BIAS OF PHENCYCLIDINE DISCRIMINATION BY THE SCHEDULE OF REINFORCEMENT

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Pigeons, trained to discriminate phencyclidine from saline under a procedure requiring the bird to track the location of a color, received cumulative doses of phencyclidine, pentobarbital, or *d*-amphetamine with a variety of schedules of reinforcement in effect (across phases). When the same second-order schedules were used to reinforce responding after either saline or phencyclidine administration, stimulus control by phencyclidine did not depend on the schedule parameter. When different second-order schedules were used that biased responding toward the phencyclidine-correlated key color, pigeons responded on the phencyclidine-correlated key at lower doses of phencyclidine and pentobarbital than when the second-order schedule biased responding toward the saline key color. A similar but less marked effect was obtained with *d*-amphetamine. Attempts to produce bias by changing reinforcement magnitude (duration of food availability) were less successful. A signal-detection analysis of dose-effect curves for phencyclidine under two of the second-order schedules employed suggested that at low doses of phencyclidine, response bias is a major determinant of responding. As doses were increased, position preferences occurred and response bias decreased; at higher doses both response bias and position preference decreased and discriminability increased. With low doses of pentobarbital, responding again was biased but increasing doses produced position preference with only small increases in discriminability. At low doses of *d*-amphetamine responding also was biased, but bias did not decrease consistently with dose nor did discriminability increase. These experiments suggest that the schedule of reinforcement can be used to bias responding toward or away from making the drug-correlated response in drug discrimination experiments, and that signal-detection analysis and analysis of responding at a position can be used to separate the discriminability of the drug state from other effects of the drug on responding.

Key words: drug discrimination, bias, signal detection, second-order schedules, phencyclidine, pentobarbital, *d*-amphetamine, key peck, pigeons

In 1937 Girden and Culler demonstrated that the internal state produced by a drug can act as a discriminative stimulus to control responding. During the past decade the study of such stimulus properties of drugs

has become an area of tremendous interest to behavioral pharmacologists. The discriminative-stimulus properties of a drug are sometimes shared with other drugs that produce similar pharmacological effects and these similarities have been used to define drug classes (Weissman, Milne, & Melvin, 1982) and even to suggest that drugs with diverse chemical structures may exert their effects by acting at the same or similar receptor sites in the nervous system.

Although experiments such as those mentioned above reveal important information about the pharmacology of discriminative-stimulus control by drugs, behavioral aspects of discriminative-stimulus control have been largely ignored. It is frequently stated that the stimulus properties of drugs

This work was supported by the National Institute on Drug Abuse, Grant #DA 02251. Phencyclidine was provided by the National Institute on Drug Abuse.

This paper is dedicated to the memory of Dr. Robert A. Patton, whose guidance and support inspired a number of his students to pursue careers in behavioral pharmacology. Through these students his influence on the field will continue for many years.

We wish to thank W. C. Hardwick for preparing the figures and Brenda Selby for typing the manuscript.

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are profoundly dependent on behavioral variables, yet there are few experimental demonstrations of such effects. As a first step toward studying the role of behavioral variables in stimulus control by drugs, we adopted a technique that has been used previously to separate drug effects on response "bias" from those on stimulus discriminability (Dykstra & Appel, 1974). This technique involved systematically changing the schedule of reinforcement to produce bias either toward the drug-correlated or toward the alternative response.

In these experiments, pigeons trained to discriminate phencyclidine (PCP) from saline (McMillan, Cole-Fullenwider, Hardwick, & Wenger, 1982) were studied under a variety of schedules of reinforcement. In addition, generalization of responding to the stimulus correlated with PCP following the administration of pentobarbital or *d*-amphetamine also was determined under a variety of schedules.

METHOD

Subjects

The same five male White Carneaux pigeons used in previous experiments in this series on phencyclidine discrimination (McMillan, 1982; McMillan et al., 1982; McMillan & Wenger, 1983) were used. With free access to food and water the birds had weighed 589 to 703 g, but they were maintained at 80% of these weights throughout these experiments.

Apparatus

The experimental chamber was a Gerbrands Model G7313 pigeon test cage equipped with a Gerbrands feeder and three response keys, each of which could be transilluminated with several colors by a Gerbrands 28-V dc Key Light Assembly containing two 0.04-W bulbs for each key color. The chamber was enclosed inside a Gerbrands Model G7211 sound and light attenuating enclosure. The minimum force required to operate the keys was 0.05 N. A

relay mounted inside the chamber operated whenever the key contacts were opened on a side key. Two 28-V dc houselights illuminated the experimental chamber during the session except during a food cycle. A TRS-80, Model III (Radio Shack) computer, located in a separate room adjacent to the room containing the experimental chamber, controlled the schedule and recorded the data.

