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Pimozide-Induced Suppression of Responding: Evidence Against a Block of Food Reward

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MASON, S. T., R. J. BENINGER, H. C. FIBIGER AND A. G. PHILLIPS. *Pimozide-induced suppression of responding: Evidence against a block of food reward.* PHARMAC. BIOCHEM. BEHAV. 12(6) 917–923, 1980.—Male albino rats injected with 0.5 or 1.0 mg/kg pimozide showed a decline in the rate of lever pressing on a continuously reinforced schedule for food reward. A similar decline was seen when responding was no longer reinforced (extinction). On this basis, Wise *et al.* [15] have previously hypothesized that pimozide blocks the reinforceing effects of the food pellets. However, in the present experiments the effects of pimozide were found to be additive with those of extinction so that animals treated with pimozide and placed into extinction ceased responding more quickly than animals subjected to either manipulation on its own. In addition, the effects of one condition failed to transfer to the other condition so that animals exposed to three days of pimozide failed to show a further decline when exposed to a day of extinction under vehicle and vice versa. Similar additivity and failure of transfer were seen on a DRL schedule for food reward; however, using this schedule pimozide failed to produce a decline in reinforced responding. In a further experiment pimozide failed to mimic extinction by blocking the reinforcing effects of food so as to cause a partial reinforcement extinction effect in a runway. It is concluded that these effects of pimozide on operant behavior are not mediated by a block of reward.

Pimozide Reward Eating

THE neuroleptic drug, pimozide, attenuates lever-pressing and alley-running of hungry rats for food [1, 4, 15]. This effect might occur because the drug blocks the reinforcing effect of the food, or alternatively, because it impairs initiation of the motor response (for reviews see [3,14]). Wise *et al.* [15] have compared the effects of pimozide on food reinforced lever pressing with its effects on responding when the reinforcer is no longer presented (extinction) in the undrugged state; both procedures progressively reduced responding. These authors concluded that this similarity of operational effect indicates an identity of mechanism, namely that in both cases reinforcement no longer occurs.

If this conclusion is correct, responding seen under the drug should be identical in time course to that seen in extinction; moreover, the two manipulations should fail to be additive. That is, simultaneous application of both pimozide and extinction should not do anymore than one or the other on its own. Further, if both pimozide and extinction have the same effect, the effects of experience of one should transfer to test sessions under the other. If the two manipulations reduced responding by different mechanisms, however, such transfer would not be expected.

METHOD

Pimozide and CRF Responding

The behavioral paradigm was modelled on that used by Wise *et al.* [15]. Seventy male albino Sprague Dawley rats (Canadian Breeding Farms, Quebec) weighing about 200 g were housed in groups of 5, given two-hour daily access to food and after five days of such deprivation trained to lever-press in standard operant test chambers (BRS/LVE RTC 022) for food (45 mg; P.J. Noyes) on a CRF schedule (each response produced food). They received two-hour access to food after the daily operant session. Contingencies were controlled and data recorded by solid state logic units (Digi-bits, BRS/LVE). Training sessions of 15 min, seven days a week for three weeks generated stable lever pressing.

At this point drug and extinction testing commenced. Ten animals received intraperitoneal injection of 0.5 mg/kg pimozide dissolved in a 3:1 solution of tartaric acid four hours prior to behavioral testing [15]. These animals continued to receive the food pellet after each lever-press (0.5 PIM-CRF group). A similar group of ten rats was injected with 1.0 mg/kg pimozide as above (1.0 PIM-CRF). A control group of ten rats received intraperitoneal injection of the tartaric acid vehicle (VEH-CRF). Ten rats received vehicle injection but were placed into extinction, in which no food pellet was delivered although the click of the feeder continued to occur (VEH-EXT group). Ten rats each received injection of 0.5 or 1.0 mg/kg pimozide and were placed into extinction (0.5 PIM-EXT and 1.0 PIM-EXT groups). These test sessions were 36 mins in duration and between each test

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session two drug-free days were allowed without further behavioral testing. Total lever presses over the session and three minute subtotals were recorded using a print-out counter (BRS/LVE).

Three such test days were administered and then on the scheduled fourth day, some of the groups were transferred to the complementary condition. That is, if the group had been receiving pimozide and food delivery for the last three days it was transferred to extinction under vehicle. If it had been in extinction under vehicle for the last three test days, it was transferred to food delivery under pimozide for the fourth test day. An additional group of ten rats was injected with 1.0 mg/kg pimozide in their home cage on three occasions with two drug free days in between each (thus mimicking the pharmacological but not behavioral history of the 1.0 PIM-CRF animals on their 3rd test session) and then tested in the pimozide plus reinforcement condition to determine whether there might be a comulative effect of the drug.

