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Cocaine and automaintained responding in pigeons: Rate-reducing effects and tolerance thereto with different CS–US pairing probabilities

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Abstract

To examine whether CS–US pairing probability, hence rate (or probability) of food delivery, modulated the effects of cocaine, pigeons were exposed to an autoshaping procedure in which 6-s red, green, and white illuminations of a response key were immediately followed by response-independent food delivery with a probability of 1.0, 0.5, and 0.25, respectively. Substantial responding occurred at all probabilities. Pre- and post-chronic administrations of cocaine (1.0–17.8 mg/kg) produced dose-dependent decreases in mean percent trials (key illuminations) with a response and total responses per session at all probabilities. In general, sensitivity to the drug was lowest at the highest probability, suggesting that rate (or probability) of food delivery influenced the behavioral effects of cocaine.

Keywords: Autoshaping; Automaintenance; Behavioral momentum; Tolerance; Cocaine; Pigeons

1. Introduction

In 1968, Brown and Jenkins (1968) reported that food-deprived, experimentally-naïve pigeons reliably pecked a response key that was briefly illuminated just prior to response-independent food deliveries. They called their procedure "autoshaping" and noted that it involved "the standard arrangement for classical conditioning" (p. 7). That is, pairings were arranged between a conditional stimulus (CS), key illumination, and an unconditional stimulus (US), food, and pecks did not produce food, although they could have been adventitiously (or superstitiously) reinforced by subsequent response-independent food deliveries. Subsequent studies extended autoshaping to other species, other CSs (e.g., lever insertion), and other USs (e.g., water), and examined how a wide variety of variables influence autoshaped, or automaintained, responding (e.g., Locurto et al., 1981). (Automaintained responding is responding that persists under an autoshaping procedure.)

In general, autoshaping occurs whenever the CS is predictive of the US, and studies from our laboratory and elsewhere have demonstrated robust autoshaping in pigeons with, for example, CS–US pairing probabilities of 0.25, 0.5, and 1.0 (e.g., Gibbon et al., 1980; Gonzales, 1974; Picker and Poling, 1982; Poling and Thompson, 1977). Interestingly, these studies found that less responding occurred when the CS–US pairing probability was 1.0 (i.e., when all key illuminations were followed by food) than when it was lower.

Several studies have examined drug effects on the acquisition (e.g., Aubert et al., 1995; Coveney and Sparber, 1981) and performance (e.g., Messing et al., 1989; Picker et al., 1986; Poling and Appel, 1978) of responding under autoshaping procedures when the CS–US pairing probability was 1.0 (see review by Sparber, 2001), but to our knowledge only one study has compared drug effects across different pairing probabilities. In that study, Poling and Thompson (1977) examined the effects of d-amphetamine on pigeons' key pecking under conditions where the probability of food delivery following key illuminations was 0.025, 0.1, 0.25, 0.5, and 1.0. Key pecking occurred under all conditions, with the 0.5 pairing probability engendering the most responding and the 0.025 pairing probability the least. Under all conditions, acute exposure to d-amphetamine (0.5, 1.0, and 2.0 mg/kg) produced similar dose-dependent decreases in responding. To our knowledge, no one has examined the development of tolerance

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to any drug as a function of CS–US (e.g., keylight–food) pairing probability.

Doing so is of some interest, because it appears that post-chronic drug effects on schedule-controlled operant responding are sometimes, but not always, influenced by probability (or rate) of food delivery. For example, cocaine typically reduces rates of food-maintained responding under fixed-ratio (FR) schedules of food delivery. Under simple (Nickel et al., 1993) and multiple schedule arrangements (Hoffman et al., 1987; Hughes and Branch, 1991), greater tolerance develops to this effect under relatively small FR schedules (e.g., FR 5) than under relatively large FR schedules (e.g., FR 125). In general, rate of food delivery varies inversely with FR size, thus these data suggest that rate of food delivery may modulate tolerance to cocaine's rate-reducing effects. Ratio size (hence probability, or rate, or food delivery) did not, however, modulate the development of tolerance to cocaine's rate-reducing effect when FR schedules were presented to pigeons in a mixed schedule arrangement, where stimulus conditions were equivalent regardless of the ratio in effect (Poling et al., 2000). Rate of food delivery also was unrelated to tolerance development in two studies in which tolerance to cocaine was examined under fixed- and random-interval schedules that varied in length (Branch, 1990; Schama and Branch, 1989).