Procedure

The training of these pigeons has been discussed in detail previously (McMillan et al., 1982). The schedule in effect at the beginning of these experiments required the pigeon to peck a center key illuminated with a white light. A peck on the center key extinguished it and lighted the two side keys, one with a red light and one with a green light. Five responses on either side key (fixed-ratio, or FR, 5 component) extinguished both side-key lights, reset the ratios on the side keys to 5, and relighted the center key to reinstate the original condition. Food (6-s access to grain) was presented only after 10 FR-5 components had been completed on the correct side key. Using the terminology of Kelleher (1966) for second-order schedules, this schedule is referred to as FR 10 (FR 5). Pecks on the red key were defined as correct and produced food under the FR-10 (FR-5) schedule if 1.5 mg/kg phencyclidine had been administered before the session, and pecks on the green key were defined as correct if saline had been administered before the session. Pecks on the key not defined as correct counted down the FR-5 component, but did not decrease the number of FR 5s required for food delivery. Position of the red and green colors on the side keys varied randomly after each center-key response. The session (on training days) terminated after food presentation had occurred six times, or after 1800 s, whichever occurred first. Sessions were conducted Monday through Friday.

During the first 2 or 4 days of the week, the pigeons were given saline or 1.5 mg/kg PCP 15 min before the session (the number

of days depended on the stability of performance). The final injection of each substance (saline or 1.5 mg/kg PCP) each week was used as a measure of baseline control by the presence or absence of the drug stimulus. On Fridays, cumulative dose-effect curves (McMillan et al., 1982) were determined to measure generalization from the training dose of PCP to other doses of PCP, pentobarbital, or *d*-amphetamine. To summarize briefly, a bird was injected intramuscularly and placed into the chamber. After 15 min, the session was initiated and it was terminated with the first food delivery. Immediately after food delivery, the bird was removed from the chamber and given a second injection and the process was repeated. Repetitions of the procedure continued until a cumulative dose was reached that disrupted responding such that the bird did not obtain food within 1800 s, or until a predetermined maximum cumulative dose of drug was reached (1.7 mg/kg PCP, 17.0 mg/kg pentobarbital, or 3 mg/kg *d*-amphetamine). All doses shown in the figures are cumulative doses (the sum of all doses given to the bird during that session). Drugs were administered and doses calculated as follows: phencyclidine hydrochloride, sodium pentobarbital, or *d*-amphetamine sulfate was dissolved in 0.9% saline and administered in a volume of 0.1 ml/100 g of body weight.

Discrimination data prior to the first food delivery were plotted as a percentage of fixed-ratio components completed on the red key (hereafter referred to as the PCP key). The average latency to respond on the center key and average rate of responding on the side keys also were determined.

Three series of experiments were performed. In the first series, the schedule of reinforcement for both keys was varied simultaneously. No cumulative dose-effect curves were determined during these experiments; the purpose was to determine if changes in the number of responses required, or other changes in second-order schedules, affected stimulus control by PCP and saline. In these experiments, responding on the correct key was reinforced under a

variety of schedules, but the schedules of reinforcement were the same for correct responses on both key colors during each phase of these experiments. Second-order schedules studied were FR 5 (FR 10); FR 10 (FR 20); FR 1 (FR 200); FR 10 (FR 1); FR 10 (FR 5) in that order. The birds received 8 days of training under each of these schedules, with PCP given before the session on 4 days and saline given before the session on 4 days.

In the second series of experiments, the schedule of reinforcement was again varied on both keys; however, different schedules were in effect on each key. In these experiments, 4 weeks of training under each schedule preceded three weeks during which cumulative dose-effect curves for PCP, pentobarbital, and *d*-amphetamine were studied. In some experiments, a cumulative saline curve also was determined. The schedules employed were FR 25 (FR 5), FR 10 (FR 5), FR 5 (FR 5), FR 10 (FR 15) and FR 10 (FR 3).

In the final series of experiments, the schedule of reinforcement was FR 10 (FR 5) for both key colors and the duration of the food cycle was manipulated. Food cycles of 4 and 16 s were studied. As in the previous series of experiments, 4 weeks of training occurred for each reinforcement duration and then cumulative dose-effect curves were determined during the next three weeks.

Data obtained in the second series of experiments under two different schedules of reinforcement—FR 25 (FR 5) and FR 5 (FR 5)—were subjected to a signal-detection analysis. The analysis was by the point estimates of discrimination (sensitivity: PED) and bias (PEB) as developed by McCarthy and Davison (1980) and as employed by Logue (1983). The proportion of responses (completed ratios) on the PCP key after each dose of PCP during the determination of the cumulative dose-effect curve was compared with the corresponding cumulative administration of saline given under similar conditions. Each dose was compared with the corresponding saline administration to classify responses for signal-detection

analysis as shown in the computational formulae below:

no consistent differences across schedules. Except for Birds 61 and 62, which responded

Point Estimate of Discrimination (PED)	$= \frac{1}{2} \log$	Proportion of drug responses after drug (hits)	$\times$	Proportion of saline responses after saline (correct rejections)
		Proportion of drug responses after saline (false alarms)	$\times$	Proportion of saline responses after drug (misses)
and				
Point Estimate of Bias (PEB)	$= \frac{1}{2} \log$	Proportion of drug responses after drug (hits)	$\times$	Proportion of drug responses after saline (false alarms)
		Proportion of saline responses after saline (correct rejections)	$\times$	Proportion of saline responses after drug (misses)

The PED and PEB were calculated for individual animals. Frequently, individual birds made no responses on the drug key after saline. When this happened in all five birds, it introduced a zero into the calculation formulae (correct rejections) and did not permit the log calculation. Therefore, when 100% of the responses occurred on one key for all birds, for purpose of the calculation, 99.9% was entered into the formulae. PED and PEB were plotted against the schedule of reinforcement and the changes in stimulus (drug dose) after Logue (1983).

