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Impact of d-Amphetamine on Temporal Estimation in Pigeons Tested with a Production Procedure

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KRAEMER, P. J., C. K. RANDALL, J. M. DOSE AND R. W. BROWN. *Impact of d-amphetamine on temporal estimation in pigeons tested with a production procedure.* PHARMACOL BIOCHEM BEHAV **58**(2) 323–327, 1997.—The influence of d-amphetamine on timing in pigeons was examined with a production procedure. Birds were trained with a fixed time schedule in which food reinforcement was contingent on the first response made after a duration signal had appeared for 30 s. Probe tests involved trials in which the duration signal was extended to 90 s and reinforcement was omitted. In Experiment 1, 2.0 mg/kg d-amphetamine shifted peak responding to a duration shorter than that found with saline. In Experiment 2, the dose–response function for this drug effect was examined. A 0.3-mg/kg dose of d-amphetamine had no impact on performance, but a 1.0-mg/kg dose shifted the peak duration significantly relative to saline; a 2.0-mg/kg dose shifted the function even more. These results complement previous findings with rats tested with the peak procedure and pigeons tested with a discrimination procedure. © 1997 Elsevier Science Inc.

Timing d-Amphetamine Pigeons Perception

THERE is considerable evidence that amphetamines affect temporal processing. Humans (5), rats (6) and pigeons (8) overestimate brief durations when tested under the influence of amphetamines. The general interpretation of this effect is that amphetamines cause brief durations to be perceived as longer than would normally be the case. This conclusion has been based on results from two different test procedures, each of which measures a different aspect of temporal processing.

In the discrimination procedure, the subject is trained to make different responses to each of two durations. For example, a rat might be trained to press one lever after a 2-s light and a different lever after a 10-s light. Subsequent test trials present durations between the two training values, and performance on these trials is used to measure how the subject categorizes "short" and "long" durations. The duration that the subject categorizes as long on half of the trials defines the point of subjective equality (PSE), which reflects the subjective boundary between short and long durations. The PSE is usually equivalent to the geometric mean of the two training durations (3). When tested following an injection of an amphetamine, however, rats (2) and pigeons (8) show a significant decrease in the PSE.

The other technique used to investigate drug effects on timing is the production or "peak" procedure. This procedure requires the subject to produce a criterion duration by regulating its behavior along a temporal dimension. For example, a rat might be reinforced with food for its first lever-press response after a stimulus has appeared for some set duration (e.g., 30 s). With sufficient training, rats display an impressive temporal regularity in their behavior; rate of responding during the duration signal gradually accelerates to a peak at or slightly above the criterion interval, at which point response rate gradually declines. When tested with amphetamines, two behavioral changes appear. First, there is an overall increase in rate of responding, which reflects the behavioral activating effect of the drug (1,4). Second, there is a leftward shift of the response function; amphetamines cause peak responding to appear sooner during the duration signal than would occur otherwise (6).

The ability to judge a fixed duration (production procedure) is related to, but not the same as, the ability to discrimi-

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nate two durations. For that reason, it is important to integrate data from both test procedures, especially with drugs like amphetamines that can influence performance on a timing task without necessarily influencing the timing process. For example, the tendency for amphetamines to produce a shift in the PSE in a discrimination task does not by itself indicate that temporal processing has been effected by the drug; rather, the shift might indicate that the animal's criterion for classifying a duration as short or long has changed.

EXPERIMENT 1

Although there is evidence with the discrimination procedure that amphetamines alter PSEs similarly in pigeons and rats (4,6,8), there is no evidence available on the influence of amphetamines on pigeons tested with the production procedure. The purpose of the present study was to provide preliminary data on this question. The first experiment tested pigeons with a peak procedure with or without d-amphetamine.

Method

Subjects. Three naive White Carneux pigeons served as subjects. The birds were housed in individual stainless steel cages in a climate-controlled vivarium that operated on a 12:12-h light:dark cycle. All testing occurred during the light phase of the cycle. The test procedures and animal maintenance protocols were approved by the University of Kentucky Animal Care and Use Committee (Protocol 89-0014L).