Clearly, probability (or rate) of food delivery does not consistently predict the extent to which tolerance develops to the effects of cocaine on schedule-controlled operant responding. It also fails to predict acute effects reliably (e.g., Cohen, 1986; Lucki and DeLong, 1983). Schedules that produce different rates of food delivery inevitably differ in other regards. For example, small and large FR schedules require different amounts of effort (work expended) per food delivery and mixed and multiple schedules differ with respect to the degree to which responding is stimulus controlled. These and other variables, as well as rate of food delivery, may well influence the development of tolerance. Autoshaping procedures allow for the control of some of the variables that make it difficult to isolate the effects of rate of reinforcement as a determinant of tolerance under various schedules of reinforcement. Such procedures obviously differ from operant schedules, in that the former does not involve a response-reinforcer dependency and paradigmatically involves classical, not operant, conditioning. Whether this difference significantly alters responsivity to cocaine is unknown and worthy of investigation. The purpose of the present study was to examine rate, or probability, of food delivery as a determinant of cocaine's effects on automaintained responding. To do so, pre- and post-chronic effects of cocaine were examined on responding under an automaintenance procedure in which the probability of food delivery following brief key illuminations was 0.25, 0.5, or 1.0 (depending on color). These CS–US pairing probabilities were chosen because they engendered consistent and relatively high-rate responding in a previous study (Poling and Thompson, 1977), making it unlikely that possible rate-dependent effects of cocaine would confound findings of the present study.

2. Methods

2.1. Subjects

Seven experimentally-naïve white Carnau pigeons served as subjects. Each bird was individually housed in a colony room maintained under a 12-hour light/12-hour dark schedule. The colony room was kept at a relatively constant temperature (20–22 °C). The pigeons were given unlimited access to food for 1 month when first procured, then their free-feeding weights were determined by calculating their average daily weights over a 7-day period with continued free access to food. Throughout the experiment, the pigeons were maintained at approximately 80% of their free-feeding weights by providing only a limited amount of food in the home cages, where water and grit were constantly available. This study was conducted in accordance with the Guide for the Care and Use of Laboratory Animals promulgated by the National Research Council (1996) and was approved by our Institutional Animal Care and Use Committee.

2.2. Apparatus

Four commercially available test chambers (MED Associates, St. Albans, VT.) housed in sound attenuating shells were used. The front wall of each chamber contained three response keys, symmetrically located 24 cm above the floor, and a horizontally centered opening through which mixed grain could be reached when the food hopper was raised. Each response key could be illuminated in red, white, or green. A white bulb centered at the top of the back wall provided ambient chamber illumination and an exhaust fan provided continuous ventilation and masking noise. A personal computer equipped with MED PC software was used to collect data and to arrange experimental events.

2.3. Behavioral procedure

Throughout the study a discrete-trials procedure in which 6-s key illuminations were immediately followed by 3.5-s food deliveries with a specified probability was arranged. Under this arrangement, pecks had no effect on food delivery. Each session comprised 45 trials, with all trials separated by a variable intertrial interval (ITI) with a mean length of 45 s. All keys were darkened during the ITI. In 15 of the 45 trials, selected at random, the key was lighted red, in 15 it was lighted green, and in 15 it was lighted white. The probability of food delivery following red, white, and green key illuminations was 1.0, 0.5, and 0.25, respectively. The key (left, right, center) that was illuminated on a particular trial was selected at random. A single session was conducted for each bird every day, 7 days a week, at about the same time each day (during the light portion of the light/dark cycle).