Statistical data were analysed by a repeated measures analysis of variance [13]. Two analyses were run, one for the time-course within the session on the first test day and the second for the response totals on the three successive test days. A conventional two-tailed level of significance at the 5% level was required.

Pimozide and DRL Responding

This experiment was undertaken to determine the effects of pimozide on a second operant schedule, one of differential reinforcement of low rates of responding (DRL). Since the CRF study had revealed the dose of 1.0 mg/kg of pimozide to be the most effective (see also [15]), this was employed in the following studies.

Eighteen experimentally naive male albino rats of the Wistar strain with weights ranging from 260 to 328 g were housed individually in a climatically controlled colony room on a 12 hr light-dark cycle. All rats were deprived to 80% of their free-feeding weights and were maintained at those weights throughout the experiment by daily feeding with measured rations. Standard operant test chambers were used with environmental control and data collection effected by a Data General Nova 3 computer, using INTERACT software.

Twenty-one sessions of 30 mins occurred five days a week. During the first two sessions a CRF schedule of food reinforcement (45 mg food pellets) was in effect. The schedule was then changed to differential reinforcement of low rates of responding (DRL) 5-sec for two sessions followed by 3 sessions of DRL 10-sec and then 14 sessions of DRL 15-sec.

Following training, rats were randomly assigned to one of three groups; the pimozide-DRL (N=6), pimozide-EXT (N=6) or vehicle-EXT (N=6) groups. The pimozide-DRL group received three sessions of DRL 15-sec but 4 hr prior to each session each rat received an intraperitoneal (IP) injection of 1.0 mg/kg pimozide. The pimozide-EXT group received the same drug treatment but pellets were no longer presented during the three test sessions. The vehicle-EXT group was given IP injections of vehicle 4 hr prior to each of three extinction sessions. Response rate and distribution of interresponse times were recorded.

The pimozide-DRL and vehicle-EXT groups received a fourth session. This was a test for transfer between pimozide and extinction conditions. Prior to this session the pimozide-DRL group received a vehicle injection; this group was then given a session of extinction. The vehicle-EXT group received pimozide (1.0 mg/kg) 4 hr prior to this session and then was tested on DRL 15-sec with delivery of food pellets.

Pimozide and Partial Reinforcement

Occasional omissions of reinforcement during the acquisition of a runway response for food are known to lead to greater resistance in subsequent extinction. This is called the partial reinforcement extinction effect (PREE); for review see [7]. If pimozide blocks the reinforcing effects of a food pellet it should be possible to cause a PREE in rats that always receive food but sometimes also receive pimozide to block the reinforcement of food.

Thirty-nine male albino Wistar rats weighing about 300 g were food deprived by being placed on a one-hour per day food access schedule for five days and then trained to run in a wooden L-shaped alleyway measuring 170 cm by 12 cm wide with a metal grid floor, and a goal box 30 cm by 12 cm wide located at the end of the main alleyway. The time to run the alleyway was recorded by means of photocells placed immediately outside the start box and at the entrance to the goal box. Breaking the beam of the first photocell started a millisecond clock which continued to run until the animal broke the second photocell beam near the goal box. Present in the goal box was a metal food cup containing four 45 mg food pellets (P.J. Noyes Ltd). Animals initially were familiarized with the apparatus in groups of four with the food cup overflowing for fifteen minutes on two consecutive days. On the third and fourth days all animals received one trial per day of being placed in the start box, running up the alleyway and finding four food pellets in the goal box.

The animals were then divided into three groups of ten and one group of nine and the following conditions pertained. One group of ten was trained on a continuously reinforced (CRF) schedule in the alleyway for ten trials, one trial per day (CRF-10 group). The group of nine rats was similarly trained for twenty days (CRF-20 group) one trial per day. Another group of ten rats was trained on a partially reinforced (PR) schedule in the alleyway for twenty days (PR group), one trial per day. On a random one half of the trials food was not present, the animal was merely confined to the empty goal box for 15 secs. Thus, this group received 20 training trials and ten rewards. The CRF-10 and CRF-20 groups thus compare to the PR group in terms of the number of reinforcements received in one case and the number of trials experienced in the other. The remaining group of ten rats received food on all daily trials in the alleyway, but whenever the PR group was scheduled for non-reinforcement, these animals received 1.0 mg/kg pimozide intraperitoneally four hours before their trial (PIM group). Thus, this latter group was on a CRF schedule of reinforcement in terms of food presentations but, since it received pimozide before a random one-half of these food presentations, should effectively have experienced partial reinforcement if pimozide indeed blocked food reinforcement. Following completion of the above training all groups were placed into extinction (5 trials per day without drug injection) in which no food was presented in the goal box.

