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d-Amphetamine Effects on Behavior Produced by Periodic Food Deliveries in the Rat[1]

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NIETO, J., C. MAKHLOUF AND R. RODRIGUEZ. *d-Amphetamine effects on behavior produced by periodic food deliveries in the rat.* PHARMAC. BIOCHEM. BEHAV. 11(4) 423–430, 1979.—In Experiment 1, four food deprived rats were given milk every 60-sec irrespective of their behavior, and various doses of d-amphetamine were administered. Subsequently, rats were food satiated and exposed to the same reinforcement schedule for further sessions. Temporal patterns of tray-directed activities and other activities were recorded by direct observations. d-Amphetamine increased tray-directed activities, reduced grooming and produced mixed effects on rearing/sniffing. In Experiment 2, food deprived rats were given a pellet every 60-sec irrespective of their behavior and drinking was allowed to occur. Observational recording was supplemented by automatic measurement of time spent in contact with food tray and time spent drinking. d-Amphetamine increased the time spent in contact with tray, but reduced time spent drinking: grooming and rearing/sniffing were also reduced. The results were interpreted in terms of direct facilitation of tray-directed activities by d-amphetamine and reductions of the other activities by competition from tray-directed activities.

d-Amphetamine Food anticipation Schedule-induced behavior Drinking Grooming Fixed-time schedule Rat

PERIODIC deliveries of food engender a regular pattern of behavior within each interfood interval, and once this pattern has stabilized two classes of behavior may be distinguished: first, terminal responses which increase monotonically with time since food and are contiguous with food delivery; and second, interim activities which show bitonic temporal patterns, peaking soon after food delivery and receding as time since food delivery increases [12,25]. In fixed-time (FT) schedules, where food is delivered at fixed intervals independently of the subject's behavior, rats show an increasing tendency to visit the food tray, rearing or sniffing at it, and even chewing it as the moment of food delivery approaches [4,24]. In fixed-interval (FI) schedules, where food delivery is dependent on the occurrence of a particular response, bar-pressing is usually chosen as the terminal response in rats (e.g., [9]). Several interim activities can occur in FT and FI schedules, their characteristics depending on the opportunities afforded by the experimental situation and on the species used, but common examples are drinking, aggression, grooming and other activities (see reviews [8,23]).

There is a good deal of evidence on the effects of amphetamine on terminal behavior, but mostly from situations using response dependent schedules such as FI. These studies have typically found that amphetamine administration increases the low rates of bar-pressing or key-pecking at the beginning of the interval, while it can decrease the higher rates of later portions in the interval (see reviews [10,18]). On the other hand, it has been reported that d-amphetamine reduced the number of visits to a food tray and the amount of water ingested per session in rats exposed to a FT schedule [17], although in this study data on the effects on amphetamine on the temporal pattern of tray visits were not presented. Nevertheless, this study raises the question of whether amphetamine effects are dependent on response-reinforcer contingencies or on the type of terminal response being studied.

Evidence on the effects of amphetamine on interim activities is more limited. The most frequently studied activity is drinking, which is usually reduced by amphetamine [3, 7, 14, 17, 19, 20, 21, 26, 27]. A further example is hose-biting in monkeys and this is also reduced by amphetamine [6]. One possible reason for the decrement in interim drinking produced by amphetamine is the anorexic properties of this drug [11], since a reduction in hunger is known to reduce drinking (e.g. [8]).

The present experiments are concerned with the effects of d-amphetamine on terminal and interim behavior of rats exposed to FT schedules. Experiment 1 assessed the effects of d-amphetamine, and attempted to determine whether the

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effects of the drug could be attributed to reductions in hunger by comparing drug effects with those of food satiation. Experiment 2 assessed the effects of d-amphetamine on time spent engaged in tray directed activities and drinking.

EXPERIMENT 1

METHOD

Subjects

Four naive male albino rats weighing between 250–310 g at the beginning of the experiment were maintained at approximately 80% of their initial body weight until the final part of the experiment, when they were allowed free access to food in their home cages. They were housed individually with water always available.

Apparatus

A modular Coulbourn Instruments chamber measuring 27×25×30 cm was used. Its side walls were transparent plastic; the ceiling, back and front walls were aluminum; and the floor was formed by stainless steel rods. A metallic cup was attached to the front wall 9 cm to the right of the midline of the front wall, and 6 cm above the floor level, and extended 2 cm into the chamber. An 8 W houselight centered on the upper part of the front wall provided general illumination. The chamber was enclosed in a sound attenuating box fitted with a one-way observation window and an exhaust fan. Solid state equipment in an adjoining room controlled events in the chamber.

