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Effects of Drugs on Response Duration Differentiation III. Acute Variation of Reinforced Duration

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McMILLAN, D. E., S. L. ADAMS, G. R. WENGER, G. Y. H. McCLURE AND W. C. HARDWICK. *Effects of drugs on response duration III. Acute variation of reinforced duration.* PHARMACOL BIOCHEM BEHAV **48**(4) 941–957, 1994.—Rats trained to hold a lever down for at least 1.0 s but less than 1.3 s could differentiate the reinforced response duration on about 50% of the trials. The response duration frequency distribution was a normal distribution with a peak near the minimum reinforced response duration. Dose–effect curves were determined for the effects of phencyclidine (PCP) and methamphetamine. Subsequently, rats continued to be trained for 3 days a week with responses between 1.0 and 1.3 s reinforced, but on days when injections were given either the maximum reinforced duration was increased to 2.3 s, or the minimum reinforced duration was lowered to 0.5. When the maximum duration was increased to 2.3 s, the percentage of reinforced responses increased to 60% and when the minimum reinforced duration was decreased to 0.5 s, the percentage of reinforced responses increased to 89%. Despite the increased percentage of reinforced responses when the time window was widened, the effects of PCP and methamphetamine were not changed. These data suggest that the effects of drugs on response duration differentiation are not greatly influenced by transient changes in reinforcement frequency.

Response duration differentiation Reinforcement frequency Phencyclidine Methamphetamine Rats

THE differentiation of response durations can be established by differentially reinforcing only those responses that terminate with durations longer than some predetermined minimum, but shorter than a somewhat longer maximum duration (1,2,5–9). Recently, Hudzik and McMillan (3,4) reinforced lever-press durations of rats that were greater than 1.0 s in duration but less than 1.3 s. The rats generated a normal distribution of response durations with a peak near the minimum reinforced duration. This performance was sensitive to the effects of a variety of drugs.

When response durations greater than 1.0 s in duration but less than 1.3 s were reinforced, methamphetamine decreased the percentage of responses falling within the reinforced interval at doses of 1 and 3 mg/kg. The decreased accuracy was caused by a flattening of the distribution of response durations with increases in response durations both too short and too long to produce the reinforcer (3). Phencyclidine (PCP) also decreased the percentage of responses falling within the reinforced interval, but did so primarily by shifting the distribution of response durations toward shorter times (3).

Unlike many schedules of reinforcement (e.g., fixed-interval schedules) where performance can vary over a wide range without affecting reinforcement frequency, changes in performance under schedules such as the response duration differentiation often change reinforcement frequency considerably. Thus, there are two behavioral variables that can contribute to the effects of a drug on response duration differentiation, the effect of the drug on the animal's ability to differentiate duration and the subsequent effects of a lowered rate of reinforcement. The present study was a first attempt to separate these factors. Rats trained previously to differentiate response durations greater than 1.0 but less than 1.3 s were tested with a wider reinforcement window on days after injections were given, in an attempt to keep the rate of reinforcement high after the administration of methamphetamine and PCP, drugs that flatten (methamphetamine), or shift to the

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left (PCP) the distribution of response durations. The reinforcement window was broadened in separate experiments by decreasing the minimum response duration required for reinforcement from 1.0 to 0.5 s and increasing the maximum duration that could be reinforced from less than 1.3 s to less than 2.3 s on days when drug or placebo injections were given.

METHOD

Subjects

Four of the same five male Sprague–Dawley rats used in a previous experiment (4) were used in these experiments. At the beginning of the experiments two of the rats were 18 months of age and the other two were 14 months old. The rats were individually housed in a room on a 12L : 12D cycle (illuminated from 0700 to 1900 h) and maintained at 85% of their free-feeding weights by food earned during testing and supplemental postsession feeding. They had free access to water in the home cage, but not in the test cage. All of the rats had considerable experience in responding under the schedule and had received a number of drugs prior to these experiments (3,4).

Apparatus

Rats were tested in Gerbrands (Model #7400) two-lever chambers enclosed in Gerbrands (Model #7200) sound-attenuating chambers. The test chambers were equipped with stimulus lights over the levers and a houselight on the chamber ceiling. A pellet feeder permitted the delivery of 97 mg food pellets (Noyes Corp.) into a food cup mounted between the levers. Programming and recording were controlled by microprocessor equipment located in an adjacent room.

Procedure

All rats had been trained previously to differentiate response durations by differential reinforcement as described previously (3,4). At the beginning of these experiments, the rats were performing at a mean accuracy level of about 50%, that is, 50% of the durations were at least 1.0 but less than 1.3 s (hereafter referred to as 1.0 to 1.3 s schedule) and produced the food-pellet reinforcer. On Mondays, Wednesdays, and Thursdays baseline training continued under this schedule. On Tuesdays and Fridays for two animals the maximum lever-press duration that produced the reinforcer was increased from less than 1.3 s to less than 2.3 s, while the minimum reinforced duration remained at 1.0 s (hereafter referred to as 1.0 to 2.3 s schedule). For the other two animals, on these same days the minimum reinforced duration was decreased to 0.5 s, while the maximum reinforced duration remained at less than 1.3 s (referred to as 0.5 to 1.3 s schedule).

Prior to Tuesday and Friday sessions during which the size of the reinforcement window was expanded, injections of saline, or various doses of PCP and methamphetamine were given. After completion of the dose-effect curves, the reinforcement window was returned to the original size (1.0–1.3 s) on Tuesdays and Fridays and all dose-effect curves were repeated again. Next, the animals that had been reinforced for responses greater than 1.0 s but less than 2.3 s in the first phase of testing had their minimum reinforced response duration lowered to 0.5 s on Tuesdays and Fridays when saline or drug injections were given, while the maximum reinforced duration of lever press that was reinforced remained at less than 1.3 s. The other two animals had their maximum reinforced response duration increased to less than 2.3 s. Thus, all animals were trained 3 days a week under the original schedule that reinforced responses between 1.0 and 1.3 s, but when injections were given, the reinforcement interval for lever press durations was 0.5 to 1.3 s, 1.0 to 1.3 s, or 1.0 to 2.3 s in a counterbalanced order. Finally, the rats were tested during two sessions, one on a Tuesday and one on a Friday, where only every other response with a duration of 1.0 to 1.3 s produced the reinforcer. These experiments were performed without drugs to determine if a decrease in the percentage of

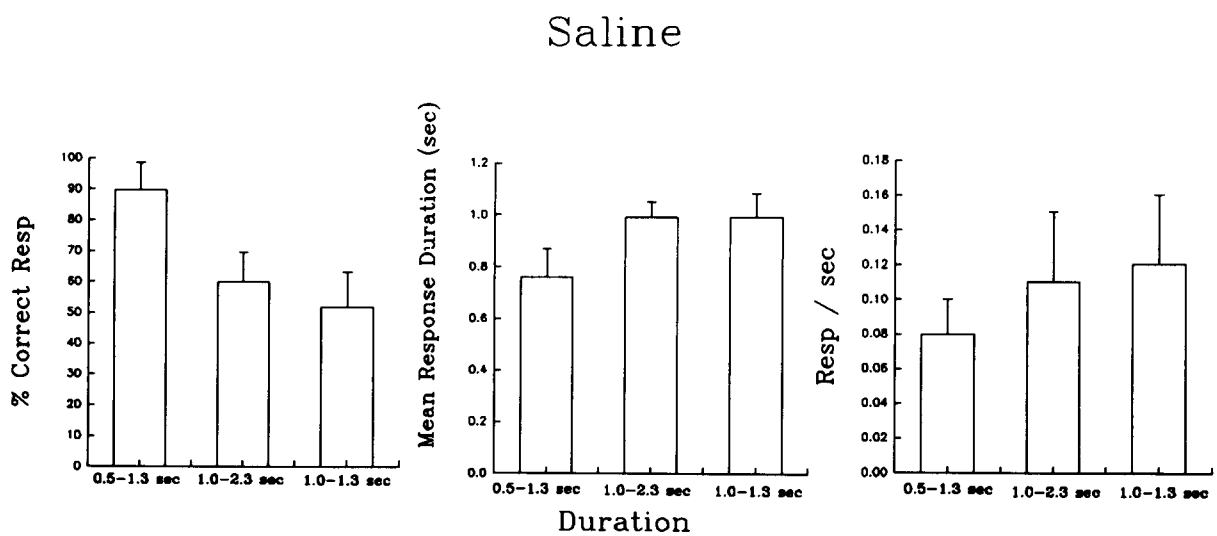

FIG. 1. Effects of varying the size of the reinforcement window on percentage of reinforced responses (left frame), mean response duration (middle frame), and response rate (right frame). Each point shows a mean for four rats. Brackets show one standard deviation above and below the control mean.

reinforced responses would disrupt performance on the response duration differentiation task. Throughout all sessions, rats were tested until they had received 50 food pellets, or until 30 min had elapsed, whichever occurred first.

