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# Effects of *d*-Amphetamine, Methaqualone, and Phencyclidine on the Reaction Time of Pigeons

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KACZOR, T., E. BLAKELY AND A. POLING. *Effects of* d-*amphetamine, methaqualone, and phencyclidine on the reaction time of pigeons.* PHARMACOL BIOCHEM BEHAV 45(2) 351–357, 1993.—The effects of acute administrations of *d*-amphetamine (0.56, 1.0, 1.78, 3.2, and 5.6 mg/kg), methaqualone (5.6, 10, 18, 32, and 56 mg/kg), and phencyclidine (0.3, 0.56, 1.0, and 1.78 mg/kg) on the reaction time of pigeons were examined. In the reaction time assay, birds were trained to depress and hold a foot treadle until a stimulus change occurred. Releases within 2 s of the stimulus change were reinforced with food; premature releases or releases occurring after the 2-s limited hold were not reinforced. At relatively high doses, each of the drugs decreased the percentage of responses that were reinforced. Methaqualone and phencyclidine usually increased median reaction times at these doses, whereas the effects of *d*-amphetamine on reaction time were less clear.

*d*-Amphetamine Methaqualone Phencyclidine Reaction time Pigeons

IN a recent study, Blakely, Starin, and Poling (1) described a novel behavioral procedure for studying reaction time in pigeons and the effects of drugs thereon. In that study, pigeons were trained to depress a foot treadle when a window located above the treadle was lighted in white and to release the treadle within 2 s when the light turned red. This stimulus change occurred after a variable period of time, termed the foreperiod.

This procedure was an apparent improvement over prior procedures used to measure reaction time in pigeons (4,7,9) in two regards. First, in those studies no preparatory response was required; a discriminative stimulus was simply presented after an intertrial interval (ITI) and the time to respond was recorded. With this arrangement, there is no guarantee that the bird attends to the stimulus or is in a position to respond when it appears. Second, keypecking was the instrumental response in those studies. Because discrete visual stimuli (e.g., key illuminations) correlated with a change from a low probability of food delivery to a high probability of food delivery elicit keypecking in pigeons (2,8), reaction times possibly were contaminated by variables controlling elicited pecking. In the study by Blakely et al. (1), subjects were required to emit a preparatory response (treadle depression), the nature of which maximized the possibility of contact with the signal to respond. Moreover, to avoid possible problems with elicited responses, treadle release was used as the operant response.

The procedure used by Blakely et al. produced relatively consistent reaction times in the absence of drug, and both mephenytoin (40, 60, 80, 120, and 160 mg/kg) and methsuximide (25, 50, 75, and 100 mg/kg) produced orderly effects (generally dose-dependent increases in median reaction times and decreases in percent responses that were reinforced). Given these findings, the procedure appears promising as an assay of drug effects on reaction time in pigeons. The present study extended the work of Blakely et al. by examining the effects of *d*-amphetamine, methaqualone, and phencyclidine on the reaction time of pigeons. These drugs were chosen because they represent three different drug classes: stimulants, sedative-hypnotics, and dissociative anesthetics, respectively. If reaction time is selectively affected by particular kinds of drugs, one would expect dissimilar results across the three agents studied.

Procedures used in the present study were similar to those employed by Blakely et al. (1), with the exception that "catch trials" were arranged in the present experiment. In these trials, the white light did not change to red when the foreperiod ended. Under the procedures used by Blakely et al., birds could obtain at least occasional reinforcement by merely depressing the treadle for a period of time when the white stimulus was present and then releasing it without attending to the red stimulus. Although all birds in the study by Blakely et al. exhibited control levels of accuracy well in excess of those that

The reported data were collected as part of the M.A. thesis of the senior author.

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would be expected if birds never attended to the red stimulus, it is possible that in some proportion of trials they simply stepped on and off the treadle without attending to it. The inclusion of catch trials evaluated whether or not this occurred in the present study. If treadle releases were controlled by the red stimulus, response latencies in such trials should exceed 3 s, the longest foreperiod duration.

