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The Acute Effects of Caffeine, Cocaine and *d*-Amphetamine on the Repeated Acquisition Responding of Pigeons[1]

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EVANS, E. B. AND G. R. WENGER. *The acute effects of caffeine, cocaine and* d*-amphetamine on the repeated acquisition responding of pigeons.* PHARMACOL BIOCHEM BEHAV **35**(3) 631–636, 1990.—The acute effects of caffeine, cocaine and *d*-amphetamine on the repeated acquisition of a four-response chain were investigated in pigeons. Subjects responded on three response keys under different predetermined sequences. Food was presented upon the completion of the four-response sequence under a fixed-ratio schedule. Incorrect responses resulted in a five-second timeout. No consistent increases in within session percent correct were observed following caffeine or *d*-amphetamine administration. However, cocaine (1.0 mg/kg) did produce consistent increases in within session percent correct. At higher doses of cocaine, *d*-amphetamine and caffeine the effects observed were similar in that there was a decrease in response rate and percent correct. The drugs did differ in the dose (potency) which decreased response rate and percent correct. Following all three drugs if percent correct was decreased there was a concurrent decrease in response rate.

Behavior Cocaine *d*-Amphetamine Caffeine Repeated acquisition Pigeon Learning

THE behavioral effects of caffeine, cocaine and *d*-amphetamine have been studied extensively. Many of the behavioral studies have found that these central nervous system stimulants often have similar behavioral effects but vary in their potency and efficacy (5, 6, 9, 11). Historically the psychomotor stimulants, primarily caffeine and *d*-amphetamine, have been shown to enhance performance of a wide variety of behaviors (21). These studies often measure the ability of stimulants such as caffeine to maintain or improve an ongoing physical or mental performance, or their ability to improve mental and physical performance deteriorated by fatigue. Improvement produced by caffeine in these performances, although small in magnitude, is now well documented (2, 4, 13, 21, 22). However, if caffeine is tested on rested subjects no improvement is observed (8).

The present experiment differs from previous studies in that it measures the psychomotor stimulant's ability to alter the rate at which a new task is acquired ("learning") in rested subjects. In a previously published report, the effect of caffeine on learning was studied utilizing a maze with multiple choice points (14). In this experiment trials and errors to criterion were used as measures of "learning." The number of trials and errors accumulated before achieving a predetermined criterion was compared following drug administration to a vehicle control performance. The administration of caffeine (20 and 80 mg/kg) prior to maze testing did not reduce the errors or trials necessary to reach criterion as compared to saline control. It should be noted, however, that any effect of caffeine in this experiment (14) is questionable since the last dose of the drug was administered 48 hours before the first trial in the maze.

Therefore, since there are so few experiments testing the effects of caffeine on the rate at which a behavior is acquired, the present experiment studied the effects of caffeine on "learning." A modification of a schedule of reinforcement was used which was originally developed by Boren (1) in rhesus monkeys to permit the study and measurement of behavior in transition. The schedule was altered by Thompson (15) for application to pigeons and for testing the effects of drugs. Under the schedule, a new sequence of position responses on three response keys must be "learned" each session in order to obtain food presentation. Once the sequence of responses is "learned" the performance is measured in terms of

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the number of correct responses made in relation to the total number of responses emitted, i.e., percent correct. After training, a baseline was established, demonstrated by little session to session variation in terms of total percent correct and pattern of within session increases in percent correct ("learning" curve). The main objective of the present experiment was to measure the effects of caffeine on the pattern of acquisition of behavioral chains (within session percent correct). Once the dose effect relationship of caffeine was determined, results were compared and contrasted with those of *d*-amphetamine and cocaine.

METHOD

Animals

Five adult male White Carneaux pigeons with free feeding weights between 562–645 g were used. All of the subjects were experimentally naive at the start of the experiment. The subjects were maintained at 80% of their free feeding weight by postsession feedings. Water and grit were continuously available in their home cages.