Drugs

Drug or saline was administered intraperitoneally, 10 min before the session began. Both methamphetamine and phencyclidine were given as the hydrochlorides, and dose levels were calculated and reported as the hydrochlorides. Methamphetamine was studied before PCP. Doses were given in an ascending (beginning with saline administration) or descending dose order with random assignment of the rat to a dose order.

Data Analysis

Three saline sessions were used as baseline control sessions against which to evaluate drug effects. For each rat on each day the percentage of responses falling within the reinforced duration, the rate of responding, and the mean response duration were calculated for the plotting of mean dose response curves. Response durations were also collected in consecutive 0.1 s bins and plotted as a percentage of the total number of response durations to construct a relative-frequency response-duration distribution. Except for rate of responding, data were not plotted when animals made fewer than 10 responses. Response duration distributions were not calculated unless three of the four rats completed the test session following drug administration.

The response duration distribution also was analyzed by calculating an initial and a terminal quarter life, which is equivalent to the 25th and 75th percentile of response durations. For example, initial quarter life was calculated by determining the 0.1 s bin below which the 25% of the response durations fell. Similarly, the terminal quarter life was calculated by determining the bin above which the last 25% of the response durations fell.

RESULTS

A summary of the baseline data under the three different response duration reinforcement schedules is shown in Figs. 1 and 2. Figure 1 shows that under the 1.0–1.3 s schedule a group average of 51% of the responses were reinforced. The mean response duration was 0.98 s and the rate of responding was 0.12 responses/s. When the maximum response duration that was reinforced was raised to 2.3 s the percentage of response durations within the reinforcement window increased to 60%, but the mean response duration and response rate were little affected. When the minimum response duration necessary for reinforcement was lowered to 0.5 s, the percentage of reinforced response durations increased to 89% and the mean response duration decreased to 0.77 s. The response rate also decreased slightly.

Figure 2 shows the response duration distributions for all three reinforcement schedules. When response durations of 1.0 to 1.3 s were reinforced, a normal distribution of response durations resulted with a peak at the minimum reinforced duration. A very similar distribution occurred when the maximum response duration that was reinforced was increased to 2.3 s, although as Fig. 2 shows, the additional response durations that fell between 1.3 and 2.3 s and were reinforced, accounted for the higher rate of reinforcement under this schedule (Fig. 1). The higher reinforcement rate did not cause a change in the shape of the distribution. When the minimum duration required for reinforcement was decreased to 0.5 s, the response duration distribution shifted to the left with the peak occurring at 0.8–0.9 s. The reinforcement of these shorter response durations was responsible for the increase in percentage of reinforced responses shown in Fig. 1.

Figure 3 summarizes the effects of methamphetamine and PCP on the percentage of reinforced responses under the three reinforcement schedules. Methamphetamine produced only small decreases in the percentage of reinforced response durations under any of the three schedules at doses that did not eliminate responding. In contrast, PCP produced dose-

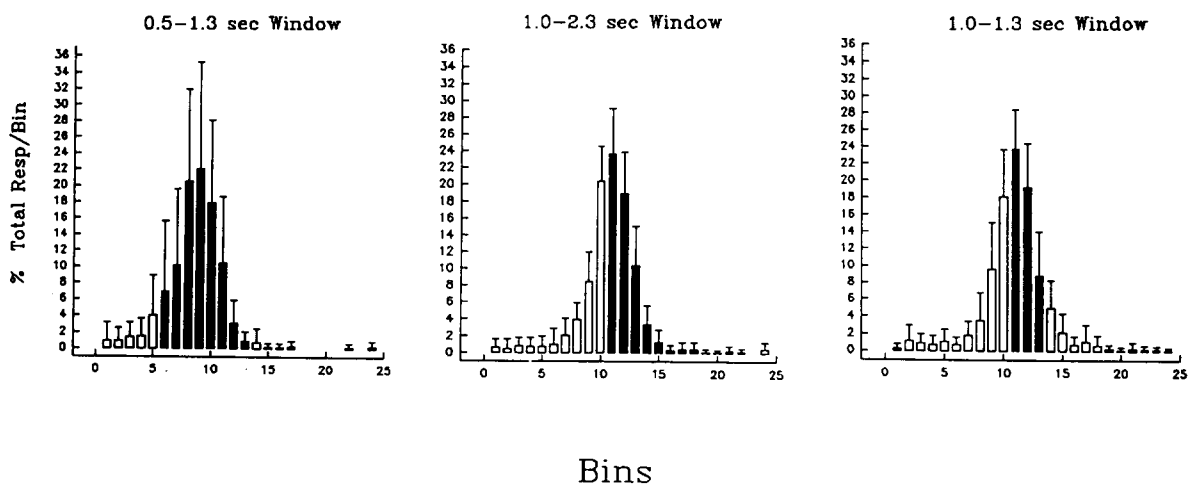

FIG. 2. Response duration distributions following saline administration with response durations reinforced between 0.5 and 1.3 s (left frame), 1.0 and 2.3 s (middle frame), and 1.0 and 1.3 s (right frame). Abscissa: response durations in 0.1 s bins. Ordinate: percentage of total response durations in each bin. Shaded bars show reinforced response durations. Brackets show one standard deviation. Each figure is based on three saline observations in each of four rats.

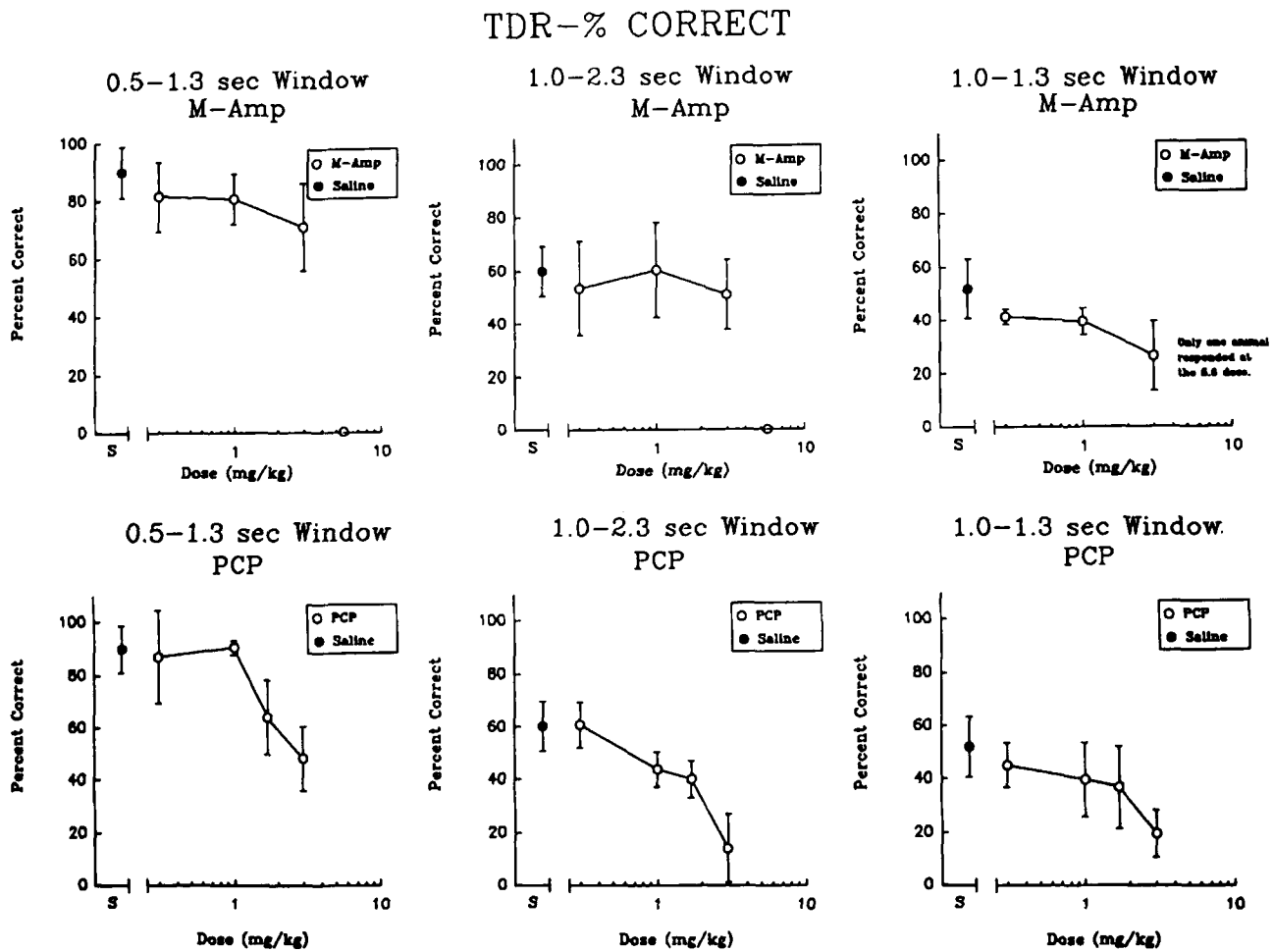

FIG. 3. Dose–effect curves for methamphetamine (M-amp, top row) and PCP (bottom row) on the percentage of reinforced response durations for response durations reinforced between 0.5 and 1.3 s (left column), 1.0 and 2.3 s (middle column), and 1.0 and 1.3 s (right column). Abscissa: dose, log scale. Ordinate: percentage of total response durations within the reinforcement interval. Brackets and points at S show ± one standard deviation around the postsaline mean based on three observations in each rat. All other points are based on single observations in each rat.

