Pharmacology Biochemistry & Behavior, Vol. 15, pp. 145–148, 1981. Printed in the U.S.A.

Effects of Phencyclidine and Ketamine on Punished and Unpunished Responding by Pigeons[1]

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Received 12 December 1980

CHAIT, L. D., G. R. WENGER AND D. E. McMILLAN. *Effects of phencyclidine and ketamine on punished and unpunished responding by pigeons.* PHARMAC. BIOCHEM. BEHAV. **15**(1) 145–148, 1981.—Pigeons responded under a multiple fixed-interval fixed-interval schedule of food presentation in which responding in one component was suppressed by presentation of electric shock (punishment). High doses of pentobarbital, ketamine and phencyclidine produced decreases in rates of unpunished responding. At least two doses of each drug produced mean rates of punished responding greater than 200% of control rates. All three drugs disrupted normal patterning of both unpunished and punished fixed-interval responding. These results demonstrate that phencyclidine and ketamine have activity qualitatively similar to that of pentobarbital on schedule-controlled responding suppressed by electric shock presentation.

Pigeons Fixed-interval Punishment Phencyclidine Ketamine Pentobarbital

IN a preliminary study [4] we reported that phencyclidine increased rates of punished responding of pigeons trained under a multiple fixed-interval fixed-interval schedule of food presentation. More recently, two papers [3,10] have appeared which also examined the effects of phencyclidine and/or ketamine (a phencyclidine analogue) on punished responding by pigeons. Wenger [10] found that both phencyclidine and ketamine increased rates of punished responding under a two component fixed-ratio schedule, although to a much lesser extent than did pentobarbital. In the same study *d*-amphetamine did not increase rates of punished responding. The other study [3], using a multiple fixed-interval fixed-interval schedule, also showed that ketamine produced moderate increases in rates of punished responding. Pentobarbital produced greater increases in rates of punished responding than did ketamine, while *dl*-amphetamine caused only decreases in rates of punished responding. Phencyclidine was not examined in this study. Thus, in these two studies, phencyclidine and ketamine had effects on punished behavior similar to that of pentobarbital, and dissimilar to that of amphetamine.

The present study examined the effects of phencyclidine, ketamine and pentobarbital on punished and unpunished responding using the same schedule of reinforcement as that used by Brandão *et al.* [3]. The results demonstrate that phencyclidine, as well as ketamine and pentobarbital, increased rates of fixed-interval responding suppressed by electric shock presentation.

METHOD

Subjects

Four male White Carneaux pigeons, weighing between 587 and 678 g under a regimen of free food and water, served as subjects. These birds had received acute doses of phencyclidine, ketamine and pentobarbital in a preliminary study [4] but had not received any drugs for at least 90 days prior to beginning the present experiment. Throughout the study the birds were housed individually and maintained at 70% of their free-feeding weights. Water and grit were freely available in the home cages, but not in the test chamber.

Apparatus

A single-key pigeon operant chamber (Gerbrands Model G7311) was enclosed in a ventilated, sound attenuating box. A translucent plastic response key, 1.9 cm in diameter, was mounted in the center of a wall inside the chamber 20 cm above the chamber floor. This key could be transilluminated by various colored lights. A minimum force of 20 g was required to operate the response key. Opening of the key contacts defined a response. Each response produced auditory feedback by operating a relay. Directly below the re-

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sponse key was a rectangular opening through which the pigeon could be given access to the feeder. The chamber was illuminated during experimental sessions by two 4.5 W bulbs. During reinforcement the keylight and houselights were off and the feeder was illuminated by a different light. Electromechanical programming and recording equipment were located in an adjacent room.

Pigeons were implanted with stainless steel electrodes around the pubis bones [1]. The electrodes were connected to a plug attached to a leather harness which the birds wore at all times. During experimental sessions a jack was attached to the plug on the harness. The jack was connected to a flexible coiled wire attached to the ceiling of the chamber, allowing the bird free movement within the chamber. Electric current (110 V AC, 60 Hz) was delivered through a variable resistor so that the shock intensity could be adjusted for each bird (range: 2.0–8.0 mA). Shock duration was approximately 80 msec.