Procedure

Rats were given a 0.2 ml drop of Carnation evaporated milk every 60-sec independently of their behavior (FT 60-sec). Each session consisted of 50 milk deliveries; each delivery was signalled by briefly turning on an amber light located 3 cm above the cup. These reinforcement conditions were maintained throughout the experiment and each rat was given 35 sessions prior to any pharmacological intervention. A period in which various doses of d-amphetamine were administered followed. Finally, after receiving free food in their home cages during 12 days when their initial body weights were recovered, the rats were exposed to the FT 60-sec schedule for a further 10 sessions.

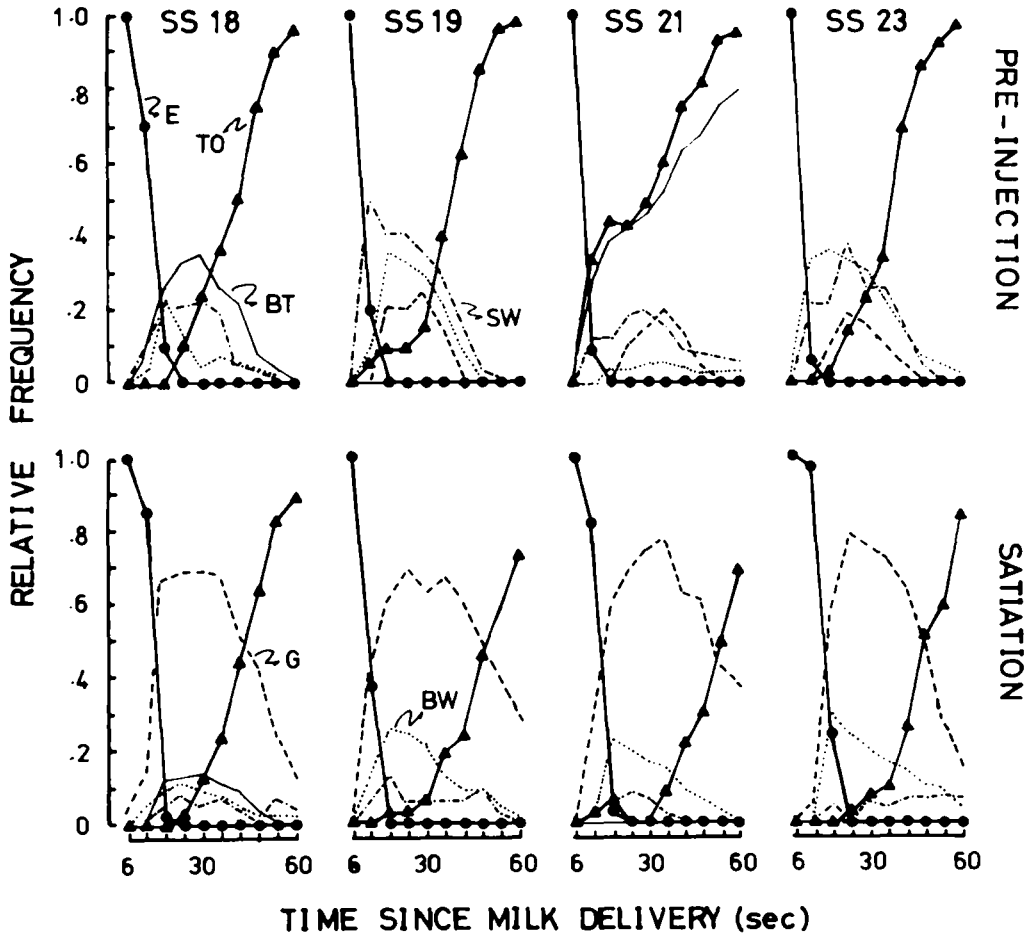

FIG. 1. Mean relative frequency of eating (E), tray orientation (TO), grooming (G), rearing/sniffing back (BW) and side wall (SW) over the last three preinjection sessions (upper part), and over the last three satiation sessions (bottom part), as a function of time since milk delivery.

