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Effects of Morphine on Fixed Interval-Induced Escape from Food Reinforcement

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SLIFER, B. E. *Effects of morphine on fixed interval-induced escape from food reinforcement.* PHARMAC. BIOCHEM. BEHAV. 16(5) 683–687, 1982.—Pigeons were trained to respond on a fixed-interval 3-min (FI 3 min) schedule of food reinforcement. During each 1-hr session responses on a second response key produced a timeout from the FI schedule. The food reinforcement schedule maintained characteristic FI responding. The escape-timeout responses occurred during the period of low response rates following reinforcement. Morphine (0.25, 0.5, 1.0 mg/kg) produced dose-related rate-dependent decreases in mean fixed-interval response rates. As morphine dose increased, there was an increased tendency for the rates within the interval to converge from a variety of predrug rates to a common, low rate of responding. The effect of morphine on the schedule-induced escape responses was to increase the mean number of escapes at doses of 0.25–0.5 mg/kg and to decrease the escapes at the highest dose of 1.0 mg/kg. The mean duration of the escape-timeouts was increased by the 3 doses of the drug, with the longest durations occurring at the 0.5 mg/kg dose. There was a great deal of variability between subjects on these measures and the dose effects did not reach statistical significance. The present study extends the analysis of drug effects on schedule-induced escape to fixed-interval-induced escape responding and includes the drug morphine.

Fixed-interval Schedule-induced escape Morphine Pigeons

ESCAPE from a schedule of positive reinforcement, as a schedule-induced behavior, has been demonstrated with different types of controlling schedules. Escape in this instance means the organism will respond to initiate a timeout from a schedule or stimulus associated with positive reinforcement. Azrin [1], who first reported the occurrence of schedule-induced escape, recorded the responses as an adjunct to a fixed-ratio schedule of food reinforcement. Since Azrin's study several others have reported fixed-ratio induced escape in pigeons [19,23] and rats [22]. Spealman [21] recently reported escape from a reinforcement schedule in squirrel monkeys using a variable-interval schedule of intravenous cocaine reinforcement. In 1972, Brown and Flory [2] studied schedule-induced escape in pigeons key pecking on a fixed-interval of food reinforcement.

It has been demonstrated that a drug can have similar effects on behaviors maintained by different types of reinforcing stimuli. Now, with schedule induction producing a separate class of behaviors (i.e., schedule-induced), behavioral pharmacological studies of these behaviors can provide information as to whether a drug has similar effects on behaviors generated and maintained by different events. Studies which have examined the effects of drugs on the schedule-controlled and schedule-induced behaviors within the same experimental session report differential drug effects on the two types of behaviors. For example, Moore and Thompson [15] found that cocaine decreased schedule-induced attack responding in pigeons at doses that did not affect the food schedule-controlled responding. Byrd [5] reported that cocaine had differential effects on schedule-controlled key pressing and schedule-induced drinking in the chimpanzee. Differential effects have also been found for chlordiazepoxide [20], chlorpromazine [4,20], scopolamine [16], haloperidol [8] and *d*-amphetamine [3, 7, 17]. In these studies, however, the schedule-controlled and schedule-induced responses differed in their response topography (e.g., bar pressing and licking). This might account for the different effects of a drug on each type of response. A few studies have addressed this question of response topography [6, 10, 18, 19]. McKearney [10] conducted a study with rats which involved licking as the fixed-interval schedule-controlled and the schedule-induced response. Chlordiazepoxide and methamphetamine produced different effects on the two types of responses.