Apparatus

The apparatus consisted of a standard three-key pigeon chamber (Model G7312, Gerbrands Corp., Arlington, MA). The chamber was housed in a ventilated, sound- and light-attenuating enclosure. Three translucent response keys, 2 cm in diameter, were mounted 5 cm apart, 22 cm above the chamber floor. A force of at least 0.17 N was required to open the key contacts and define the response. Each translucent response key could be transilluminated by lights mounted behind the keys. Located below the response keys, 5 cm above the wire mesh floor, was a rectangular opening providing pigeons access to Purina pigeon chow. The chamber was illuminated by two bulbs (No. 1819) (houselights) mounted on the ceiling of the chamber. Programming of the schedule and recording of responses were accomplished by a microcomputer located in a separate room (TRS-80, Model 4, Tandy Corp., Fort Worth, TX).

Schedule

Under the chain schedule, each subject was required to peck the correct key in the presence of each color. A correct response produced a change in key color (stimulus) to the color appropriate for the next step in the chain. The order of presentation of the stimulus colors remained the same throughout the experiment; yellow, red, green, blue. All three keys were illuminated with the same colored stimulus at the same time. The completion of the four response chain was followed by the brief (0.5-sec) raising of the food hopper. The sequence had to be completed four times (fixed ratio 4, FR 4) before receiving 3-second access to food. Incorrect responses resulted in a 5-second timeout during which all lights in the chamber were extinguished and responses were of no programmed consequence. After the timeout, the response keys were illuminated with the same color corresponding to the step in the chain where the error occurred, the chain did not reset. A session ended after 40 food presentations or 1 hour, whichever came first. There were ten sequences in all and sequences were changed from session to session.

Drugs

The drugs studied were caffeine sodium benzoate, cocaine hydrochloride and *d*-amphetamine sulfate. All drugs were dissolved in physiologic saline to a concentration that permitted the desired dose to be injected in a volume of 1 ml/kg body weight. All doses were calculated and are expressed as the salt. The drugs were administered by deep intramuscular injection into the pectoral muscle. Following drug administration, the subject was placed in a darkened experimental chamber. The session began after the elapse of the appropriate presession time allowing for the onset of drug effect. The presession or onset times were: 1800 seconds for caffeine sodium benzoate, and 300 seconds for cocaine hydrochloride and *d*-amphetamine sulfate. The birds were tested between 08:30 and 17:00 hours, Monday through Friday. Drug effects were tested on Tuesday and Friday with Thursdays used as a vehicle test day.

Data Analysis

The group data were analyzed by comparing drug effects to the mean of five saline control sessions. The five saline sessions bracketed each dose-effect determination. To measure the drug effects on within session percent correct or "learning," percent correct was plotted over blocks of reinforcers received. The session was divided into 5 blocks. Each of the first 4 blocks contained data for 4 reinforcers. Block five contained data for the last 24 reinforcers received. Percent correct was not plotted for any one block if total responses emitted in a block fell below 10 responses. Within session percent correct was determined to be significant using the two-sample rank test or Mann-Whitney U-test ($p \leq 0.05$) (7).

RESULTS

Figure 1 illustrates the effects of 1 and 3 mg/kg caffeine on within session percent correct in all pigeons. In pigeons P221, P223 and P224 doses of 1 and/or 3 mg/kg caffeine produced increases in within session percent correct. However, the improvements observed in within session percent correct in individual subjects were not consistent enough to produce a statistically significant upward and left shift of the relative position of the mean "learning" curves compared to control. Higher doses of caffeine (not shown) produced no improvement in within session percent correct and consequently no shifts in the relative position of the "learning" curves compared to the saline control curve. Following administration of 180 mg/kg caffeine, the within session percent correct was unaffected in P220 (not shown), the only subject which completed the session at this dose.

