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Effects of Pimozide on the Hedonic Properties of Sucrose: Analysis by the Taste Reactivity Test

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LEEB, K., L. PARKER AND R. EIKELBOOM. *Effects of pimozide on the hedonic properties of sucrose: Analysis by the taste reactivity test.* PHARMACOL BIOCHEM BEHAV **39**(4) 895–901, 1991.—The ability of the neuroleptic agent, pimozide, to modify sucrose palatability was assessed using three 10-min taste reactivity test sessions. Pimozide was found to suppress the ingestive response of tongue protrusions, but enhance the mildly ingestive/neutral response of mouth movements elicited by an intraoral infusion of sucrose solution. Since the pattern of taste reactivity responding shifted from highly ingestive to mildly ingestive/neutral, our results suggest that pimozide pretreatment reduces the palatability of sucrose solution. The temporal pattern of the modification of these taste reactivity responses was predicted by the Anhedonia Hypothesis.

Anhedonia Pimozide Neuroleptic Taste reactivity Ingestive behavior Dopamine Sucrose Palatability Psychopharmacology

NEUROLEPTIC drugs, such as pimozide, attenuate the activity of the dopamine system by blocking dopamine receptors. These agents have been shown to disrupt the learning and/or performance of responses motivated by positive reinforcers [e.g., (28)]. Neuroleptic drugs also have been shown to suppress food intake [e.g., (12, 25, 27, 29, 30)] as well as the consumption and sham consumption of sucrose solution [e.g., (9, 31, 32)]. One problem evident in paradigms that require a rat to approach an object in order to gain exposure to the food or drink is that pimozide has been demonstrated to have inhibitory effects on motor responding at similar doses as those employed in studies which show a pimozide-induced decrease in consumption [e.g., (6, 14, 20, 21, 25, 27)].

A more direct measure of the hedonic properties of tastants is the Taste Reactivity (TR) Test designed by Grill and Norgren (11). When flavored solutions are infused directly into rats' mouths, they display a characteristic set of orofacial and somatic responses. Flavors with positive hedonic properties elicit an ingestive response pattern which includes tongue protrusions and paw licks [e.g., (1, 10, 11, 16, 17)]. Flavors with neutral hedonic properties elicit either the mildly ingestive/neutral response of mouth movements [e.g., (1, 7, 10, 24)] or the mildly aversive/neutral response of passive drips [e.g., (1,24)]. Flavors with negative hedonic properties elicit an aversive pattern which includes gapes, chin rubs and paw pushes [e.g., (1, 10, 11, 16, 17)]. Parker and Lopez (18) reported that pimozide enhances the aversive properties of quinine solution as measured by increased aversive TR responding. However, pimozide did not modify the TR responses elicited by sucrose solution. Berridge, Venier and Robinson (2) also reported that depletion of dopamine by 6-hydroxydopamine lesions produced no modification of TR responding elicited by sucrose solution. Finally, Treit and Berridge (24) have recently reported that haloperidol has no effect on TR responding elicited by sucrose solution.

In all of the above studies which employed the TR test (2, 18, 24), the rats received a single, relatively brief exposure to sucrose solution. Wise and his colleagues have recently demonstrated that the effects of pimozide on both instrumental (8, 28, 33) and consummatory (12, 29, 30) behavior motivated by positive reinforcers are generally not immediate, but instead increase with the test duration and increase over test trials. They argue that neuroleptics disrupt the maintenance of instrumental responding and free feeding before they disrupt the initiation of responding. This decrease in responding across repeated tests is believed to be analogous to the gradual decrease in responding under extinction. That is, the rats must gradually learn that the reinforcer (food) is less reinforcing under the influence of pimozide. The effect of pimozide on both free feeding and instrumental responding for a reinforcer is similar to the effect of nonreward on responding previously maintained by a reinforcer. Therefore, the previously described failures to demonstrate pimozide-induced (18), haloperidol-induced (24) or 6-OHDA-induced (2) modification of taste reactivity elicited by sucrose solution may have been the result of the brevity of the sucrose exposure and lack of repeated testing. As Wise and his colleagues (12, 29, 30) have demonstrated with free feeding in rats, a rat may require a given period of exposure to sucrose solution under the influence of pimozide in order to learn that the taste of sucrose is no longer reinforcing.