RESULTS

Simultaneous Variation of the Schedules on Both Keys

Table 1 shows for each bird the percentage of ratios completed on the "correct" key (Column 1) following PCP administration (top half of table) or saline administration (bottom half), the average latency to respond on the center key, and the average rate of responding on the side key during the last four sessions at each schedule value. The first five data columns of Table 1 show that stimulus control frequently was greater following saline administration than following PCP administration; however, there were

only slightly more often on the red key than on the green key under the FR 1 (FR 200) schedule after PCP administration, birds completed 74 to 100% of their ratios on the PCP key after PCP administration. After saline administration, the birds consistently completed nearly 100% of the ratios on the saline key.

The mean latency to respond on the center key (i.e., time from center-key illumination to the first peck) was longer for all 5 birds after both PCP and saline under the FR 1 (FR 200) schedule than under the other schedules. There were no consistent differences in rate of responding on the side key across schedules.

This series of experiments showed that changing the schedule of reinforcement had little effect on stimulus control when the same schedule of reinforcement was in effect on both keys. Moreover, stimulus control did not differ when a large number of responses—for example 200 under FR 10 (FR 20) or FR 1 (FR 200)—were required versus when only 10 responses were required [FR 10 (FR 1)]. Similarly, other second-order schedule variations had little effect on stimulus control when the schedule required the same number of responses in the presence of PCP or saline [e.g., the degree of

Table 1

Effects of changes in the schedule of reinforcement on stimulus control by PCP (top half of table) and saline (bottom half of table) injections. The first 5 data columns show the percentage of responses on the "correct" key (red key after PCP and green key after saline), the second 5 columns show the center-key latency in seconds, and the final 5 columns show the FR rate in responses per second for individual birds. Each value is a mean value for four sessions for each bird.

Schedule	Percentage of Responses on Red Key					Center-key Latency (Seconds)					Fixed-ratio Rate (Responses/sec)				
	Pigeon	62	61	58	60	59	62	61	58	60	59	62	61	58	60
FR 5 (FR 10)	97	81	85	88	85	3.0	4.9	10.4	3.2	27.2	0.7	1.9	1.8	1.2	2.1
FR 10 (FR 20)	97	86	100	91	75	1.7	2.6	3.8	2.5	4.5	1.4	2.0	2.1	1.7	1.8
FR 1 (FR 200)	100	68	96	61	88	26.2	98.4	400.0	20.6	108.8	0.3	0.8	1.0	0.8	0.6
FR 10 (FR 1)	96	99	95	89	92	7.9	5.4	9.8	2.9	22.6	0.5	0.7	0.9	0.6	0.4
FR 10 (FR 5)	86	79	82	95	74	5.4	1.3	2.3	2.4	3.7	1.0	1.2	1.8	1.4	1.5
	Percentage of Responses on Green Key					Center-key Latency					Fixed-ratio Rate				
	Pigeon	62	61	58	60	59	62	61	58	60	59	62	61	58	60
FR 5 (FR 10)	95	100	85	99	100	1.6	1.7	3.0	2.7	1.8	1.4	2.2	2.2	1.6	1.9
FR 10 (FR 20)	99	100	100	100	97	1.8	2.4	1.8	2.5	1.8	1.6	1.6	3.0	1.5	1.9
FR 1 (FR 200)	97	99	100	100	97	9.4	3.0	16.3	13.8	11.4	0.9	1.2	2.7	0.8	2.1
FR 10 (FR 1)	95	99	100	100	99	1.7	1.4	1.9	1.7	1.1	1.1	1.1	1.0	1.0	1.1
FR 10 (FR 5)	98	100	100	100	99	1.2	1.1	1.5	2.5	1.5	1.3	1.3	2.1	1.2	1.7

control under FR 5 (FR 10) and FR 10 (FR 5) was virtually identical].

Biasing Responding Toward One Key by Differential Schedule Variation

Figure 1 shows cumulative dose-effect curves for phencyclidine, pentobarbital, *d*-amphetamine, and repeated saline administration when biases toward responding on the PCP key were produced by reinforcing responding on the red key after PCP under FR 5 (FR 5) and reinforcing responding on the green key after saline under FR 25 (FR 5), or biases toward responding on the green key were produced by reversing these schedule contingencies, or no biases were produced by the schedule toward responding on either key by reinforcing responding on both keys under FR 10 (FR 5).