The fixed-interval schedule generates, within an inter-reinforcement interval, a positively accelerating pattern of responding characterized by low rates of responding in the initial segments of the inerval immediately following reinforcement followed by high rates of responding just prior to the next reinforcement. Brown and Flory [2] found that the

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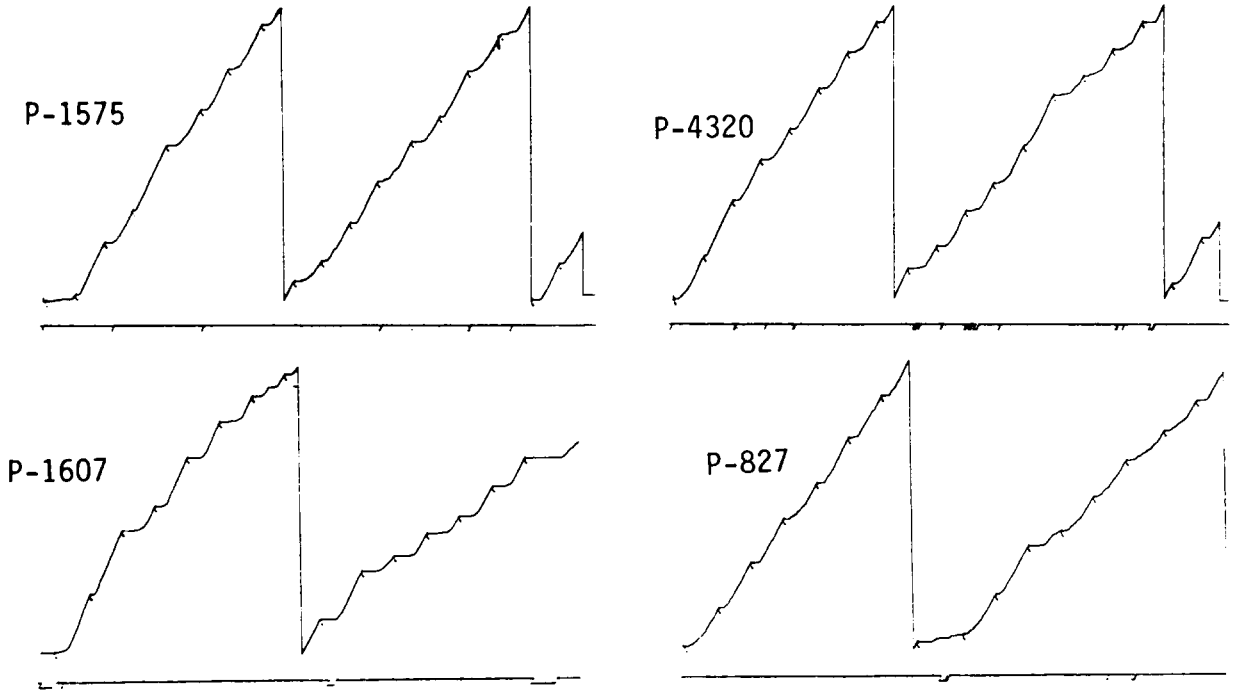

FIG. 1. Cumulative records for key pecking on a FI-escape schedule. The escape responses are shown on the bottom line (event pen).

schedule-induced escape response occurred, as other schedule-induced behaviors, most frequently during the immediate post-reinforcement period which included the first two quarters of the interval when FI responding was relatively low. The FI schedule is particularly well suited for pharmacological studies because the effects of a drug on both low and high baseline rates of responding can be measured within a single component. The present experiment was designed to extend the previous findings [19] of differential effects on schedule-induced-escape responding in pigeons to another drug (morphine) and the fixed-interval-escape schedule where the gross, physical topography of the two responses were similar.

METHOD

Subjects

The subjects were four adult, male White Carneaux pigeons. The subjects had had brief experience in an operant schedule-induced attack situation. The birds were individually housed and maintained at 70–80% of their free feeding weight by post-session feedings and had free access to water and pigeon grit in their home cages.

Apparatus

The sessions were conducted in a three-key pigeon chamber within a ventilated, sound attenuation enclosure. The three response keys were located on the front panel, 18 cm above the grid floor and 4 cm apart. The keys were illuminated by 7 W bulbs. The left key was covered and inoperative. The grain reinforcement magazine was present through an opening on the front panel below the center key. During presentation, the grain magazine was illuminated. A 28 W houselight was centered above the front panel. Events within the chamber were controlled and recorded by electromechanical equipment located in a separate room. White masking noise was present, immediately outside the chamber.