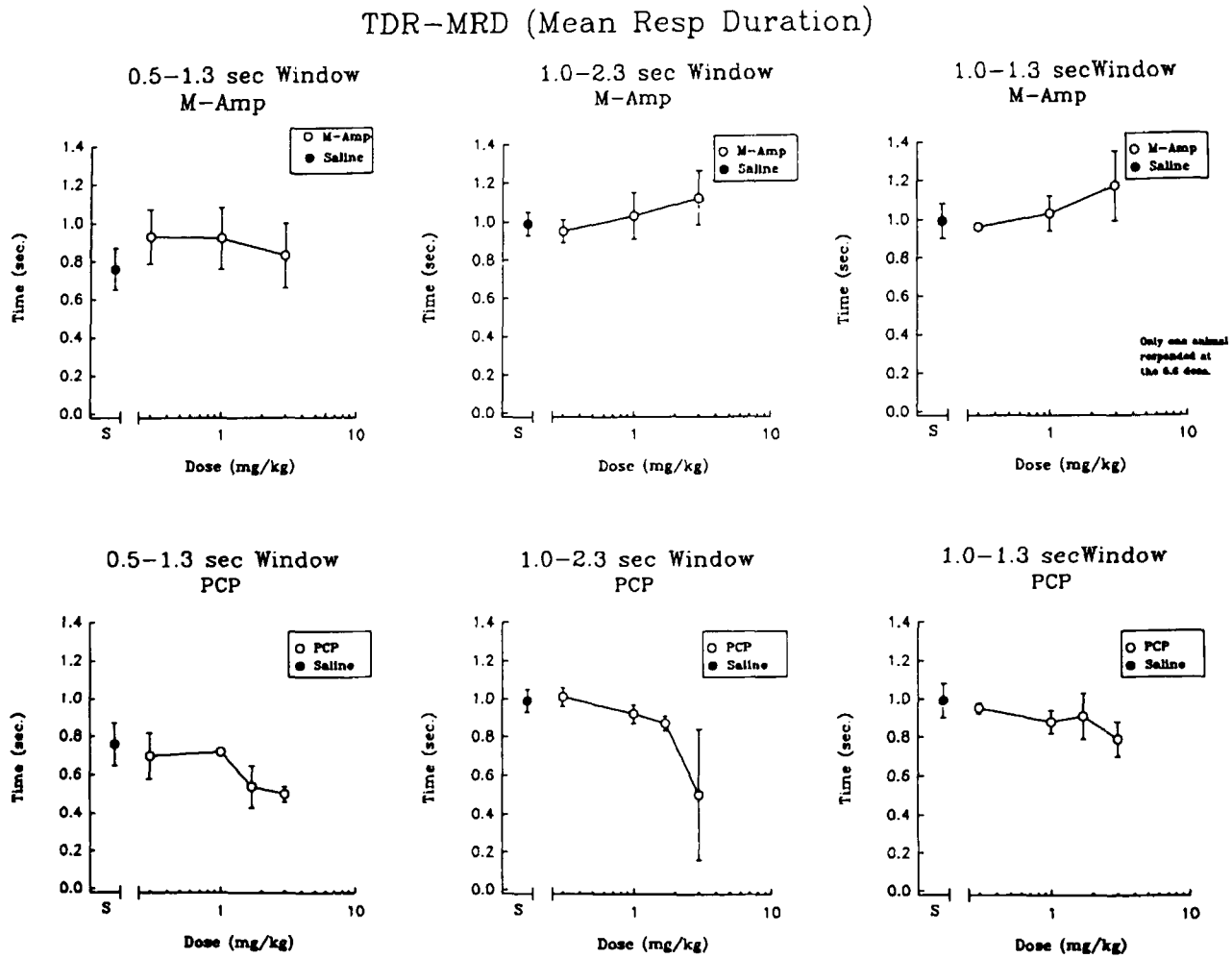

FIG. 4. Dose-effect curves for the effects of methamphetamine and PCP on mean response duration. Ordinate: mean response duration in seconds. Other details as in Fig. 3.

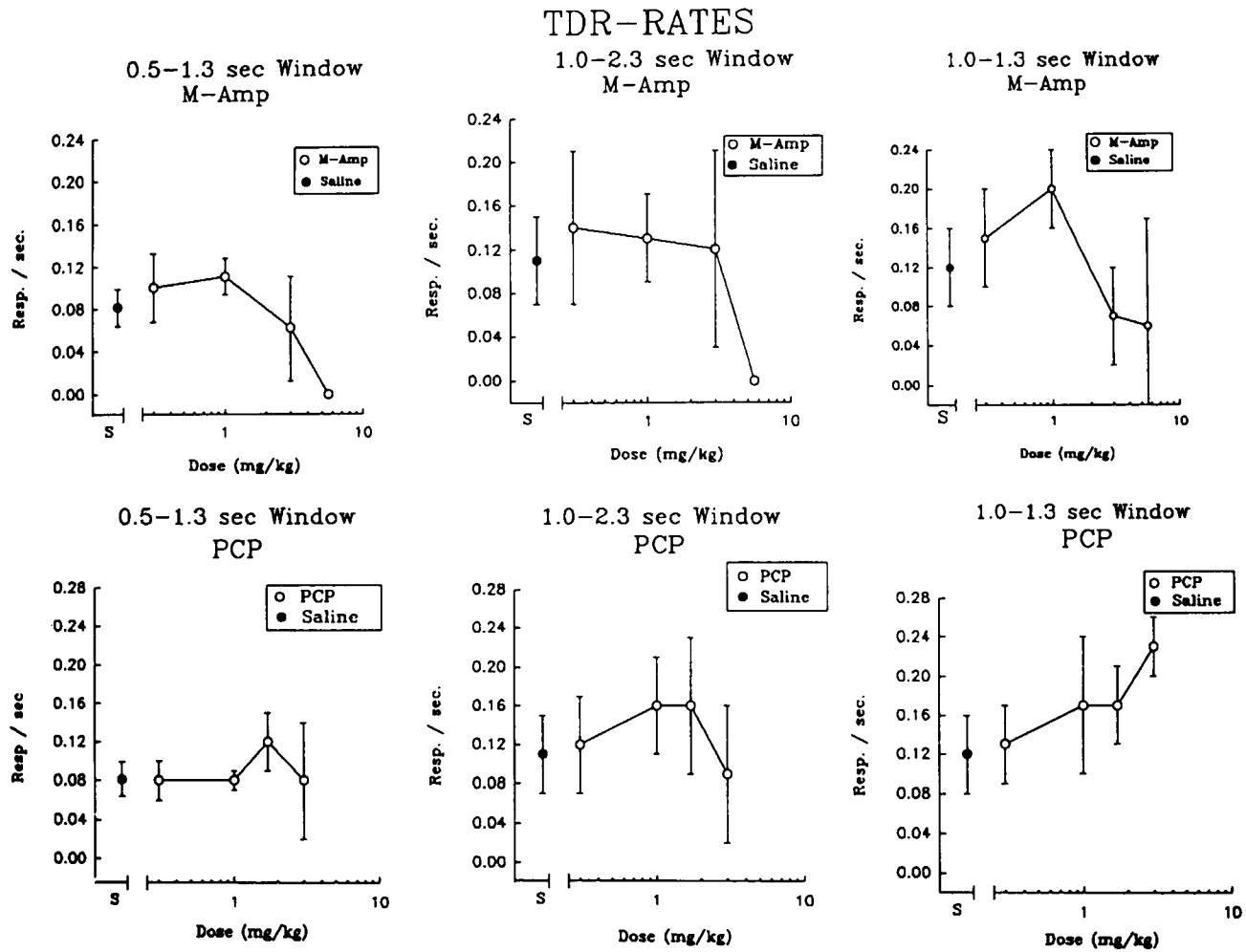

FIG. 5. Dose–effect curves for the effects of methamphetamine and PCP on mean rates of responding. Ordinate: mean response rate in responses/s for the entire session. Other details as in Fig. 3.