Baseline performance after PCP administration was fairly similar across all three schedules for all birds; however, when the schedule biased responding toward the PCP key [red key: FR 5 (FR 5), green key: FR 25 (FR 5)] Birds 62, 58, and 60 showed a greater tendency to respond on the PCP key after saline (brackets at G25 R5) than was

observed under other schedules employed in this study or under conditions of nonschedule bias in previous studies (McMillan, 1982; McMillan et al., 1982; McMillan & Wenger, 1983).

When the PCP cumulative dose-effect curves were determined, under conditions in which the schedule biased responding toward the PCP key, the generalization curve for PCP always fell to the left of the dose-effect curve for PCP that was obtained when the schedule biased responding toward the saline key. When the schedule was changed so as not to bias the birds toward either key, the cumulative dose-effect curve fell between the biased curves for 3 of 5 birds (Birds 62, 60, and 59).

These results show that the schedule of reinforcement is an important determinant of the generalization gradient for PCP. When the schedule biased responding toward the PCP key, there was an increased likelihood that low doses of PCP would result in responding on the PCP key, as compared to when responding was biased by the schedule toward the saline key.

It might be argued that these effects on

Fig. 1. Cumulative dose-effect curves for PCP (Column 1), pentobarbital (Column 2), *d*-amphetamine (Column 3), and saline (Column 4) with bias toward the PCP key [●, FR 5 (FR 5) red key and FR 25 (FR 5) green key], bias toward the saline key [○, FR 5 (FR 5) green key and FR 25 (FR 5) red key], and no bias [▲, FR 10 (FR 10) for both key colors]. Ordinate: percentage of ratios completed on the red (PCP) key (repeated on the right side of the figure for convenience). Abscissa: dose, log scale. Brackets show the range of control performances after 1.5 mg/kg PCP during control sessions and after saline administration at the beginning of the session during which the cumulative dose-effect curve was determined. Points represent single observations in each pigeon.

Table 2

Mean latency to respond on the center key and rate of FR responding on the side keys when responding was biased toward the PCP key (top frames) or toward the saline key (bottom frames), during determination of the cumulative dose-effect curve for phen-cyclidine.

Schedule	PCP Dose (mg/kg)	Center-key latency (seconds)					Choice-key rate (response/sec)				
		BIRD					BIRD				
		62	61	58	60	59	62	61	58	60	59
PCP: FR 5 (FR 5)	0	6.3	1.1	1.2	1.7	1.3	1.0	1.9	2.2	2.1	2.2
Saline: FR 25 (FR 5)	0.3	2.7	1.2	1.7	2.2	1.4	0.8	2.1	0.9	2.0	1.8
	0.56	2.3	2.1	17.2	2.5	2.3	0.6	1.3	2.0	1.9	1.3
	1.0	3.4	1.1	5.3	27.8	2.4	0.8	1.1	2.4	1.7	1.0
	1.7	2.4	2.2	7.6	27.8	5.4	1.0	0.8	2.5	2.7	1.2
PCP: FR 25 (FR 5)	0	1.4	1.1	1.1	1.2	1.5	1.8	1.6	1.7	1.8	2.4
Saline: FR 5 (FR 5)	0.3	1.1	1.3	2.4	1.6	1.3	1.8	1.7	2.2	1.5	1.8
	0.56	1.6	1.4	18.4	2.5	1.3	1.9	1.5	1.4	1.5	1.9
	1.0	1.4	1.4	6.8	2.2	1.5	1.3	1.7	2.0	1.2	1.5
	1.7	1.0	2.3	—	1.6	128.4	1.3	2.0	—	1.4	0.2

stimulus control are secondary to changes in rate of responding. For example, if PCP decreased rates of responding more under one schedule than another, the birds would require more time to finish the session. Because PCP is a relatively short-acting drug, the decreased blood levels of PCP toward the end of a long session might result in an apparent shift to the right in the dose-effect curve. Latencies to respond on the center key and rate of responding on the side keys during determination of the cumulative dose-effect curve for PCP are shown in Table 2 for the FR 25 (FR 5) and FR 5 (FR 5) schedules. The table shows that no such systematic rate or latency differences occurred.

Figure 1 also shows cumulative dose-effect curves for pentobarbital under the same conditions. As with PCP when the schedule biased responding toward the PCP key, lower doses of pentobarbital frequently produced more responding on the PCP key than occurred when the schedule biased responding toward the saline key. There were, however, some differences between the PCP and pentobarbital dose-effect curves. First, after pentobarbital, Bird 59 rarely responded on the PCP key under any condition. Second, there was a tendency for most behavior not to be as well controlled by pentobarbital as

by PCP, as shown by dose-effect curves that did not approach 100% responding on the PCP key after pentobarbital. Nevertheless, 4 of the 5 birds showed increased responding on the PCP key at lower doses of pentobarbital under conditions in which responding was biased toward the PCP key.

These experiments show that when the schedule biases responding toward the PCP key, pigeons are more likely to respond on the PCP key after low doses of pentobarbital than when the schedule biases responding toward the saline key.