2.4. Pharmacological procedure

The autoshaping procedure was in effect for 36 sessions prior to pharmacological testing. By the end of this period, the percentage of trials (key illuminations) in which each bird emitted one or more responses (percent trials with a response) showed no

upward or downward trend over 5 consecutive sessions. The same is true of the total number of responses emitted each session. Pre-chronic drug testing involved administering an ascending series of cocaine doses (1.0, 3.2, 5.6, and 10 mg/kg). No higher dose was given because 10 mg/kg substantially reduced responding. Cocaine was given every third day; the session immediately preceding drug testing was a vehicle-control session and the day preceding vehicle injections was a baseline session not preceded by an injection. After the 10-mg/kg dose was tested, a second ascending series of doses was administered as previously described. Throughout the study, cocaine hydrochloride (Sigma, St. Louis) was dissolved in isotonic saline solution and injected into the breast muscles at a volume of 1 ml/kg 5 min prior to behavioral testing. Vehicle (isotonic saline solution) was administered in comparable fashion.

Pre-chronic testing was followed by three consecutive baseline sessions, after which chronic exposure to cocaine began. During chronic exposure, for 20 consecutive sessions each bird received a dose of cocaine that when administered pre-chronically reduced overall percent trials with a response to approximately 50% of the vehicle-control level. The chronic dose of cocaine was 3.2 mg/kg for three birds and 5.6 mg/kg for four birds. By the end of this 20-session period, percent trials with a response and total responses per session showed no upward or downward trend across 5 consecutive sessions. Post-chronic dose–response tests were then conducted. During these tests, vehicle, and 1.0-, 3.2-, 5.6-, 10-, and 17.8-mg/kg cocaine injections were administered 5 min prior to test sessions in two ascending series, with test session separated by one session in which the chronic dose was administered 5 min prior to the experimental session. Two baseline test sessions, in which no injections were given prior to testing, were also arranged; they preceded vehicle tests. If the test condition involved administering less than the chronic dose, sufficient cocaine to make the total daily dose equal to the usual chronic daily dose was given immediately after behavioral testing.

2.5. Data collection and analysis

Each session, the number of responses emitted during each trial and during each ITI was recorded. Very few ITI responses occurred, therefore, this measure is not reported. Two response measures are reported: (a) the percent of trials with at least one response, and (b) the total number of responses each session in all trials with a given CS–US pairing probability (15 trials per session). These data were analyzed by means of two-way repeated measures analysis of variance followed by Bonferroni planned comparison tests. The two factors analyzed were CS–US pairing probability (0.25, 0.5, 1.0) and drug dose (1.0, 3.2, 5,6, 10, and where administered 17.8 mg/kg). Results of all analyzes were considered as significant if $p < .05$.

3. Results

Fig. 1 depicts mean total responses (±95% CI) and mean (±95% CI) percent trials with a response during baseline and vehicle-control sessions and during sessions in which the indicated cocaine doses were administered pre- and post-chronically. Because control performance and sensitivity to cocaine did not differ in the birds that received chronic doses of 3.2 and 5.6 mg/kg, their data are combined.

Performance was comparable in baseline and vehicle-control sessions. In the absence of drug, substantial levels of responding were evident under all conditions. During pre-chronic vehicle sessions, mean values for total responses per session were 187, 178, and 71 for the 0.25, 0.5, and 1.0 CS–US pairing probability conditions, respectively. Mean percent trials with a response for these same respective conditions were 97.1, 88.6, and 63. Thus, with both dependent variables, the 0.25 and 0.5 probability conditions engendered more responding than the 1.0 probability condition during the pre-chronic phase of the study.

3.1. Pre-chronic drug effects

Pre-chronic administrations of cocaine produced generally dose-dependent reductions in both measures of responding. Pre-chronic data for each of seven birds at each of three CS–US pairing probabilities involved 25 baseline sessions, 10 vehicle sessions, and two sessions at each of four doses, for a total of 301 observations per pairing and 903 total observations. Two-factor repeated measures analysis of variance of mean total responses per session, with drug dose and CS–US pairing probability as factors, revealed significant effects for dose ($F = 92.59$, $df = 5, 879$, $p < .001$) and CS–US pairing probability ($F = 37.95$, $df = 2, 879$, $p < .001$), as well as a significant interaction between these factors ($F = 6.14$, $df = 10, 879$, $p < .001$). Planned comparisons of within-factor data from the 0.25, 0.5, and 1.0 pairing probability conditions revealed significantly fewer responses per session than the vehicle-control mean at cocaine doses of 3.2, 5.6 and 10; 3.2, 5.6, and 10, and; 5.6 and 10 mg/kg, respectively.