Behavioral Procedure

The subjects had been trained to work on a fixed interval schedule with the maximum interval value of 3 minutes (FI 3 min). The center green key was the fixed-interval key. The first response on this key after 3 minutes had elapsed resulted in 4 seconds access to grain. The sessions were conducted at least 6 days a week and were 60 minutes in duration. The right key was the red escape key. At the start of the session, a response on this key was required to turn on the fixed interval, the houselight and the green center key light. During the session, escape key responses turned off the fixed interval contingency, the key light and houselight. The interval timer stopped while in the timeout. The escape timeout remained in effect until the bird made another response on the escape key to turn on the stimulus lights, reinstate the fixed interval schedule contingencies and resume timing the interval.

Pharmacological Procedure

Morphine sulfate was administered 30 minutes before the sessions. Two injections of each of the following doses (salt weight) were given in descending then ascending order: 0.25, 0.5, 1.0 mg/kg body weight. The injections were i.m. into the pectoral muscle in a volume of 1 ml/kg, with 50% of the injection given into each side. Drug test days were separated

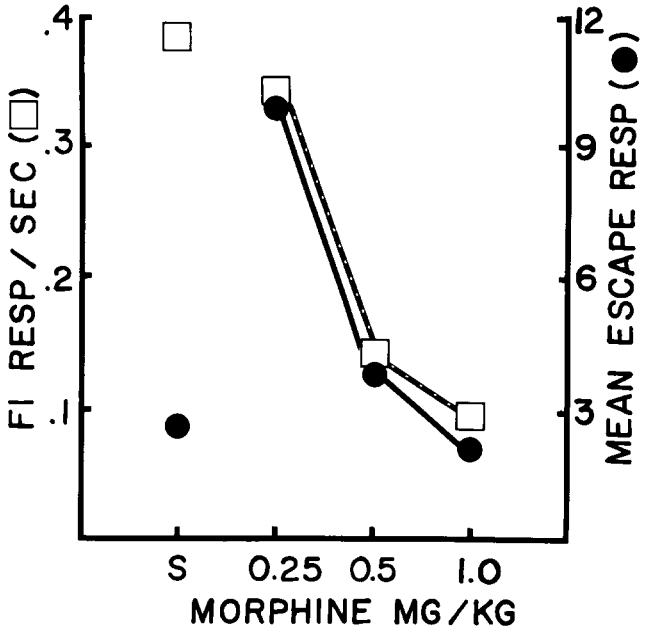

FIG. 2. The effects of the three doses of morphine on the rates of fixed-interval responding (□) and escape responses (●). Each data point is the mean of all four birds. Saline control is indicated at point S.

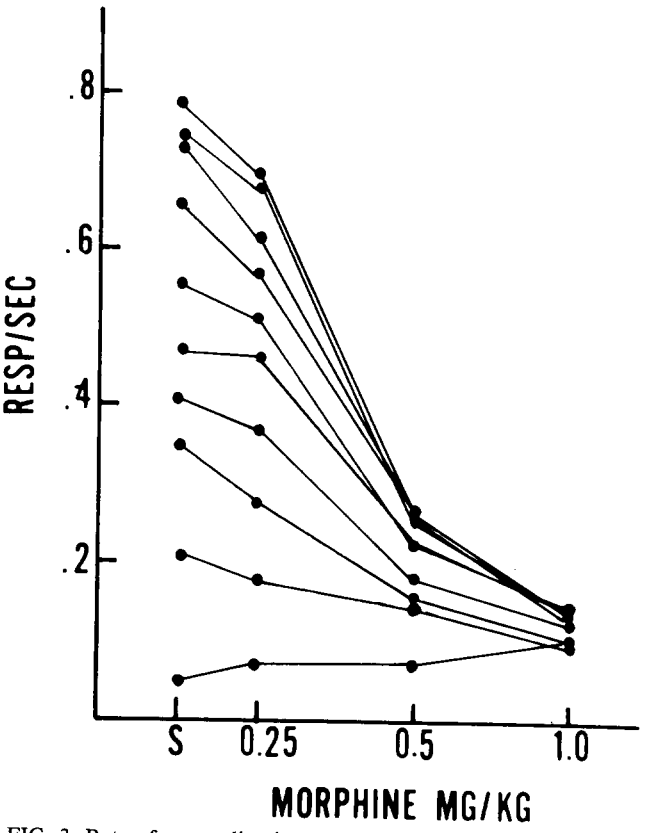

FIG. 3. Rate of responding in each tenth of the 3 min interval as a function of morphine dose. Each data point represents the mean of all subjects during an interval segment.