Procedure

The birds responded under a multiple fixed-interval 300-sec fixed-interval 300-sec schedule of food presentation (mult FI 300-sec FI 300-sec). One component of the multiple schedule was associated with a red keylight, and the other component with a green keylight. In each component the first response after 300 sec had elapsed produced 5-sec access to mixed grain, at which point the component ended. Components ended automatically without food presentation if a response did not occur within 60 sec after the 300-sec fixed-interval had elapsed. A 60-sec time-out period, during which the houselights and keylight were extinguished and responses had no programmed consequence, followed each component. The two fixed-interval components alternated throughout the session. Sessions ended after five presentations of each schedule component (about 60 min).

After typical patterns of responding were established under both components of the mult FI 300-sec FI 300-sec schedule, responses during one of the two FI components were programmed to produce electric shock (punishment component). For two birds (P-8 and P-16) every response in the presence of a green keylight produced an electric shock, while for the other two birds (P-9 and P-17) every response in the presence of a red keylight produced shock. All birds began the session with the nonpunishment component. Shock intensities were adjusted for each bird in an attempt to produce rates of responding during the punishment components that were less than 25% of the rates during the nonpunishment components. Before drug treatments began, a modification was made in the schedule such that the session began with presentation of a white keylight. Thirty responses on the key (fixed-ratio 30) resulted in 5-sec access to grain, followed by a 60-sec time-out and presentation of the first fixed-interval component. This modification was made in an attempt to reduce variability in responding during the first fixed-interval.

Phencyclidine hydrochloride, ketamine hydrochloride and sodium pentobarbital were dissolved in 0.9% NaCl solution. All drug injections were given into the breast muscle immediately before the start of the session in a volume of 1.0 ml/kg body weight. Similar volumes of 0.9% NaCl served as control injections. All doses are expressed as the salt. The dose-effect curve for pentobarbital was determined first followed by ketamine and phencyclidine. Doses of each drug (or saline) were given in mixed order, no more than twice

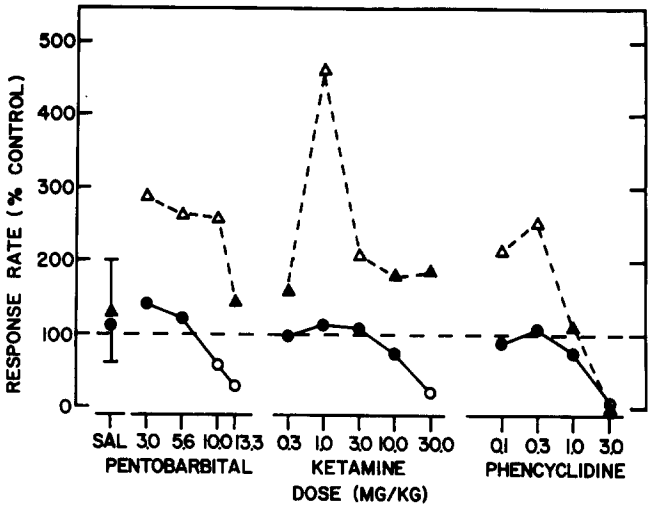

FIG. 1. Mean rates of fixed-interval responding in nonpunishment (circles) and punishment (triangles) components. Points at SAL represent the mean of three saline determinations for each of four birds; bars around these points indicate the 95% confidence intervals calculated using n=4, the smallest n used for the dose-effect curve determinations. All other points represent the mean of one or two determinations for each of four birds. Open points (those which lie outside the appropriate confidence interval around SAL) represent significant changes.

weekly, usually on Tuesdays and Fridays. Generally one determination at each dose level was made for each bird; redetermination of some doses were made for birds that finished the protocol before the others. When two determinations of a dose were made, the mean of the dependent variable was employed. One saline determination was made during each of the three dose-effect curve determinations. A noninjection control session preceded each drug session.

Measurement of Drug Effects

Average rates of responding were computed in responses per sec from elapsed time meters and digital counters for both components. All days immediately preceding drug days for each dose-effect curve determination were used to calculate a control mean and standard deviation. Response rates after drug or saline injections are expressed as percent of that control value. For the analysis of quarter-life [6], responses were collected separately for each 30-sec segment of the 300-sec fixed-intervals and were cumulated over the entire session for both schedule components. Quarter-life values were determined by linear interpolation as the proportion of the interval elapsed before 25% of the total responses in the interval were made [5].