Similarly, two-factor repeated measures analysis of variance of mean percent trials with a response, with drug dose and CS–US pairing probability as factors, revealed significant effects for dose ($F = 161.58$, $df = 5, 879$, $p < .001$) and pairing probability ($F = 15.26$, $df = 2, 879$, $p < .001$), as well as a significant interaction between these factors ($F = 4.63$, $df = 10, 879$, $p < .001$). Planned comparisons of within-factor data from the 0.25, 0.5, and 1.0 pairing probability conditions revealed significantly fewer trials with a response than the vehicle-control mean at cocaine doses of 3.2, 5.6, and 10; 3.2, 5.6, and 10, and; 5.6 and 10 mg/kg, respectively. For both dependent variables, the interaction between dose and pairing probability appears to involve diminished sensitivity to cocaine under conditions where the probability of CS–US pairing was highest (i.e., 1.0).

3.2. Post-chronic drug effects

The post-chronic effects of cocaine were similar to its pre-chronic effects, that is, the drug reduced responding in a generally dose-dependent fashion. Post-chronic data for each of seven birds at each of three CS–US pairing probabilities involved two baseline sessions, two vehicle sessions, 12

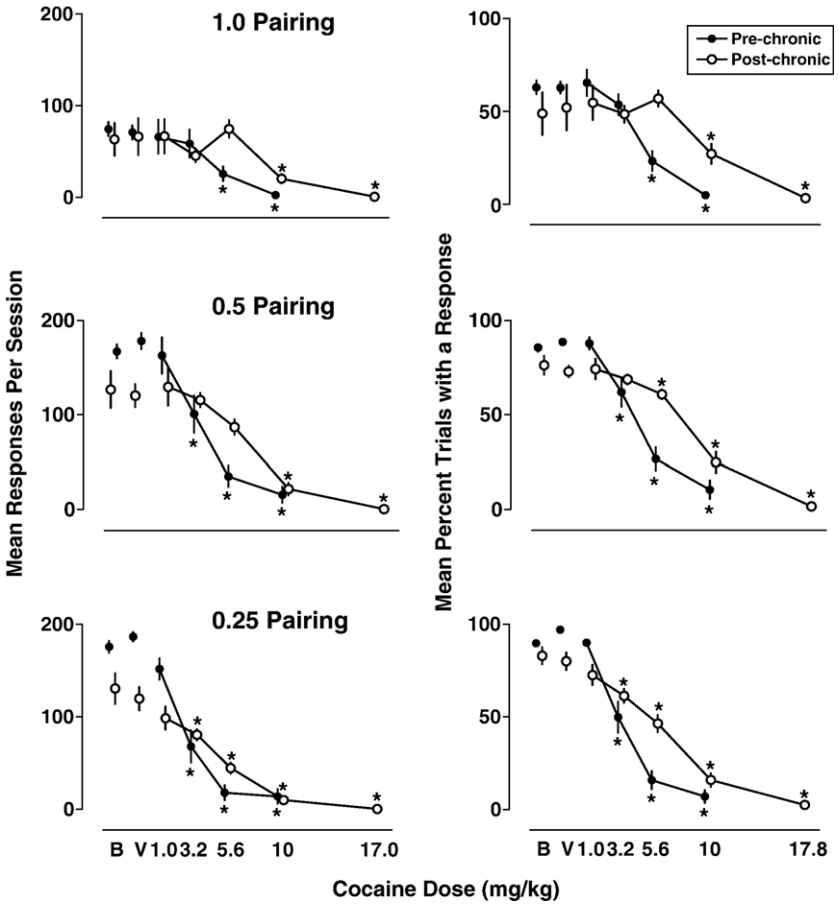

Fig. 1. Pre- and post-chronic effects of cocaine on automaintained key-peck responding of pigeons. Each dose was administered to seven birds on two occasions. B represents baseline (no injection) sessions, V represents vehicle-control sessions. Asterisks indicate drug data points that differ significantly ($p<.05$) from vehicle-control means. Data, which represent means (±95% CIs) are presented separately for trials in which the CS–US (keylight–food) pairing probability was 0.25, 0.5, and 1.