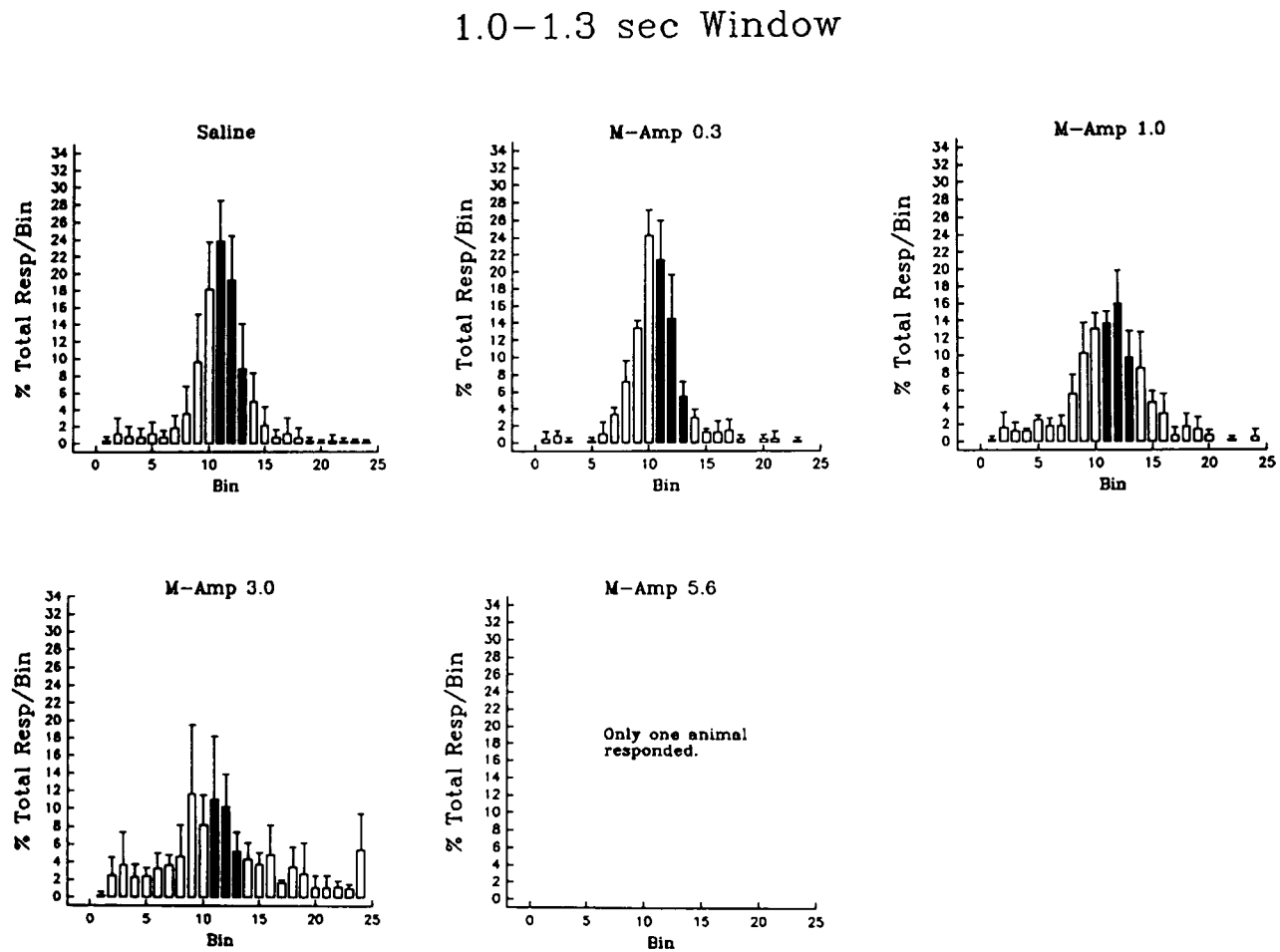

FIG. 6. Response duration distributions for methamphetamine with response durations between 1.0 and 1.3 s reinforced. Details as in Fig. 2.

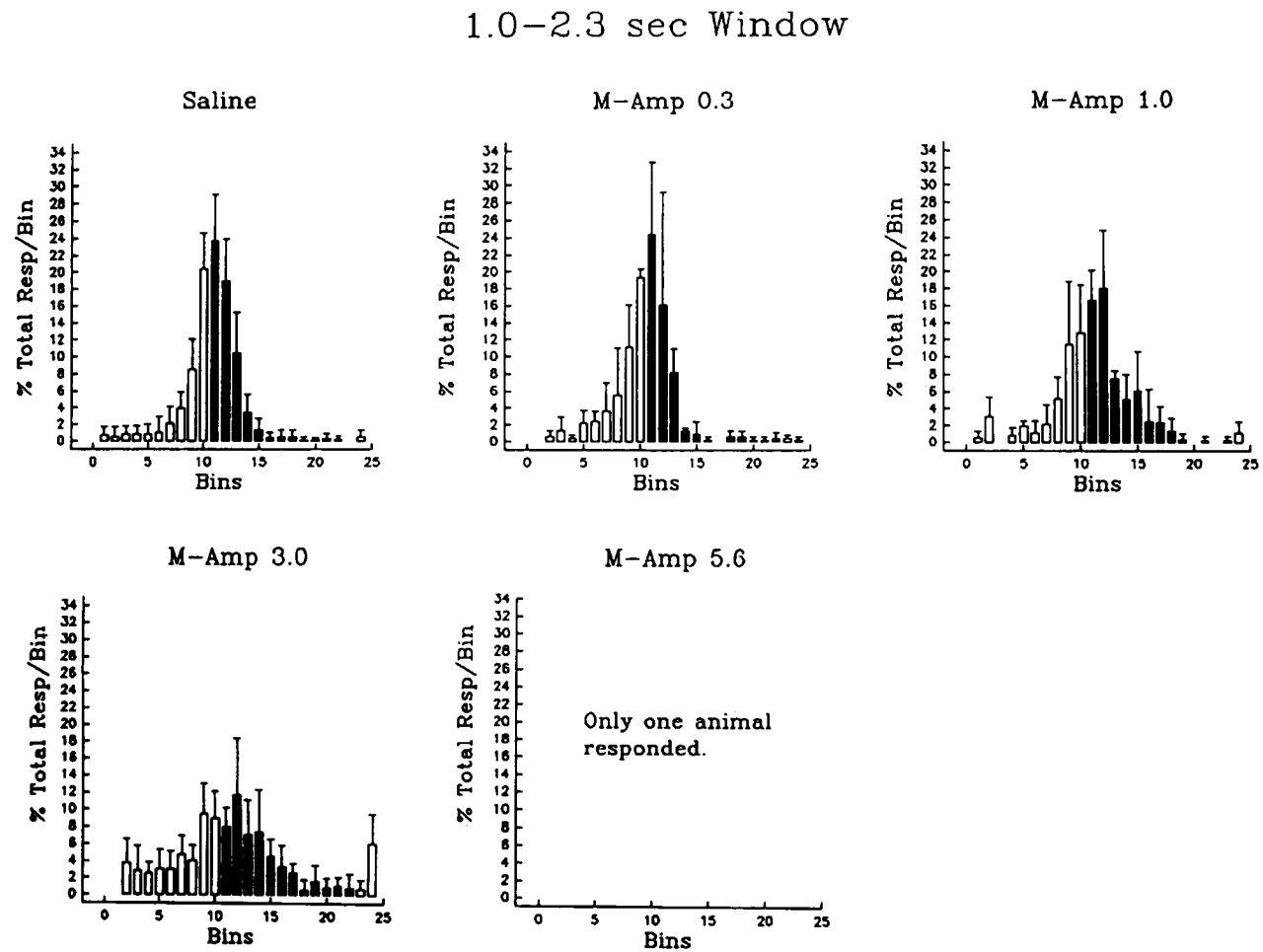

FIG. 7. Response duration distributions for methamphetamine with response durations between 1.0 and 2.3 s reinforced. Details as in Fig. 2.