Acquisition and extinction times were analysed by a repeated measures analysis of variance [13]. The acquisition data were broken up into two blocks of ten trials to compare the groups with different amounts of acquisition training.

RESULTS

Pimozide and CRF Responding

All groups finished preliminary CRF training responding

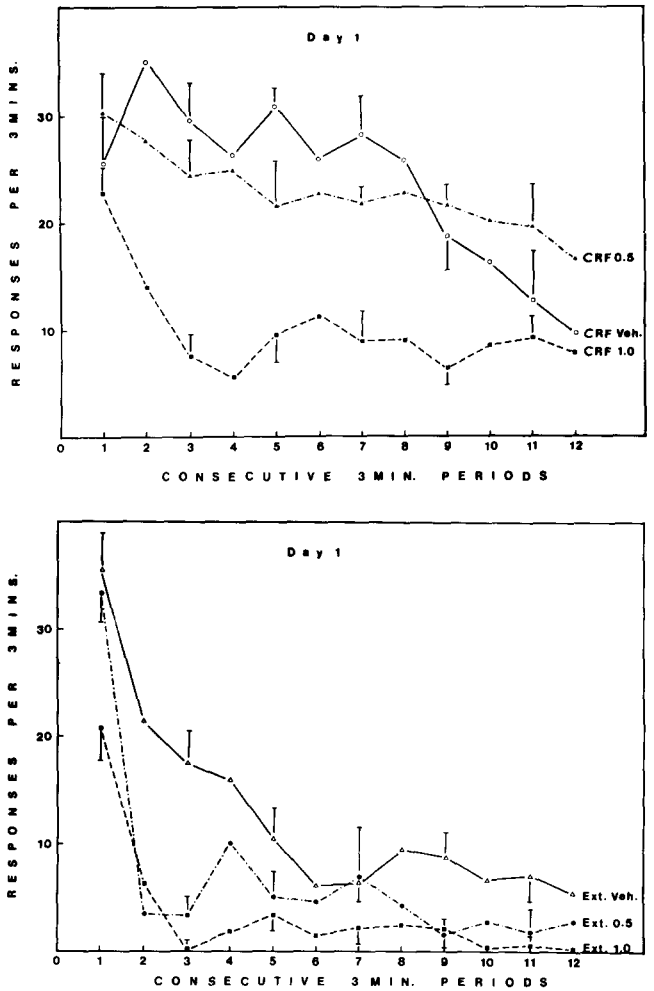

FIG. 1. Time-course of lever-pressing within the session on day one of pimozide administration during a CRF schedule (upper frame) or during the first day of extinction (lower frame). Values are mean response rate of ten rats in each group (vertical lines are SEM's) plotted against successive three minute periods in the session.

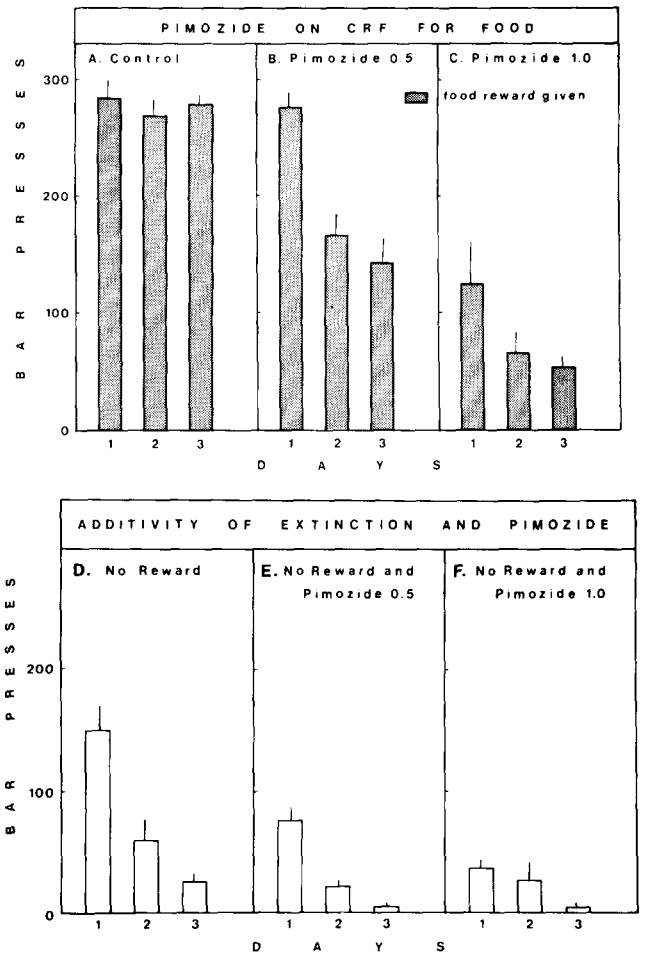

FIG. 2. The effect of pimozide on the number of lever presses on each of three days of CRF testing (upper panel) or extinction (lower panel). Values represent the mean (±SEM) of 10 rats in each group. A: VEH-CRF B: 0.5 PIM-CRF C: 1.0 PIM-CRF D: VEH-EXT E: 0.5 PIM-EXT F: 1.0 PIM-EXT. See test for details of abbreviations.

at similar levels (all F's less than 0.21, NS).