Apparatus. The test box was a standard operant chamber for pigeons. A single 2.7-cm pecking key was centered on the front wall, 12 cm above a 5-cm^2 food receptacle through which pigeons received controlled access to mixed grain. The pecking key was always illuminated with a red light. The duration signal consisted of a white houselight located in the center of the ceiling.

Procedure. Each bird was reduced to 80% of their free-feeding weights and pretrained to peck the red key for 3-s access to grain in the absence of the duration signal. During the subsequent training phase, each pigeon received daily sessions consisting of 48 trials. A trial was defined by the appearance of the duration signal. The first response to the red key 30 s after the duration signal appeared produced 3-s access to grain and terminated the duration signal. All other responses to the red key had no programmed effect. Trials were separated by a variable interval schedule (mean = 90 s, range = 15–180 s).

Test sessions began once performance stabilized. The test sessions were of two types: drug and nondrug. Every drug session began with a 1-ml/kg intraperitoneal (IP) injection of d-amphetamine (2 mg/kg) administered 10 min before the bird was placed into the test chamber. Nondrug sessions were identical to drug sessions except that saline was substituted for d-amphetamine. Each bird received two blocks of testing in which drug and nondrug sessions alternated regularly over 8 days. Test sessions differed from training sessions only with respect to a change in the nature of 6 of the 48 trials. On these probe trials, the duration signal was extended to 90 s and responding to the red key had no effect (i.e., reinforcement was omitted). Peck responses to the red key were monitored continuously throughout each session and were summated separately for each 3-s bin of every trial.