by at least two nondrug days. Saline was given as a control (placebo) injection.

RESULTS

The fixed-interval 3-min schedule of reinforcement generated positively accelerated patterns of responding characteristic of fixed-interval performance. The escape-timeout responses occurred during the first quarter of the interval following the grain reinforcer. Figure 1 shows an example of cumulative records from a control session which show the scallop pattern of FI responding and the schedule-induced escape responses.

The group means for rates of FI responding (calculated minus the time in escape-timeout) and the mean number of escape responses are presented in Fig. 2. The three doses of morphine produced a dose related decrease in the mean rates of fixed-interval responding. Analysis of variance revealed highly significant dose effects, $F(3,21)=13.60$, $p<0.001$. A post-hoc Tukey test showed significant effects for the 1.0 mg/kg morphine dose. The mean number of escape-timeout responses were increased above saline rates by the 0.25 and 0.5 mg/kg dose of the drug while the highest dose of 1.0 mg/kg morphine resulted in escape responses just below saline control rates. The dose effects did not reach statistical significance, $F(3,21)=1.51$, due to the large variability between subjects.

Figure 3 shows the rate of food maintained responding in each tenth of the interval as plotted against the drug treatments. Each data point is the mean rate of responding for all subjects during the interval segments. This type of plot demonstrated a dose related convergence in the pattern of responding from a variety of predrug rates to a common rate [9]. The convergence was slight at the lowest morphine dose of 0.25 mg/kg but increased with the 0.5 mg/kg dose and still more convergence was seen with the highest dose of 1.0 mg/kg. This tendency to converge to a common rate throughout the interval is shown on the cumulative records from a session at the 0.5 mg/kg dose (Fig. 4). The positive acceleration, or scallop pattern, is disrupted and the inter-reinforcement rate of responding becomes more consistent. The response pattern of bird P-4320, in contrast to the other 3 birds, was variable between the individual 3 minute intervals with some intervals showing a flattening of the scallop, and other intervals maintaining the characteristic FI pattern.

When the total minutes in timeouts are compared with the mean number of escape responses (Fig. 5), it can be seen that, while all 3 doses of morphine produced increases in the duration of the schedule-induced timeouts, the dose of 0.5 mg/kg resulted in the greatest increase. The peak in the dose-effect curve then, differs for the escape-timeout durations and the mean number of escapes.

Upon visual observation of the cumulative records there appeared to be a tendency for the temporal location of the escape responses to change with morphine administration which was seen as a shifting from the first quarter of the interval to later into the FI.

DISCUSSION

The present study shows that morphine at the lowest dose (0.25 mg/kg) produced differential effects on the two types of behavior: fixed-interval schedule-controlled and schedule-induced key-peck responses of pigeons. The positively ac-