## METHOD

### *Subjects*

Three White Carneau pigeons, all with previous exposure to anticonvulsant drugs and histories of treadle-pressing, were used as subjects. Birds were maintained at 80% of their free-feeding weights and were individually housed. Water and grit were available continuously in the home cages.

### *Apparatus*

Sessions were conducted in three operant conditioning chambers, each measuring 40 cm long, 30 cm wide, and 38 cm high. On the front panel of each were located a 1.5 × 1.5-cm translucent stimulus window, an 8 × 8-cm plastic foot treadle, and a 6 × 6-cm opening giving access to a food hopper. The window could be illuminated in red or white. The treadle, covered on top by a coarse, high-friction material, was mounted on the front panel 7 cm from the right corner of the wall and 2 cm from the floor. A microswitch was activated when a downward force of at least 0.5 N was applied to the treadle. General chamber illumination was provided by a 7-W white houselight centrally located on the ceiling of each chamber. White noise was present continuously, and ventilation was provided by exhaust fans. A PDP8-E minicomputer (Digital Equipment Corporation, Maynard, MA), equipped with electromechanical interfacing and SUPERSKED® software (State Systems, Inc., Kalamazoo, MI), controlled the experiment and collected data.

### *Behavioral Procedure*

Subjects had been previously trained to depress the treadle when the white stimulus was illuminated and release it when the stimulus turned red, which occurred after a variable period of time (the foreperiod). The mean foreperiod was 1.75 s, and the individual durations were 0.5, 1.0, 1.5, 2.0, 2.5, and 3.0 s. The foreperiod on a given trial was randomly selected from this distribution, which is the same as that used by Blakely et al. (1). Timing of each foreperiod began when the treadle was depressed; thus, trials did not advance until the bird stepped on the treadle. With this arrangement, trials without a response could not occur. All trials ended when the bird stepped off (i.e., released) the treadle.

Correct responses were defined as treadle releases that occurred within a 2-s limited hold after the stimulus changed color. A correct release produced 3-s access to grain. Premature releases (those that occurred before the stimulus changed color) resulted in darkening of the stimulus, no access to grain, and reprogramming of the same foreperiod duration for the next trial. If a release occurred after the 2-s limited hold (an aborted trial), no grain was presented and a new foreperiod was programmed for the next trial. A 5-s intertrial interval (ITI) followed access to grain and incorrect releases. If the treadle was depressed during the ITI, the houselight was extinguished until the treadle was released, at which time the ITI was restarted. Each daily session ended after 40 grain deliveries, 45 min, or 100 trials, whichever came first.

Each session, 8% of all trials, selected at random, were designated as catch trials. Catch trials were identical to regular trials, with two exceptions: The stimulus did not change from white to red when the foreperiod ended and food was never delivered.

### *Pharmacological Procedure*

Drug testing began after 10 consecutive sessions in which percent correct on normal trials for each bird was at least 70 and for catch trials was less than 20, and there was no trend in median reaction times as determined by visual inspection. The criteria were met in 56 days for both P1 and P2 and in 30 days for P3.

*d*-Amphetamine (0.56, 1.0, 1.78, 3.2, and 5.6 mg/kg), methaqualone (5.6, 10, 18, 32, and 56 mg/kg), and phencyclidine (0.3, 0.56, 1.0, and 1.78 mg/kg) were then tested. The drugs were administered acutely under a BBCDBBCD regimen, where B, C, and D represent baseline, vehicle control, and drug sessions, respectively. All birds received two determinations at each dose; doses were given in an irregular order that differed for each bird. Both dose–response determinations were made with one drug before proceeding to the next.