sessions of exposure to the chronic dose, and two sessions of exposure to each of four other drug doses, for a total of 168 observations per pairing and 503 total observations. Two-factor repeated measures analysis of variance of mean total responses per session, with post-chronic drug dose and CS–US pairing probability as factors, revealed significant effects for dose ($F=28.78$, $df=6, 477$, $p<.001$) and CS–US pairing probability ($F=14.63$, $df=2, 477$, $p=.008$), as well as a significant interaction between these factors ($F=3.88$, $df=12, 477$, $p<.001$). Planned comparisons of within-factor data from the 0.25, 0.5, and 1.0 pairing probability conditions revealed significantly fewer responses per session than the vehicle-control mean at cocaine doses of 3.2, 5.6, 10, and 17.8; 5.6, 10, and 17.8, and; 10 and 17.8 mg/kg, respectively.

Two-factor repeated measures analysis of variance of mean percent trials with a response, with drug dose and CS–US pairing probability as factors, revealed significant effects for post-chronic dose ($F=47.44$, $df=6, 477$, $p<.001$) and CS–US pairing probability ($F=7.32$, $df=2, 477$, $p=.001$), as well as a significant interaction between these factors ($F=2.90$, $df=12, 477$, $p<.001$). Planned comparisons of within-factor data from the 0.25, 0.5, and 1.0 pairing probability conditions revealed significantly fewer trials with a response than the vehicle-control mean at post-chronic cocaine doses of 3.2, 5.6, 10, and 17.8 mg/kg; 5.6, 10, and 17.8 mg/kg, and; 10 and 17.8 mg/kg, respectively. For both dependent variables, the interaction between dose and pairing probability appears to involve diminished sensitivity to cocaine under conditions where the probability of CS–US pairing was highest (i.e., 1.0).

It is noteworthy that vehicle-control (and baseline) means for total responses per session were lower during the post-chronic phase than during the pre-chronic phase. During post-chronic vehicle sessions, mean values for total responses per session were 120, 120, and 66.4 for the 0.25, 0.5, and 1.0 CS–US pairing probability conditions, respectively. Mean percent trials with a response for these same respective conditions were 80.1, 72.9, and 52.1. While mean percent trials with a response were lower during the post-chronic phase at all CS–US pairing probabilities, differences between pre- and post-chronic means were larger at probabilities of 0.25 and 0.5 (17 and 15.7%, respectively) than at the 1.0 probability (11.9%). Statistical analysis (two-way repeated measures analysis of variance with pre-chronic vs. post-chronic × dose as factors) of data from vehicle-control and baseline sessions revealed a significant effect of pre- vs. post-chronic phase for the 0.5 and 0.25 pairings on both mean total responses per session ($F=10.79$, $df=1, 164$, $p=0.001$; $F=23.65$, $df=1, 164$, $p<0.001$; respectively) and mean percent trials with a response ($F=5.23$, $df=1, 164$, $p=0.022$; $F=11.36$, $df=1, 164$,

$p=0.001$; respectively). Planned comparisons indicated significant ($p<.05$) differences in mean responses per session after vehicle administrations for the 0.5 and 0.25 pairing, and baseline sessions for the 0.25 pairing. Planned comparisons also indicated a significant difference between pre- and post-chronic mean percent trials with a response after vehicle administrations for the 0.25 pairing only.