Figure 2 illustrates the effect of 1, 3, and 5.6 mg/kg cocaine on within session percent correct in all pigeons. Doses lower than 1 mg/kg cocaine (not shown) had no effect on within session percent correct. An improvement in within session percent correct was observed following 1 mg/kg cocaine. The dose of 1 mg/kg cocaine produced a shift of the relative position of the "learning" curves upward and to left from the saline control curve as shown in pigeons P220, P221 and 222 and produced improvements in within session percent correct in P223 and P224 though not in all blocks. At 1 mg/kg cocaine, the improvement in within session percent correct was consistent enough to produce a statistically significant shift in the mean "learning" curve upward and to left from the saline control curve. In two of the three subjects still responding at 3 mg/kg cocaine, within session percent correct was unaffected (P223 and P224), though an increase was observed in pigeon P222. Responding was so severely reduced at 3 mg/kg and/or particularly at 5.6 mg/kg cocaine in some subjects that

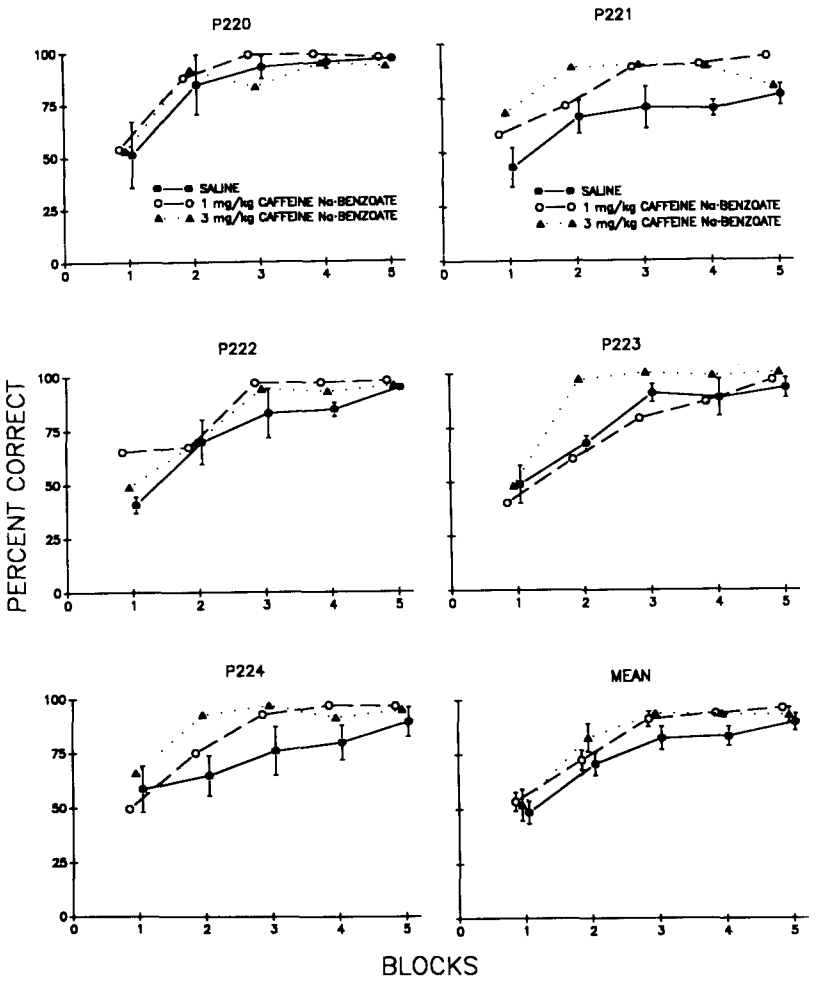

FIG. 1. Effects of caffeine Na·benzoate on within session percent correct. Abscissa: blocks of reinforcers per session, 4 reinforcers for each block 1 thru 4, 24 reinforcers in block 5. Ordinate: percentage of total responses emitted per block that were correct. Individual subject plots: each point represents a single observation. Mean plots: points and vertical lines represent the mean ± S.E.M. of single observations in 5 pigeons. Points and vertical lines for saline represents the mean ± S.E.M. from 5 saline sessions.

either within session percent correct was only plotted in the first few blocks (P221 and P222) or not at all (P223 and P224).