Figure 1 also shows cumulative dose-effect curves for *d*-amphetamine under the same schedules. Birds 62, 60, and 58 showed a greater tendency to respond on the PCP key after *d*-amphetamine administration than after saline administration when the schedule biased responding toward the PCP key. In previous experiments in which responding was not biased by the schedule of reinforcement (McMillan, 1982; McMillan & Wenger, 1983), responses on the PCP key rarely occurred after *d*-amphetamine administration. Thus, biasing some birds' responding toward the phencyclidine key appeared to extend the response generalization curve to a drug (e.g., *d*-amphetamine) that did not show generalization under unbiased conditions.

Figure 1 also shows the effects of repeated administration of saline to these birds when the schedule of reinforcement biased responding toward the phencyclidine key. All birds showed values similar to control sessions after repeated saline administration during the same session. These experiments show that it is not the cumulative injections that result in drug-key responding, but rather it is the drug that produces this effect. Although the birds did make some responses on the PCP key after saline, when the schedule biased responding toward the PCP key, the amount of responding was similar to that seen during training sessions under saline, which was less than that seen during determination of the *d*-amphetamine dose-effect curve and considerably less than that seen during determinations of the PCP and pentobarbital cumulative dose-effect curves.

In the next series of experiments, the size of the FR unit was varied, rather than the number of FR units as had been done in the previous series. Responding was biased toward the PCP key by requiring smaller FR units when phencyclidine had been administered before the session [FR 10 (FR 3)] and larger FR units when saline had been administered before the session [FR 10 (FR 15)]. Subsequently, responding was biased toward the saline key by reversing these schedule contingencies. As in the previous series of experiments, the pigeons were trained for 4 weeks at each schedule parameter, with cumulative dose-effect curves for PCP, pentobarbital, and *d*-amphetamine being determined during the following 3 weeks.

Figure 2 shows the effects of PCP under these schedules. During control sessions, only Bird 58 responded on the PCP key after saline administration when responding was biased toward the PCP key [red key: FR 10 (FR 3), green key: FR 10 (FR 15)]. When responding was biased toward the saline key, virtually all responses after saline occurred on the saline key, and fewer responses occurred on the PCP key following PCP than when responding was biased toward the PCP key.

When cumulative dose-effect curves were determined for PCP (Figure 2), as in previous experiments, a greater percentage of responses occurred on the PCP key with schedule bias toward phencyclidine than occurred with schedule bias toward saline. For Birds 60 and 61, the PCP curve with schedule bias toward responding on the PCP key fell to the left of the PCP curve with responding biased toward the saline key. For Birds 58 and 59, the values were higher on the ordinate with PCP bias than with saline bias. (Bird 59 showed little responding on either key after PCP administration with saline bias.) Only Bird 62 showed little difference between the PCP cumulative dose-effect curves under the different schedule biases.

These experiments confirm observations made in the previous series of experiments: Biasing responding toward the PCP key by varying the schedule of reinforcement can result in a shift of the PCP curve to the left (the bird is "more sensitive" to lower PCP doses). The schedule manipulation in the second set of experiments (variation of FR unit size) did not appear to be as effective as the manipulation in the first set of experiments (variation of the number of FR units), since the separation of the PCP curves by schedule bias in the second set of experiments was not as great. However, these differences may be due to the exact parameters of the schedules that were studied. Nevertheless, in terms of relative numbers of key pecks required to produce the reinforcer, the FR 5 (FR 5) and FR 25 (FR 5) schedules show a total response ratio of 1:5 with a greater degree of PCP curve separation than is seen with FR 10 (FR 3) and FR 10 (FR 15) schedules in which the ratio of total responses under the two schedules is also 1:5.

Figure 2 also shows the effects of pentobarbital under the FR 10 (FR 3) and FR 10 (FR 15) schedules. For Birds 62, 61, and 60, the pentobarbital cumulative dose-effect curve under schedules biasing responding toward the PCP key fell to the left of this curve when the schedules biased responding toward the saline key. For Bird 59, the trend

Fig. 2. Cumulative dose-effect curves for PCP with bias toward the PCP key [●, FR 10 (FR 3) red key and FR 10 (FR 15) green key], or bias toward the saline key [○, FR 10 (FR 3) green key and FR 10 (FR 15) red key]. Ordinate: percentage of ratios completed on the red (PCP) key (repeated on the right side of the figure). Abscissa: dose, log scale. Brackets show the range of control performances after 1.5 mg/kg PCP or saline during control sessions and after saline administration at the beginning of the session during which the cumulative dose-effect curve was determined. Points represent single observations in each pigeon.

was in the same direction, although the shift in the curve was largely a function of effects at the 17 mg/kg dose. For Bird 58, there was a trend in the opposite direction. Despite this one exception, once again schedules that biased responding toward the PCP key tended to produce increased responding on the PCP key after pentobarbital.

Figure 2 also shows similar data for *d*-amphetamine under these schedules. Only Bird 58 showed appreciably more responding on the PCP key after *d*-amphetamine when schedules biased responding toward the PCP key.