The effects of the various drug and reinforcement conditions on CRF lever pressing are shown in Fig. 1 for the time-course of the first test day. It may be seen that all groups responded rapidly in the first three minutes in the session. The VEH-CRF and 0.5 PIM-CRF groups declined only slightly over the remainder of the 36 min session. The 1.0 PIM-CRF group, however, declined precipitously in responding and emitted few lever-presses for most of the second half of the test session. A similar but less severe decline was seen for the undrugged animals in the extinction condition (VEH-EXT). Both groups which received the combination of pimozide and extinction (0.5 PIM-EXT and 1.0 PIM-EXT) ceased responding more rapidly than either group receiving each manipulation on its own (PIM-CRF or VEH-EXT).

These observations were confirmed statistically in that the effect of reinforcement condition (food or extinction) was highly significant, $F(1,54)=72.6$, $p<0.001$, as was the effect of drug dosage. $F(2,54)=26.2$, $p<0.001$. The effect of drug dosage also depended on the reinforcement condition, interaction $F(2,54)=4.5$, $p<0.02$. Individual comparisons revealed that the 1.0 PIM-EXT group responded significantly less than the 1.0 PIM-CRF group, $F(1,18)=7.7$, $p<0.02$, and that the VEH-EXT group responded more than the 1.0 PIM-CRF group, $F(1,18)=25.9$, $p<0.001$.

The effects of drug and reinforcement conditions over the three days of testing are shown in Fig. 2. Repeated administration of pimozide (0.5 or 1.0 mg/kg) resulted in a decline in responding over days, despite the continued presentation of the food pellet (PIM-CRF groups; Fig. 2B and C). This effect was more marked for the 1.0 mg/kg dose than for the 0.5 mg/kg and did not occur for vehicle injected rats (Fig. 2A). Repeated presentations of extinction to undrugged rats also resulted in a progressive decline in response rate over days (VEH-EXT; Fig. 2D). Combination of these manipulations resulted in a faster decline in responding over days than either manipulation on its own (PIM-EXT groups; Figs. E and F compared to Fig. 2D). Transfer from one condition to the other failed to yield a further decline in responding. In fact, a marked increase in response rate was seen in both the group transferred from PIM-CRF to VEH-EXT and the