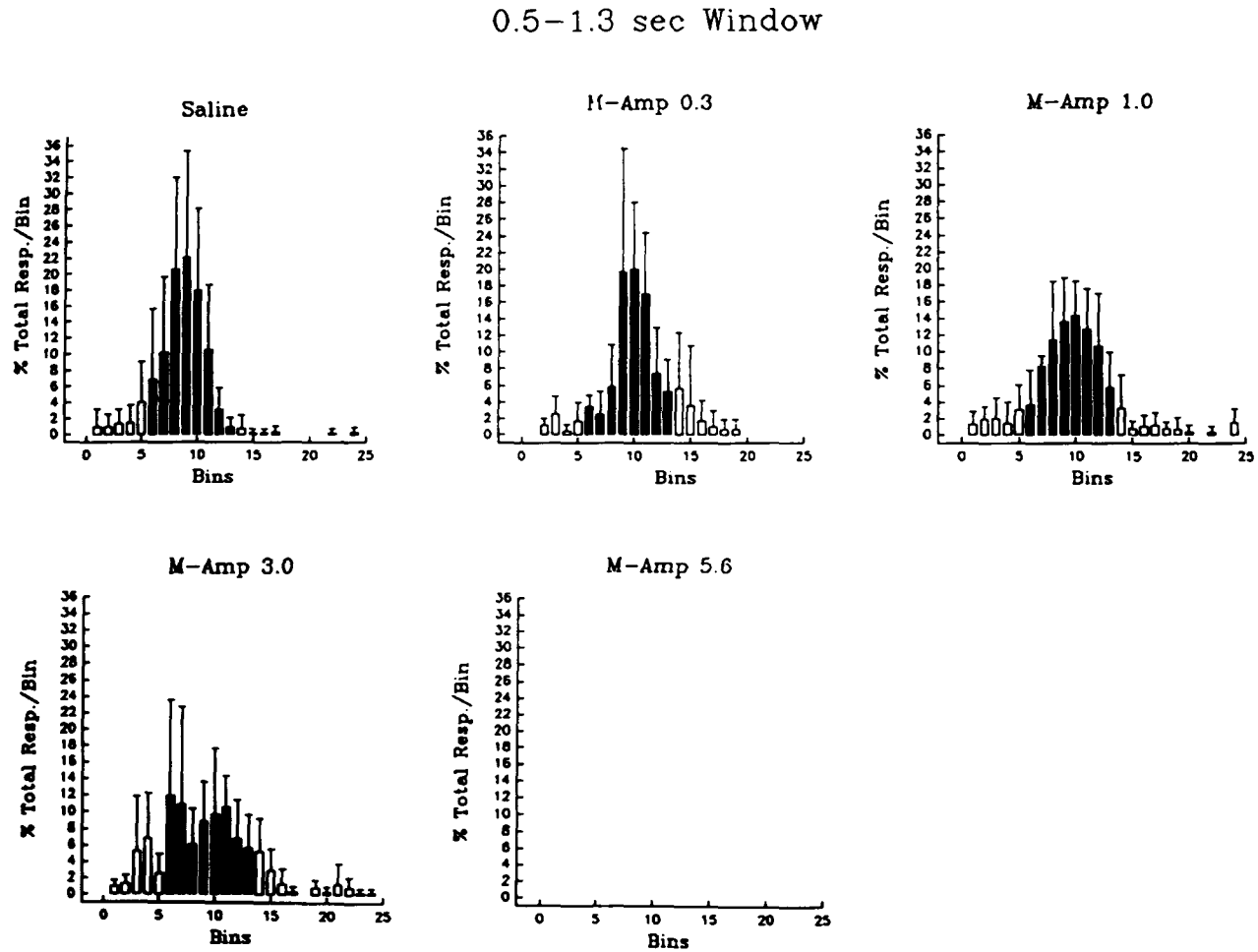

FIG. 8. Response duration distributions for methamphetamine with response durations between 0.5 and 1.3 s reinforced. Details as in Fig. 2.

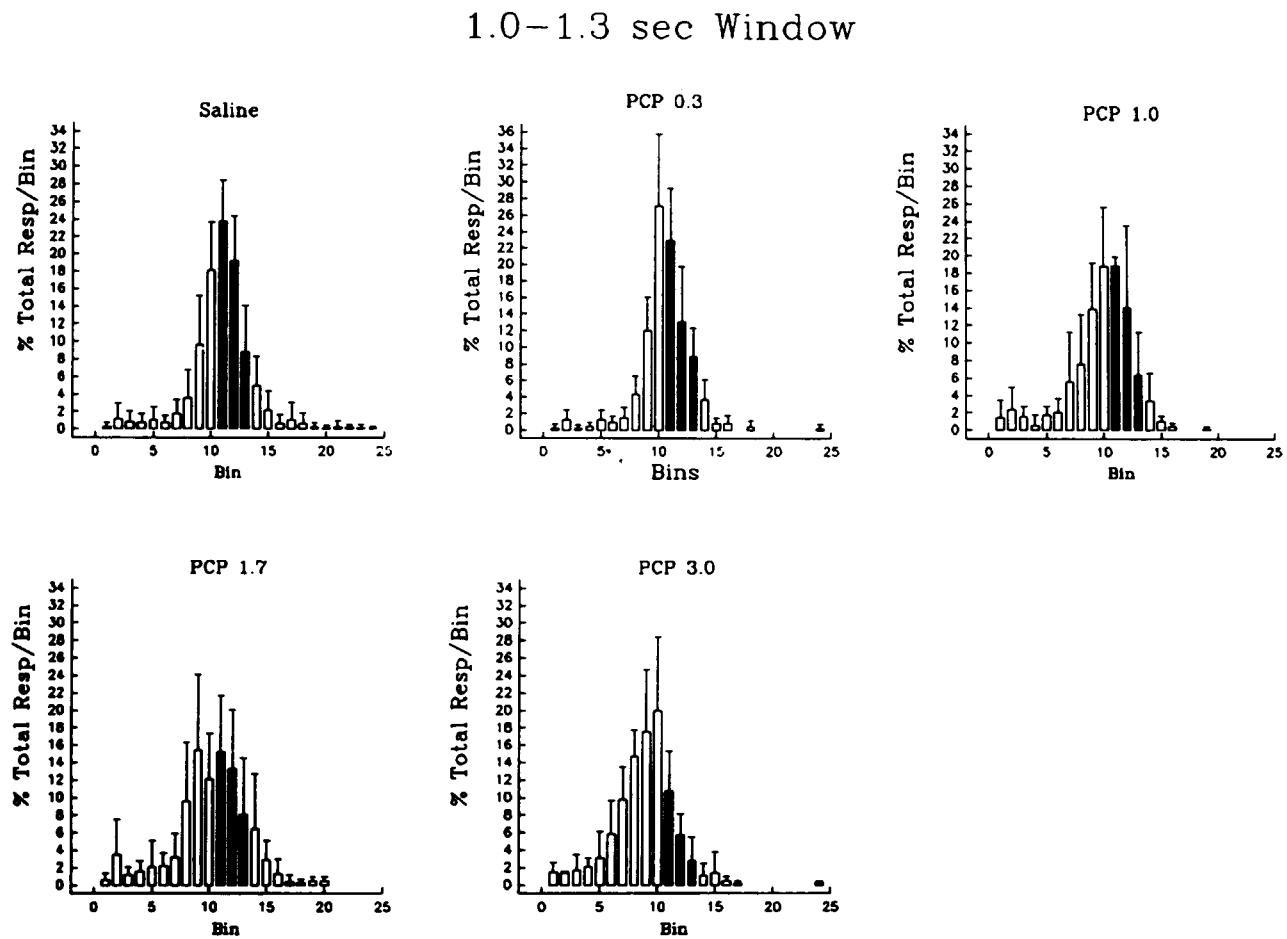

FIG. 9. Response duration distributions for PCP with response durations between 1.0 and 1.3 s reinforced. Details as in Fig. 2.