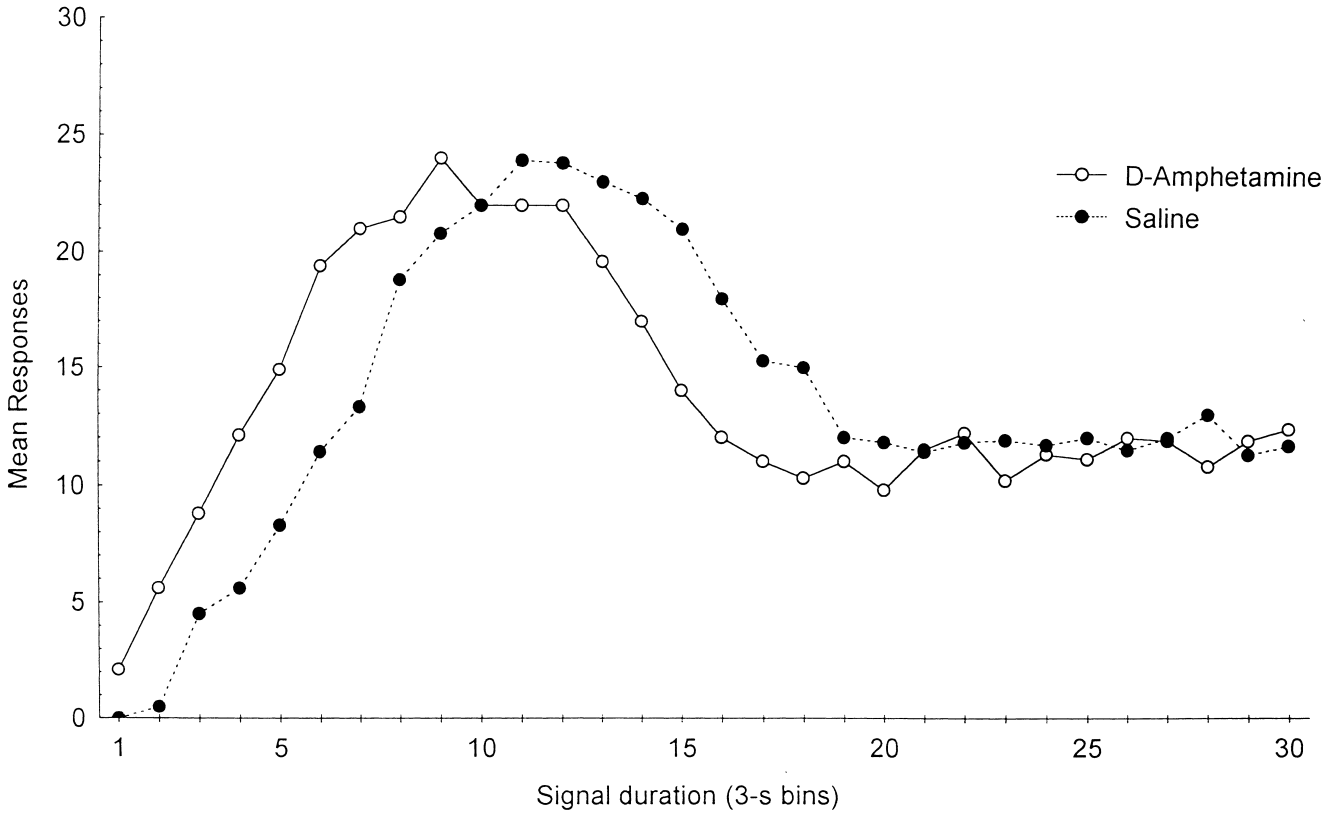

FIG. 1. Mean responses for each 3-s bin on probe trials plotted separately for d-amphetamine and saline sessions tested in Experiment 1.

Results and Discussion

Mean peck responses during each 3-s bin are plotted in Fig. 1 as a function of signal duration. The response function for drug and nondrug conditions closely resembles that typically found with pigeons tested with this production procedure (7). Response rate increased gradually to a peak and then gradually declined to an asymptote substantially above zero. The most important feature of these data is the leftward shift in the peak of the response function due to d-amphetamine. The mean peak duration was lower with d-amphetamine (mean = 9.3, SEM = 0.33) than with saline (mean = 12.0, SEM = 0.99), and the difference between the two means was statistically significant [$t(2) = 4.4$, $p < 0.05$]. The mean peak response rate, however, did not differ significantly between the two conditions [saline: mean = 25.6, SEM = 4.0; d-amphetamine: mean = 23.7, SEM = 2.9; $t(2) = 0.56$, $p < 0.63$].

The significant leftward shift in peak responding due to d-amphetamine replicates findings with rats tested with the same basic procedure (2,6). These results also complement findings with pigeons tested with a discrimination procedure (8). Thus, it is now possible to conclude that amphetamines exert a similar influence on timing in pigeons and rats. There is a salient difference, however, between these results and those with rats. There was no evidence from Experiment 1 that response rate was influenced by d-amphetamine. The mean peck rate at the peak of responding during saline test sessions was no different from that during d-amphetamine test sessions. Thus, the influence of d-amphetamine on timing in this experiment apparently cannot be attributed exclusively to the stimulating effects of the drug on arousal or behavioral activity (1,4).

EXPERIMENT 2

The second experiment was designed to replicate and extend findings from Experiment 1. A group of three naive, white Carneux pigeons were trained with the same procedure and apparatus as used in the first experiment. Testing involved sessions of 48 trials. Six trials within each session were probe trials in which the duration signal remained on for 60 s and food reinforcement was omitted. Each subject received a 1-ml/kg IP injection of either saline or one of three doses of d-amphetamine: 0.3, 1.0, or 2.0 mg/kg. A block of trials consisted of 6 sessions that were alternated regularly between saline and d-amphetamine injections. Each dose of d-amphetamine was tested once within a trial block, and the order in which these doses were tested within a trial block differed randomly across subjects. Each subject received 3 blocks of testing.