In general, the data obtained under schedules where FR unit size was varied support the data obtained when the number of FR units was varied. Biasing responding toward the PCP key resulted in increased responding on the PCP key at lower doses of PCP, a similar effect with pentobarbital, and in one bird, increased responding on the PCP key after *d*-amphetamine. Thus, schedule-produced bias extended the PCP generalization curve to lower doses of the training drug (PCP), to lower doses of a drug (pentobarbital) with stimulus properties that may be similar to PCP (see McMillan, 1982; McMillan & Wenger, 1983), and in one bird even to a drug (*d*-amphetamine) which previously has not been shown to have discriminative-stimulus properties similar to PCP in the pigeon (McMillan, 1982; McMillan & Wenger, 1983).

Schedules Varying the Magnitude of Reinforcement

In experiments described previously, we attempted to produce bias toward responding on the PCP key by decreasing the response requirements after PCP administration relative to the response requirements after saline administration. In the next series of experiments, the response requirements were held constant by maintaining responding under a FR 10 (FR 5) schedule, while the duration of the food cycle was varied from 4 to 16 s.

Figure 3 shows the effects of PCP when responding was biased toward the PCP key

by providing a 16-s food cycle for responses on the red key after PCP administration and a 4-s food cycle for responses on the green key after saline administration, or when the conditions were reversed to bias responding toward the saline key. Under baseline conditions, the degree of stimulus control was similar across birds at both food-cycle durations with essentially no responding occurring on the saline key after PCP administration.

When cumulative dose-effect curves for PCP were determined, there were no consistent differences across birds. Birds 61 and 60 produced a PCP curve that fell to the left when responding was biased toward the saline key, but Bird 59 showed the opposite effect; the curves for Birds 62 and 58 were similar under both schedules. Thus, attempting to bias responding toward the PCP key by giving the bird a longer food cycle after PCP-key responding than after saline-key responding was not effective in shifting the PCP dose-effect curve toward responding on the PCP key at lower doses.

Table 3

Weight changes (grams) in individual birds during sessions when 4- and 16-s food cycles were correlated with saline or PCP administration. Each value is a mean of three determinations taken from the sessions immediately prior to sessions during which cumulative dose-effect curves were determined.

BIRD	Food-cycle duration (sec)			
	16-sec	4-sec	4-sec	16-sec
	Saline	PCP	Saline	PCP
62	9.7	3.0	1.3	0.7
61	6.7	-1.3	0.3	4.0
58	3.7	-3.0	0.9	3.7
60	6.0	0.3	1.3	2.3
59	8.0	-6.0	1.0	1.0

It might be argued that manipulation of the food cycle was ineffective in shifting the PCP dose-effect curves because the difference between 4- and 16-s food cycles was not sufficient to allow the birds to consume more food at the longer cycle duration. This was not the case, as shown in Table 3. With a 16-s food cycle after saline, all birds showed a mean weight gain during the three

Fig. 3. Cumulative dose-effect curves for PCP with bias toward the PCP key (●, 16-s food cycle with the red key and 4-s food cycle with the green key) or the saline key (○, 16-s food cycle with the green key and 4-s food cycle with the red key). Ordinate: percentage of ratios completed on the red (PCP) key (repeated on the right side of the figure). Abscissa: dose, log scale. Brackets show the range of control performances after 1.5 mg/kg PCP during control sessions, or saline during control sessions and after saline administration at the beginning of the session during which the cumulative dose-effect curve was determined. Points represent single observations in each pigeon.

baseline sessions immediately preceding the determination of the cumulative dose-effect curves, but 3 of 5 of those same birds lost weight during the corresponding PCP session with a 4-s food cycle. Similarly, after the PCP session with a 16-s food cycle, all birds showed a mean weight gain, but during the corresponding saline session with a 4-s food cycle, 3 of 5 birds gained less weight and one bird showed no difference. Thus, the longer food cycles resulted in greater weight gains, especially when the long food cycle was correlated with saline administration. PCP administration may have limited eating during the 16-s food cycle so that weight gains were less impressive than when the 16-s food cycle was correlated with saline administration.

The effects of pentobarbital on responding under the different durations of the food cycle are shown in Figure 3. Manipulation of the food-cycle duration was somewhat more effective in shifting the pentobarbital dose-effect curves than had been the case for PCP. When correct responses on the PCP key produced a 16-s food cycle and those on the saline key produced only a 4-s food cycle, the dose-effect curve was shifted to the left for Birds 58, 59, and 60, relative to the reciprocal condition. For the other two birds, the cumulative pentobarbital dose-effect curves were almost identical under both conditions.

It is not clear why biasing the birds' responding toward the PCP key by manipulation of the food-cycle duration should be more effective in shifting the pentobarbital dose-effect curves than in shifting those of PCP itself. We have suggested previously that with drugs where there is only partial overlap in stimulus properties between the training drug and the test drug, other effects of the drug (e.g., the degree to which it produces position responding or errors in discrimination) may play an important role (McMillan & Wenger, 1983). Perhaps the role of bias becomes more important when stimulus properties of the drugs only partially overlap; however, in the present studies there was no such tendency for bias

to be more effective with pentobarbital than PCP when the schedule of food delivery was manipulated rather than when the duration of food availability was changed.