Figure 3 illustrates the effects of 1 and 1.8 mg/kg *d*-amphetamine on within session percent correct in all pigeons. Low doses of *d*-amphetamine (0.1 and 0.3 mg/kg, not shown) had no effect on within session percent correct compared to saline control sessions. Higher doses of 1 and 1.8 mg/kg *d*-amphetamine produced infrequent and inconsistent increases in within session percent correct. In P221 a substantial improvement in within session percent correct was produced following 1 mg/kg *d*-amphetamine, though this dose produced no changes in P220 and P223, and inconsistent increases in P222 and P224. At 1.8 mg/kg *d*-amphetamine, within session percent correct was unaffected in two subjects (P220 and P223) and increased in one subject (P222). Increasing the dose to 1.8 mg/kg *d*-amphetamine severely suppressed responding in two pigeons (P221 and P224). There was no change in within session percent correct responding at 3 mg/kg *d*-amphetamine compared to saline sessions in birds still able to respond at this dose. None of the doses of *d*-amphetamine tested produced a consistent increase in within session percent correct in the majority of subjects.

DISCUSSION

In previous experiments caffeine administration has been demonstrated to improve performance which has been decreased by fatigue or sleep deprivation, see review by Weiss and Laties (21). By contrast, in this experiment and in another experiment using human subjects (8) the effects of caffeine were tested on a rested performance. In both experiments caffeine did not produce a consistent improvement in performance. Similarly, in the present study, within session percent correct was not improved following *d*-amphetamine administration. This is in concordance with previous experiments in which acute *d*-amphetamine did not increase the degree of negative acceleration (increases within session percent correct) as measured by the index of curvature (15,16).

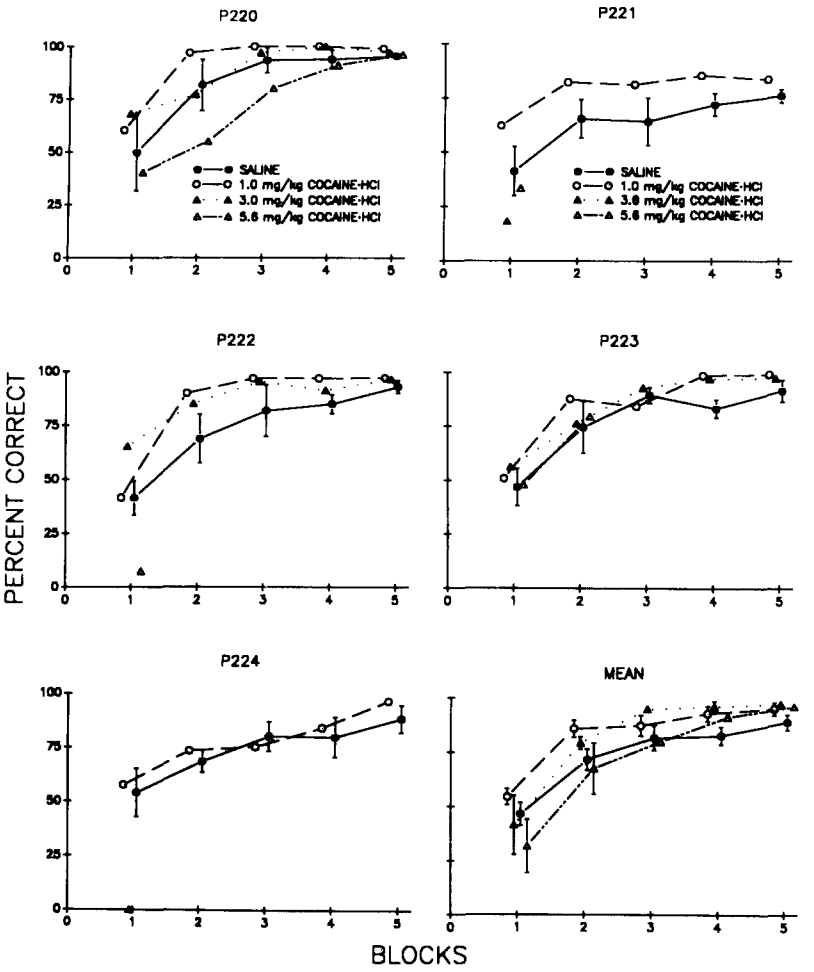

FIG. 2. Effects of cocaine·HCl on within session percent correct. Data as presented in Fig. 1.