Drug Administration

d-Amphetamine sulfate was administered in doses of 0.65, 1.1, 2.0 and 3.6 mg/kg. Each dose was dissolved in 0.9% saline solution to provide an injection volume of 2 ml/kg and was injected intraperitoneally 15 min before the start of the session. Dose administration order was mixed, and at least 4 days were allowed to elapse between each dose. Saline solution was injected on all non-drug sessions. Rat SS 18 received the dose of 0.65 mg/kg once and the remaining doses twice; Rats SS 19, SS 21 and SS 23 received the doses of 0.65 and 1.1 mg/kg once and the remaining doses twice.

Observations

The following categories of behavior were recorded: (a) Eating—defined as licking or chewing the reinforcer; (b) Tray orientation—defined as sniffing at the cup or tray, touching it, or any movement ostensibly directed towards the cup or tray in the absence of the reinforcer; (c) Grooming—defined as rubbing body with forepaws, or scratching or licking any part of the body; (d) Biting tray—defined as gripping the cup or tray with teeth; and (e) Rearing/sniffing at the back or side walls. Each interfood interval was divided into 10 bins of 6-sec each, and the observer (CM) using check sheets recorded, every 6th sec, which categories had occurred during each bin (i.e., one-zero method of sampling, see [22]). This was carried out during the last three preinjection sessions, on those saline sessions immediately preceding each dose, during each drug session, and on the last three satiation sessions.

RESULTS

Figure 1 shows for each subject the sequence of interreinforcement activities during the last three preinjection sessions (upper part), and during the last three satiation sessions (bottom part).

In both conditions rats always licked at the cup during milk delivery; then, they engaged in some activities such as rearing/sniffing or grooming; finally, the rats were more likely to approach, touch or bite the cup as time since milk delivery increased. Thus, tray orientation can be considered as the terminal response for all subjects, and grooming and rearing/sniffing as interim activities. In Rat SS 21, biting the tray also appeared as a terminal response during preinjection sessions, although this activity disappeared during the subsequent conditions. Food satiation reduced tray orientation and increased grooming in all rats, whereas rearing/sniffing was not greatly altered.

Figure 2 shows for each subject the effects of d-amphetamine on the categories recorded under these sessions. The upper row shows that tray orientation was increased as the dose increased; it started earlier and remained at a constant level throughout the interval. At high doses, rats showed little movement about the chamber, but displayed a great deal of activity—rearing, touching, and swaying—in the immediate area of the food cup. On all drug sessions the rats were observed to drink the milk soon after it was delivered. Grooming and rearing/sniffing at the back wall were reduced as the dose was raised, while rearing/sniffing at the side wall was increased, as seen in the middle and bottom rows of Fig. 2.

DISCUSSION

The results show that d-amphetamine administration increases tray orientation by making the rats engage in rearing, touching and swaying at the food cup. Conversely, it eliminates activities in other areas of the chamber. Food satiation, on the other hand, reduced orientation towards the food tray. Thus, it seems unlikely that amphetamine affects behavior by reducing hunger, especially since the rats continued to drink the milk as soon as it was presented.

The effects of d-amphetamine on tray orientation found in this experiment seem to contradict Sanger's [17] finding that the number of tray entries per session in rats exposed to a FT 60-sec schedule is reduced by d-amphetamine. This discrepancy may be due to differences in the way of recording behavior directed toward the tray. In Sanger's experiment a tray entry response was defined by the displacement of a hinged plastic flap connected to a microswitch. In the present experiment a much broader class of responses was included within the category of tray oriented behavior. Hence, it is possible that amphetamine increases the frequency, but also changes the topography, of behavior directed toward the tray. A further problem in the comparison between this and Sanger's experiment is that in the latter, as in most drug studies employing response-dependent reinforcement (e.g. [2,3]), solid food was used as the reinforcer. Consequently, the second experiment determines the extent to which the effects of d-amphetamine found in Experiment 1 was specific to the use of sweetened milk as a reinforcer. In addition to using food pellets, a further change was to allow access to water, so that drinking could occur as an interim activity. The automatic measurement of time spent in contact with the food tray and with the water provided a check on the reliability of observational data.

EXPERIMENT 2

METHOD

Subjects

Four male albino rats weighing between 287–350 g at the beginning of the experiment were maintained at 80% of their initial body weights. They were housed individually with water always available.

Apparatus

The chamber was the same as in Experiment 1, except that the cup was removed, and a metallic tray and a glass spout were used instead. The tray extended 3 cm into the chamber and was placed 9 cm to the left of the mid line of the front wall, and 1 cm above the floor. The spout extended 3 cm into the chamber and was 18 cm to the right of the tray, and 6 cm above the floor level; it was attached to a calibrated reservoir placed outside the chamber. Time spent in contact with the tray and with the water in the spout were automatically recorded to the nearest tenth of a second by means of contact sensors.

