

*DISCRIMINATION OF METHADONE AND COCAINE BY
PIGEONS WITHOUT EXPLICIT DISCRIMINATION TRAINING*

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Pigeons were trained to peck a key on a variable-interval 2-min schedule of food reinforcement. Prior to each session, either 2.0 mg/kg methadone ($n = 3$), 3.0 mg/kg cocaine ($n = 4$), or 5.6 mg/kg cocaine ($n = 2$) was administered. When each pigeon's rate of pecking was stable, a range of doses of the training drug and saline were administered prior to 20-min extinction sessions separated by at least four training sessions. Rate of pecking during these extinction tests was generally an increasing function of dose, with the lowest rates obtained following saline and low doses and the highest rates obtained following doses near the training doses. Dose functions from pigeons trained with 5.6 mg/kg cocaine were steeper than those from pigeons trained with 3.0 mg/kg cocaine. Pigeons trained with methadone or 3.0 mg/kg cocaine were then given discrimination training, in which food reinforcement followed drug administration and 20-min extinction sessions followed saline administration. Rates of pecking under these conditions quickly diverged until near-zero rates were obtained following saline and high rates were obtained following drug. Discrimination training steepened dose functions for the training drugs, and the effects of several other substituted drugs depended on the pharmacology of the training drug. The pigeons trained with 5.6 mg/kg cocaine were tested with *d*-amphetamine, methadone, and morphine prior to discrimination training. *d*-Amphetamine increased rates dose dependently, and methadone and morphine did not. The results suggest that discriminative control by methadone and cocaine was established without explicit discrimination training.

Key words: drug discrimination, state-dependent learning, stimulus control, methadone, cocaine, key peck, pigeons

In the classic study of stimulus generalization by Guttman and Kalish (1956), different pigeons were trained to peck a key lit from behind with lights of various wavelengths. Pecks were reinforced with food according to a variable-interval (VI) 1-min schedule. When a range of other wavelength stimuli were presented during 30-s extinction periods, inverted U-shaped generalization gradients were obtained, with the highest rate of pecking occurring during the wavelength presented during training (S+). This study introduced methods for the study of generalization in individual subjects, and inspired much research on factors that determine the form of generalization gradients (see Honig & Urcuioli, 1981, for a review). The purpose of the present experiment was to determine whether the

internal stimuli produced by drugs could exert discriminative stimulus control over pecking using a procedure similar to that employed by Guttman and Kalish.

In the experiment by Guttman and Kalish (1956), generalization gradients were obtained prior to explicit discrimination training. That is, pigeons could peck only the training stimulus, which produced food, prior to tests of other wavelengths. This procedure does not always produce inverted U-shaped generalization gradients. For example, using similar procedures, Jenkins and Harrison (1960) found no evidence for discrimination of the frequency of a tone. After training in which a tone-plus-food condition alternated with a no-tone-plus-extinction condition, however, an inverted U-shaped gradient was obtained. Although the reasons for the flat gradients have been traced to overshadowing (Rudolph & Van Houten, 1977), the Jenkins and Harrison experiment established that inverted U-shaped gradients along the targeted stimulus dimension are not guaranteed to occur following training with S+ only (see Dinsmoor, 1995, for a systematic discussion of these and related phenomena). It is of inter-

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est, therefore, whether such gradients would be obtained along a drug-stimulus dimension following drug-only training.

This question was addressed in an experiment by Koek and Slangen (1982). They trained 2 rats, using food pellets as reinforcers, to press a lever after administration of 0.02 mg/kg fentanyl (an opioid drug) administered 30 min before sessions. A tandem VI 60-s fixed-ratio (FR) 10 schedule was employed. Fentanyl doses and other drugs were tested during occasional 5-min extinction tests. Latencies to the first lever press of the test sessions depended on the drug and dose administered; high doses of fentanyl and another opioid, morphine, produced short latencies, whereas low doses, saline, and non-opioid drugs produced longer latencies. These results suggest that fentanyl was acquired discriminative control even though no explicit discrimination training had been given. Experiments using similar procedures have produced similar effects with chlordiazepoxide and yohimbine, but not with cocaine (Colpaert, 1986, 1990).

In the present experiments, pigeons were used to test whether discrimination training is required to produce methadone or cocaine discrimination. Three groups of pigeons were studied. In one group of 3 pigeons, 2.0 mg/kg methadone was the S+, and in the other two groups one of two doses of cocaine, 3.0 ($n = 4$) or 5.6 mg/kg ($n = 2$), was the S+. The experiments were designed to increase the confidence with which the resulting dose functions could be attributed to discriminative processes rather than drug effects unrelated to discrimination. First, methadone and cocaine, both drugs known to be discriminable by pigeons at doses at least as high as those used here (Johanson & Barrett, 1993; Schaal, Jewett, & Schuh, 1994), were used as the S+. Using drug (as opposed to saline) as the S+ allowed their discriminative function to be indicated by dose functions that peak near the training dose, with the lowest response rates obtained following very low drug doses and saline. A dose function such as this would be unlike the dose-effect curve that is obtained in subjects trained in the absence of drug, which, with these drugs under similar baseline conditions, is typically a monotonically decreasing function (Branch, 1990; Cleary, Nader, & Thompson, 1986). Second,