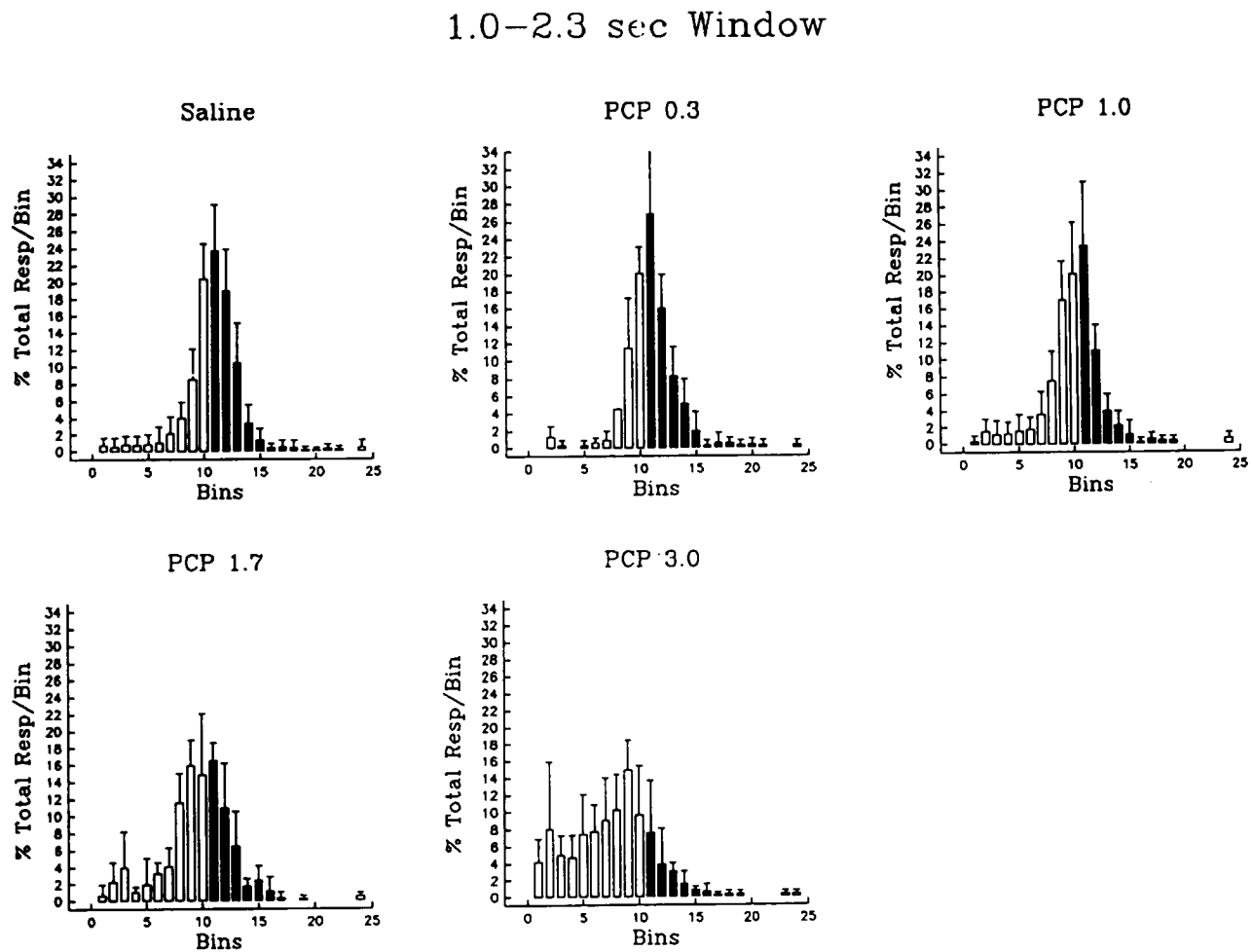

FIG. 10. Response duration distributions for PCP with response durations between 1.0 and 2.3 s reinforced. Details as in Fig. 2.

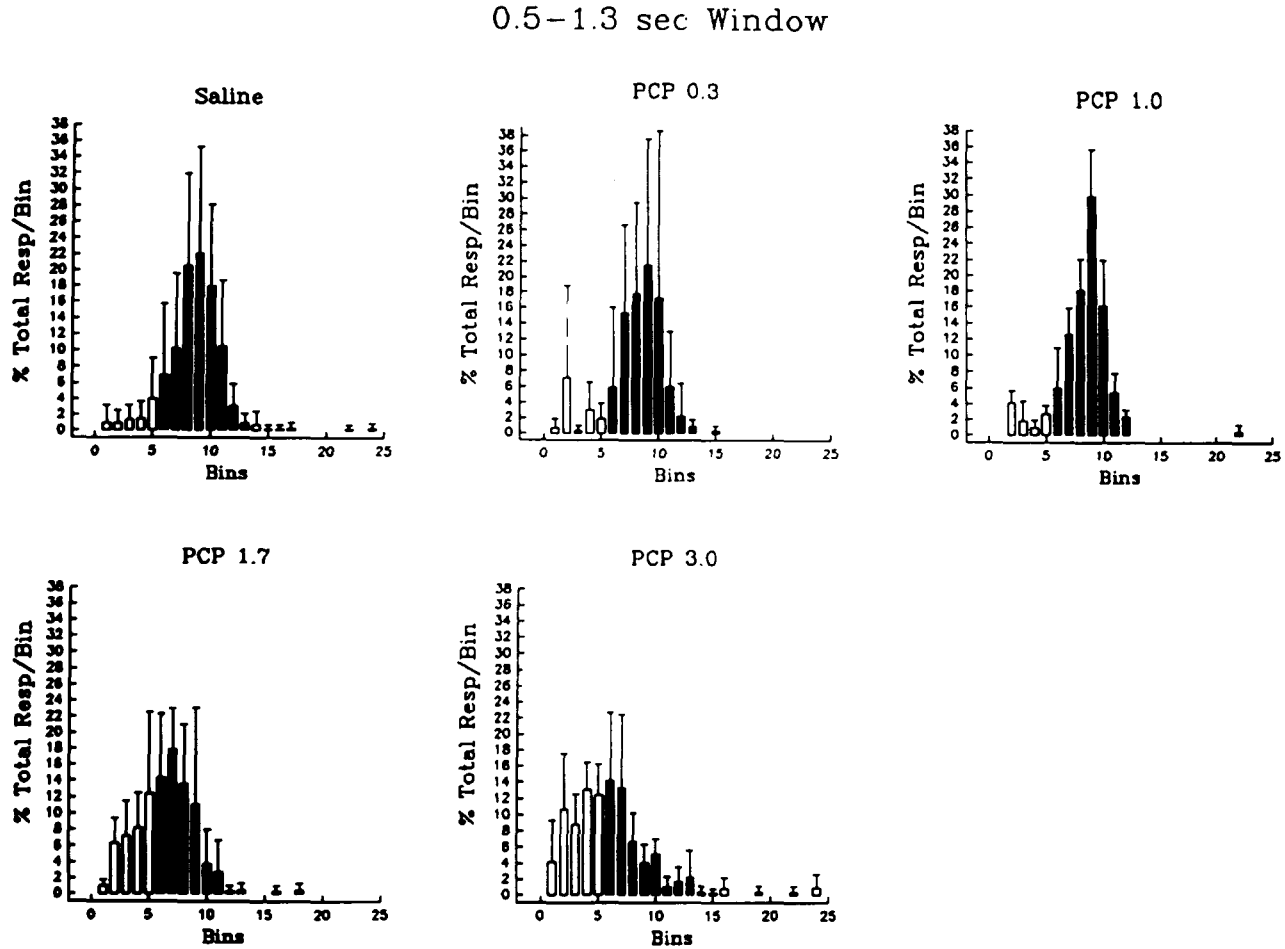

Fig. 11. Response duration distributions for PCP with response durations between 0.5 and 1.3 s reinforced. Details as in Fig. 2.