Procedure

The rats were exposed to a FT 60-sec schedule, that is, every 60-sec a single 45-mg Noyes pellet (Formula A) was delivered independently of the rat's behavior. These conditions were maintained throughout the experiment and 30 sessions were given to each rat before any injection was

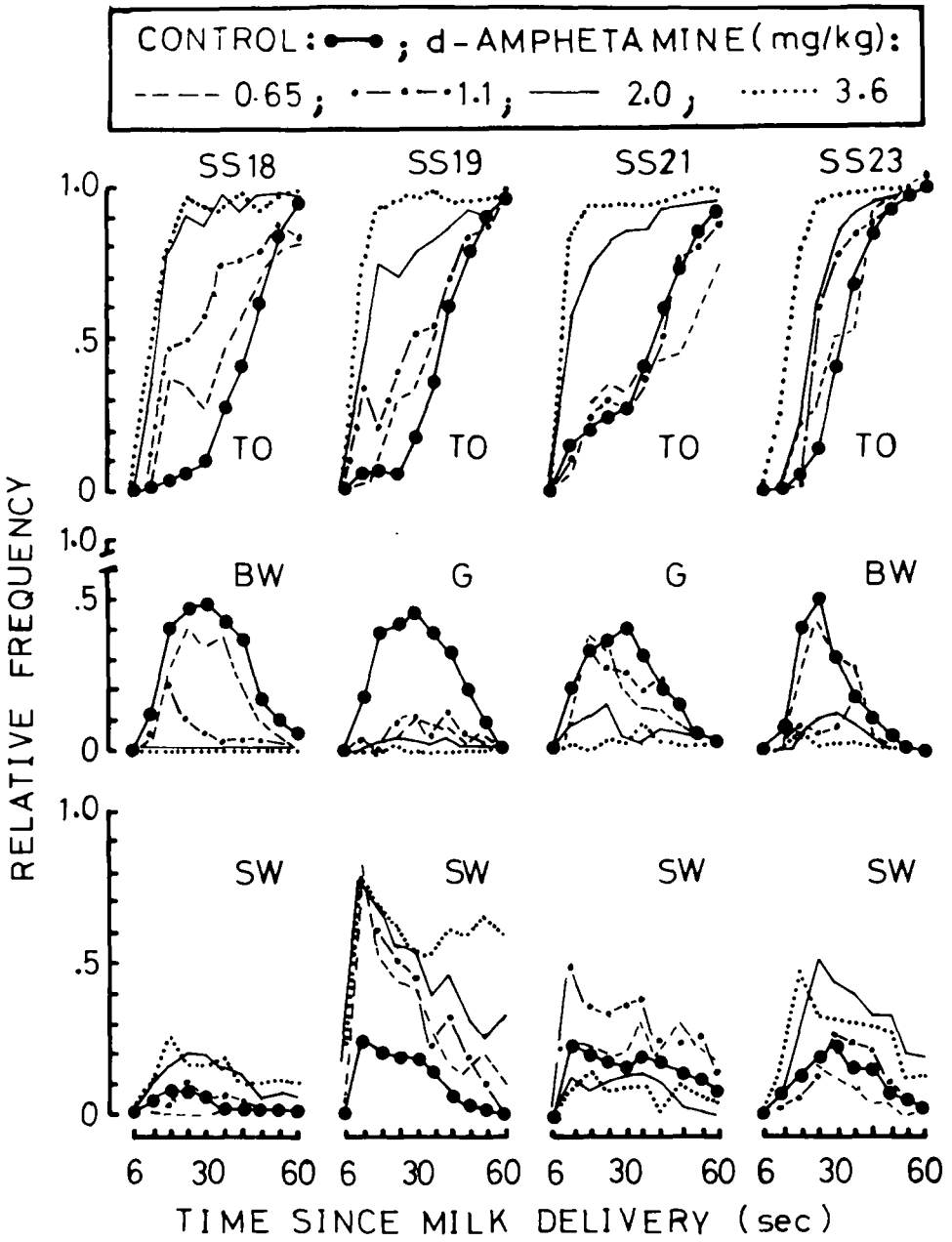

FIG. 2. Mean relative frequency of each behavioral category during saline and drug administration, as a function of time since milk delivery. Conventions for categories are as in Fig. 1. Filled circles connected by heavy lines represent saline sessions: ---, ·--, ——and. . . . represent 0.65, 1.1, 2.0 and 3.6 mg/kg of d-amphetamine, respectively.