The experiment below employed a 10-min TR test in contrast to the 1–5-min tests employed in the previous attempts to modify sucrose TR responding with disruption of the dopamine

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system (2, 18, 24). Furthermore, the rats were given three test trials with each test separated by 3 days. The sucrose solution was novel for half of the rats, consistent with the procedures of previous research (2, 18, 24), and was familiar for the other half of the rats. Schallert and Whishaw (22) have reported that changes in taste reactivity following lateral hypothalamic lesions are more pronounced when sucrose is familiar than when it is novel. Presumably, neophobia may mask some of the change in responsivity to novel sucrose.

METHOD

Subjects

Forty-one male Sprague-Dawley rats weighing between 366 and 434 g on the first test day served as subjects. They were maintained on ad lib access to food and water except as indicated below.

Apparatus

The taste reactivity test was conducted in a glass chamber ($22.5 \times 26 \times 20$ cm). The room was illuminated by two 40-watt light bulbs placed on each side of the test chamber. Once the animals were placed in the chamber, their cannulae were connected to the infusion pump. A 35-cm-long tube connected the infusion pump to the plastic adapter of the cannulae. A Hitachi HV-62 facilitated viewing of the rat's ventral surface. The rat's image was transmitted to a Panasonic videorecorder. The tapes were later scored by a rater blind to the experimental conditions via an event recorder attached to an Apple IIe microcomputer.

Procedure

One week after the arrival of the rats in the laboratory, they were surgically implanted with intraoral cannulae as described by Parker (15). The rats were then given one week to recover. Following the one-week recovery period, the rats were randomly divided into two initial groups which were tested one week apart. Half of the rats in each group were familiarized to the sucrose solution for 7 days. The familiarization trials consisted of placing two bottles on each home cage. One bottle contained water while the other bottle contained sucrose solution. The remaining rats received only water on their home cages. The groups were as follows: Familiar 17% Sucrose (F17; $n=11$), Familiar 25% Sucrose (F25; $n=10$), Novel 17% Sucrose (N17; $n=9$) and Novel 25% Sucrose (N25; $n=11$).

On the seventh day of the familiarization trials, all the rats received their first of 3 successive adaptation trials in the test chamber. Prior to the second adaptation trial, the two bottles were removed from the cages of the rats receiving sucrose familiarization trials and were replaced by one bottle containing water. On each of the 3 days prior to the first test trial, each rat was placed in the TR test chamber with the plastic tube from the infusion pump attached to its cannula. After 1 minute, the rat received a 10-ml intraoral infusion of water at the rate of 1 ml/min for 10 minutes. The cannulae were then briefly flushed with water, and the rats were returned to their home cages.

Twenty-four hours after the final adaptation trial, the rats were given the first of 3 test trials. Four hours prior to testing, half of the rats in each group were injected intraperitoneally (IP) with 0.5 mg/kg of pimozide solution ($n=20$), and half of the rats in each group were injected with the drug vehicle ($n=21$). The pimozide was dissolved in a vehicle of 1.5% tartaric acid and distilled water in a volume of 1 mg/ml. During the TR test, the rats in each of the pretreatment groups received a 10-ml infusion of either 17% sucrose solution or 25% sucrose solution over a 10-minute period at the rate of 1 ml/min; however, since the analyses revealed no effects of concentration, these groups were combined for further discussion and analyses. After each test trial, each rat's cannula was flushed with water and the rat was then returned to its home cage. The groups were as follows: Pimozide Familiar (PF; $n=11$), Pimozide Novel (PN; $n=9$), Vehicle Familiar (VF; $n=10$), and Vehicle Novel (VN; $n=11$). The orofacial and somatic responses of the rats during the test sessions were recorded on videotape. Two additional identical test trials were conducted, with each trial separated by 3 days.