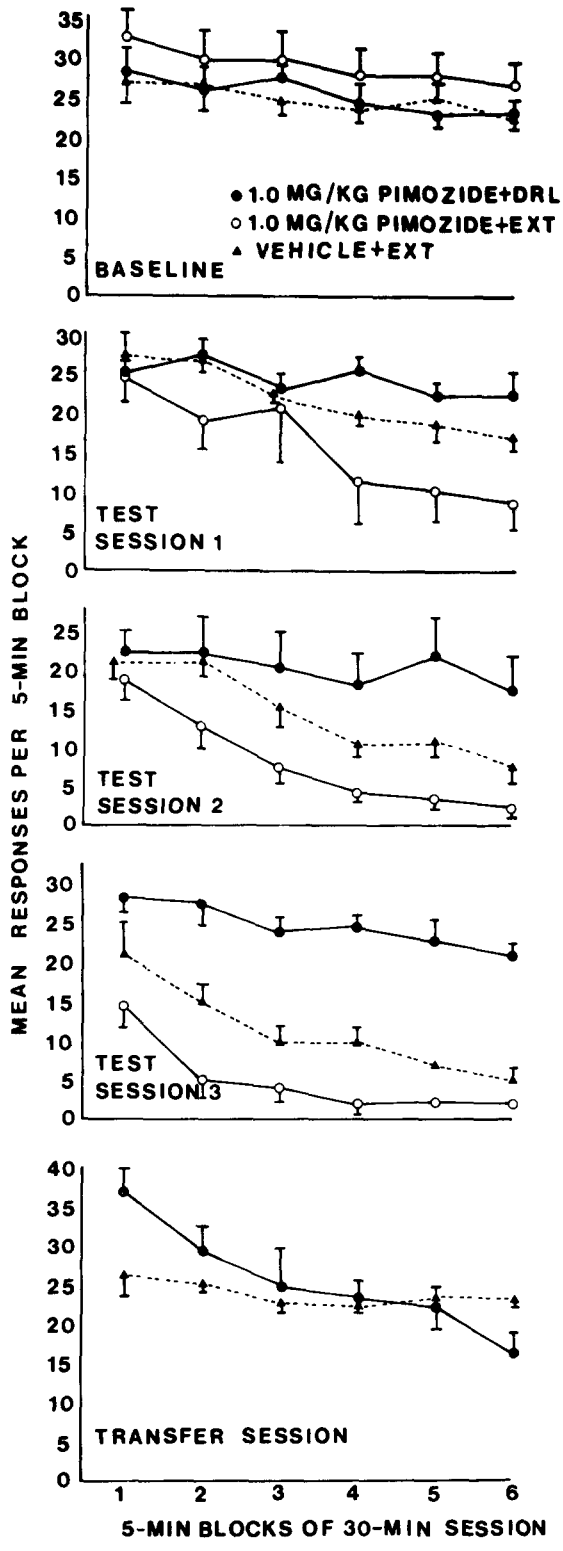

FIG. 3. Mean response rate (responses per five-min block) for the last three training sessions combined (Baseline), the three test sessions and the transfer session. During transfer the pimozide plus DRL group received vehicle and extinction whereas the vehicle plus extinction group received pimozide plus DRL. Verticle lines from each point indicate standard error on the mean.

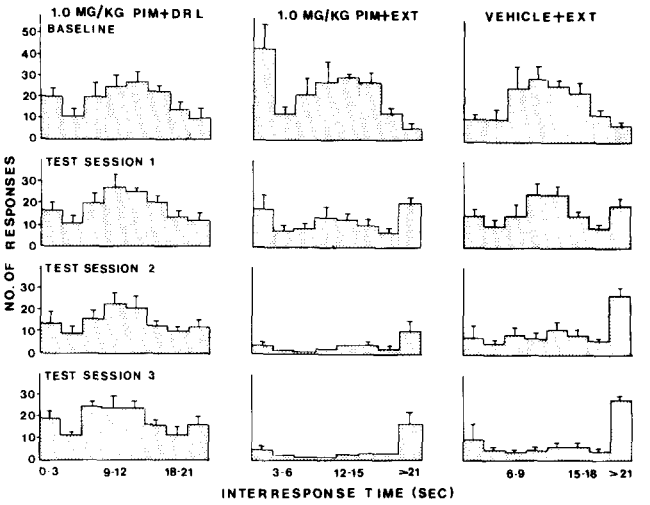

FIG. 4. Mean (±SEM) number of responses in three-sec interresponse time (IRT) bins ranging from 0–3 sec IRT's to IRT's of more than 21 sec for each group during the last three training sessions combined (Baseline) and during the three test sessions. Abbreviations. PIM, pimozide; EXT, extinction.

group transferred from VEH-EXT to PIM-CRF. A 4th day of extinction would indeed have resulted in a further decline in response rate (Group VEH-EXT, not shown).

Pretreatment with 3 doses of 1.0 pimozide in the home cage failed to yield any evidence of a cumulative effect of the drug, in that the response rate of this group when given pimozide in the *behavioral* test for the first time was not less than that of similar animals without prior drug history.

These effects were confirmed statistically in that the effect of reinforcement condition was highly significant, $F(1,54)=141.8$, $p<0.001$, as was the effect of drug dosage, $F(2,54)=42.9$, $p<0.001$. Further, the effect of the drug depended on the reinforcement condition, interaction $F(2,54)=12.5$, $p<0.001$. A progressive change occurred over days, $F(2,108)=67.2$, $p<0.001$, and this change depended on the drug dosage, $F(4,108)=2.9$, $p<0.03$. Individual comparisons revealed that the PIM-EXT group ceased responding more rapidly than the PIM-CRF groups at both the 0.5 mg/kg, $F(1,18)=87.6$, $p<0.001$, and the 1.0 mg/kg dose, $F(1,18)=9.4$, $p<0.01$. The PIM-CRF group at the 1.0 mg/kg dose failed to differ from the VEH-EXT group, $F(1,18)=0.84$, NS, but the 0.5 mg/kg PIM-CRF group declined less severely than the VEH-EXT group, $F(1,18)=10.8$, $p<0.005$.

Pimozide and DRL Responding

The number of responses for each rat during each five-min block of the 30-min sessions was recorded. The mean response rate (responses per 5-min block) for each block and for each group averaged over the last three training sessions (Baseline) is shown in Fig. 3. Two-way analysis of variance with repeated measures on the blocks variable revealed that the groups did not differ significantly during the acquisition training.