made. Time spent in contact with the tray (tray time) and with the water (water time), latencies to the first postpellet contact with the tray and spout, and the amount of water ingested were recorded for every session. As the rats were consistently in contact with the tray soon after pellet delivery, tray latencies were recorded from 4 sec after pellet delivery to the next contact with the tray. An observer (JN) using the same observing procedure as in Experiment 1 recorded behavior during drug administration and on those saline sessions immediately preceding each drug session. The behavioral categories were the same as in Experiment 1, except that drinking was also recorded.

Drug Administration

The procedure for drug administration was similar to the one used in the previous experiment. After initial exposure to the FT schedule, the rats were injected intraperitoneally every session with either saline solution or 0.65, 1.1, 2.0 and 3.6 mg/kg of d-amphetamine in mixed order. Each dose was administered twice.

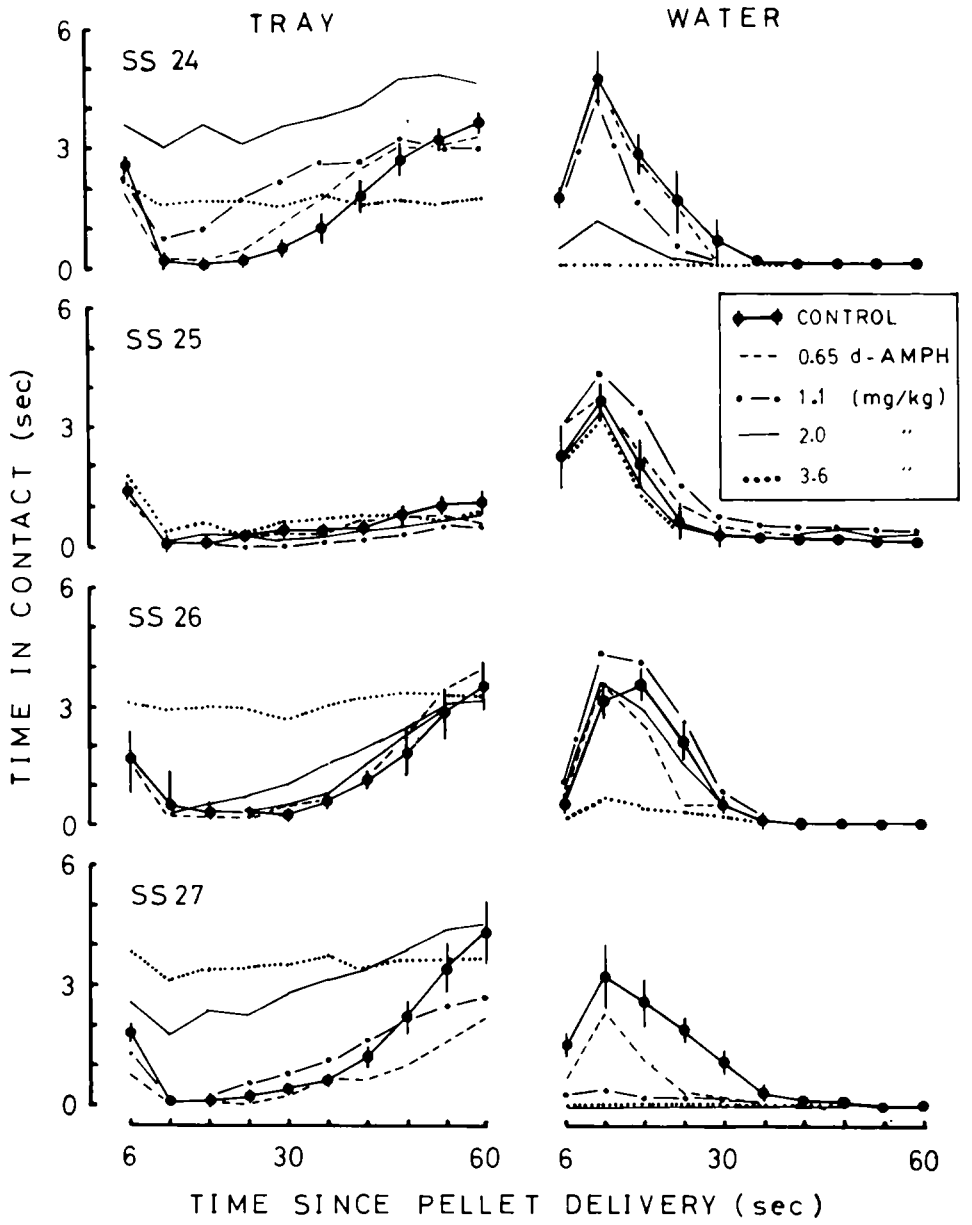

FIG. 3. Mean tray and water time for each subject during saline and drug administration as a function of time since pellet delivery. Filled circles connected by heavy lines represent saline effects; brackets are ± one standard deviation. Conventions for drug effect are as in Fig. 2.

RESULTS

The effects of d-amphetamine on the patterns of tray and water times are shown in Fig. 3, where tray time is on the left and water time on the right.