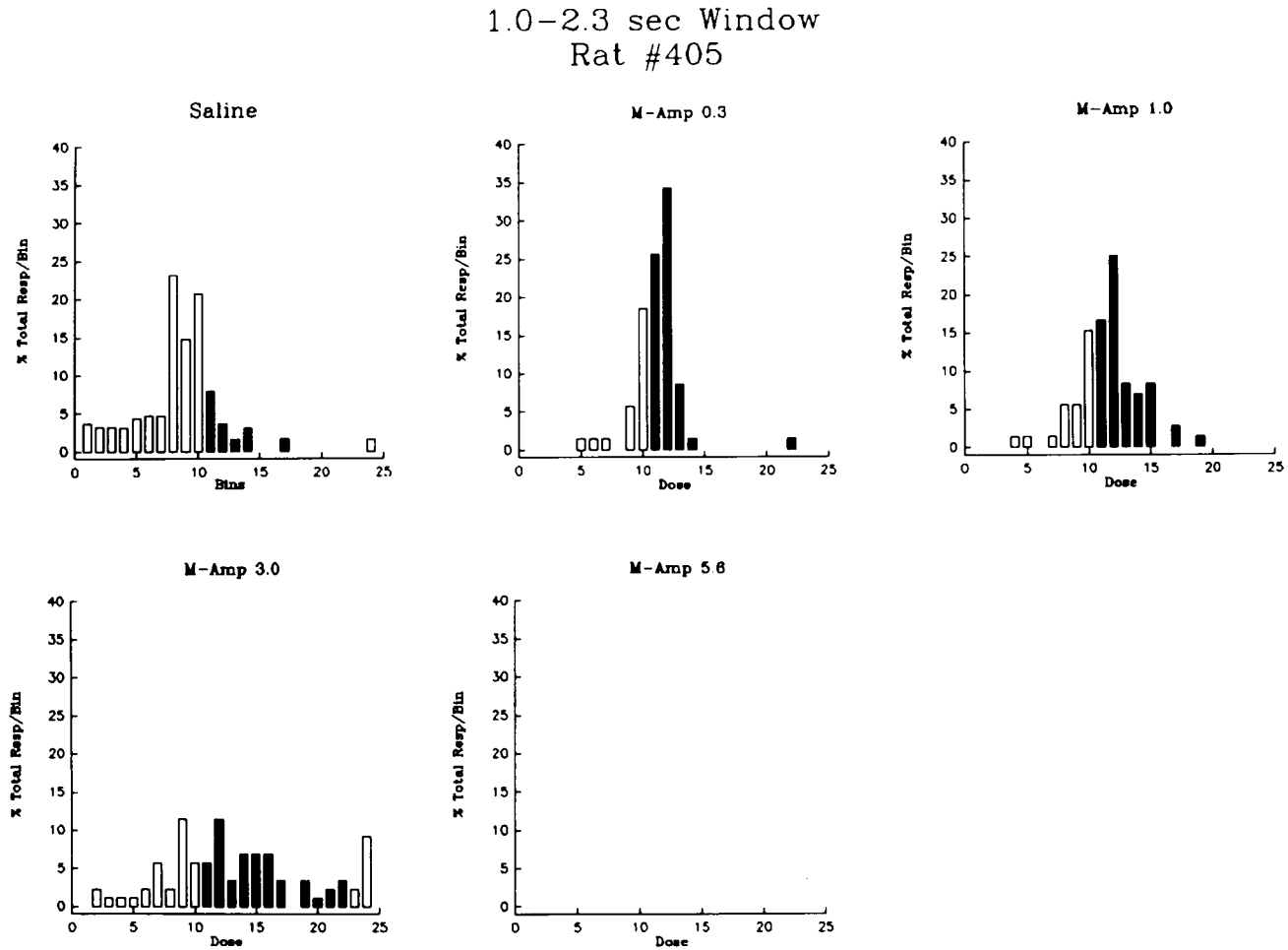

FIG. 12. Response duration distributions for methamphetamine in rat #405 with response durations between 1.0 and 2.3 s reinforced. Details as in Fig. 2.

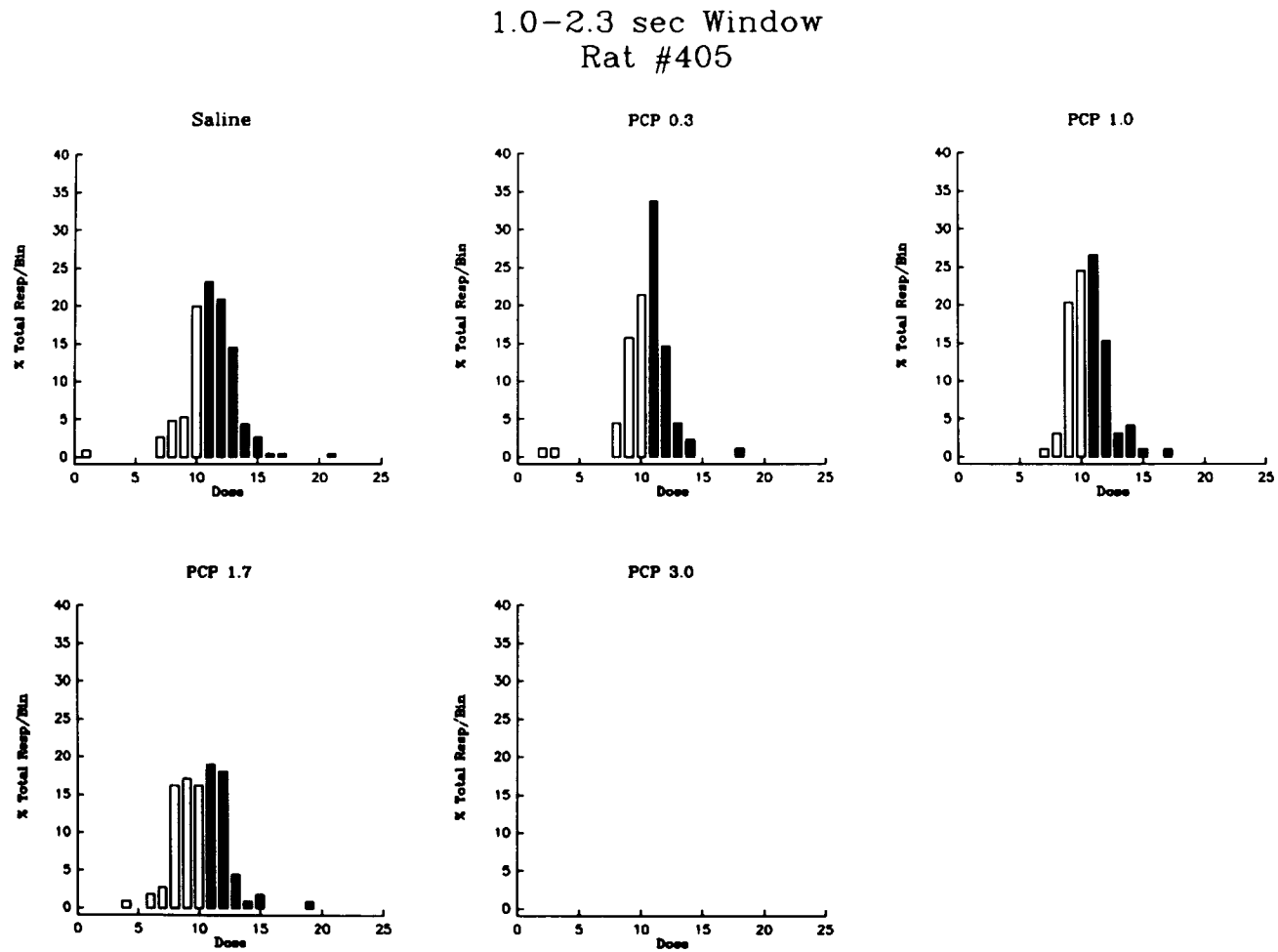

FIG. 13. Response duration distributions for PCP in rat #405 with response durations between 1.0 and 2.3 s reinforced.

dependent decreases in the percentage of reinforced response durations under all three schedules. Figure 4 shows summary data for the mean response duration. At doses that did not eliminate responding, methamphetamine had little effect on mean response duration, although there was a suggestion that the 3.0 mg/kg dose slightly lengthened the response duration under the two schedules that reinforced minimum response durations of 1.0 s. Again, in contrast, PCP produced small decreases in the mean response duration at higher dose levels. Figure 5 shows the effects of both drugs on rates of responding. Higher doses of methamphetamine reduced rates of responding, but PCP did not. In fact, PCP showed some tendency to increase rates of responding, especially after the 3.0 mg/kg dose under the schedule that reinforced response durations greater than 1.0 s, but less than 1.3 s.

Figure 6 shows the mean response duration distributions for methamphetamine with response durations of 1.0 to 1.3 s reinforced. The 0.3 mg/kg dose had little effect. As the dose increased, the distribution flattened with increases in both response durations too long and too short to produce the reinforcer.

Figure 7 shows similar response duration distributions for the schedule where responses longer than 1.0 but shorter than 2.3 s were reinforced. Methamphetamine effects on the distribution were remarkably similar under this schedule to those shown in Fig. 6 for the 1.0 to 1.3 s schedule.

Figure 8 shows the response duration distributions following methamphetamine with response durations of 0.5 but less than 1.3 s reinforced. Although the distribution after saline is shifted to the left compared to the distributions under the other two schedules (Fig. 1), the effect of methamphetamine remains the same, that is, the 0.3 mg/kg dose had little effect on the distribution with higher doses (1.0 and 3.0 mg/kg) flattening the distribution. The rate of reinforcement under this schedule remained high due to the reinforcement of the increased number of short response durations. In summary, by varying the reinforced response duration, the percentage of reinforced responses changed, but the effect of methamphetamine on the response duration distributions did not change. Figure 3 showed that PCP produced a dose-dependent decrease in the percentage of reinforced response durations under all three schedules. The decreases in reinforcement occurred at doses that had little effect on rate of responding (Fig. 5).