3.3. Analysis of transformed data

Because vehicle-control performance in some conditions differed significantly during the pre- and post-chronic phases, drug effects across CS–US pairing probabilities may be easier to compare when data from drug sessions are expressed as a percentage of vehicle-control means, as in Fig. 2. Unlike Figs. 1, 2 facilitates comparison of the effects of cocaine not as a function of pre- and post-chronic exposures, but rather as a function of CS–US pairing probability.

Visual inspection of Fig. 2 suggests that both pre- and post-chronic cocaine administrations produced dose-dependent reductions in both response measures at all CS–US pairing probabilities. Visual inspection also suggests that the magnitude of the disruptive effects of both pre-chronic and post-chronic exposure to cocaine varied inversely with CS–US pairing probability. That is, with both dependent variables, the largest disruption at a given dose typically was observed when the pairing probability was 0.25 and the smallest disruption consistently observed when the probability was 1.0. The difference in effects across probabilities was small in magnitude in many cases, however.

Like the data in Fig. 1, the data in Fig. 2 were analyzed by two-way analysis of variance with drug dose and CS–US pairing probability as factors. Pre-chronic percent control data for each of seven birds at each of three CS–US pairing probabilities involved two sessions at each of four doses, for a total of 56 observations per pairing and 168 total observations. Analysis of mean total responses per session indicated a significant effect for pre-chronic dose ($F=19.81$, $df=3$, 150, $p<.001$) and CS–US pairing probability ($p=6.56$, $df=2$, 150, $p=.002$). There was no significant interaction between these factors ($F=1.08$, $df=6$, 150, $p>.05$). Similarly, analysis of mean trials with a response revealed a significant effect for pre-chronic dose ($F=46.59$, $df=3$, 150, $p<.001$) and CS–US pairing probability ($F=6.65$, $df=2$, 150, $p=.002$) and no significant interaction ($F=0.96$, $df=6$, 150, $p>.05$).

Post-chronic percent control data for each of seven birds at each of three CS–US pairing probabilities involved 12 sessions of exposure to the chronic dose and two sessions of exposure to each of four other drug doses for a total of 140 observations per pairing and 420 total observations. Analysis of mean total responses per session indicated a significant effect for pre-chronic dose ($F=29.52$, $df=4$, 399, $p<.001$) and CS–US pairing probability ($F=9.85$, $df=2$, 399, $p=.001$), as well as a significant interaction between these factors ($F=3.75$, $df=8$, 399, $p<.001$). Analysis of mean trials with a response revealed a significant effect for pre-chronic dose ($F=66.20$, $df=4$, 399, $p<.001$) and CS–US pairing probability ($F=13.42$, $df=2$, 399, $p=.001$). The interaction between these factors approached, but did not achieve significance ($F=1.86$, $df=8$, 399, $p=0.065$).