However, the present results contradict with those of Harting and McMillan (10) who reported that following low doses of *d*-amphetamine (0.1 and 0.3 mg/kg) total percent correct was increased.

In contrast to the effects of caffeine and *d*-amphetamine, cocaine (1 mg/kg) administration resulted in consistent increases on within session percent correct. The increase in within session percent correct found here with cocaine is inconsistent with a previous report of cocaine's effect on accuracy employing a very similar procedure (17). These findings are also in contrast to the effects of cocaine on accuracy on matching to the sample examined by Branch *et al.* (3). In that experiment, acute cocaine administration produced only dose related decreases in accuracy at all delay periods.

At higher doses of caffeine, cocaine and *d*-amphetamine within session percent correct was decreased as a function of dose. The drugs differed in the dose (potency) at which the decrease was observed. The lowest dose producing a significant decrease in within session percent correct was: caffeine, 100 mg/kg; cocaine, 5.6 mg/kg; and *d*-amphetamine, 1.8 mg/kg. Plots of individual subjects revealed that at the higher doses of the three drugs tested, within session percent correct was decreased only when response rate was decreased (not shown). The converse was not necessarily true, responding could be reduced without a decrease in within session percent correct observed. In previous experiments in both pigeon and monkey following *d*-amphetamine and cocaine administration a decrease in percent correct was most often observed only when there was a decrease in response rate (15–20).

The discrepancies between this report and previous reports in the literature with respect to the effects of cocaine and *d*-amphetamine on within session percent correct may be partially accounted for if the schedule on which these experiments were run is examined. For example, in a study by Thompson and Moerschbaecher (19), the effects of these drugs varied according to the schedule on which the four response chain was tested. In that experiment three schedules were employed: one in which the chain had to be completed 5 times to gain access to the reinforcer (FR 5), one in which the reinforcer was presented upon the 20th completion of the chain (FR 20), and one in which the chain had to be completed 50 times (FR 50). The results of the experiment (19) demonstrated the effects of cocaine on within session percent correct varied according to the schedule. Under the FR 5, cocaine