*d*-Amphetamine sulfate (Sigma Chemical Co., St. Louis, MO) and phencyclidine HCl (Sigma) were dissolved in a vehicle of 0.9% sodium chloride (saline) solution. Methaqualone HCl (Sigma) was dissolved in a vehicle of 80% propylene glycol and 20% ethyl alcohol. Injections, at a volume of 1 ml/kg, were administered IM 30 min prior to test sessions. Isotonic (0.9%) saline solution was administered in all vehicle sessions that preceded injection of *d*-amphetamine and phencyclidine and, for each bird, in 8 of 10 vehicle sessions that preceded injection of methaqualone. The methaqualone vehicle (80% propylene glycol, 20% ethyl alcohol) was administered in the other two vehicle sessions.

## RESULTS

Data of primary interest were percent correct responses and median response latencies. These data are shown for individual subjects in Figs. 1, 2, and 3, which present dose–response relations for *d*-amphetamine, methaqualone, and phencyclidine, respectively. The percent of responses that met the criterion for reinforcement (percent correct) during control and drug sessions are shown in the left panels. These data represent trials in which the treadle was released within the 2-s limited hold after the foreperiod elapsed; thus, trials in which the criterion for reinforcement was not met included premature releases and releases after the 2-s limited hold (aborted trials). Median reaction time data are presented in the right panels. A reaction time was defined as the elapsed time from the end of the foreperiod to the release of the treadle. Thus, the medians were computed using the reaction times in trials with correct responses and in trials in which releases occurred after the 2-s limited hold (i.e., aborted trials). Premature releases, which occurred before the foreperiod ended, did not yield reaction times and thus did not figure into the medians.

Reaction time and percent correct data are presented separately for the first and second exposures to each dose. Therefore, control data points for each subject represent the mean of four (phencyclidine) or five (*d*-amphetamine and methaqualone) sessions (one control session prior to each dose). There was no evidence that the methaqualone vehicle was behaviorally active; therefore, saline and methaqualone vehicle