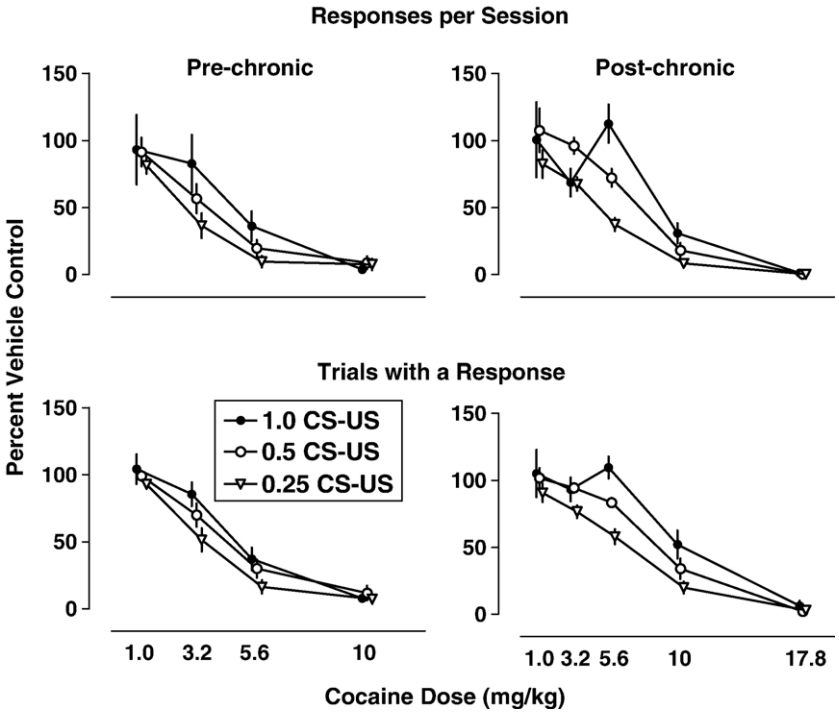

Fig. 2. Pre- and post-chronic effects of cocaine when data for drug sessions are expressed as percentages of vehicle-control means. Details are as in Fig. 1.

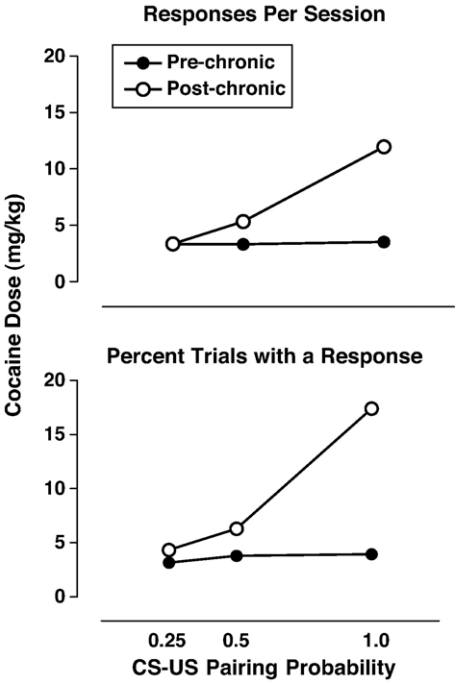

Fig. 3. Pre- and post-chronic ED_{50} doses for both dependent variables (mean total responses, mean percent trials with a response) as a function of the probability of CS–US (keylight–food) pairing probability.

To quantify the extent to which tolerance developed to the response-reducing effects of cocaine, linear regression lines were fitted to the data in Fig. 2 and ED_{50} doses based on lines of best fit were calculated. Because the 17.8-mg/kg dose was not given pre-chronically, this dose was not used in calculating post-chronic ED_{50} doses.

As shown in Fig. 3, pre-chronic ED_{50} doses for both dependent variables were comparable across the three CS–US pairing probabilities. Post-chronic ED_{50} doses, however, were directly related to CS–US pairing probability. For each individual bird at each of the three CS–US pairing probabilities, a change score was calculated for each dependent variable by subtracting that bird's pre-chronic ED_{50} dose from its post-chronic ED_{50} dose. Change scores were analyzed by one-factor repeated measures analysis of variance, with CS–US pairing probability as the factor and seven observations (one for each bird) in each of the three cells. There was a significant effect of CS–US pairing probability on both responses per session ($F=14.98$, $df=2, 12$, $p=0.001$) and percent trials with a response ($F=4.72$, $df=2, 12$, $p=0.031$). Bonferroni tests revealed that for both dependent measures change scores differed significantly only between the 0.25 and 1.0 CS–US pairing probabilities.

4. Discussion

In the absence of drug, mean responses per session in the present study were higher when the CS–US pairing probability was 0.25 or 0.5 than when it was 1.0. That is, the rate of responding was higher in the two former conditions than in the latter one. This finding, which has been reported in prior studies (e.g., Gibbon et al., 1980; Gonzales, 1974; Picker and Poling, 1982; Poling and Thompson, 1977), suggests that responding was "stronger" when the pairing probability was 0.25 or 0.5 than when it was 1.0.