training doses that do not have drastic rate-altering effects were chosen. The methadone training dose (2.0 mg/kg) and both cocaine training doses (3.0 and 5.6 mg/kg) have been shown to suppress somewhat or leave unaffected response rates in pigeons under similar VI schedules of food reinforcement (Branch, 1990; Cleary *et al.*, 1986). Third, following assessment of the dose functions under drug-only training conditions for two groups (those trained with 2.0 mg/kg methadone or 3.0 mg/kg cocaine), a discrimination procedure, with drug as S+ and saline as S-, was conducted. Steeper dose functions following such training would support the assertion that the initial dose functions were generalization gradients (Jenkins & Harrison, 1960; Switalski, Lyons, & Thomas, 1966). Fourth, in addition to tests of different doses of training drug following discrimination training, other drugs, both pharmacologically similar and dissimilar to the training drugs, were tested. Dose functions that revealed the pharmacological specificity obtained using two-response procedures would also support the contention that discriminative stimulus effects were observed. Fifth, 2 pigeons were trained with a stimulus of greater magnitude (*i.e.*, 5.6 mg/kg *vs.* 3.0 mg/kg cocaine). Steeper dose functions in these birds relative to those trained with the lower dose would be consistent with the interpretation of those functions as generalization gradients. Finally, in the birds trained with 5.6 mg/kg cocaine, several drugs were tested prior to drug versus saline discrimination training. The effects of test drugs should, if training produced discriminative stimulus control by the test drug, depend on the pharmacologies of the test drugs (*i.e.*, pharmacologically similar drugs should produce high response rates, and dissimilar drugs should produce rates near those obtained following saline).

METHOD

Subjects

Three adult female White Carneau pigeons (trained with methadone), 4 adult male White Carneau pigeons (trained with 3.0 mg/kg cocaine), and 2 adult male White Carneau pigeons (trained with 5.6 mg/kg cocaine) were used as subjects. A 3rd pigeon

began the study in the group trained to discriminate 5.6 mg/kg cocaine, but despite repeated attempts to establish and maintain pecking, the pigeon would not peck following even low doses (i.e., 1.0 mg/kg) of cocaine, and so was dropped from the study. The methadone-trained females were housed in the Department of Psychology vivarium at the University of Minnesota, and the cocaine-trained males were housed at the Department of Psychology vivarium at West Virginia University. All birds were housed individually and had free access to water and grit. Their weights were maintained, by supplemental feedings following sessions, at 80% of those obtained with continuous access to food. Lights in the Minnesota vivarium were on continuously; lights in the West Virginia vivarium were on from 7:00 a.m. to 5:30 p.m.

Apparatus

The methadone-trained females were studied in one standard three-key Lehigh Valley operant conditioning chamber. The cocaine-trained males were studied in four custom-built three-key chambers with similar dimensions and characteristics. In both cases the center key, located above the food hopper, could be illuminated from behind with a green light. A peck required a force of approximately 0.14 N to be counted as a response. General illumination was provided by 28-V 1.1-W lamps mounted 4 cm (West Virginia) or 8 cm (Minnesota) above the center keys. Houselights in the Minnesota chamber were shielded with a stainless steel shade that prevented direct downward illumination; in the West Virginia chambers, houselights were covered with a white plastic cap. Chambers were equipped with identical solenoid-operated hoppers that were lit with a white light when they were raised. Contingencies were programmed and data were collected using MS-DOS-based microcomputers programmed in MEDState Notation (MED Associates, Inc. & Tatham, 1991). White noise and ventilation fans masked extraneous sounds.

Procedure

Initial training. Experimental sessions were conducted 6 or 7 days per week. Following two 30-min periods of adaptation to the chambers, the pigeons were trained to eat from the magazine. Key pecking was auto-

shaped to a green key; following a 45-s interval, the key was lit green for 8 s, after which houselights and keylights were extinguished and the hopper was raised for 3 s. After one to three sessions in which each peck produced 3-s access to the hopper, pigeons were exposed to a VI schedule. During the next one to five sessions, administration of the training drug began (see below). The mean value of the VI was increased gradually during the next one to 10 sessions by increasing the duration of the longest intervals until a mean of 120 s was reached. The VI schedule was composed of 20 intervals determined using the progression of Fleshler and Hoffman (1962). Sessions began with illumination of the houselight and the green keylight. The first peck after each interval elapsed extinguished the houselight and keylight, illuminated the light in the hopper, and raised the hopper for 3 s. Sessions lasted for 40 reinforcers (approximately 80 min) in the case of the methadone-trained pigeons, and for 20 reinforcers (approximately 40 min) in the case of the cocaine-trained pigeons.

Drug administration. All drugs were dissolved in 0.9% saline and injected into the breast muscle in a volume of 1.0 ml/kg body weight. Methadone HCl (Sigma), morphine sulfate (Sigma in Minnesota; NIDA in West Virginia), and *d*-amphetamine sulfate (Sigma) were injected 10 min prior to the start of a session. Cocaine HCl (Sigma) was injected 5 min prior to sessions. Doses are expressed in terms of the salts.