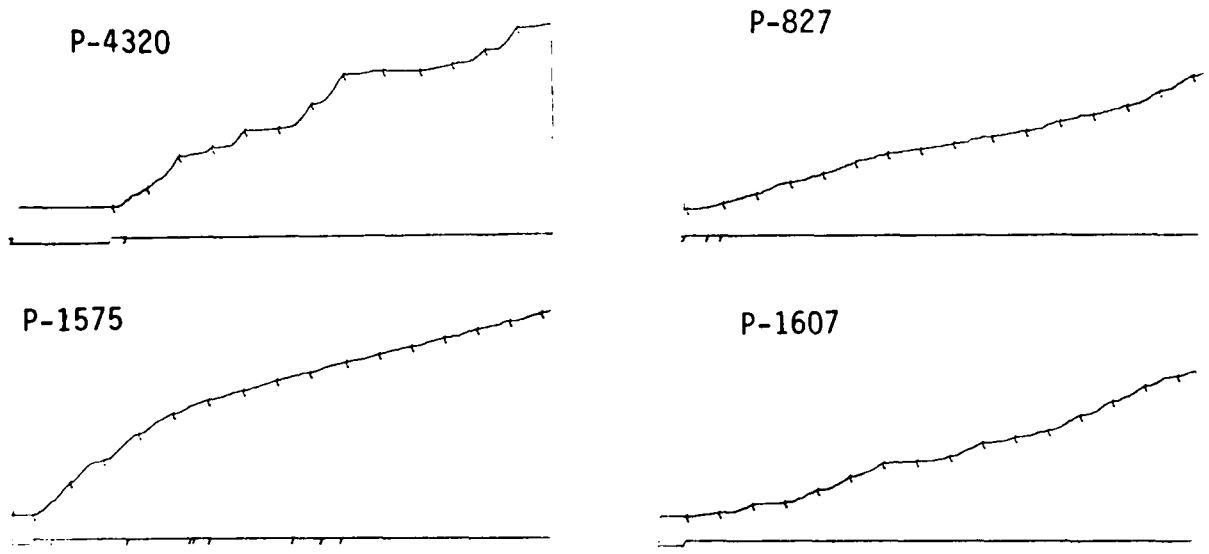

FIG. 4. FI-escape responding for the four birds with the 0.5 mg/kg dose of morphine.

celerated FI responding with the escape-timeout responses occurring during the period of low response rates following reinforcement is similar to the FI-escape responding in pigeons reported by Brown and Flory [2] and consistent with other schedule-induced behaviors.

The rate decreasing effect of morphine on the fixed-interval schedule-controlled responding was dose dependent with the greatest reduction in rates produced by the highest dose of 1.0 mg/kg. The disruption of FI patterning is observed when the rates for each tenth of the FI are plotted against morphine dose (Fig. 3). A dose related convergence in rates is seen. As morphine dose increased, there was an increased tendency for the rates within the interval to converge from a variety of predrug rates to a common low rate of responding typical of many other psychoactive drugs, amphetamine being the classic example. Only the lowest rate of responding (the first tenth of the interval) was increased by all three doses of morphine. The failure to find increases in FI responding was surprising in light of other reports of rate increases in FI responding by morphine in pigeons [13,14].

The increase in the schedule-induced escape responses with the lower doses of morphine occurred in three of the four subjects. The fourth bird (P-4320) showed only decreases by the drug. This might have been related to the fact that this subject had the highest baseline rate of escape responding, although no consistent relationship of drug effect to baseline rate of escape was seen with the other three individual subjects. Still, these morphine effects on responding may be due to the baseline rate of the ongoing behaviors, that is the effects maybe rate-dependent. The overall, higher fixed-interval rates were only decreased while the schedule-induced escape responses, by their very nature (e.g., producing a timeout) low rate responses relative to the schedule-controlled key pecking, were increased by the low dose of morphine. The rate convergency plot (Fig. 3) indicates a modest rate-dependent effect within the fixed-intervals. McMillan [11] reported the effects of *d*-amphetamine and caffeine on schedule-controlled FI lever pressing and schedule-induced licking in rats to be rate-dependent and caffeine also produced differential effects on the two behaviors. The escape rate increase produced by morphine is opposite the effect seen with amphetamine. An earlier report [19] found dose-related decrease in schedule-induced escape responses with *d*-amphetamine. These findings are nonetheless, in agreement with the McMillan and other reports of differential drug effects on schedule-controlled operants and various schedule-induced behaviors [3, 5, 6, 7, 10, 11, 15, 20]. There are two studies which, because of their emphasis on response topographies, are