RESULTS

Control Responding

Mean rates of unpunished responding ranged from 0.38 (bird P-17) to 0.49 (bird P-9) resp/sec, and remained stable throughout the study. Mean rates of punished responding ranged from 0.051 (bird P-8) to 0.071 (bird P-9) resp/sec, but tended to decrease over time, so that by the end of the experiment the mean ratio of rates of punished to unpunished responding (0.08) was one-third its initial value (0.24), de-

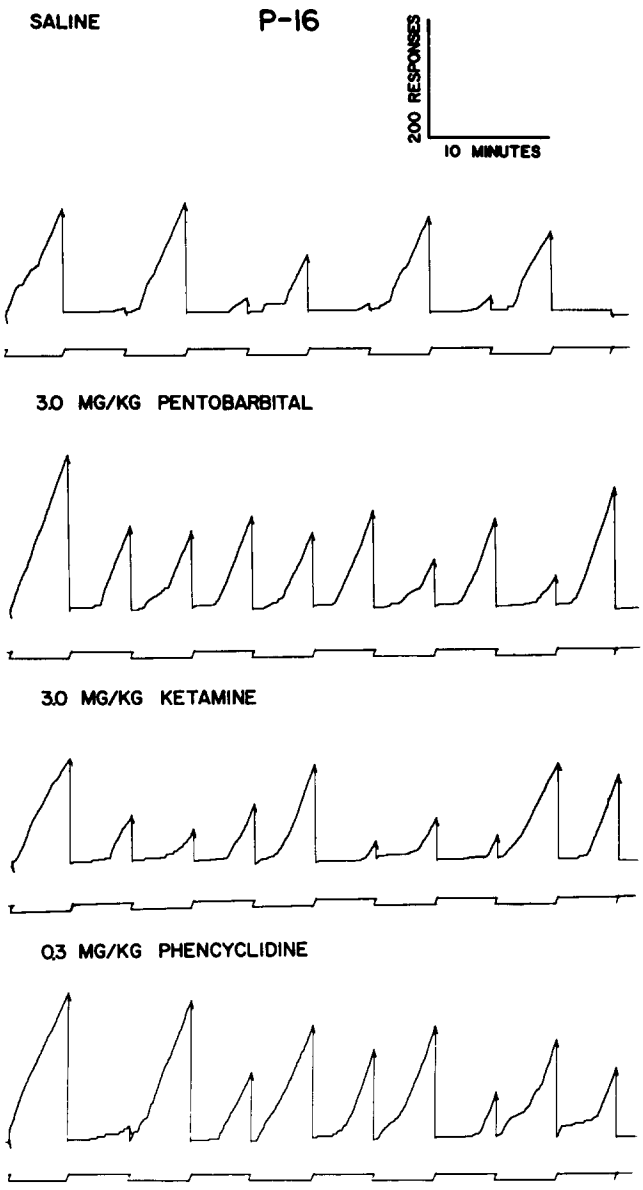

FIG. 2. Cumulative records for subject P-16. Time is displayed along the x-axis; responses along the y-axis. Downward deflection of the bottom pen tracing indicates the nonpunishment component was in effect. The response pen reset after each change of components. Short diagonal deflections of the response pen indicate food delivery.

spite the fact that the shock intensities were in the same range as those used initially. Mean ratios of rates of punished to unpunished responding (across the entire study) ranged from 0.11 (bird P-8) to 0.18 (bird P-17).

There was a consistent difference throughout the study in control quarter-life values for punished vs unpunished responding. Quarter-life values were larger for punished (group mean 0.75) than for unpunished (group mean 0.51) responding; this effect was observed for all birds and was statistically significant (Student's t test, $p<0.05$). Examination of cumulative records indicated that the higher quarter-life values observed with punished responding were the result of longer periods of no responding at the beginning of punishment intervals.

TABLE 1

EFFECTS OF PENTOBARBITAL (PB), KETAMINE (K) AND PHENCYCLIDINE (PCP) ON GROUP MEAN QUARTER-LIFE VALUES*

Drug	Dose	Quarter-life	
		Unpunished component	Punished component
SAL†		0.49	0.71
PB	3.0	0.41	0.66
	5.6	0.41	0.57
	10.0	0.37	0.27
	13.3	0.16	—
K	0.3	0.54	0.72
	1.0	0.50	0.70
	3.0	0.45	0.68
	10.0	0.51	0.53
	30.0	0.37	0.32
PCP	0.1	0.57	0.73
	0.3	0.47	0.73
	1.0	0.36	0.46
	3.0	—	—

*Quarter-life values were not calculated if the total number of responses cumulated over the entire session for a component was less than ten. Mean quarter-life values are not shown for doses for which the values for two or more birds were uncalculable.