Results

Figure 2 presents mean performance on probe trials for each of the four drug conditions. The response rate increased to a peak and then decreased with saline and with each of the three doses of d-amphetamine. Peak duration differed as a function of the dose of d-amphetamine administered. This latter effect is more clearly evident in Fig. 3, which plots mean

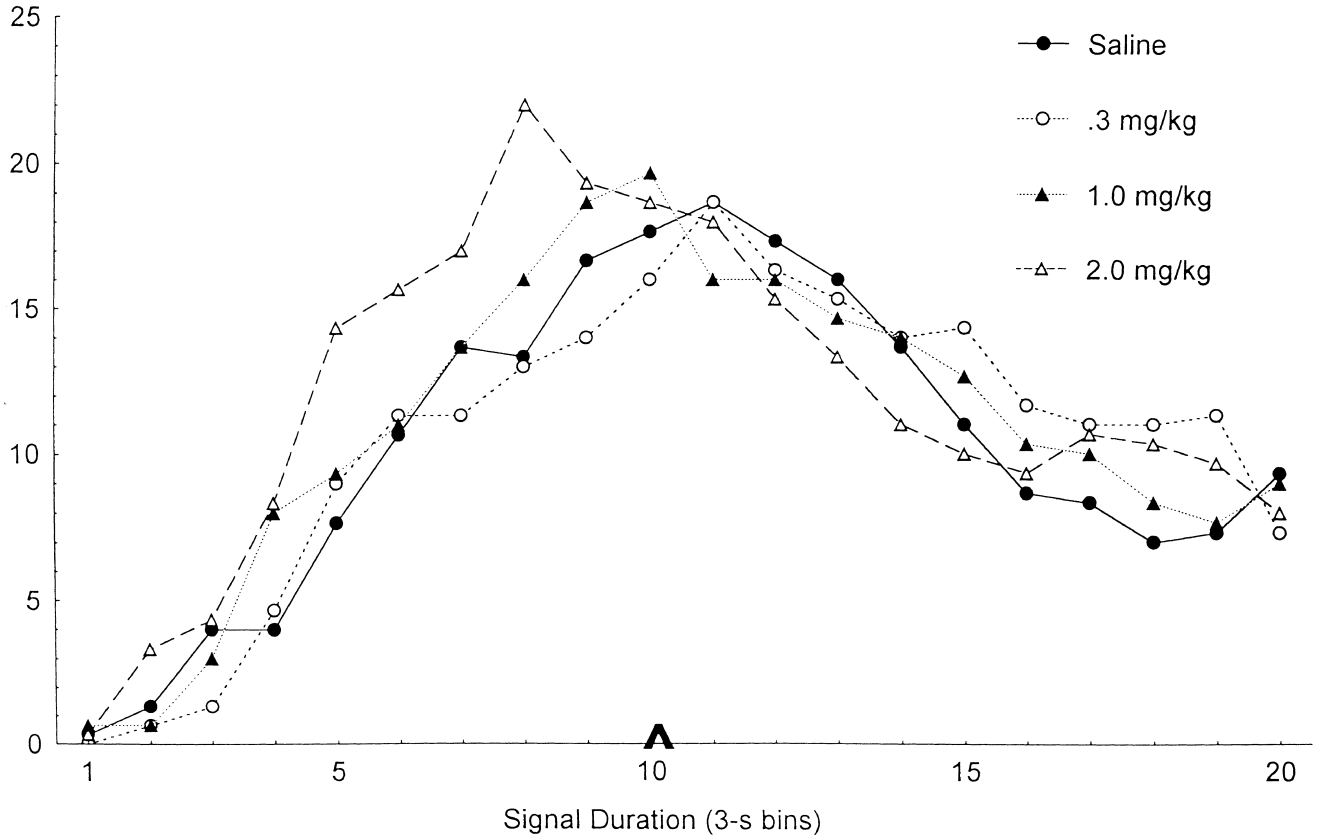

FIG. 2. Mean responses for each 3-s bin on probe trials plotted separately for sessions involving saline and each of the three (0.3, 1.0, 2.0 mg/kg) doses of d-amphetamine tested in Experiment 2.