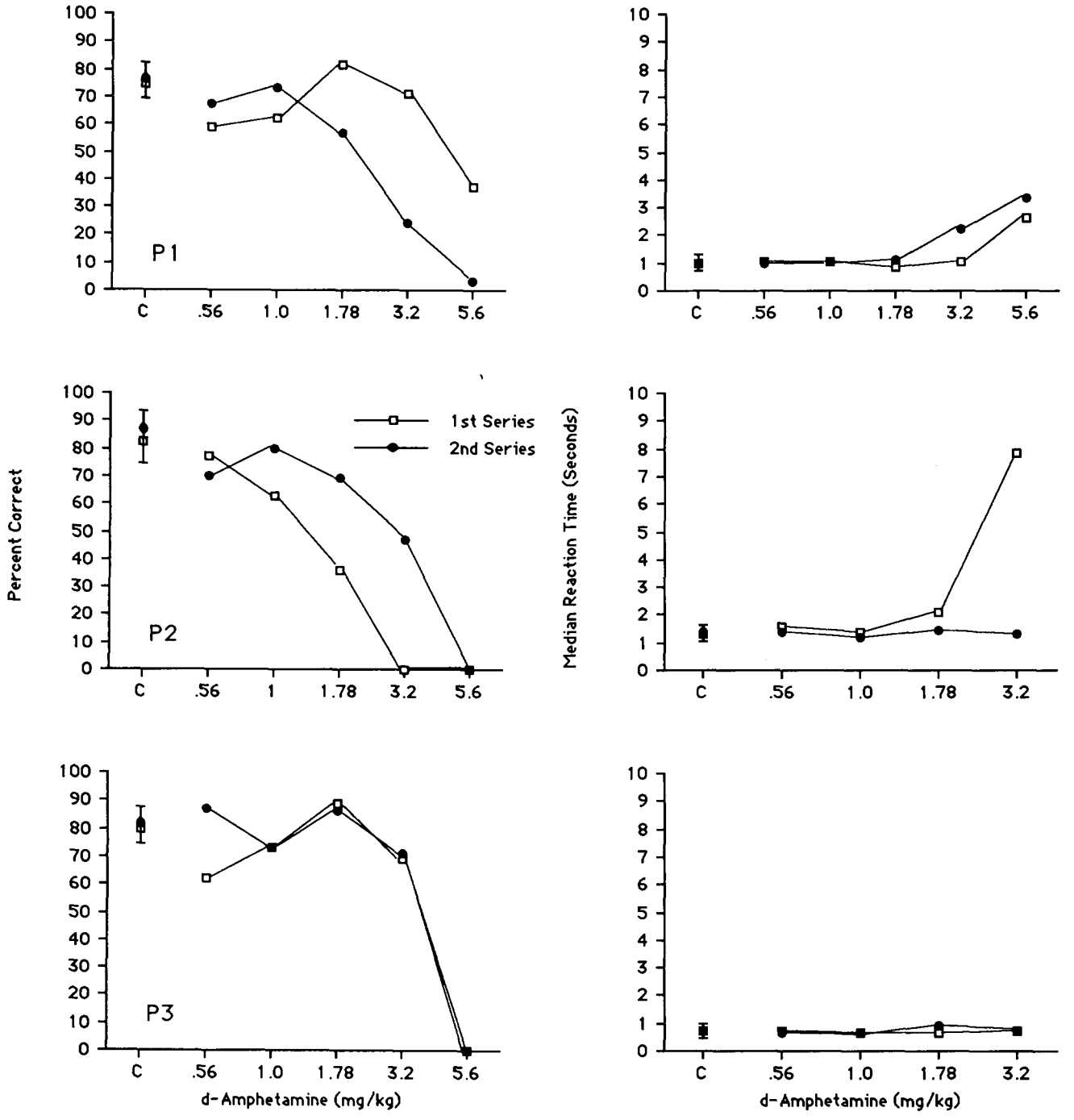


FIG. 1. Effects of *d*-amphetamine on the percent correct responses and median reaction time of individual pigeons. Drug data are presented separately for each of two series of administrations. Vehicle control data (C) represent all control sessions immediately before the drug sessions in each series. Vertical lines through control data points represent the range across these sessions.

control sessions are combined in Fig. 2. All drug data points in each figure represent a single session.

In the absence of drug, median reaction times and percent correct responses were relatively consistent within and between subjects. In all three subjects, methaqualone and phencyclidine produced substantial and generally dose-dependent decreases in percent correct responses and increases in median reaction times. No consistent differences were evident in the results of the two dose-response determinations.

*d*-Amphetamine also produced generally dose-dependent decreases in percent correct responses. The effects of this drug on median reaction time were inconsistent, although at high doses (3.2 and 5.6 mg/kg) it increased the median reaction time in two of three subjects. The median reaction time of