In order to ensure that any modification in TR responding was not the result of the development of a conditioned taste aversion in the pimozide-pretreated group, six days after the third test trial, the rats were given a two-bottle sucrose solution consumption test. Twenty-two hours prior to the consumption test, the rats were water deprived. The rats were then given access to two bottles for a twenty-four-hour period. One bottle contained water and the other bottle contained the sucrose solution at the concentration with which each rat had been tested. The amounts consumed at intervals of 15 min, 30 min, 60 min, 120 min, 240 min, and 24 h were measured. These measures were converted into sucrose preference ratios, which were determined by dividing the total amount of sucrose consumed at each interval by the total amount of sucrose plus the total amount of water consumed at the interval. A value of 0.5 would indicate that the rat consumed an equal amount of sucrose and water.

Data Analysis

The TR responses measured were identical to those that have been previously described [e.g., (1, 2, 7, 10, 11, 16–18, 24)]. Since none of the aversive responses of chin rubbing, gaping and paw treading were displayed on any one of the tests, these behaviors were excluded from the analysis. The TR responses that were analyzed included the following. The neutral responses [e.g., (1, 7, 10, 24)] included neutral/mildly aversive Passive Dripping (PD: number of drops of solution that fall to the floor of the cage when the rat is not actively ejecting the solution by a rejection response) and neutral/mildly ingestive Mouth Movements (MM: amount of time displaying movement of the lower mandible). The highly ingestive responses included Tongue Protrusions (TP: amount of time spent extending tongue from mouth) and Paw Licking (PL: amount of time spent licking solution from paws). The activity responses included Rearing (R: forelimbs off of the floor of the cage) and Horizontal Activity (HA: movement in a horizontal orientation with the forelimbs on the floor of the cage). The frequency of occurrence of the final two responses (R + HA) were summated to produce a composite Activity (ACT) score. The ingestive TR responses were analyzed separately, rather than as a combined score as described by Berridge and Grill (1), because tongue protrusions and paw licking are highly ingestive responses, and mouth movements are mildly ingestive/neutral responses, as described by Berridge and Grill (1). A shift in palatability might be expected to involve a redistribution among these ingestive responses. Although data was analyzed for the response of passive drips, the pretreatment effect was not significant; therefore, these data will not be presented.

The 10-min total scores for each behavior were analyzed as a 2 by 2 by 3 mixed ANOVA with the between-groups factors of pretreatment condition (Pimozide, Vehicle) and familiarity of sucrose (Familiar, Novel) and the within-groups factor of test trial (Trial 1, 2 or 3). The data for the behaviors of Tongue Pro-

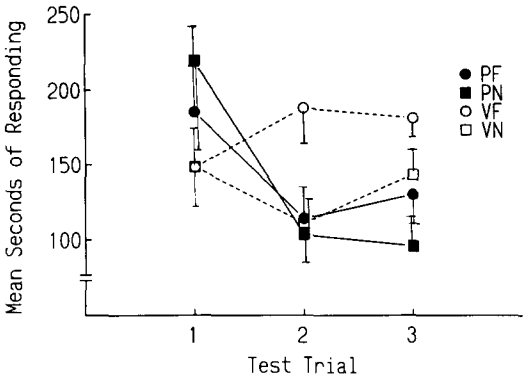

FIG. 1. Mean amount of time during each 10-min test trial that the rats in each group engaged in tongue protrusions. The solid lines represent the pimozide-pretreated groups, and the broken lines represent the vehicle-pretreated groups.

trusions, Paw Licking, Mouth Movements, and General Activity were also subjected to a minute-by-minute analysis on each test trial. On each test trial, the within-groups factor of minutes of testing (minute 1–minute 10) was included to produce a 2 by 2 by 10 mixed ANOVA.