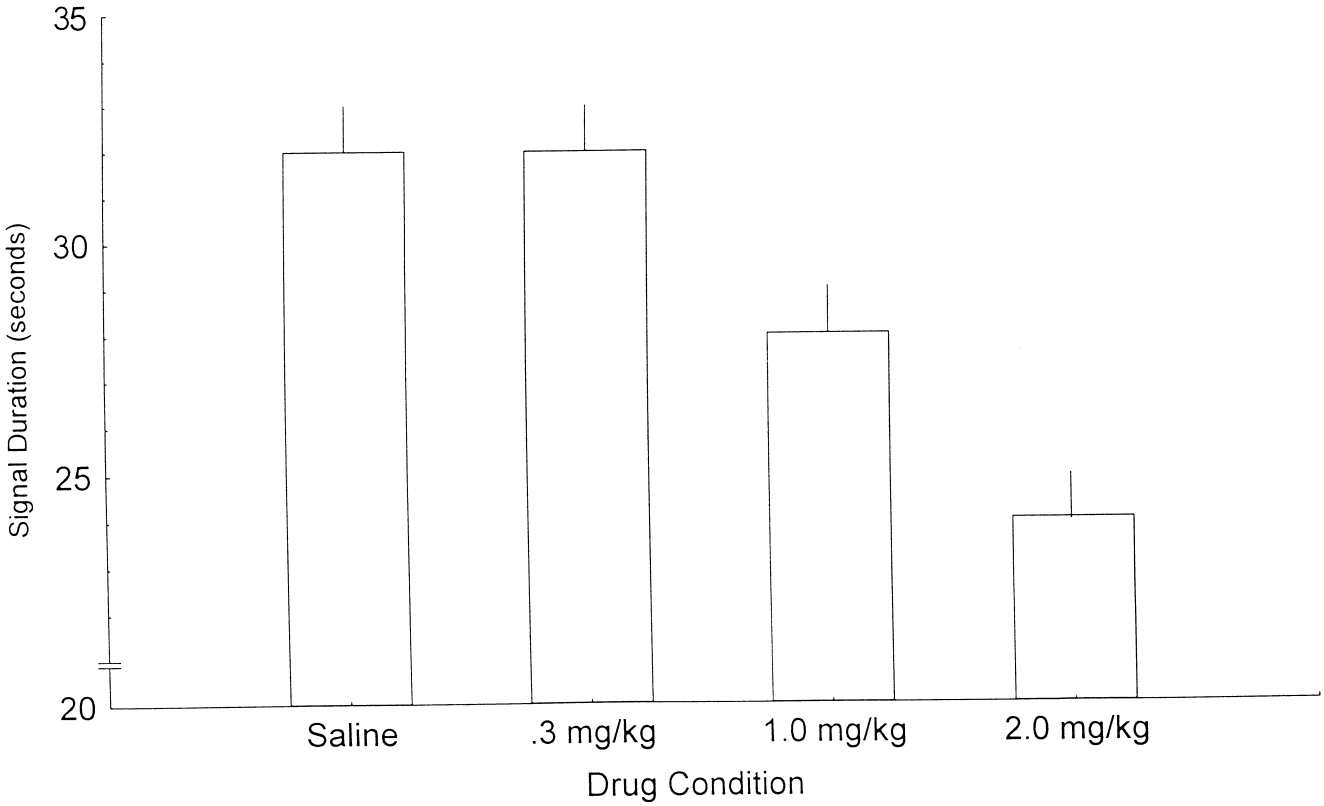

FIG. 3. Mean signal duration at which peck responses were highest for sessions involving saline and each of the three (0.3, 1.0, 2.0 mg/kg) doses of d-amphetamine tested in Experiment 2.