Drug-only training and testing. During drug-only training, methadone (2.0 mg/kg) was administered prior to every session to 3 pigeons (P4565, P3890, and P4882), 3.0 mg/kg cocaine was administered to 4 pigeons (P1, P2, P3, and P4), and 5.6 mg/kg cocaine was administered to 2 pigeons (P1061, P1100). Sessions were conducted until daily response rates became stable as judged visually. Table 1 lists the number of sessions prior to the initial tests for each pigeon and their respective drug-training conditions. In methadone-trained pigeons, a range of methadone doses (0.25, 0.5, 1.0, 2.0, and 3.0 mg/kg) and saline were administered, in mixed order, 10 min prior to 20-min extinction sessions. During these test sessions, pecks were counted but no reinforcers were delivered. External stimuli were identical to those present during train-

Table 1

Number of sessions prior to drug tests before discrimination training, number of sessions prior to drug tests during discrimination training, and drug training conditions.

Subject	Condition	Before S- training	During S- training ^a
3890	2.0 mg/ml methadone	59	172
4565	2.0 mg/ml methadone	65	163
4882	2.0 mg/ml methadone	63	173
1	3.0 mg/ml cocaine	197	215
2	3.0 mg/ml cocaine	86	251
3	3.0 mg/ml cocaine	87	136
4	3.0 mg/ml cocaine	69	70
1100	5.6 mg/ml cocaine	83	
1061	5.6 mg/ml cocaine	135	

^a Includes both drug and no-drug sessions.

ing sessions. For the cocaine-trained pigeons, a range of cocaine doses (0.3, 1.0, 1.7, 3.0, and 5.6 mg/kg) and saline were administered 5 min prior to identical 20-min extinction sessions. Test sessions were separated by at least 3 days (determined by the stability of the control sessions) in which the VI 120-s schedule operated in the presence of the training doses of the drugs. Each dose was tested twice, and a test of saline occurred during dose-effect tests with each drug.

Immediately following cocaine dose-effect tests, other drugs were tested in the 2 pigeons trained with 5.6 mg/kg cocaine. *d*-Amphetamine (0.3, 1.0, and 1.7 mg/kg), methadone (1.0, 2.0, and 3.0 mg/kg), and morphine (1.0, 2.0, and 3.0 mg/kg) were tested in mixed order, both with respect to doses and drugs. One of these pigeons (P1061) occasionally began exhibiting long latencies (e.g., 3 to 10 min) to its first peck during training sessions. Therefore, for this pigeon an additional criterion had to be reached before drug tests were conducted; latencies to the first peck had to be shorter than 2 min from

the start of the session for at least three consecutive sessions. The experiment was terminated for these pigeons after these substitution tests.