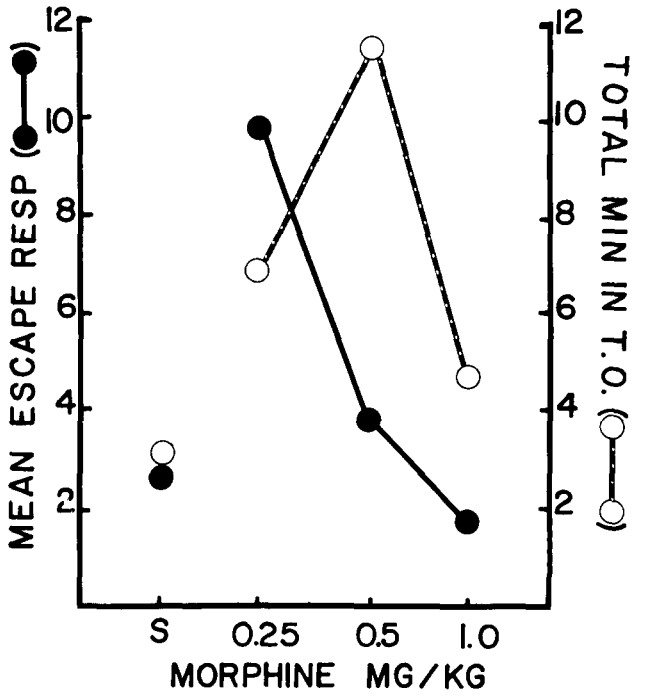

FIG. 5. Morphine effects on the mean number of escape responses (●) and the total minutes in escape-timeout (○). Each data point is the mean of all four birds. Saline control is indicated at point S.

particularly relevant. In the 1973 McKearney study [10] rates of fixed-interval schedule-controlled licking responses were increased by the lowest dose of methamphetamine and decreased by the highest dose, while schedule-induced licking was unaffected except by the highest dose.

The morphine dose-effect curve also differs for the two measures of the schedule-induced response (i.e., mean number of responses, timeout duration). While the pigeons are making the greatest number of escapes at the 0.25 mg/kg level they are spending less absolute time in the escape condition than they do at the 0.5 mg/kg dose of morphine. This difference in the drug effect on the escape response may be due to the fact that a response on the escape key was required to initiate the session and may thus be confounding the results. The most disparate effects of the drug occur at the 0.5 mg/kg dose. The average number of escape responses was near saline levels, however the absolute time in the escape-timeout was increased to the longest mean duration by this dose. Additionally, the responses on the fixed interval were markedly decreased by this dose.

In general, it appears that the low dose of morphine (0.25 mg/kg) resulted in differential effects on the two behaviors producing a slight decrease in food-controlled responding and an increase in schedule-induced escape responses and a corresponding increase in escape-timeout duration. At the higher doses the drug produced a general depression of operant behaviors. When not in the timeout the bird's FI response rates were decreased; in addition, although the number of escape responses differed only slightly from saline, when the animals did make escape responses they stayed in the timeout condition for longer periods of time.

The absence of a rate increasing effect by morphine on the fixed-interval schedule-controlled responding parallels the findings by McMillan and Leander in their 1976 study [12]. The authors reported only rate decreases in rat's fixed-interval responding with morphine administration. The drug also produced a decrease in the concurrent schedule-induced polydipsia. Although different species of subjects were used, these results plus those of the current study, suggest that the drug effects on the FI schedule-controlled responding may be related to the occurrence of a concurrent schedule-induced behavior. In the McMillan and Leander experiment [12] the effects of the drug were similar for the schedule-controlled and schedule-induced behaviors. The present findings of an increase by morphine in the schedule-induced escape responding suggests that the drug may diversely affect different forms of schedule-induced behaviors, just as it has disparate effects on schedule-controlled versus schedule-induced behaviors.

Although the rate changes were in different directions, the present study extended the analysis of drug effects on schedule-induced escape to fixed-interval-escape responding and includes the drug morphine. Additionally, the present results further demonstrate the contrasting effects of a drug, within a session, on two topographically similar responses which are differentially maintained.

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