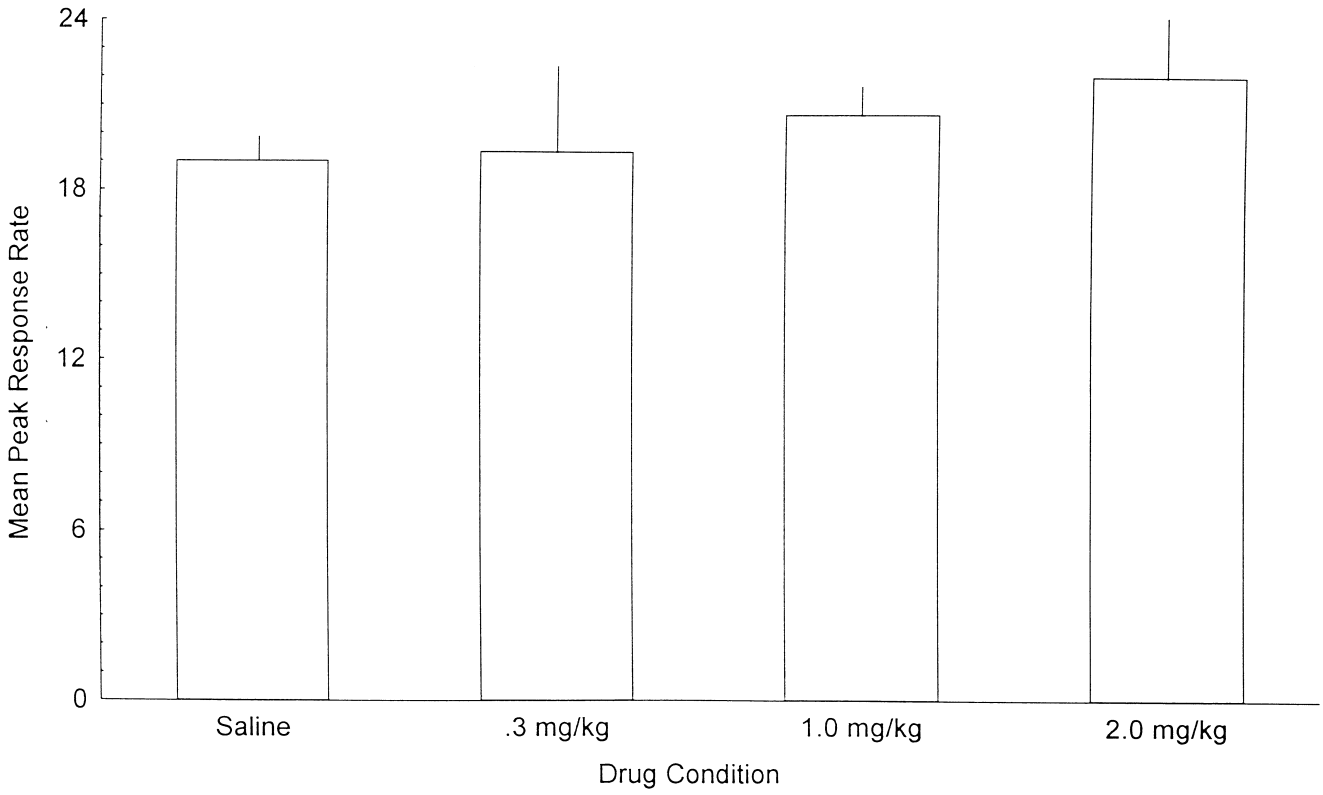

FIG. 4. Mean peck rate at the signal duration at which peck responses were highest for sessions involving saline and each of the three (0.3, 1.0, 2.0 mg/kg) doses of d-amphetamine tested in Experiment 2.

peak duration for each of the four drug conditions. Although performance at the 0.3-mg/kg concentration was almost identical to that with saline, the mean peak duration was lower with 1.0 mg/kg and lower yet with 2.0 mg/kg. A repeated measures analysis of variance confirmed that peak duration changed significantly across the four conditions [$F(1, 3) = 16$, $p < 0.003$]. Post hoc comparisons indicated that mean peak duration was equal for saline and 0.3-mg/kg conditions, but it was significantly longer under these conditions than it was under the two higher doses of d-amphetamine. The mean peak duration was also significantly higher at the 1.0-mg/kg dose than it was at the 2.0-mg/kg dose. Peak rate of responding, however, did not differ significantly across the four conditions (Fig. 4) [$F(3, 6) = .51$, $p > 0.6$].