Figure 9 shows the response duration distributions for PCP when response durations of 1.0 to 1.3 were reinforced. As the dose of PCP increased, longer response durations were eliminated and the distribution shifted toward shorter response durations without losing it's bell shape. Figure 10 shows similar distributions for the schedule that reinforced response durations of 1.0 to 2.3 s. The data were remarkably similar, except at the highest dose of PCP (3.0 mg/kg) there was a greater tendency for short response durations to occur.

Figure 11 shows the response duration distribution following PCP with the schedule that reinforced response durations of 0.5 to 1.3 responses/s. As shown in Fig. 2, reinforcement of the response durations between 0.5 and 1.0 s resulted in a shift in the response duration to the left after saline, relative to the distributions after saline for the other two schedules. The 0.3 and 1.0 mg/kg doses of PCP had little effect on the response duration distribution, aside from eliminating most of the longer response durations. The higher doses (1.7 and 3.0 mg/kg) shifted the distribution to the left with an increase in the frequency of short response durations. The increase in the percentage of responses less than 0.5 responses in duration was sufficient to lower the reinforcement rate significantly (Fig. 1). Thus, PCP also produced similar effects across all three schedules of response duration differentiation, despite differences in reinforcement frequency under these schedules.

Figures 12 and 13 show the response-duration distributions for rat #405 under the 1.0 to 2.3 s schedule to demonstrate that the effects of methamphetamine and PCP seen in the group data of Figs. 6 to 11 are shown in the distributions of individual animals and are not an artifact of group averaging. As with the group data, in rat #405 methamphetamine increased the proportion of long duration responses, while PCP shifted the response duration distribution to the left.

The differences between methamphetamine and PCP in their effects on response durations is emphasized in Fig. 14. Figure 14 shows initial quarter life and terminal quarter life

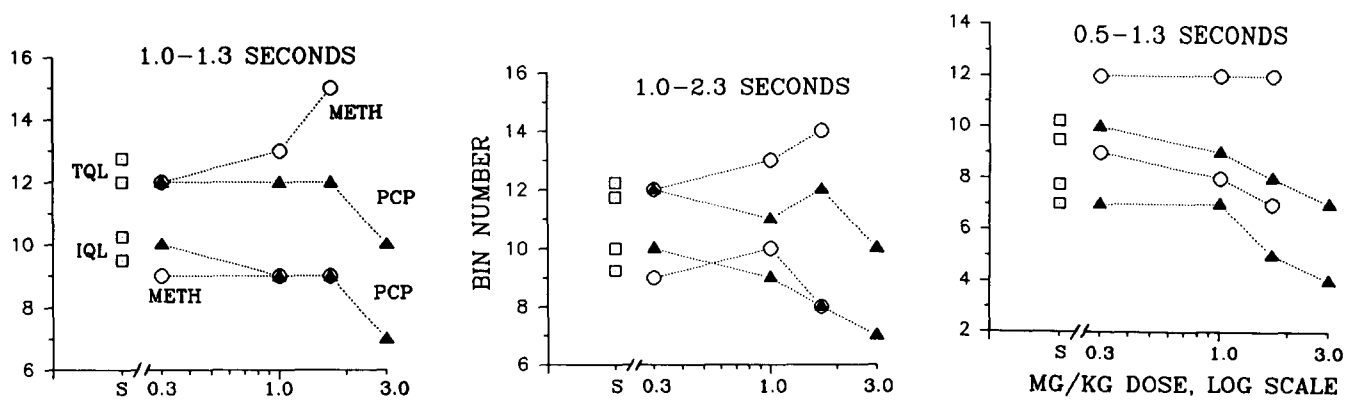

FIG. 14. Effects of methamphetamine (unfilled circles) and PCP (filled triangles) on intial quarter life (IQL) and terminal quarter life (TQL) under the schedules that reinforced responses with durations of 1.0 to 1.3 s (left frame), 1.0 to 2.3 s (middle frame), and 0.5 to 1.3 s (right frame). Squares at S show a range of three control observations. Abscissa: dose, log scale. Ordinate: bin number. Each point represents a mean of observations in each of four rats.

values for these drugs. PCP decreased both the initial and the terminal quarter life, which is consistent with the observed shift of the response duration distribution to the left. In contrast, methamphetamine increased the terminal quarter life.

In the final experiment, only every other response with a response duration between 1.0 and 1.3 s was reinforced during two session 3 days apart. The percentage of responses with durations between 1.0 and 1.3 s and the mean response durations are shown for individual rats on the 2 days when only every other response between 1.0 and 1.3 s was reinforced and for the 2 days preceeding these session when all responses within this time window were reinforced, are shown in Table 1. The table shows that reinforcing only every other response that fell within the reinforcement window did not disrupt response differentiation. In fact, the precentage of responses between 1.0 and 1.3 s was slightly higher when only every other response was reinforced. Although the percentage of responses between 1.0 and 1.3 s did not change much when every other response was reinforced, the mean response duration was increased slightly in seven of the eight observations. The increase in response duration was reflected in small shifts in the response duration distributions. For example, for five of the eight response duration distributions, the peak of the distribution shifted one bin toward longer response durations (data not shown).

DISCUSSION

These experiments showed that by temporarily changing the schedule to increase the range of response durations that were reinforced the percentage of response durations that were reinforced could be increased under control conditions (e.g., after saline). Decreasing the minimum response duration necessary for reinforcement from 1.0 to 0.5 s increased the frequency of reinforcement considerably more than increasing the maximum reinforced response duration from 1.3 to 2.3 s.

When the upper limit duration was increased, there was little effect on the distribution, despite the slightly increased reinforcement rate; however, when the lower limit was decreased, the response duration distribution was shifted to the left and the reinforcement rate increased. This effect probably occurred because under the schedule where the rats had received extensive training (response durations of 1.0 to 1.3 were reinforced) considerably more responses occurred with durations between 0.5 and 1.0 s than occurred between 1.3 and 2.3 s. When the schedule was changed so that shorter response durations were reinforced, the increased frequency of reinforcement of short response durations might have served to pull the distribution toward the left. Under the training schedule, the less frequent occurrence of longer response durations might have caused the reinforcement of these longer response durations when the schedule was changed to have less influence on the response duration distribution.

The most important finding of the study was that despite the difference in reinforcement frequency across schedules and the shift of the distribution to the left when the minimum response duration needed for reinforcement was decreased to 0.5 s, the effects of both methamphetamine and PCP did not change with the schedule. Methamphetamine flattened the response duration distributions under all three schedules with the longer response durations being retained after drug. In contrast, PCP shifted the response duration distributions to the left with a near elimination of the longer response durations. These data suggest that the effects observed were much more a function of the drug than the schedule and that these effects were primarily effects of the drugs on the animals ability to differentiate response duration, with little influence of changes in baseline reinforcement frequency.

Although the effects of methamphetamine and PCP on response duration differentiation did not seem to depend on the reinforcement frequency, it should be pointed out that these observations are based on increases in baseline reinforcement frequency. We have not yet attempted to determine the extent to which decreases in baseline reinforcement frequency might affect the response to drugs; however, we did do experiments where we decreased the rate of reinforcement by only reinforcing every other response that fell within the reinforced response duration. When we did so, the percentage of responses that fell within that interval was unchanged, suggesting that merely decreasing the rate of reinforcement does not disrupt performance, although mean response duration increased slightly. Also, we have studied the effects of increasing reinforcement frequency on only two drugs and different effects might be obtained with other drugs. Nevertheless, we picked two drugs that we had observed previously to have different effects on response duration differentiation (3,4), and both of these drugs showed their characteristic effects across all three schedules. The data strongly suggest that changes in response duration differentiation produced by drugs is a direct effect on the differentiation process and is not powerfully affected by resultant changes in reinforcement frequency.

TABLE 1

EFFECTS OF REINFORCING ONLY EVERY OTHER RESPONSE (50% REINFORCEMENT) ON RESPONSE DURATION AND ON THE PERCENTAGE OF RESPONSES WITH DURATIONS OF 1.00 TO 1.30 s

Rat Number	Reinforcement Percentage	Percent Responses of 1.00–1.30 s	Mean Response Duration in s
402	100	49.5	0.86
	50	53.2	0.99
	100	39.1	0.83
	50	53.8	0.96
405	100	76.9	1.01
	50	75.8	1.03
	100	62.5	0.95
	50	58.8	1.05
408	100	69.4	0.98
	50	58.8	0.95
	100	41.7	0.91
	50	62.5	0.96
413	100	56.2	0.95
	50	74.6	1.01
	100	51.0	0.94
	50	61.7	1.00

ACKNOWLEDGMENTS

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