Dose-effect curves for *d*-amphetamine were also determined with manipulation of the duration of the food cycle (data not shown). Under neither condition did any of the birds respond on the PCP key after *d*-amphetamine administration.

Signal-Detection Analysis

Figure 4 shows a signal-detection analysis for FR 25 (FR 5) and FR 5 (FR 5) schedules by the point estimate of discrimination (sensitivity) and of bias for PCP. The data show that as the dose of PCP increased (i.e., the intensity of the drug stimulus increased), the sensitivity increased (top row). The increase in sensitivity with dose was seen under both schedules, but the increases in sensitivity began to occur at a lower dose (0.56 mg/kg) under the schedule that biased responding toward the PCP key than under the schedule that biased responding toward the saline key.

The second row of Figure 4 shows similar data for bias. These data suggest that the birds showed a bias toward the saline key under both schedules (PEB was generally negative), even when one of the schedules was designed to bias responding toward the PCP key. At low doses of PCP (i.e., when the drug stimulus and the saline stimulus are presumed to be difficult to discriminate), there was a greater bias toward responding on the saline key under the schedule in which the lower response requirements were correlated with the saline key. As the dose of PCP increased, the bias decreased (became less negative) across both schedules, but higher doses were required to overcome the bias and the bias was overcome to a lesser extent when the schedule required fewer responses on the saline key than on the PCP key. Thus with low doses of PCP, responding is heavily biased, but as the dose increases the influence of bias becomes less and that of sensitivity becomes more important.

Fig. 4. Signal-detection analysis for FR 25 (FR 5) and FR 5 (FR 5) schedules by the point estimate of discrimination (PED) and point estimate of bias (PEB) and position-preference analysis for PCP. The top row shows the point estimate of discrimination, the second row shows the point estimate of bias, and the bottom row shows the percentage of FRs completed on the preferred (left or right) key. Movement of the points up the ordinate in the top row (from negative to positive) represents an increase in sensitivity (or discriminability). Movement of the points up the ordinate in the second row (from negative values toward zero) represents a decrease in bias. The preferred key is defined as that key position at which more than 50% of the responses occur. Each point represents a single observation in each bird as follows: ●, Bird 62; ○, Bird 61; ▲, Bird 58; △, Bird 60; □, Bird 59.

We have shown previously (McMillan & Wenger, 1983) that pigeons trained to discriminate phencyclidine from saline tend to respond at a particular position following some doses of PCP rather than tracking a key color. An analysis of position responding is shown in the bottom row of Figure 4 where the percentage of total responses on the preferred key is plotted. The preferred key was defined as the key position at which the bird responded most frequently; hence, responding on the preferred key was always greater than 50%. Responding on the preferred key is determined by the degree to which the random switching of colors from one key to another varies from a 50:50 ratio, as well as by any tendency of the bird to favor a particular position; however, casual observation suggests that it was unusual for more than 80% of the FRs at a particular key to be correlated with one color. The bottom row of Figure 4 suggests that considerable position responding occurred.

Comparison of sensitivity, bias, and position responding in individual birds is quite revealing. For example, under the schedule that biased responding toward PCP, Bird 58 (▲) showed little bias (PEB near zero), or sensitivity (PED near zero), after the 0.3 mg/kg dose of PCP, because this bird responded entirely at one position. As the PCP dose increased, there was an increase in sensitivity and a decrease in position responding. The other birds showed greater bias under this schedule at low doses of PCP, but three of these four birds also went through a phase in which responding occurred exclusively at one position before, at higher doses, position responding decreased and sensitivity increased. Thus, the picture that emerges under this schedule is that at low doses of PCP, sensitivity is low and bias is marked. As the dose increases, bias decreases, partly due to increased position responding and partly due to increased sensitivity. At high doses of PCP, sensitivity to the drug stimulus exerts the most powerful control with that of bias and position responding becoming less.

Under the reinforcement schedule that

biased responding toward saline, less position responding occurred, although Birds 61 (O) and 60 (Δ) did make all of their responses on one key after 1.0 mg/kg PCP. The modest PED value for these birds at 1.0 mg/kg PCP suggests that the birds' responding was under the control of the key position rather than the key color. In general, under this schedule, bias toward saline responding was

greater and there was less tendency for position responding to decrease bias before the increase in discriminability of the highest drug doses decreased bias.

Figure 5 shows a similar analysis for pentobarbital. The major difference between pentobarbital and PCP as shown by the signal-detection analysis and position-response analysis is that increasing doses of pentobarbital did not increase sensitivity to the same degree that increasing doses of PCP did. Position responding often was pronounced. Thus at low doses of pentobarbital, bias was frequently a major determinant of responding, especially under the schedule designed to bias responding toward saline. At higher doses, position responding tended to increase for most birds. If bias was already low, as with Bird 62 ($\bullet$) and Bird 60 (Δ) under the schedule designed to bias responding toward the PCP key, an increase in position responding did not reduce bias.