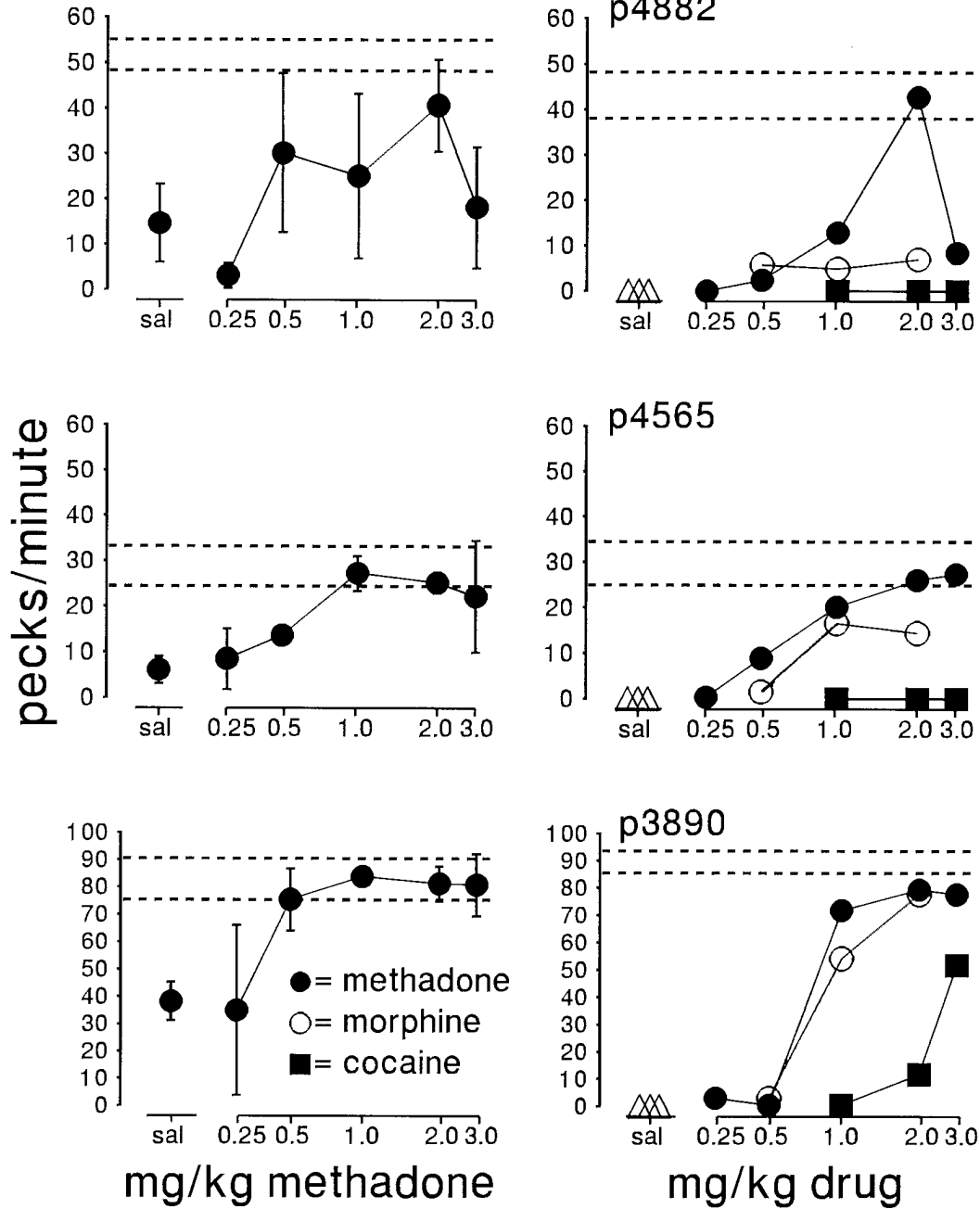
Discrimination training and testing. Following completion of dose-effect determinations during drug-only training, pigeons trained with methadone or 3.0 mg/kg cocaine were exposed to conditions in which the training dose alternated with sessions in which saline was administered. Following drug, the VI 120-s schedule operated; a 20-min extinction period (identical to test sessions) followed saline administration. The type of session was chosen randomly in four-session blocks, with the restriction that no more than two consecutive sessions of one type could occur. The session length for methadone-trained pigeons was reduced to 20 reinforcers (approximately 40 min) during this training. Forty-eight sessions into discrimination training, 2 of the pigeons trained with methadone were given saline and were accidentally exposed to the VI 120-s schedule of food reinforcement. A transient increase in response rates following saline, lasting 10 to 20 sessions, was observed (data not shown). When rates of pecking under these conditions became stable, methadone, morphine (0.5, 1.0, and 2.0 mg/kg), and cocaine (1.0, 2.0, and 3.0 mg/kg) were tested, in the same manner as described previously, in pigeons trained with methadone. Because of time constraints, each dose was tested only once. In the pigeons trained with 3.0 mg/kg cocaine, cocaine (0.3, 1.0, 1.7, 3.0, and 5.6 mg/kg), methadone (1.0, 2.0, and 3.0 mg/kg), *d*-amphetamine (0.1, 0.3, and 1.0 mg/kg), and morphine (1.0, 2.0, and 3.0 mg/kg) were also tested following discrimination training, again following the procedures used for other dose-effect tests.

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Fig. 1. Effects of a range of doses of methadone and saline (sal) on mean response rates during 20-min extinction sessions prior to discrimination training (left panels), and the effects of methadone, morphine, and cocaine during discrimination training (right panels). Vertical bars in the left panels depict ranges of two determinations at each dose. Only single determinations of drug doses in the right panels are represented. The effects of saline during tests of other drugs (right panels) are represented by open triangles. Dashed lines represent the variability in baseline rates during training sessions prior to discrimination training and during discrimination training. Baseline variability was determined by calculating the mean of rates obtained from 10 sessions prior to the first test of drug or saline before S- training and during S- training. The standard deviation of the mean was added to and subtracted from the mean rate to yield the values shown by the dashed lines.

before S- training

during S- training



RESULTS

Methadone-Trained Pigeons

For all pigeons (including those trained with cocaine) patterns of pecking under the VI 120-s schedule were typical of those ordinarily obtained under such conditions (i.e., continuous, uniform rates throughout the session). Response rates of pigeons that received 2.0 mg/kg methadone prior to each session ranged from about 30 pecks per minute (for P4565) to about 80 pecks per minute (for P3890). This variability in baseline rates across subjects is not uncommon for similar VI schedules (see, e.g., Schaal, Schuh, & Branch, 1992).

Figure 1 shows the effects of methadone on rates of pecking obtained during 20-min extinction tests given both prior to discrimination training and during discrimination training. The highest rates were obtained following doses of 0.5 to 3.0 mg/kg, and the lowest were obtained following saline and 0.25 mg/kg methadone. During discrimination training, rates of pecking usually increased dose dependently following methadone. The dose functions following methadone obtained during discrimination training were considerably sharper than the ones obtained prior to discrimination training for P4882 and P3890. Lower rates were observed following saline and 0.25 and 0.5 mg/kg methadone for these 2 pigeons. For P4565 the shapes of the dose functions determined before and during discrimination training were similar; however, rates were lower following saline and 0.25 mg/kg methadone during discrimination training. Morphine produced dose-dependent increases in rates for 2 of 3 subjects; although the gradient for P4882 was very flat, response rates were still increased relative to those obtained after saline. For 2 subjects (P4565 and P4882), no dose of cocaine increased response rates, but for P3890 dose-dependent increases in rates were obtained.