Shown in Fig. 3 are the mean response rates for each group for each 5-min block of the three drug or extinction test sessions. These data were subjected to a three-way analysis of variance with repeated measures on the blocks

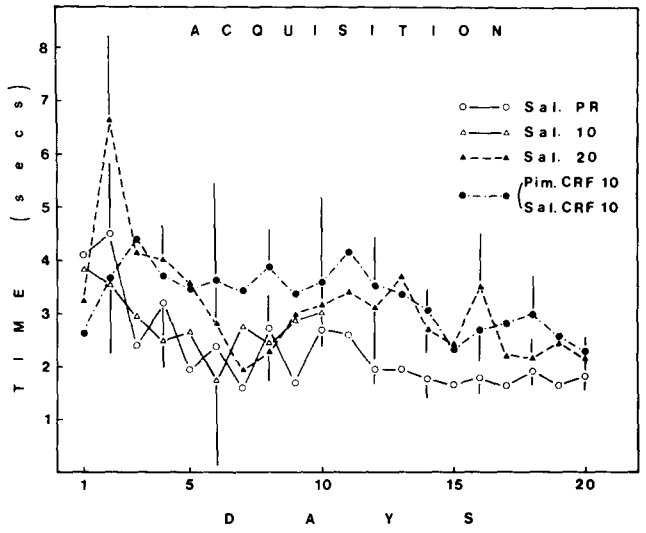

FIG. 5. Acquisition running times in alleyway for twenty daily trials. Abbreviations as in text.

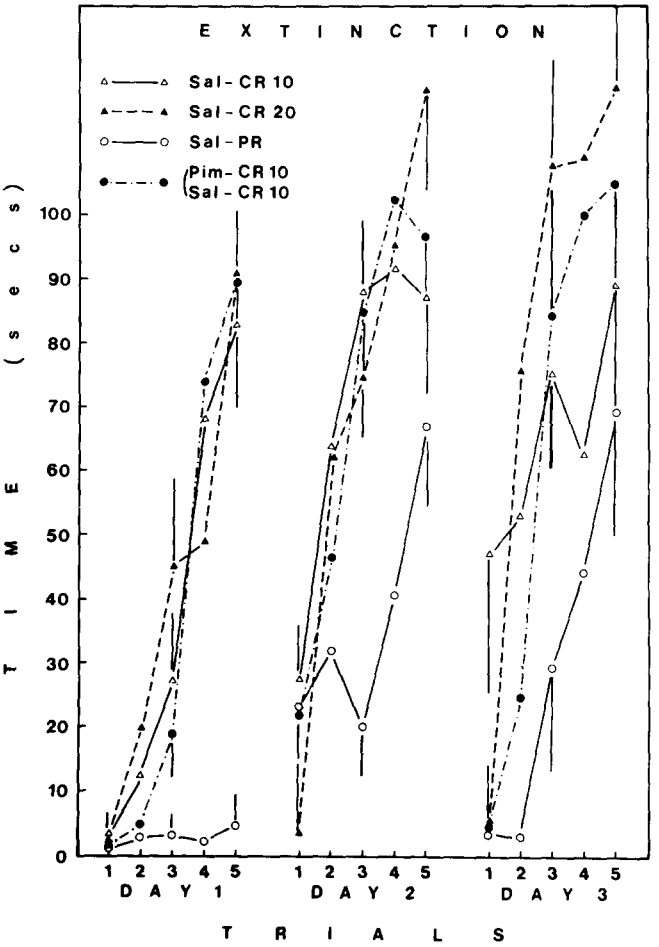

FIG. 6. Extinction running times in alleyway in absence of food pellets for three days of five trials per day.

and sessions variables. The groups differed, $F(2,15)=20.3$, $p<0.001$, there was a sessions effect, $F(2,30)=13.4$, $p<0.001$, and an interaction between groups and sessions, $F(4,30)=3.0$, $p<0.04$. Thus, the effect of pimozide depended on the reinforcement condition, being without effect in the group which continued to receive food on a DRL schedule but significantly reducing the response rate of the group experiencing extinction compared to the vehicle-injected extinction group. This is supported by the results of post hoc tests of simple main effects which revealed no significant group effect in test session one, $F(2,15)=2.7$, $p<0.05$ but group differences in test sessions two, $F(2,15)=5.8$, $p<0.01$, and three, $F(2,15)=14.9$, $p<0.01$.