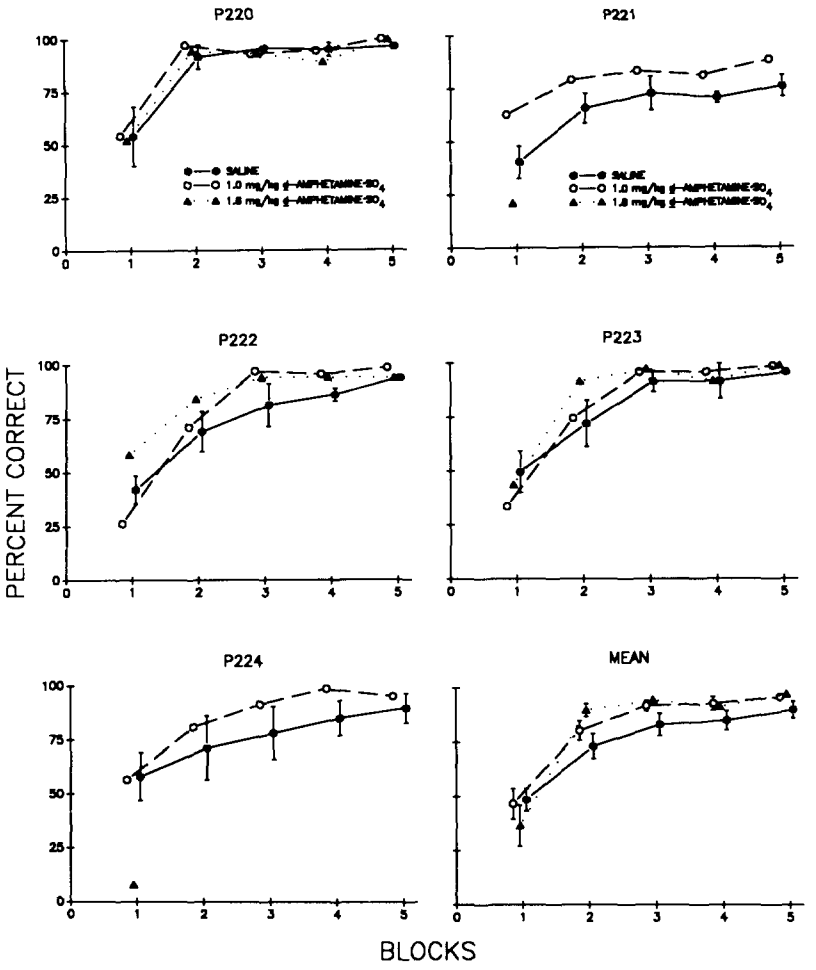

FIG. 3. Effects of *d*-amphetamine·SO_4 on within session percent correct. Data as presented in Fig. 1.

produced decreases in within session percent correct during the first part of the session. Under the FR 20 and FR 50 schedules, cocaine increased within session percent correct. Similar results were obtained following *d*-amphetamine administration (19). Like cocaine, *d*-amphetamine did not improve within session percent correct under the FR 5 schedule, but did under the FR 20 and FR 50 schedules. The three schedules used (19) generated a different baseline accuracy (percent correct) on which the drug effects were tested, and the baseline accuracy appeared to be an important modifier of the drug effect. Thus, Thompson (19) stated; "The effects of *d*-amphetamine and cocaine on accuracy may depend upon the control accuracy in the same way that the effects on rate may depend upon the control rate." It may be that the closer control accuracy is to an errorless performance the more difficult it is to observe a psychomotor stimulant induced increase in accuracy. In this respect, it should be noted that in the present experiment the control accuracy (total percent correct) resembles that of the FR 20 and FR 50 schedules in the Thompson experiment (19), and the effects of cocaine were similar. Therefore, these differing effects of cocaine and *d*-amphetamine on accuracy could be due to these schedule differences and consequently the baseline behavior. Other differences which cannot be ruled out include: length of error produced timeout and session length.

The failure to see an increase in accuracy following caffeine may also be related to baseline performance. As discussed above, if a psychomotor stimulant produced an improvement in a performance, it seemed the results often depended on the baseline performance on which the drug was tested. In experiments where cocaine and *d*-amphetamine produced no improvement in accuracy the baseline control accuracy was higher than in experiments where an improvement was observed. The role of the baseline control accuracy in modulating the drug effect is further evidenced in this study by noting the large increases in within session percent correct in pigeon P221 produced by 3 mg/kg caffeine, 1 mg/kg cocaine and 1 mg/kg *d*-amphetamine (Figs. 1, 2, and 3). Subject P221's baseline accuracy was invariably lower than the other subjects and consequently a larger margin for a drug-induced improvement in accuracy was present. The large drug-induced improvements in accuracy observed in this subject may be a reflection of this subject's lower baseline control accuracy. A comparison of this study with other reports in the literature indicates that caffeine seems to only produce an improvement in a mental performance where the baseline is deteriorated by fatigue.

The fact that cocaine increased accuracy in this experiment and caffeine did not may be related to differences in efficacy among these stimulants. Control accuracy may need to be lower to observe an effect of caffeine.

The effects of these psychomotor stimulants were measured over blocks of reinforcers received on a continually improving performance. Therefore, this experiment tests the effects of drugs on learning, if defined operationally as an improvement in performance with reinforced practice. In light of the fact that cocaine abuse has escalated in recent years, the use of caffeine is ubiquitous in today's society and amphetamine abuse remains, their effects on learning would be of paramount concern. The present analyses suggest that there is no detrimental effect of these psychomotor stimulants on "learning" until doses which produce a general behavioral disruption are achieved.

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