Cocaine-Trained Pigeons (3.0 mg/kg)

More sessions had to be conducted prior to the first dose-effect tests of cocaine than for tests of methadone (listed in Table 1) to achieve stability. But rates of pecking eventually became stable at levels that are not unusual under similar conditions (Schaal *et al.*, 1992). Figure 2 shows the effects on response

rate of a range of doses of cocaine and saline prior to discrimination training. Near-baseline rates of pecking were obtained following doses that exceeded saline. For P1, P2, and P4, the lowest rates were obtained following saline or 0.3 mg/kg cocaine and the highest rates were obtained following doses near the training dose. For P3 the function was nearly flat. The right panels of Figure 2 depict rates obtained during dose-effect tests following discrimination training. In each case the difference in rates obtained following low cocaine doses and saline and those obtained following higher cocaine doses was much greater than the differences obtained prior to discrimination training.

Tests of methadone, morphine, and *d*-amphetamine in these pigeons are depicted in Figure 3. Although neither methadone nor morphine produced dose-dependent increases in response rates, *d*-amphetamine did increase rates dose dependently.

Cocaine-Trained Pigeons (5.6 mg/kg)

Figure 4 shows the effects of cocaine, methadone, morphine, and *d*-amphetamine in pigeons trained only in the presence of 5.6 mg/kg cocaine. Again, the highest rates were obtained following administration of doses of cocaine near the training dose, and the lowest were obtained following saline. Although no dose of methadone or morphine increased rates in these pigeons, *d*-amphetamine increased rates dose dependently.

DISCUSSION

In general, dose functions for methadone and cocaine sloped upward, from low rates after saline and low doses of drug to relatively high rates as the training dose was approached. These curves were obtained without explicit discrimination training (i.e., without exposing pigeons to extended experience with extinction following administration of saline). In this discussion we will (a) present arguments in favor of calling these dose functions generalization gradients, (b) consider alternative explanations that focus on direct rate-altering effects of drugs, (c) relate these findings to those obtained with state-dependent learning procedures (Overton, 1983), and (d) suggest a link between these effects and those that indicate that tolerance to