The distribution of interresponse times (IRT) was obtained by setting up seven 3-sec class intervals up to 21 sec and one interval for all responses that followed the preceding response by more than 21 sec. The IRT distributions for each group averaged over the last three training sessions (Baseline) are shown in Fig. 4. Two-way analysis of variance with repeated measures on the intervals variable revealed that the groups did not differ significantly, $F(2,15)=1.2$, $p<0.05$. As inspection of Fig. 4 might suggest, there was an effect of intervals, $F(7,105)=6.1$, $p<0.001$ but no significant interaction, $F(14,105)=1.14$, $p<0.05$. These results indicate that the groups did not differ in their patterning of responses during acquisition baseline training and that the most frequent IRT's, for all groups tended to be from 6 to 18 sec.

From inspection of Fig. 4 it appears that the pimozide-DRL group continued to respond most frequently with IRT's ranging from 6 to 15 sec whereas the pimozide-EXT and vehicle-EXT groups tended to show fewer short IRT responses, making most responses with IRT's greater than 21 sec., (a significant effect of class intervals, $F(7,105)=7.7$, $p<0.001$, and an interaction between groups and class intervals, $F(14,105)=3.6$, $p<0.001$).

For transfer tests the pimozide-DRL group received a vehicle injection and testing in extinction while the vehicle-EXT group received pimozide and was tested on DRL with delivery of food pellets. The response rates during each 5-min block of the 30-min transfer session are shown in Fig. 3. The pimozide-DRL group showed a declining response rate throughout the session when injected with vehicle and tested in extinction whereas the vehicle-EXT group responded at a fairly constant rate when tested on DRL 15-sec while treated with pimozide. Thus, groups did not differ significantly, $F(1,10)=1$, $p<0.05$; however, there was an effect of blocks, $F(5,50)=9.3$, $p<0.001$, and an interaction of blocks with groups, $F(5,50)=4.8$, $p<0.001$.

The overall response rate (±SEM) in responses per 5-min block of the vehicle-EXT group during the third test session was 11.5 (±1.4). During the transfer session when this group was run under the pimozide and DRL condition the response rate was 24.2 (±1.0). Comparison of these rates revealed that they differed, $t(5)=7.7$, $p<0.01$. The respective overall response rates of the pimozide-DRL group during test session three and transfer to vehicle-extinction were 24.7 (±1.3) and 26.4 (±2.4) respectively, and failed to differ significantly, $t(5)<1$, $p>0.05$.

Pimozide and Partial Reinforcement

The running times in the acquisition trials are shown in Fig. 5. It can be seen that towards the end of the twenty acquisition trials the PR group was running slightly faster than the other groups. This is an example of the partial rein-

forcement acquisition effect (PRAE: see [7]). It failed to reach conventional levels of significance, $F(2,26)=2.71$, $0.10>p>0.05$, due possibly to the low number of acquisition trials [9]. It was not present in the pimozide treated animals.

The running times in extinction, five trials per day over three days, are shown in Fig. 6. It can be seen that over the five trials per day the CRF-10, CRF-20 and PIM groups showed a rapid slowing of running upon encountering the absence of the food pellet in the goal box. The PR group however continued to run rapidly to the goal box, even after encountering the absence of the food pellet. This effect was noticeable on days one and two but tended to disappear by day three of extinction. Analysis of variance revealed a significant slowing over days, $F(2,68)=11.6$, $p<0.001$, and a significant slowing over five trials within days, $F(4,136)=78.0$, $p<0.001$. This did not occur equally for all groups, however, since there was a significant group effect, $F(3,34)=5.6$, $p<0.003$, a significant group by trials interaction, $F(12,136)=5.5$, $p<0.001$, and a significant three-way interaction, $F(24,272)=2.22$, $p<0.001$.

DISCUSSION

Pimozide and CRF Responding

Animals treated with pimozide progressively decreased lever-pressing for food over days. This effect, at the 1.0 mg/kg dose, was similar to that caused by omitting the food pellet (extinction) over days. As such, it might be argued that pimozide was blocking the reinforcing effects of the food pellets, were it not for two additional groups of animals. The PIM-EXT groups indicated that the effects of pimozide added to the effects of extinction. This confirms a similar observation with rats responding for food pellets on variable interval schedule [11]. As such it cannot be argued that these two manipulations have an identity of action. Nor can it be argued that in addition to blocking the primary reinforcing effects of the food pellet, pimozide also blocked secondary (or conditioned) reinforcement present in the VEH-EXT group to cause an additive effect. These conditioned secondary reinforcers would also have been present in the PIM-CRF group, and therefore there should have been no difference between PIM-CRF and PIM-EXT groups. However, large differences were observed between these groups (Fig. 2).