Although frequency, or more often rate, of responding is a popular measure of response strength, Nevin (e.g., 1988, 1992) has argued that it is not an especially good one when operant behavior is considered, because variables that theoretically should affect response strength (e.g., size of the reinforcer, the number of responses required to produce the reinforcer) frequently do not produce the expected changes in response rate. Moreover, conditions that engender the most responding do not necessarily produce the strongest responding when other tenable measures of response strength are used. For example, Picker and Poling (1982) observed more automaintained key pecking in pigeons under conditions where the probability of food delivery following key illumination was 0.5 than under conditions where the probability was 1.0. Nonetheless, when given a choice, the birds almost always pecked the key color followed by food on every occasion. Thus, choice and response rate yielded opposite results when used to index response strength. Also, Perkins et al. (1975) suggested that the lower response rate characteristically observed when the CS–US pairing probability is 1.0 may be due to the occurrence of anticipatory approach responses to the feeder during CS presentations, which are incompatible with and reduce the rate, but not necessarily other measures of the "strength", of key pecks.

As an alternative to rate as an index of response strength, Nevin (1988, 1992; Nevin et al., 1987, 1990) has proposed behavioral momentum, defined as resistance to change. Moreover, he has proposed that behavioral momentum is primarily a function of how frequently a reinforcer, such as food, is delivered in the context of the antecedent stimulus exercising control over the behavior in question. Although the behavioral momentum metaphor has been used primarily in the context of schedule-controlled operant responding, it also could be applied to automaintained behavior. From a behavioral momentum perspective, responding in the present study should have varied directly in strength with the probability of CS–US pairings. Therefore, responding should have been most resistant to change (and recovered from change most readily) when the CS–US pairing probability was 1.0.

In general, that was the case. Pre- and post-chronic exposures to cocaine produced generally dose-dependent reductions in automaintained responding regardless of the CS–US pairing probability, but the minimum dose that produced statistically significant reductions in percent trials with a response and total responses was lower when the pairing probability was 0.25 or 0.5 than when it was 1.0. Moreover, as evident by comparing pre- and post-chronic ED_{50} doses, greater tolerance developed to the rate-reducing effects of cocaine when the CS–US pairing probability was 1.0 than when it was 0.25 or 0.5. Finally, chronic exposure to cocaine (3.2 or 5.6 mg/kg) substantially reduced both measures of responding during vehicle-control sessions when the CS–US pairing probability was 0.25 or 0.5.

Control performance was reduced to a lesser degree when the probability was 1.0. All of these observations suggest that CS–US pairing probability, hence the rate (or probability) of food delivery, influenced the effects of cocaine. That is, behavior appeared to have the greatest momentum, in the sense of resistance to drug-induced change, when the CS–US pairing probability was 1.0. There was, however, no apparent difference in the effects of cocaine, and hence resistance to drug-induced change, at CS–US pairing probabilities of 0.25 and 0.5. It would be interesting to determine whether similar effects would be observed with other disruptors, such as pre-feeding, but this was not attempted in the present study.

Poling and Thompson (1977) previously reported that acute administrations of another stimulant, d-amphetamine, reduced automaintained responding across a substantial range of CS–US pairing probabilities and Miller (2005) demonstrated that cocaine reduced responding when the CS–US probability was 1.0. Findings from the pre-chronic phase of the present study are generally consistent with these earlier results.

Interestingly, Poling and Thompson (1977) found that acute exposure to d-amphetamine (0.5, l, and 2 mg/kg) produced similar dose-dependent decreases in mean responses per key illumination regardless of whether the CS–US probability was 0.025, 0.1, 0.25, 0.5, or 1.0. In their study, a single response key lighted in red was used as the CS and dose–response curves were determined across the five CS–US probabilities in descending order. The use of the same key color as the CS in all conditions or the sequential evaluation of different CS–US probabilities in the study by Poling and Thompson, but not in the present study, may have contributed to the difference in results. Further investigation is needed to determine the range of conditions under which rate (or probability) of food delivery influences drug effects under autoshaping procedures and the variables that determine whether or not it does so. Given that rate of food delivery is not a strong general determinant of drug effects on schedule-controlled responding, as discussed previously, and that this variable produced inconsistent effects in the two studies that have examined it in the context of automaintained responding, it appears likely that it will join the long list of environmental variables that may affect, but do not consistently determine, the behavioral effects of drugs.

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