potential for such incompatible effects, the data suggest that, under conditions of the present study, the potential for the drug's effect on feeding being due to its competing hypermotility action is uniformly high in the case of rearing. However, the potential for the hypermotility action of the drug competing with feeding in the case of ambulation must await further experimentation which more clearly differentiates, than does the present study, the ambulatory and stereotypical effects of the drug.

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