RESULTS

Taste Reactivity Test

Tongue protrusions. Figure 1 presents the mean amount of time during each of the three 10-minute tests that the rats displayed tongue protrusions. The only significant effect was the pretreatment by test trial interaction, $F(2,74)=3.92$, $p<0.025$. Subsequent 2 by 2 between-groups ANOVAs were conducted for each test trial for the factors of pretreatment condition and familiarity of sucrose solution. On trial 1, there were no significant effects among conditions. There was a significant effect of pretreatment condition on trial 2, $F(1,37)=4.08$, $p<0.05$, and on trial 3, $F(1,37)=5.6$, $p<0.025$; the pimozide-pretreated rats spent less time displaying tongue protrusions during the sucrose infusion than the vehicle pretreated rats. On trial 2, there was also a familiarity effect, $F(1,37)=4.7$, $p<0.05$; familiar sucrose elicited more tongue protrusion activity than novel sucrose overall, which suggests that it was more preferred. Since Schallert and Whishaw (22) reported that lateral hypothalamic (LH) lesions produced a greater disruption of sucrose reactivity when sucrose was familiar than when novel, separate Newman-Keuls analyses of the group means were conducted. On test trial 2, group VF showed more tongue protrusions than all other groups (p's<0.05) which did not differ among themselves. Therefore, on trial 2, pimozide only suppressed tongue protrusions elicited by familiar sucrose, as is evident in LH-lesioned rats (22). On test trial 3, both pimozide-pretreated groups showed suppressed tongue protrusion activity in relation to the vehicle-pretreated groups exposed to either novel or familiar sucrose solution ($p<0.05$).

Figure 2 presents the mean amount of time that each group spent displaying the ingestive TR response of tongue protrusions during the sucrose infusion for each minute of testing on trials 1, 2, and 3. The analysis revealed a significant main effect of minutes on each of the three test trials, F's(9,333)>12.3, p's<0.001 regardless of pretreatment condition, the amount of

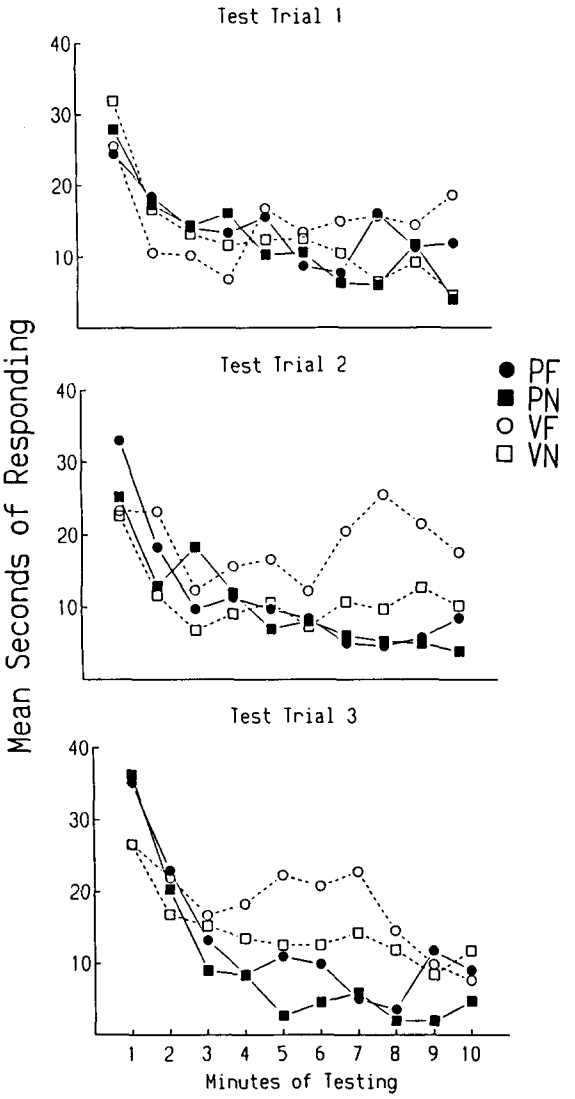

FIG. 2. Mean amount of time during each minute of testing on each test trial that the rats in each group engaged in tongue protrusions. The solid lines represent the pimozide-pretreated groups, and the broken lines represent the vehicle-pretreated groups.

time spent tongue protruding was highest during the first two minutes of testing on each test trial (p's<005). On test trials 2 and 3, but not on test trial 1, there was also a significant effect of pretreatment, F's(1,37)>3.9, p's<0.06 on each of these trials, the pimozide-pretreated rats spent less time displaying tongue protrusions overall than did the vehicle-pretreated rats. On test trials 2 and 3, there was also a significant pretreatment by minutes interaction, F's(9,333)>5.5, p's<0.001. During the latter minutes of testing, the pimozide-pretreated rats spent less time displaying tongue protrusions than the vehicle-pretreated rats; on trial 2, the groups differed during min 7–10 (p's<0.01) and on trial 3, the groups differed during min 4–8 (p's<0.05). On trial 3 only, a somewhat paradoxical effect occurred: sucrose elicited *more* tongue protrusion activity during min 1 in the pimozide-pretreated rats than in the vehicle-pretreated rats ($p<0.025$), but this difference reversed during min 4–8, as described above.