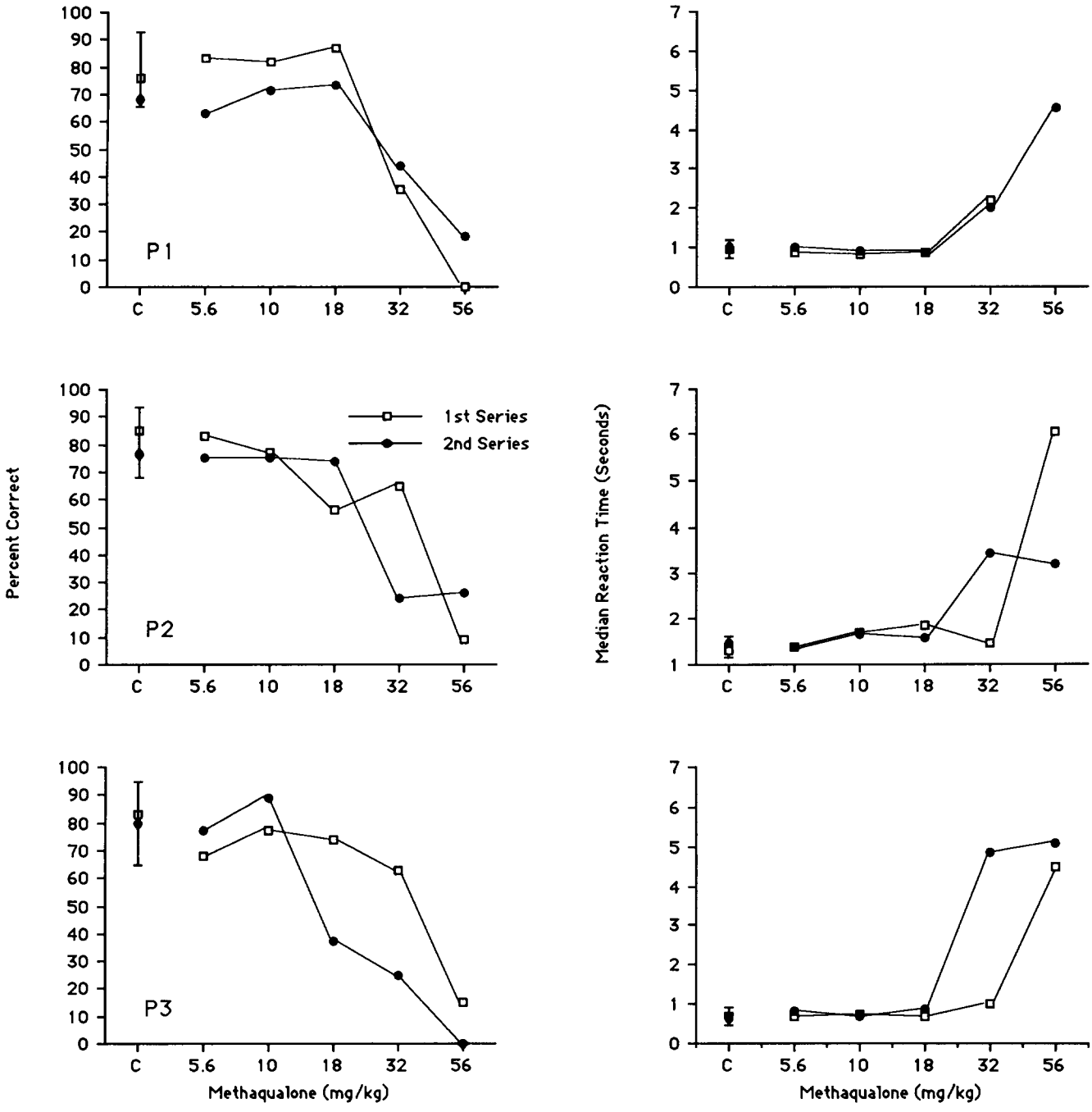


FIG. 2. Effects of methaqualone on the percent correct responses and median reaction time of individual pigeons. Details are as in Fig. 1.

one bird (P3) was not affected by *d*-amphetamine at any dose. There were no obvious differences in results of the two dose-response determinations for either median reaction time or percent of responses that were reinforced.

Table 1 summarizes the kinds of errors that occurred under all experimental conditions. This table presents for each bird the percentage of total errors that were early releases under all experimental conditions. In the absence of drug, the vast majority of errors made by one subject (P3) were early releases. For the other two, both early releases and aborts contributed substantially to the total error pool. Across all control sessions, the percent of total errors composed of early releases was 42 for P1, 62 for P2, and 89 for P3. When control data for each drug are compared, there is considerable variability within subjects.