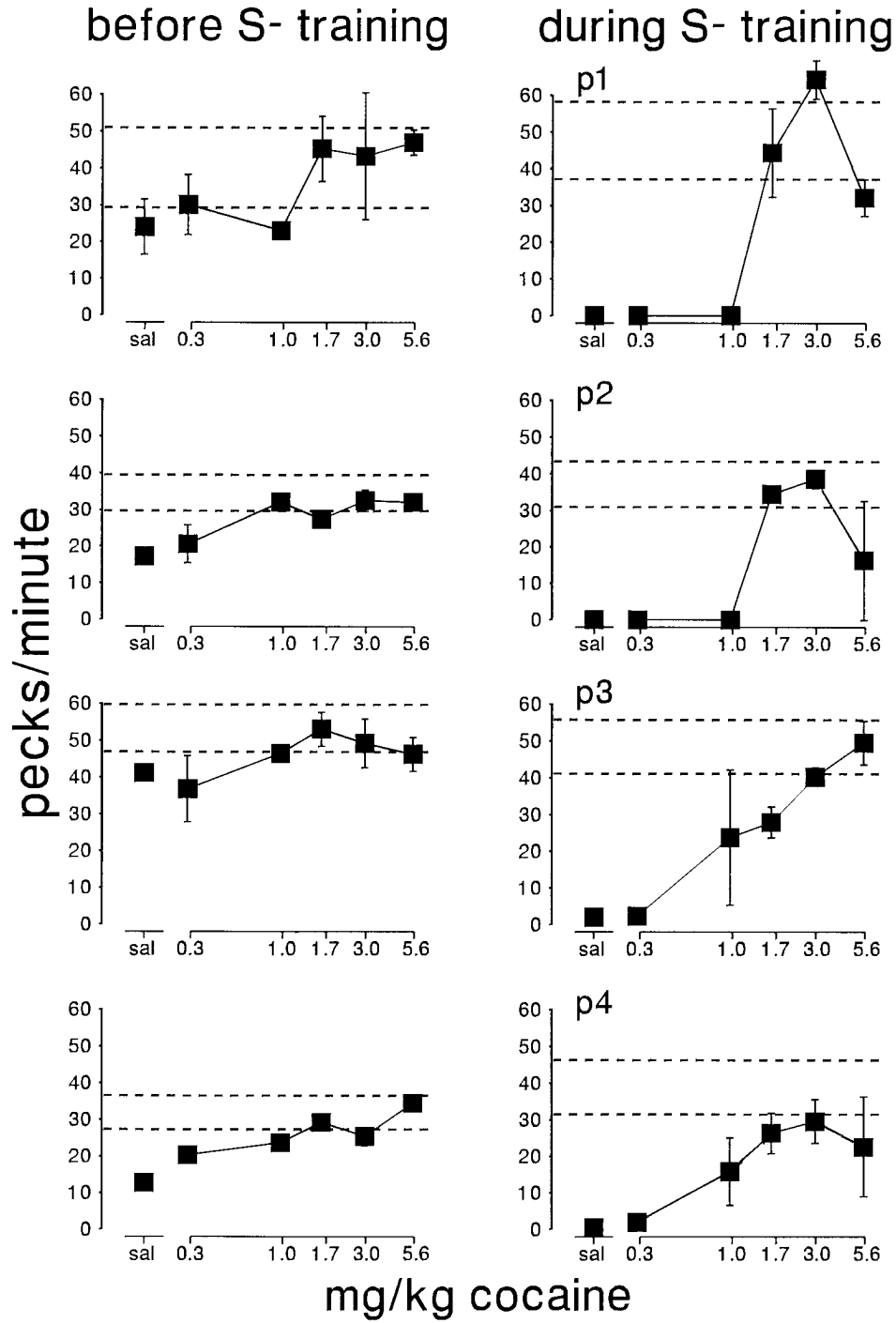


Fig. 2. Effects of a range of doses of cocaine and saline on mean response rates during 20-min extinction sessions in pigeons trained with 3.0 mg/kg cocaine prior to discrimination training (left panels) and following such training (right panels). Vertical bars depict ranges of two determinations at each dose. Other details are as in Figure 1.

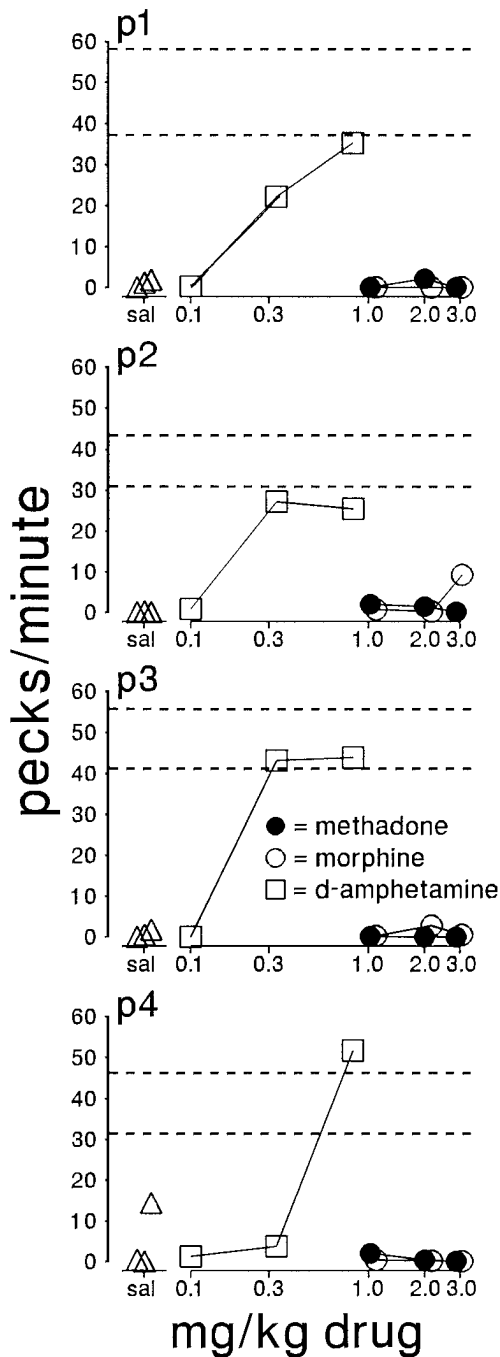


Fig. 3. Effects of single determinations of a range of doses of *d*-amphetamine, methadone, morphine, and saline in pigeons trained with 3.0 mg/kg cocaine following discrimination training. The effects of saline are represented by open triangles. Other details are as in Figure 1.

drugs can be situationally specific (e.g., Smith, 1991a, 1991b).

Arguments in favor of calling these dose functions generalization gradients. First, the shapes of the obtained functions differ considerably from what would have been obtained in the absence of the drug-schedule history. They resemble, in fact, inverted U-shaped generalization gradients, at least from the training dose of drug to saline. This assertion is based on the similarity of these dose functions and those obtained under comparable conditions in pigeons without prolonged training with drug. In particular, compared to response rates obtained after saline administration, 2.0 mg/kg methadone reliably reduced rates of pigeons' responding on a VI 150-s schedule (Cleary *et al.*, 1986). Likewise, acute administration of 3.0 mg/kg cocaine did not affect response rates of pigeons responding on a random-interval (RI) 120-s schedule, and 5.6 mg/kg cocaine either did not affect or reduced rates (Branch, 1990). Therefore, the shapes of the dose functions in each methadone-trained pigeon, in 3 of 4 pigeons trained with 3.0 mg/kg, and in both of the pigeons trained with 5.6 mg/kg cocaine, differ considerably from those likely to be obtained in drug-naive animals.