In three subjects (SS 24, SS 26, SS 27), increasing doses of d-amphetamine resulted in approximately equal amounts of time in contact with the tray throughout the interval. The increments in tray time produced by the drug were greater during the early portions of the interval than during later portions. These alterations in tray time patterns were associated with reductions in the peak frequency of drinking, but only in one subject (SS 26) was the temporal locus of the peak altered by the drug. In the fourth rat (SS 25), tray time was very low during saline sessions and was not increased by the drug, while water time displayed the same temporal pattern as in the other rats, but was not reduced by the drug. However, as Fig. 4 shows, the latencies to contact the tray and water were similarly altered in all rats. As the dose increased, latency to contact the tray was reduced, whereas latency to contact the water was increased.

In order to assess whether the drug altered the absolute values of tray and water times, as well as their temporal patterns, the overall times per session in contact with the tray and water were computed. They are shown in the left of Fig. 5, and the amount of water ingested per session in on the

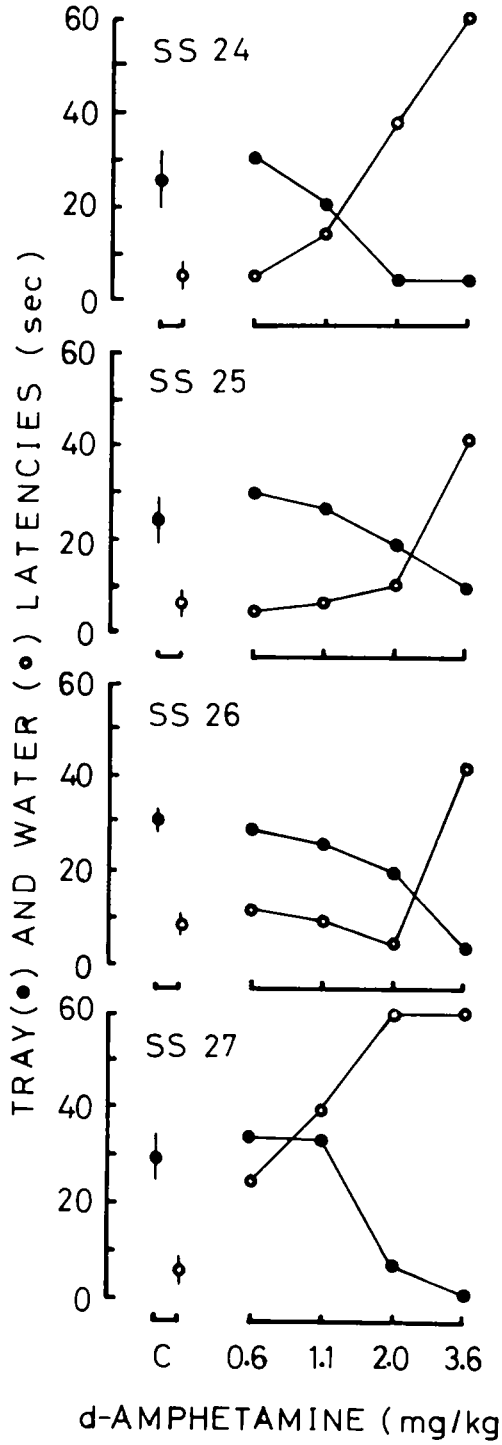

FIG. 4. Mean tray and water latencies during saline (C) and drug administration; brackets are ± one standard deviation.