It is difficult to summarize how drugs affected the distribution of errors. In all birds, *d*-amphetamine at the two highest doses (1.78 and 3.2 mg/kg) slightly decreased the percentage of errors that were early releases. Phencyclidine at 0.3, 0.56, and 1.0 mg/kg produced a similar, but stronger, effect on this

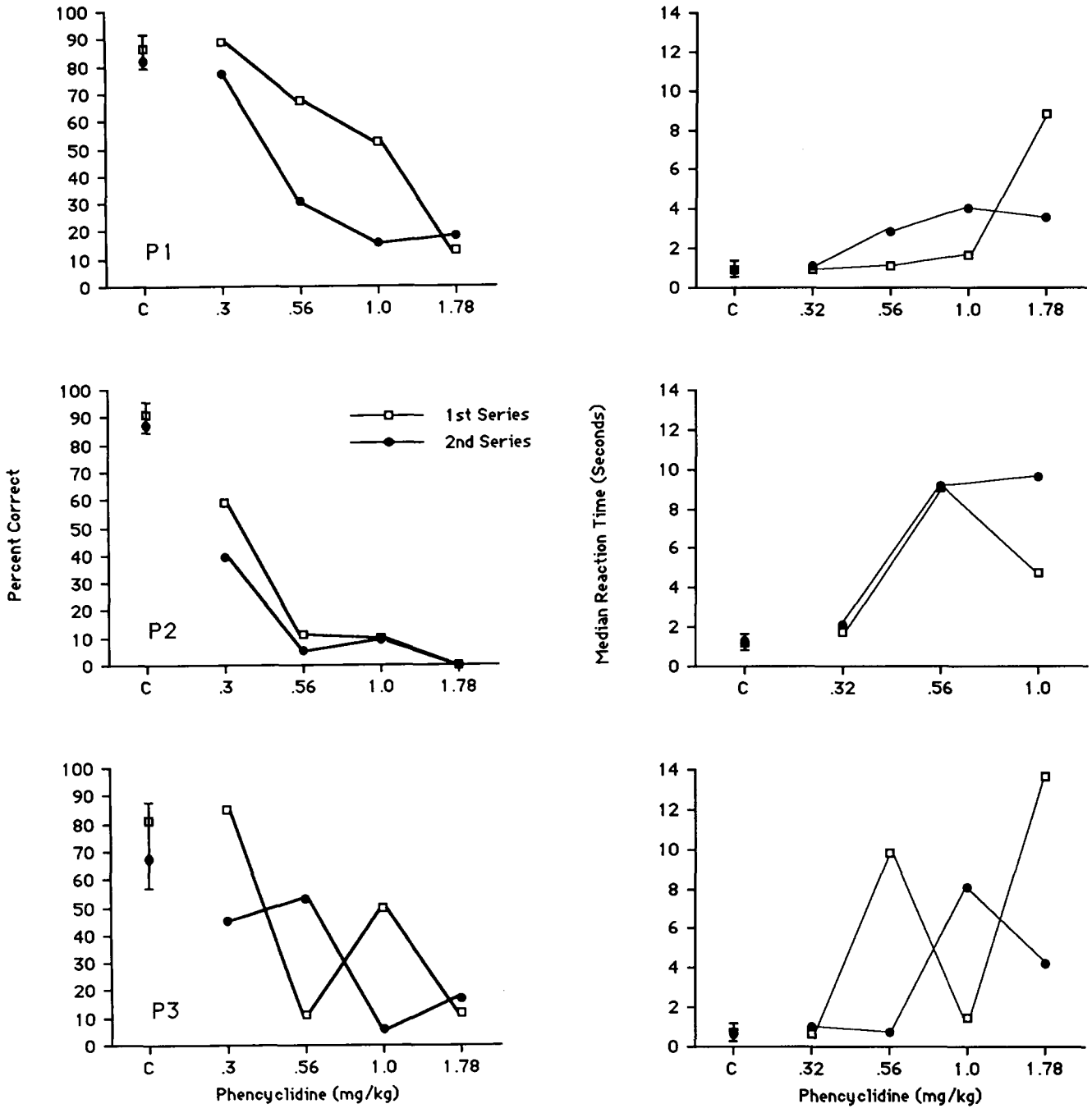


FIG. 3. Effects of phencyclidine on the percent correct responses and median reaction time of individual pigeons. Details are as in Fig. 1.

measure. In all birds, the percentage of errors that were early releases increased at 1.78 mg/kg phencyclidine relative to 1.0 mg/kg. In two birds (P2, P3) methaqualone generally decreased the percentage of errors that were early releases. Effects in the other bird (P1) were inconsistent.