A signal-detection and position-preference analysis for *d*-amphetamine is shown in Figure 6. There was little tendency for sensitivity to increase with dose of *d*-amphetamine, and bias also showed minimal changes with dose. Bird 62 ($\bullet$) responded entirely at one position after all three doses of *d*-amphetamine, but the increase in position responding observed with intermediate doses of PCP and pentobarbital did not occur with *d*-amphetamine. Thus bias appeared to be the major determinant of where the bird responded, except for the bird that confined responding to one key after this drug under the schedule designed to bias responding toward PCP.

DISCUSSION

These experiments demonstrate clearly that, in pigeons trained to discriminate phencyclidine from saline, changes in the schedule of reinforcement can be made that bias responding either toward or away from increased responding on the drug key. Furthermore, these changes in the schedule of reinforcement also produce changes in responding on the PCP key when the pigeons

Fig. 5. Signal-detection analysis and position-preference analysis for pentobarbital under FR 25 (FR 5) and FR 5 (FR 5) schedules. Symbols and details as in Figure 4.

Fig. 6. Signal-detection analysis and position-preference analysis for *d*-amphetamine under FR 25 (FR 5) and FR 5 (FR 5) schedules. Symbols and details as in Figure 4.

are given pentobarbital, a drug which usually produces only partial response generalization in PCP-trained pigeons (McMillan & Wenger, 1983). In some cases, responding also occurred on the PCP key when pigeons were given *d*-amphetamine, a drug which does not produce response generalization from PCP without schedule bias (McMillan, 1982; McMillan & Wenger, 1983).

In these experiments, schedule changes in

which the number of FR units required to produce reinforcement was varied were more effective in separating the PCP dose-effect curves than were variations in the size of the FR unit required. It is not clear why this is so, inasmuch as the ratio of responses under the schedule requiring the fewest responses to the schedule requiring the largest number of responses was 1:5 under both sets of schedules. The absolute number of correct responses required was only slightly greater (30 and 150 responses) under the schedules in which the size of the FR unit was varied than the absolute number of correct responses required (25 and 125) under the schedule in which the number of FR units was varied.

The consequences of completing an FR on the incorrect key did vary across these schedules. Completing one FR on the incorrect key under FR 25 (FR 5), or FR 5 (FR 5) added only 5 additional responses to the total number emitted before reinforcement, whereas completion of one ratio on the incorrect key under FR 10 (FR 15) added 15 responses to the sequence. The consequences of large additions in the number of responses emitted prior to reinforcement if "errors" occurred might alter the extent to which the drug stimulus versus the schedule of reinforcement controls responding.

Both types of schedule change resulted in greater separation of the dose-effect curves for PCP than did changes in the duration of the food cycle. This does not necessarily imply that changes in the way a reinforcer is scheduled produce a greater bias than changes in the magnitude of reinforcement. It is quite possible that at other schedule values and reinforcement magnitudes, different results would have been obtained. It could be argued that bias decreased with time in these experiments, inasmuch as each procedure was less effective in separating dose-effect curves than the preceding procedure. Although the data are not presented, in subsequent experiments with these same birds we have combined some of the schedules used to bias responding in the present experiments and produced even greater

biases than those observed in the present experiments, indicating that bias does not necessarily decrease with time.

The application of signal-detection analyses to these experiments provided some especially interesting new data. Clearly, increasing the dose of the training drug (PCP) increased discriminability (sensitivity) and reduced bias. Stated differently, increasing the difficulty of the discrimination (e.g., lowering the "stimulus dose" of PCP) decreased discriminability and increased bias. This is a somewhat different result from those in several other stimulus-control experiments. For example, using tone duration as a stimulus, Logue (1983) showed that increasing the difficulty of the discrimination affected discriminability without changing bias.

With pentobarbital, there was some increase in sensitivity as the dose increased, but not as much as with PCP and the effect was not observed in all birds. Bias decreased with dose. At least part of this effect (decreased bias with little change in sensitivity) was caused by increased position responding, which tended to over-ride schedule bias. As the pigeon began to respond predominately on one key (e.g., the left key), bias was reduced because the schedule of reinforcement was randomly switching from key to key along with the key color.

In summary, the present experiments show that changes in the schedule of reinforcement in drug-discrimination experiments can shift the generalization gradient for the training drug (PCP) as well as influence response generalization for other drugs. The application of signal-detection and position-preference analyses to these drug-discrimination studies suggested that at low doses of PCP and pentobarbital, bias

was a major determinant of responding. As the drug dose increased, position responding became predominant and tended to decrease bias if the initial degree of bias was large. For PCP, further increases in dose produced an increased sensitivity (i.e., ability to discriminate between the drug and the non-drug state). *d*-Amphetamine did not produce a consistent increase in discriminability with increasing doses, nor did bias undergo much change.

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Received September 27, 1983
Final acceptance May 11, 1984