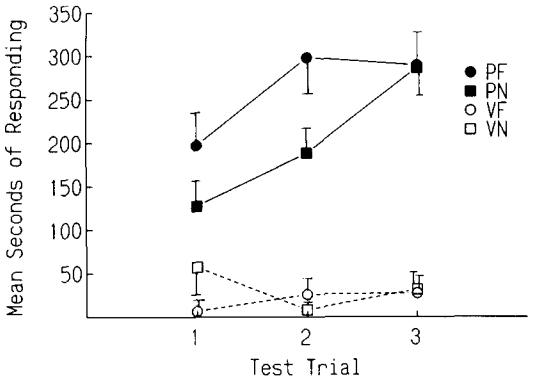

FIG. 3. Mean amount of time during each 10-min test trial that the rats in each group engaged in mouth movements.

The overall pattern of tongue protrusion activity elicited by sucrose infusion suggests that with relatively brief test periods and with a single test trial [e.g., (18)], the effects of pimozide pretreatment on tongue protrusions might not be evident. As with food intake, as demonstrated by Wise and his colleagues [e.g., (12, 29, 30)], pimozide may gradually reduce the tendency for sucrose to elicit tongue protrusions both within a test session and across test sessions. However, the enhanced tongue protrusion activity with pretreated rats during min 1 of test trial 3 suggests that the suppression is evident only after an initial increase in tongue protrusion activity. This initial increase in tongue protrusion activity may reflect an initial compensatory increase in tongue protrusions that could be analogous to the initial compensatory increase in lever pressing described by Yokel and Wise (33). When rats were pretreated with 0.5 mg/kg of pimozide prior to lever pressing for amphetamine, they demonstrated an initial compensatory increase in response rate followed by a dramatic decrease in response rate. They reasoned that this pattern was similar to the pattern of responding displayed by rats during the early period of extinction training. If dopamine blockade reduces the rewarding properties of sucrose solution, then rats may demonstrate an increased rate of tongue protrusions during early minutes in order to compensate for the loss of rewarding properties. After the first minute of testing, the rats drastically reduce their tongue protrusion activity. Albeit, this explanation is post hoc; however, it is consistent with the data presented by Yokel and Wise (33) pertaining to amphetamine self-administration.

Paw licking. The analysis of the amount of time that each group spent paw licking during the 10-min test on each trial revealed only a significant effect of pretreatment, $F(1,37)=10.4$, $p<0.01$. The rats pretreated with pimozide spent less time paw licking than the rats pretreated with the vehicle. No other effects were significant. Since this effect did not interact with the test trials, it did not appear to change across trials. The analysis of the amount of time spent paw licking during each minute on each of the three test trials revealed no significant pretreatment by minutes interactions, suggesting that the suppression of paw licking by pimozide does not vary across test interval. This may, therefore, reflect a motoric inhibitory effect of pimozide pretreatment, rather than an effect on palatability.

Mouth movements. Figure 3 presents the mean amount of time that the rats engaged in the mildly ingestive/neutral TR response of mouth movements during the total 10 minutes of testing on each of the three test trials. The analysis revealed a significant pretreatment effect, $F(1,33)=80.0$, $p<0.001$, a significant pretreatment by test trial interaction, $F(2,74)=16.9$, $p<0.001$, and a significant pretreatment by sucrose familiarization by test trial interaction, $F(2,74)=3.25$, $p<0.025$. Separate 2 by 2 ANOVAs for each trial revealed a significant pretreatment effect on each trial, $F's(1,37)>26.1$, $p's<0.001$, on each trial, sucrose elicited more mouth movement activity in the pimozide-pretreated rats than in the vehicle-pretreated rats. Additionally, on trial 1 only, the analysis revealed a significant pretreatment by sucrose familiarization interaction, $F(1,37)=5.4$, $p<0.05$. On trial 1, regardless of sucrose familiarization condition, both pimozide pretreatment groups showed greater mouth movement activity than their respective vehicle pretreatment group ($p's<0.025$). However, within pretreatment groups, vehicle-pretreated rats demonstrated greater mouth movement activity during an infusion of novel sucrose solution than a familiar sucrose infusion ($p<0.05$), whereas the sucrose familiarization treatment did not significantly modify the mouth movement activity in the pimozide pretreatment groups. This difference in mouth movement activity among vehicle-pretreated rats was no longer evident on test trials 2 and 3, presumably because sucrose was no longer novel.