Median response latencies during catch trials are shown in Table 2. Because there was no obvious difference in latencies during the first and second exposures to any drug, these data are not presented separately. Table 2 clearly reveals that treadle-releasing by all subjects in regular trials was under the control of the change in illumination from white to red. Catch trial response latencies under control and drug conditions consistently exceeded 3 s and were much longer than normal-trial latencies. Also, relatively few (i.e., less than 20% of) catch trial responses were "correct" (i.e., occurred within 2 s of the end of the foreperiod). Drug effects on median response latencies during catch trials were inconsistent within and across subjects for *d*-amphetamine, phencyclidine, and methaqualone.

Because the number of trials that occurred in each session

TABLE 1

PERCENT OF TOTAL ERRORS THAT WERE EARLY RELEASES UNDER ALL EXPERIMENTAL CONDITIONS

| Drug | mg/kg | Subject P1 | P2 | P3 |
|---|---|---|---|---|
| *d*-Amphetamine | 0.0 | 30 | 53 | 94 |
| | 0.56 | 22 | 52 | 88 |
| | 1.0 | 23 | 70 | 96 |
| | 1.78 | 21 | 50 | 76 |
| | 3.2 | 16 | 36 | 88 |
| Methaqualone | 0.0 | 33 | 41 | 100 |
| | 5.6 | 35 | 28 | 93 |
| | 10.0 | 30 | 32 | 66 |
| | 18.0 | 59 | 17 | 97 |
| | 32.0 | 26 | 27 | 33 |
| | 56.0 | 53 | 16 | 28 |
| Phencyclidine | 0.0 | 80 | 63 | 76 |
| | 0.3 | 29 | 29 | 54 |
| | 0.56 | 41 | 41 | 41 |
| | 1.0 | 39 | 27 | 31 |
| | 1.78 | 51 | 88 | 57 |

was not fixed, it is of interest to examine whether the number of trials completed changed as a function of drug and dose. Table 3 shows the number of trials completed by each bird under all experimental conditions. At relatively high doses, each drug sometimes reduced the number of trials completed compared with vehicle control values, although this effect was not consistent.

## DISCUSSION

Save for the inclusion of catch trials in the present study, the procedures employed to study reaction time were identical to those used in a prior investigation (1). The finding that median reaction times in those catch trials were relatively long (i.e., in excess of 3 s, the longest foreperiod duration) provides evidence that the change in illumination from red to white at the end of the foreperiod was controlling behavior during regular trials. Further evidence is provided by the observation that, in the vast majority of trials, all birds met the criterion for reinforcement (i.e., stepped off the treadle within 2 s of the stimulus change). Thus, it appears that Blakely et al. (1) were correct in asserting that their procedures provide a workable assay of reaction time in pigeons. Such an assay is of interest insofar as one important goal of those who conduct nonhuman research in behavioral pharmacology is to disclose drug effects that might be harmful if manifested in humans who take those drugs (6). Certainly increases in reaction time fall in this category.

Reaction time as assayed by time from the onset of a stimulus light to release of a foot treadle was sensitive to the effects of mephenytoin and methsuximide in an earlier study (1) and to the effects of *d*-amphetamine, phencyclidine, and methaqualone in the present experiment. These five drugs represent four different pharmacological classes (i.e., two anticonvulsants, a stimulant, a dissociative anesthetic, and a sedative-hyp-