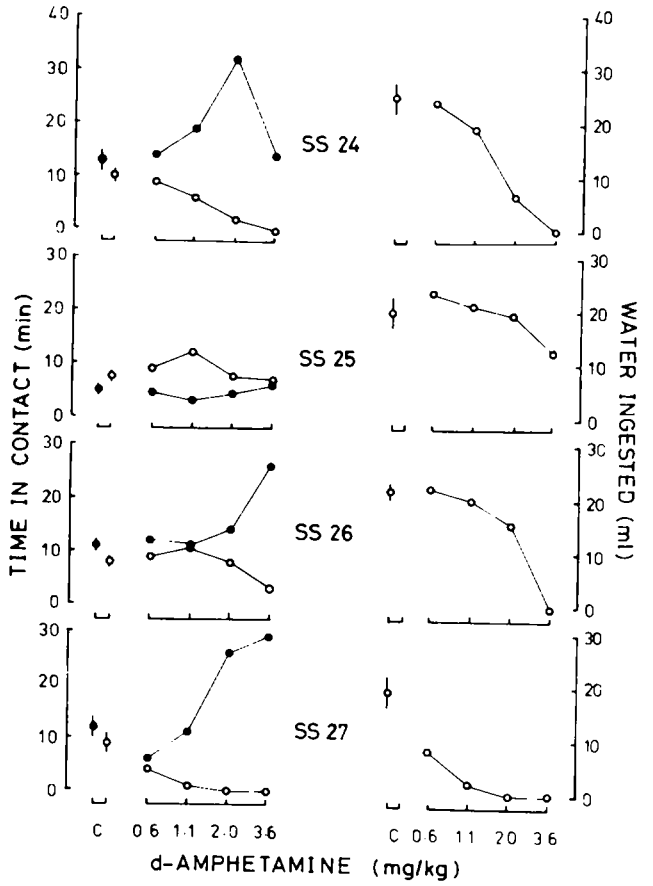

FIG. 5. Mean overall tray and water time (left hand side) and the amount of water ingested (right hand side) during saline (C) and drug administration. On the left side, filled circles represent tray time and open circles water time. Brackets are ± one standard deviation.

right. Overall tray and water times were roughly similar during saline sessions, each one accounting for about one fifth of the session time. As the dose was increased, overall tray time increased and overall water time decreased. With the highest doses tray time accounted for about one half of the session time and water time was close to zero. Rat SS 25 was again the only exception. Figure 5 also shows that the amount of water ingested was reduced in all subjects as the dose was increased.

Observational data replicated the main features of the automatic measurement: as the dose of d-amphetamine increased, the behavior of Rats SS 24, SS 26 and SS 27 became restricted to rearing, touching, sniffing and swaying in the immediate area of the tray. Figure 6 shows for Rat SS 27 the sequence of activities between pellet deliveries that occurred during saline administration, on an intermediate dose and on the highest dose of d-amphetamine. During saline sessions, eating was followed by drinking, then by other activities; and finally by the terminal response. During drug sessions, eating still persisted and the terminal response occurred throughout the interval, whereas drinking and other interim activities disappeared. A similar effect was observed with all rats, although it was less marked with SS 25, in which tray orientation never substituted for drinking or for the other interim activities.

DISCUSSION

These results confirm the findings of Experiment 1, and show that drug-induced increments in tray orientation or in