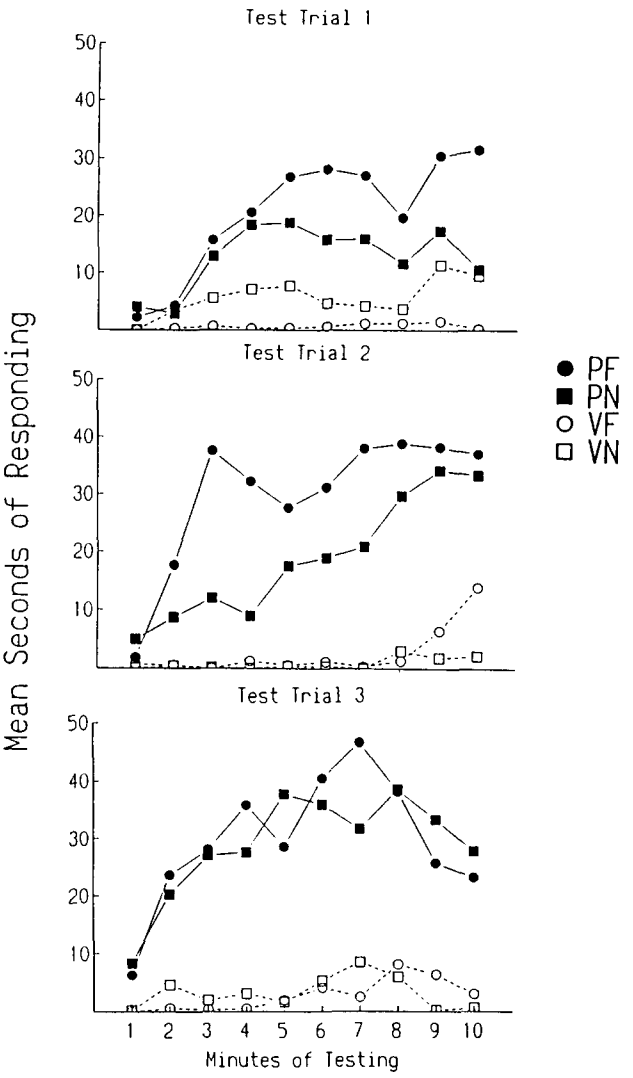

FIG. 4. Mean amount of time during each minute of testing on each test trial that the rats in each group engaged in mouth movements.

Figure 4 presents the mean amount of time spent engaged in mouth movements for each group for each minute of testing on trials 1, 2, and 3. The effects which were consistently significant on each test trial were the pretreatment effect, F's(1,37)>25.7, p's<0.001, the minute effect, F's(9,333)>7.4, p's<0.001, and the pretreatment by minutes interaction, F's(9,333)>3.7, p's<0.001. Generally, the pimozide-pretreated rats spent more time engaged in mouth movements than did the vehicle-pretreated rats, but this difference was greatest during min 3–10 on trial 1 (p's<0.05) and min 2–10 on trials 2 and 3 (p's<0.01). Therefore, the effect of pimozide pretreatment on mouth movements gradually increased within and across test sessions, as predicted by Wise and his colleagues [e.g., (8, 12, 28–31)].

General activity. The analysis of the combined frequency of vertical and horizontal movements for the various groups on each test day revealed a significant pretreatment effect, $F(1,37) = 37.9$, $p<0.001$; the pimozide-pretreated groups were less active than the vehicle-pretreated groups. Additionally, there was a significant sucrose familiarity by test trial interaction, $F(2,74) = 3.4$, $p<0.05$; on test trial 2, the rats tested with novel sucrose were more active overall than the rats tested with familiar sucrose, $F(1,39) = 35.5$, $p<0.001$. The combined activity scores at each minute interval were analyzed for each trial. The pretreatment effect did not interact with minutes on any test trial; therefore, this analysis will not be discussed.