The second evidence against interpreting the operational similarity of effect of extinction and of pimozide as an identity of mechanism comes from the transfer results. If the decline in responding seen in both pimozide and extinction groups was due to the same mechanism (removal of reinforcement) then the effects of one should transfer to a subsequent test under the other. That is, a day of PIM-CRF given after three days of VEH-EXT should have given the same results as a fourth day of VEH-EXT. It did not. Similarly, a day of VEH-EXT given after three days of PIM-CRF should also have caused a further decline in responding. Again it did not. Thus, the failure of the response reducing effects of pimozide, and of extinction, to transfer to the other condition indicates that these response reducing effects result from different mechanisms.

In summary, although the basic observation of pimozide-induced suppression of food-reinforced responding [15] has been confirmed, additional groups indicate that this operational similarity does not come about as a result of pimozide blocking food reinforcement, in contradiction to the conclusions of earlier authors [15].

Pimozide and DRL Responding

The results can be summarized as follows: (1) during the three drug or extinction test sessions the response rates of the pimozide-DRL group showed no significant change; the pimozide-EXT and vehicle-EXT groups, on the other hand, showed a decrease in response rate both within and across test sessions, the decrease being more marked for the pimozide-EXT group than for the vehicle-EXT group; (2) the IRT distributions of the pimozide-DRL group showed no significant change over the course of the three test sessions while the pimozide-EXT and vehicle-EXT groups made a higher frequency of long IRT responses; (3) in transfer tests, the pimozide-DRL group failed to show a significant decline in *total* responses when injected with vehicle and tested in extinction although this group did show a significant within-session decline in response rate during extinction; the vehiclel-EXT group made significantly more total responses when tested with food on DRL while treated with pimozide and failed to show the significant within session decline in rate which was seen under the vehicle plus extinction condition.

Thus, unlike with a CRF schedule, pimozide (1.0 mg/kg) failed to cause a decline in DRL response rate. This suggests further that the drug does not block food reinforcement, since extinction (actual omission of the food pellet) was effective in reducing DRL response rate over days (Fig. 3). As found on CRF the rate reducing effects of extinction failed to transfer to testing with pimozide and food presentation. Animals actually increased response rate in this transfer. Further, the transfer from pimozide-DRL to vehicle-EXT failed to yield further reduction in the overall response rate, although no increase was seen in this case. Thus, in agreement with the findings obtained using a CRF schedule, the effects of extinction fail to transfer to drug testing and vice versa suggesting that the two manipulations are not acting by the same mechanism (i.e., removal of food reinforcement). The additivity of pimozide with extinction, seen with a DRL schedule, also suggests an independence of mechanism of the two manipulations and extends the previous observations on a CF schedule.

Pimozide and Partial Reinforcement

Omitting food on a random one-half of the acquisition trials in a runway produced faster running in extinction than either continuously reinforced group (CRF-10 or CRF-20). A significant PREE was thus obtained. Treating animals with pimozide before a random one-half of food reinforced trials failed to cause increased resistance to extinction and did not give rise to a significant PREE. Thus, operationally, treatment with the neuroleptic drug pimozide did not produce the same effects as omission of food. This adds to the conclusions of the CRF and DRL experiments that pimozide differs from the effects of food omission in a number of aspects. The failure of pimozide to cause a PREE may be direct evidence that it does not block food reinforcement, since actual omission of food on the identical schedule to pimozide administration was successful in causing a PREE.

General

A complete explanation of the effects of pimozide on operant responding must deal with one fundamental issue; namely the progressive decline in responding under pimozide in the presence of continuous reinforcement. Ac-

cumulation of the drug over repeated injections can be discounted on the basis of there being no significant pretreatment effect. It remains to be determined empirically whether the progressive decline in responding reflects an impairment in response initiation after pimozide [2] or possibly a response-contingent aversive effect that develops slowly with repeated motor responses.

The present study should be interpreted with caution in terms of the neurotransmitter systems which mediate reinforcement processes. Much other evidence has implicated dopamine (DA) in reinforcement generated by electrical brain stimulation [5, 6, 10] or by the self-administration of psychomotor stimulant drugs [12,16]. It is possible that food reinforcement differs in its pharmacology from electrical or drug-induced reinforcement. Alternatively, it may be that the behavioral effects of pimozide seen in this experiment are not mediated through effects on dopamine but on, for example, serotonin systems [8]. A further possibility is that more than one dopamine-containing system is affected by pimozide, with the drug-induced changes in the response initiation DA system overshadowing changes simultaneously present in a second, reinforcement-related DA system, and hence not detected by the paradigms employed in the present experiments.

In summary, although pimozide in this study did cause a decline in reinforced response rate similar to that observed in extinction, this occurs only in certain limited situations (CRF but not on DRL) and seems to involve a mechanism separate from a block of food reinforcement, as evidenced by the additivity of the two manipulations, by the failure of transfer, and by the failure to cause a PREE.

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