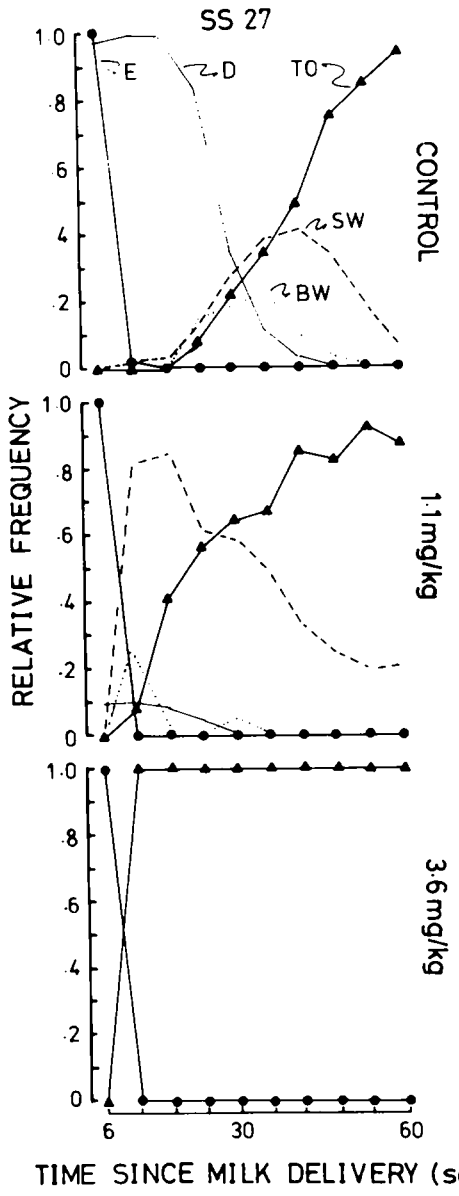

FIG. 6. Mean relative frequency of eating (E), drinking (D), tray orientation (TO), rearing/sniffing back (BW) and side wall (SW) for Rat SS 27 during saline administration (control) and two doses of d-amphetamine, as a function of time since pellet delivery.

tray time, and decrements in grooming, rearing/sniffing and drinking, are not dependent on the use of sweetened milk.

The disappearance of rearing/sniffing at high dose levels, shown for SS 27 in Fig. 6 and also found in Rats SS 24 and SS 26, was unexpected from the results of Experiment 1, when rearing/sniffing at side walls (SW) persisted even at high doses (see Fig. 2). The most probable reason for this difference was the change in the location of the reinforcer. Most side wall rearing/sniffing was directed to the wall nearest the observer. In Experiment 1 the milk cup was close to this wall, but in Experiment 2 the food tray was in the opposite wall. Thus, therefore there was greater incompatibility between tray approach and rearing/sniffing to the side wall in Experiment 2 than in Experiment 1.

The effects of d-amphetamine on tray orientation resemble previous ones obtained with FI schedules, where bar-pressing and key-pecking are increased by this drug (e.g. [15,16]). Thus neither the topography of the terminal response nor the explicit response-reinforcer contingency of an FI schedule appear to be crucial for the production of such an effect. The similarity of the present results and those from FI studies also suggests an interpretation of the increments of tray orientation in terms of the rate-dependency hypothesis [5]. This hypothesis predicts the selective facilitation of low frequency activity and the reduction of high frequency activity, regardless of the type of behavior. However, in the present experiment d-amphetamine effects were not selective, since the terminal response was increased until it approached a relatively constant level throughout the interval. This is inconsistent with the rate-dependency hypothesis. The effects of d-amphetamine on interim activities are also inconsistent with the hypothesis, since drinking, grooming, and rearing/sniffing were reduced throughout the interval (for a further discussion of similar inconsistencies see [10,18]).

GENERAL DISCUSSION

The behavior of the rats during non-drug sessions in the present experiments was similar in several respects to that reported previously with rats, hamsters and pigeons [1, 24, 25], in that characteristic terminal and interim activities were observed within each interfood interval. In both experiments the terminal response consisted of orientation, approach and contact with the cup or tray. Interim activities included grooming, rearing/sniffing and drinking, when this last activity was allowed to occur. Interim activities occupied different portions of the interval: drinking peaked soon after pellet delivery, then rearing/sniffing and grooming followed.

Increasing doses of d-amphetamine increased the relative frequency of tray orientation and reduced the relative frequency of grooming, rearing/sniffing and drinking time. Comparisons between the effects of d-amphetamine and of food satiation, and the fact that rats always consumed the reinforcer, rule out the possibility that the behavioral effects of d-amphetamine were mediated by a change in motivation for food.

Given that the terminal response was increased while interim activities were in general reduced, the increments in tray orientation could be due to a direct facilitation by amphetamine, or to release from competition from interim activities. In Experiment 2, tray and water times accounted together for about two fifths of saline session time, but tray time increased up to a half of the session time during d-amphetamine administration. This suggests that the drug directly facilitated tray orientation. Further support for this suggestion comes from the different effects on rearing/sniffing found in the two experiments. As noted above, this difference is easily accounted for if the direct effect of the drug is to increase tray orientation, so that whether rearing/sniffing increases or decreases depends on the extent to which it is incompatible with behavior around the tray area.

In conclusion, the present experiments provide support for theories that propose competitive interaction between terminal and interim behavior (e.g. [12,23]) and for the view that amphetamine acts centrally to restrict an animal's behavioral repertoire [13]. At high dose levels most of the animal's behavior is concentrated around the site of food and other kinds of behavior which compete with this are suppressed.

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