Following discrimination training with methadone versus saline and 3.0 mg/kg cocaine versus saline, the dose functions became more sharply sloped, a result routinely obtained with external stimuli (e.g., Jenkins & Harrison, 1960; Switalski *et al.*, 1966). Although the change in the steepness of dose functions following discrimination training does not prove that the original dose functions indicated discrimination of the drugs, it is consistent with this assertion. Effects of other drugs, both similar to and quite different pharmacologically from the training drugs, also support the assertion that the dose functions indicate discriminative stimulus control by the training drug. This is because of the reliable finding that behavior following tests of other drugs depends on the correspondence of the pharmacologies of the training and test drugs. Thus, morphine produced similar effects on response rates to methadone, but neither cocaine nor *d*-amphetamine generally did. Likewise, *d*-amphetamine increased response rates when cocaine

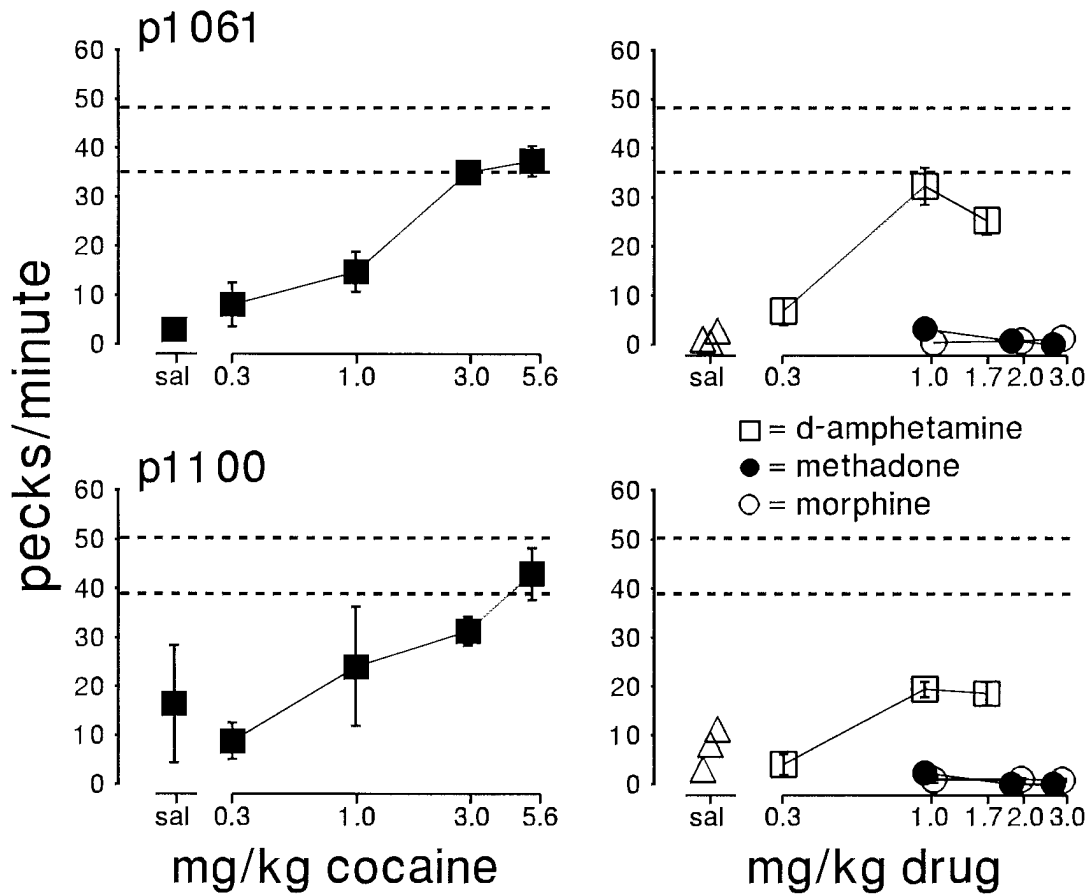


Fig. 4. Effects of a range of doses of cocaine and saline (left panels) and *d*-amphetamine, methadone, morphine, and saline (right panels) in pigeons trained with 5.6 mg/kg cocaine. Vertical bars depict ranges of two determinations. The effects of saline during tests of other drugs (right panels) are represented by open triangles. Other details are as in Figure 1.

was the training drug, but the opioids did not.

Two pigeons were trained with 5.6 mg/kg cocaine in order to strengthen the argument that the dose functions may be called generalization gradients. Steeper dose functions for cocaine, and both substitution of *d*-amphetamine for cocaine and the inability of methadone or morphine to increase response rates in these pigeons, support the drug-discrimination interpretation of these data. These results were obtained entirely without explicit S- training, which had occurred prior to substitution tests in the other pigeons. It should be noted that the highest rate of responding for P1100 following saline was obtained during its first test (see Figure 4). No test with saline produced as high a

response rate for P1061, and no other tests with saline or opioids produced high rates of pecking in these 2 pigeons.