Since the effect of pimozide pretreatment neither interacted with test trial nor with minutes of testing on any test trial, there is no evidence of a gradual change in activity across or within test trials as would be predicted by the Anhedonia Hypothesis (25). The suppression of activity, therefore, probably reflects a motoric inhibitory effect of pimozide.

Sucrose Solution Consumption Test

The mean preference ratios for each group at each interval of testing during the sucrose consumption test which followed the three test trials were analyzed as a 2 (pretreatment) by 2 (familiarization) by 5 (intervals) mixed ANOVA for the first 240 minutes. The analysis revealed only an interval effect, $F(4,132) = 55.8$, $p<0.001$. The failure to find a significant effect of pimozide pretreatment or a pimozide pretreatment interaction indicates that the sucrose consumption was not effected by the pimozide pretreatment. Analysis at the 24-h test period revealed no significant differences. Therefore, there was no evidence of the establishment of a pimozide-induced conditioned taste aversion due to the repeated test trials. Since the consumption test has been demonstrated to be more sensitive than the TR test to the conditioned aversive properties of tastes [e.g., (16,34)], it is unlikely that the modified TR responses evidenced in the pimozide-pretreated rats was the result of a conditioned taste aversion.

DISCUSSION

Pimozide pretreatment resulted in modified taste reactivity (TR) responses elicited by sucrose solution over three 10-minute test sessions. Rats pretreated with pimozide displayed enhanced neutral/mildly ingestive mouth movement TR responding, and this effect strengthened with repeated testing. On the other hand, pimozide-pretreated rats displayed suppressed ingestive TR responding of tongue protrusions during the latter minutes of testing during test trials 2 and 3. This pattern of results suggests that pimozide modified the palatability of sucrose solution from highly ingestive (tongue protrusions) to neutral mildly/ingestive (mouth movements). Pimozide pretreatment, however, did not result in aversive TR responding in rats infused with sucrose solution, nor did it systematically result in the enhancement of the neutral/mildly aversive TR response of passive dripping. The proposed palatability shift from highly ingestive to neutral/mildly ingestive was not the result of conditioning of aversive properties due to pimozide association with sucrose solution across test trials, because the subsequent conditioned taste avoidance (CTA) test revealed no evidence of a pimozide-induced CTA. The CTA test has been reported to be more sensitive to flavor-drug associations than the TR test [e.g., (16,34)].

The pattern of TR responding in the pimozide-pretreated rats provides support for the Anhedonia Hypothesis (28), which postulates that blockade of dopamine receptors by pimozide attenuates the rewarding value of stimuli. Wise and his colleagues [e.g., (8, 12, 28–30, 33, 34)] argue that the effect of pimozide on responding for reward is similar to the effect of the removal of reward on both instrumental and consummatory responding that was previously maintained by reward (i.e., extinction). The behavioral effect is not immediate, but instead increases within and across test sessions. That is, pimozide-pretreated rats do not show a reduced latency to begin eating in the first trial as would be expected by a motoric interference hypothesis; instead, they demonstrate a slower rate of feeding during a trial and across repeated test trials. As in these consummatory measures, our results provide evidence that such an extinction-like, gradual modification of the palatability of sucrose solution may also occur in rats pretreated with pimozide. Both the suppression of tongue protrusions and enhancement of mouth movements increased across the 10 min of testing and also increased with repeated testing, as would be predicted by an extinction effect.

One finding is somewhat problematical for our interpretation of the results. During minute 1 of test trial 3, the pimozide-pretreated rats showed enhanced tongue protrusion activity when compared with the vehicle-pretreated rats. This finding suggests that during the final trial, the suppression of tongue protrusion activity occurred only after an initial increase in tongue protrusion activity. There are two possible explanations for this effect: 1) On the final test trial, pimozide produced an early enhancement in tongue protrusion activity which simply decayed to normal levels; or 2) The initial increase may reflect an initial compensatory increase in tongue protrusions analogous to the initial compensatory increase in lever pressing described by Yokel and Wise (33).