TABLE 2

MEDIAN REACTION TIMES (IN SECONDS) DURING CATCH TRIALS UNDER ALL EXPERIMENTAL CONDITIONS

| Drug | mg/kg | Subject P1 | P2 | P3 |
|---|---|---|---|---|
| *d*-Amphetamine | 0.0 | 4.63 | 8.07 | 6.01 |
| | 0.56 | 6.32 | 4.72 | 3.74 |
| | 1.0 | 3.52 | 6.12 | 4.66 |
| | 1.78 | 4.50 | 3.19 | 7.42 |
| | 3.2 | 7.57 | 3.05 | 5.32 |
| Methaqualone | 0.0 | 6.89 | 8.64 | 7.98 |
| | 5.6 | 5.20 | 9.20 | 6.96 |
| | 10.0 | 5.19 | 7.63 | 10.05 |
| | 18.0 | 4.86 | 25.19 | 3.58 |
| | 32.0 | 14.57 | 8.13 | 6.34 |
| | 56.0 | 5.98 | 7.68 | 9.09 |
| Phencyclidine | 0.0 | 4.65 | 7.56 | 5.99 |
| | 0.3 | 4.08 | 15.90 | 5.51 |
| | 0.56 | 5.72 | 6.31 | 4.84 |
| | 1.0 | 4.44 | 4.66 | 8.88 |
| | 1.78 | 21.90 | * | 1.55 |

*No responding.

TABLE 3

NUMBER OF TRIALS COMPLETED

| Drug | mg/kg | Subject P1 | P2 | P3 |
|---|---|---|---|---|
| *d*-Amphetamine | 0.0* | 52 | 48 | 49 |
| | 0.56† | 68 | 52 | 65 |
| | | 60 | 57 | 46 |
| | 1.0 | 65 | 63 | 55 |
| | | 55 | 50 | 55 |
| | 1.78 | 49 | 89 | 45 |
| | | 70 | 58 | 36 |
| | 3.2 | 56 | 17 | 58 |
| | | 89 | 86 | 56 |
| Methaqualone | 0.0 | 56 | 50 | 49 |
| | 5.6 | 48 | 48 | 59 |
| | | 64 | 53 | 52 |
| | 10.0 | 49 | 52 | 52 |
| | | 56 | 53 | 45 |
| | 18.0 | 46 | 71 | 54 |
| | | 55 | 54 | 53 |
| | 32.0 | 89 | 62 | 63 |
| | | 89 | 80 | 89 |
| | 56.0 | 2 | 58 | 33 |
| | | 89 | 27 | 25 |
| Phencyclidine | 0.0 | 48 | 45 | 58 |
| | 0.3 | 45 | 68 | 47 |
| | | 52 | 89 | 88 |
| | 0.56 | 60 | 47 | 54 |
| | | 89 | 63 | 76 |
| | 1.0 | 89 | 20 | 58 |
| | | 77 | 66 | 63 |
| | 1.78 | 76 | 6 | 17 |
| | | 47 | 5 | 29 |

*Control data for all drugs are means for all vehicle sessions.

†For all drugs and doses, data for the first series appear above data for the second series.

notic) and have dissimilar neuropharmacological mechanisms of action. Nonetheless, each of them produced generally dose-dependent decreases in the percentage of responses that met the criterion for reinforcement. With the exception of *d*-amphetamine, all of the drugs also increased median reaction time. The effects of *d*-amphetamine on this measure differed across birds, although in two of three there was some evidence of increased reaction time at the highest (3.2 mg/kg) dose.

Because drugs from four different pharmacological classes produced similar effects, disruption of performance under the reaction time assay does not appear to depend upon a particular neuropharmacological mechanism of action. This limits the utility of the assay for studies designed to examine relations between the behavioral and physiological actions of drugs.

No prior reports of the effects of *d*-amphetamine or methaqualone in pigeons exposed to pure reaction time assays have appeared. In studies using human subjects and procedures different from those of the present study, both drugs have been reported to increase reaction time (3,10). In pigeons responding under a delayed-matching-to-sample procedure, *d*-amphetamine and phencyclidine increased response latencies when sample and comparison stimuli were presented (5). Insofar as response latencies in this assay can be taken as a measure of reaction time, these findings are consistent with the present results.

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