Alternative explanations that focus on direct rate-altering effects of drugs. The current design might have resulted in a more convincing case for discrimination without explicit training had the drugs been tested on a separate group of birds trained under similar conditions with a VI 2-min schedule of food reinforcement but without the extensive drug history. We have relied instead on comparisons of the effects of these doses of drugs reported in other studies in which pigeons were trained to respond for food under similar conditions. These studies (Branch, 1990; Cleary et al., 1986) indicate that dose-effect curves obtained with these drugs are either

flat or monotonically decreasing across the range of tested doses. Except perhaps for P3, trained with 3.0 mg/kg cocaine, the dose functions produced in the current study were very different from those obtained in previous ones. If repeated administration of the training doses used in this study would simply have resulted in tolerance to the rate-decreasing effects of the drugs, low response rates following saline would probably not have been obtained. Branch (1990) administered higher doses (7.4 or 10.0 mg/kg) of cocaine to pigeons prior to their sessions. The pigeons had been trained in the absence of cocaine on a three-component multiple VI schedule, one of which was similar to the VI 120-s schedule used here. In 2 of 4 pigeons, response rates following the highest doses were slightly increased relative to cocaine's effects prior to chronic administration, but the effect was not as large or reliable as that obtained in the present study (particularly in the pigeons trained with 5.6 mg/kg cocaine). Thus, a reasonable suggestion is that repeated administration of the drugs during training on a food-reinforcement schedule resulted in the stimulus effects of the drugs setting the occasion for key pecking.

Relation of these procedures to state-dependent learning procedures. The procedure used in these studies is similar to procedures employed in studies of state-dependent learning. The typical procedure used to study state-dependent learning is a 2×2 design (Overton, 1983), in which a performance is established in the presence of either drug or no drug and then is tested under drug and no-drug conditions. State-dependent learning is inferred when an impairment in performance is obtained under test conditions that differ from those arranged during training. After an extensive review of the literature, Overton concluded that state-dependent learning, when it occurs, probably reflects the discriminative stimulus effects of the training drugs. Colpaert (1986), on the other hand, suggested that state-dependent learning could underlie multiple effects of drugs, including those reported here. The present experiments used a procedure that was similar to the one used by Colpaert (1986, 1990). For example, in one of a series of experiments Colpaert (1990) trained groups of rats to lever press on FR 10 schedules of food reinforce-

ment. During training, some rats received saline and others received 40.0 mg/kg chlordiazepoxide 30 min before each session. Tests of saline and a range of doses of chlordiazepoxide were conducted for different groups of rats. The number of rats to complete 10 responses during the first 2 min of test sessions increased as a function of dose for the rats trained with drug and decreased as a function of dose for the rats trained with saline. Because the completion of the first ratio within 2 min occurred under test conditions that approximated the training conditions, Colpaert (1990) argued that state dependency was indicated. These effects may also be interpreted as indications of discriminative stimulus control by chlordiazepoxide, however. The latter interpretation may be preferable because of the similarity of Colpaert's results and the present results to those obtained in most studies of drugs as discriminative stimuli, which clearly reflect the acquisition of discriminative control by drugs.

Could "untrained" discrimination be involved in context-specific drug tolerance? In a series of studies by Smith (1990, 1991a, 1991b), it has been shown that tolerance, as indicated by reductions in the behavior-altering effects of several drugs, including cocaine (Smith, 1990), morphine (Smith, 1991a), and phenylidone (Smith, 1991b), may occur only under the conditions immediately prior to which the drug is administered. Tolerance is frequently not observed under other conditions, distinguished by different responses, contingencies, or stimuli, in the same animals despite the fact that tests in the other conditions are conducted on the same or the subsequent day. Tolerance to the effects of the drugs on the other responses can be produced, however, by administering the drug prior to those behavioral conditions. The fluidity of the changes in drug effects as they are administered in different situations suggests that mechanisms other than metabolic changes or alterations in steady-state physiological conditions produced by repeated drug administration are involved. The present results suggest that drugs can serve as discriminative stimuli even in the absence of explicit discrimination training. Perhaps the behavioral changes observed as animals experience drug stimuli in new contexts reflect, first, the disruption of behavior by the drug, followed

by the development of stimulus control by the drug over the behavior in the new situation. Disruption of behavior when the drug is newly administered prior to one of the other behavioral conditions may reflect the joint contributions of direct behavior-altering effects and the introduction of "inappropriate" drug stimuli. Several of Smith's effects suggest a drug-stimulus-control interpretation of the situational specificity of tolerance. Whether such a speculation has merit remains to be determined experimentally.

In summary, rates of pecking of pigeons under a VI 2-min schedule appear to be subject to discriminative control by drugs in a manner that is analogous to the discriminative control exerted by visual stimuli (Guttman & Kalish, 1956); that is, it may occur without explicit S- training. The discriminative stimulus function of the drugs was enhanced by explicit training, and the effects of other drugs depended on the correspondence of the pharmacologies of the trained and tested drugs, a result consistent with the drug-discrimination literature. Furthermore, training with a higher dose of cocaine enhanced discriminative control by the drug and allowed the observation of pharmacologically specific generalization prior to explicit S- training. Taken together, these results demonstrate that stimulus control by drugs can occur in the absence of explicit discrimination training.

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