These results indicate that a dose–response relationship exists in the effects of d-amphetamine on duration estimation in pigeons tested with the peak procedure. The degree to which peak responding occurred earlier during a duration signal changed with the dose of the drug. The lowest dose, 0.3 mg/kg, produced no discernible impact on performance. A moderate dose, 1.0 mg/kg, shifted the response function to the left, and the highest dose, 2.0 mg/kg, shifted the function even farther to the left. Interestingly, overall peck rate did not change across the three dose levels. The 2.0-mg/kg dose level represents the highest dose of d-amphetamine that we were able to test. A pilot experiment that included higher dose levels (e.g., 3.0 mg/kg) was aborted once it became apparent that pigeons would no longer peck at the response key while under the influence of these higher doses of the drug.

GENERAL DISCUSSION

These results establish that duration estimation in pigeons, as measured with a peak procedure, is influenced by d-amphetamine. The leftward shift in peak responding obtained in the present study is consistent with the impact of amphetamines on timing in rats (2,6). More significantly, these findings complement results obtained from pigeons tested with a discrimination procedure (9). When the present findings are combined with those obtained with the discrimination procedure, it is possible to conclude that amphetamines exert a similar influence on timing in pigeons and rats. This conclusion is premature without data from the peak procedure because it is possible to interpret the effects of d-amphetamine on performance in the discrimination task in ways that do not implicate timing. For example, a shift in the PSE with the discrimination procedure could indicate that a drug has altered the response criterion the animal uses to discriminate or classify durations as short or long, which is only one dimension of temporal processing. Data from the peak procedure provide the necessary additional information to ascribe the locus of a drug effect to timing rather than some other aspect of behavior.

There are at least two viable mechanisms that could account for the effects obtained in the present study. One approach relies on the idea of an internal clock, which consists of a number of interrelated components. The centerpiece of the model is the pacemaker, a hypothetical device that emits pulses at regular intervals. These pulses accumulate during a target event, and the animal's subjective duration for that event is based on the number of pulses that have accrued (2). It is possible that d-amphetamine increases the speed of the pacemaker, which would result in more pulses accumulating during the same absolute duration than would occur in the absence of the drug (6). The behavioral consequence of this effect would be overestimation, as occurred in the present experiments.

The other possibility is that d-amphetamine alters attention, which indirectly changes performance on a timing task. This approach assumes that the pacemaker operates at the same speed with and without d-amphetamine but the animal starts timing the signal sooner with the drug, perhaps because it more quickly identifies the presence of the duration signal (9). The present findings do not distinguish between these two possibilities, nor has this issue been resolved in other studies (6).

There is a discrepancy between the present findings and those found with rats. We discovered that d-amphetamine increased responding at signal durations up to the criterion interval (30 s) but decreased responding thereafter, but there was no apparent effect of d-amphetamine on rate of responding; the response functions were merely shifted to the left. In contrast to this pattern of results, studies with rats have found that amphetamines cause both a leftward shift in the response function and an increase in overall rate of responding (6). The latter is consistent with evidence that amphetamines have a stimulating effect on general activity (1,4).

This discrepancy might be related to our procedure, or it might indicate a species difference in the influence of d-amphetamine. Given the remarkable consistency in behavioral and pharmacological effects found in timing studies with pigeons and rats, we suspect that some aspect of our procedure and not a pharmacological difference between species is responsible for this discrepancy. Unlike other studies, our procedure measured responding to a stimulus that was different from the duration signal itself. Other studies that have used this task have trained animals to respond directly to the duration signal. Forcing subjects to respond to a stimulus different from that which provides duration information could alter the general behavioral profile expressed during testing, which is a possibility that we are now investigating.

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