†SAL values represent the mean of three saline determinations in each of four birds.

Effects of Drugs on Responding

Figure 1 shows the effects of pentobarbital, ketamine and phencyclidine on mean overall rates of unpunished (circles) and punished (triangles) responding. High doses of all three drugs produced significant decreases in rates of unpunished responding. No dose of any drug produced significant increases in rates of unpunished responding; however, small to moderate increases were observed for all birds after 3.0 mg/kg pentobarbital.

In contrast, at least two doses of each drug resulted in significant mean increases in rates of punished responding. Three of the four birds showed increased rates of punished responding after each of the three drugs, while the other bird (P-17) proved to be less sensitive to the rate-increasing effects of all three drugs. (The large increase in mean rate of punished responding seen in Fig. 1 after 1.0 mg/kg ketamine was due to a response rate of 1100% of control for bird P-9.) The highest dose of phencyclidine (3.0 mg/kg) completely suppressed punished responding of all birds, and was the only dose of any drug to produce a significant decrease in rates of punished responding.

Figure 2 shows cumulative records from bird P-16 after injection of saline, 3.0 mg/kg pentobarbital, 3.0 mg/kg ketamine and 0.3 mg/kg phencyclidine. The saline (top) record shows that responding during punishment components was consistently suppressed to levels far lower than those maintained during nonpunishment components. In addition, the periods of little or no responding early in the intervals are

much longer for punishment than nonpunishment components. The lower three records in Fig. 2 indicate that, for this bird, these doses increased rates of punished responding relative to rates of unpunished responding.

All three drugs tended to decrease quarter-life values for both punished and unpunished responding with increasing dose (Table 1). Despite the higher control quarter-life values for punished vs unpunished responding, quarter-life values for punished responding were lowered to about the same values as those for unpunished responding after high doses of each drug.

DISCUSSION

The results of the present study confirm our preliminary report [4] that phencyclidine can increase fixed-interval responding suppressed by electric shock. Similar results obtained here with pentobarbital and ketamine provide a replication of the findings of Brandão *et al.* [3]. The capacity of phencyclidine and ketamine to increase rates of fixed-ratio responding suppressed by electric shock presentation has been demonstrated by Wenger [10]. Thus, in their effects on punished responding, phencyclidine and ketamine are similar to pentobarbital and unlike amphetamine, which, under the same conditions, did not increase rates of punished responding [3,10]. In contrast, Wenger [9] concluded that the effects of phencyclidine and ketamine on unpunished responding of pigeons under a multiple fixed-ratio fixed-interval schedule more closely resembled those of *d*-amphetamine than those of pentobarbital. The present results thus further underscore the unusual spectrum of behavioral activity of phencyclidine and related compounds.

The effects of phencyclidine and ketamine on unpunished fixed-interval responding obtained here differ in one respect from those previously reported. With pigeons trained under a multiple fixed-ratio fixed-interval schedule of food presentation, low doses of phencyclidine and ketamine produced small (about 20%) but consistent increases in rates of fixed-interval responding [9]. Since baseline rates of responding and quarter-life values were very similar between that study [9] and the present one, the absence of increases in rates of unpunished responding after phencyclidine and ketamine may be due to an interaction between the nonpunishment and punishment components of the schedule or the longer fixed-interval (600 sec) used by Wenger [9]. Ketamine produced only a slight increase in rates of unpunished responding at one dose in the study that used the same schedule of reinforcement as that used here [3].

The effects of phencyclidine and ketamine on quarter-life values for unpunished responding agree well with those reported by Wenger [9]. The present results further demonstrate that these drugs also disrupt normal patterning of punished responding.

The present study found significantly higher quarter-life values for punished than for unpunished responding. Three studies which used comparable two-component fixed-interval schedules in which responses during one component were punished [3, 7, 8] did not report quarter-life values, although one of these studies [3] did note that the initial pause was longer in punishment than in nonpunishment fixed-intervals. Although it was reported that quarter-life values did not change as a function of punishment intensity [2], the present results suggest that punishment of fixed-interval responding can alter the temporal distribution of responding.

ACKNOWLEDGEMENT

The authors thank William C. Hardwick for preparation of the figures.

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