The modification of sucrose palatability by pimozide pretreatment appears to be in conflict with previous reports that pimozide (18), haloperidol (24) and 6-OHDA lesions (2) are ineffective in modifying taste reactivity elicited by sucrose solution. However, in the previous failures to demonstrate that the attenuation of the effectiveness of the dopamine system modified sucrose palatability, the rats were provided with a single, short (1–5 min) taste reactivity test. The present results indicate that previous tests (2, 18, 24) may have been too short to demonstrate a modification of taste reactivity, since the effects were not immediate. In fact, our findings are consistent with those that report that pimozide suppresses the sham drinking and drinking of sucrose solution [e.g., (9, 31, 32)]. Since pimozide modifies sucrose palatability in our paradigm, it is likely that the effect of pimozide on sucrose consumption and sham consumption is not the result of interference with motoric approach to the bottle.

Pimozide did suppress general activity level, which provides evidence for the motor deficit hypothesis [e.g., (6, 14, 20, 21, 25, 27)]. These effects, however, did not change within and between test sessions, as did the TR responses of tongue protrusions and mouth movements. Given that a motor deficit hypothesis would predict a reduction in motor activity, in general, the enhanced mouth movement activity suggests that, although pi-

mozide did suppress motor activity, it also acted to modify palatability.

The effects of neuroleptic treatment in rats has also been related to the clinical phenomenon of tardive dyskinesia evident in humans. Chronic neuroleptic treatment has been demonstrated to produce enhanced vacuous chewing movements in rats [e.g., (3–5, 13, 23, 26)]. These findings have been suggested to represent an animal model of tardive dyskinesia, apparent in humans following chronic neuroleptic treatment. Although most demonstrations of increased vacuous chewing movements have employed chronic drug regimes, Rupniak (19) has demonstrated that such effects can occur during the early trials of drug treatment. In rats that were given 5 days of haloperidol (2 mg/kg) treatment, the haloperidol-pretreated rats demonstrated a greater frequency of vacuous chewing movements than the saline-pretreated rats on Days 3, 4 and 5 of treatment. Rupniak suggests that such early effects of neuroleptic treatment indicate that neuroleptic treatment produces abnormal motoric effects, called dystonias, rather than tardive dyskinesia. Although it is conceivable that the increased mouth movements elicited by sucrose solution in the pimozide-pretreated rats of the present experiment represent a dystonia rather than a palatability shift, this explanation is unlikely because of the extinction-like pattern of responding demonstrated by the rats within a session and across sessions. That is, the pimozide-pretreated rats did not demonstrate increased mouth movements during the first few minutes of testing in each session, as would be expected if the mouth movements merely reflected bizarre motor responses induced by pimozide pretreatment. Instead, the increase in the frequency of mouth movements was evident during the latter portion of each test session. Furthermore, although an increase in the frequency of mouth movements did occur on the first test session, the effect was strengthened with further test trials, which again suggests an extinction-like effect similar to that described by Wise and colleagues [e.g., (8, 12, 28–30, 33)]. In fact, it is conceivable that the early effects of neuroleptic treatment reported by others [e.g., (19)] may actually represent a shift in the palatability of the rat's own saliva rather than a dystonia, as has been previously suggested.

The most parsimonious explanation for pimozide-induced enhanced mouth movements and suppressed tongue protrusions elicited by sucrose solution within and between test sessions is that dopamine receptor blockade produces a shift in the palatability of sucrose solution from highly ingestive to mildly ingestive. Pimozide treatment did not cause sucrose to become aversive or even neutral/aversive as reflected by passive dripping. Furthermore, the effect of dopamine blockade on the palatability of sucrose solution was not immediate, since the effect was stronger during the latter half of each 10-min test trial than during the first half, and the effect became stronger with each trial. This pattern of change is analogous to that of extinction. Since Wise and his colleagues [e.g., (8, 12, 28–30, 33)] suggest that dopamine blockade suppresses positively reinforced responding in a manner that reflects the process of extinction, our results support the Anhedonia Hypothesis (28).

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