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ENHANCEMENT OF PROGRESSIVE-RATIO PERFORMANCE BY CHLORDIAZEPOXIDE AND PHENOBARBITAL[1]

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The key pecking of two pigeons was reinforced with food on a progressive-ratio schedule, which required an increasing number of responses for each successive reinforcement: 8, 16, 24, 32, *etc.* When the subject failed to complete the next ratio in the sequence within 60 min, the session terminated. The number of responses in the final completed ratio was defined as the "breaking point". After the breaking point had stabilized (60 sessions), it served as a baseline to assess the effects of varying doses (5 to 80 mg/kg) of chlordiazepoxide and phenobarbital, administered intramuscularly 30 min before the sessions. Both drugs increased the breaking point. The dose-effect curves were inverted U-shaped, with maximum enhancement of performance occurring at 20 mg/kg for chlordiazepoxide and at 40 mg/kg for phenobarbital. A comparable enhancement was not obtained during a nondrug "probe" session, which was conducted after the subjects' body weights had been temporarily reduced from 80% to 70% of their free-feeding weights. The drug-induced enhancement of breaking point was related to the initial values of the performance and may represent a reduction in the aversiveness of the schedule.

Hodos (1961) described a technique for evaluating performance in a free-operant situation without reference to rate of responding. Rats received a liquid reinforcer for pressing a lever. Two responses were required for the first reinforcement to occur in the session, four responses for the second reinforcement, six responses for the third, *etc.* This arrangement was called a progressive-ratio schedule because the subject was required to emit an increasing number of responses at each successive reinforcement. As the schedule progressed, the subject began to pause after each reinforcement before starting the next ratio run; the length of the post-reinforcement pause generally increased as the ratio increased. Eventually, the subject failed to respond for a period of 15 min and the session was terminated. The number of responses in the final completed ratio of the session was defined as the "breaking point" of the subject's performance.

The breaking point has proved to be a sensitive measure. Functional relationships have been obtained between the breaking point and such variables as the concentration and volume of a liquid reinforcer, the degree of food deprivation, and the size of the increment in the progressive-ratio schedule (Hodos, 1961; Hodos and Kalman, 1963). The breaking-point technique has also been used with brain stimulation as the reinforcer (Hodos, 1965).

In the present research, the progressive-ratio breaking point served as a baseline to assess the behavioral effects of drugs. Dose-effect curves were obtained for two prototype drugs, phenobarbital and chlordiazepoxide.

METHOD

Subjects

Two adult male White Carneaux pigeons, with an extensive history of fixed-ratio and variable-ratio reinforcement, were maintained within 10 g of 80% of their free-feeding weights throughout the baseline and drug conditions by food presented during the sessions and by post-session supplemental feeding. Water and grit were always available in the home cages.

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Apparatus

The experimental chamber was a single-key box designed to provide a food reinforcer. A 12 by 12 by 12 in. (30 by 30 by 30 cm) aluminum enclosure with a Plexiglas door was housed in a commercial ice chest, which was fitted with an exhaust fan and a one-way observation window. The translucent response key (Gerbrands Model B) was centered on the front wall, 8 in. (20 cm) above the wire-mesh floor. The key could be illuminated from behind by two green 7.5-w bulbs. A white 7.5-w houselight was mounted on the back wall near the ceiling. A minimum force of 15 g (0.14 N) was required to operate the response key. Located 4 in. (10 cm) below the key was a 2 by 2 in. (5 by 5 cm) opening through which a solenoid-operated hopper containing mixed grain was made available as the reinforcer. White noise was continuously present in the chamber to mask extraneous sounds. The automatic scheduling and recording equipment was located in a separate room.

Procedure

Throughout the following procedures the reinforcer was 5-sec access to grain. Presentation of the food magazine was accompanied by the offset of the keylight and houselight, and the onset of the magazine light. A "blackout" (all lights off) of variable duration preceded and followed each session. With few exceptions, there were six daily sessions a week.

Baseline. The pigeons were exposed to the progressive-ratio schedule for 60 sessions to allow the breaking points to stabilize. The ratio increment was eight; *i.e.,* at the start of each session, eight responses were required for the first reinforcement, 16 responses for the second, 24 for the third, *etc.* There was no option available to the subject to reset the progressive ratio during a session (*cf.* Hurwitz and Harzem, 1968). The criterion for the breaking point was reached when the subject failed to complete the next ratio in the sequence within 60 min, at which time the session was terminated.

Drugs. After baseline session 60, the next 16 weeks were used to obtain dose-effect curves for the drugs phenobarbital sodium and chlordiazepoxide hydrochloride. Four doses of each drug were tested and two determinations of each dose were taken with each subject. The drug testing followed the counterbalanced design PCCP, where P and C represent the blocks of four doses of phenobarbital and chlordiazepoxide; within each block, the doses were tested in a random order. The drugs were dissolved in saline and injected into the pectoral muscles 30 min before the test sessions, which took place once a week. Another session in each week was preceded by the administration of saline. The volume of each injection was 0.1 ml/100g body weight.

Probe. After drug testing, the degree of food deprivation was temporarily increased to see whether a "motivational" interpretation of the drug effects could be ruled out. This probe involved discontinuing the daily sessions, without supplemental feeding, until the subjects' body weights had dropped to 70% of the free-feeding weights. Only one session was conducted under these conditions, and then the baseline deprivation (80% of free-feeding weight) was reinstated. As a control, the daily sessions were also discontinued for an equal period of time but with supplemental feeding to maintain the baseline deprivation.

RESULTS

The dose-effect data for individual subjects were analyzed by comparing the breaking point (the number of responses in the last completed ratio) for a given drug session with the breaking points for the saline sessions and all of the baseline sessions except the one after the drug session. Figure 1 shows the dose-effect curves obtained with chlordiazepoxide and phenobarbital for both subjects. The brackets indicate the ranges of variability for the baseline (B) and saline (S) sessions. A drug was considered to have an overall effect on the breaking point to the extent that the dose data fell outside of both ranges (shaded area). With only one exception (which will be described later), all of the breaking points for all of the baseline sessions during the 16 weeks of drug testing fell within the ranges indicated. The baseline of breaking points was thus relatively stable for each subject, although there were individual differences in the absolute values. Figure 1 shows that the main effect of both drugs for both subjects was to increase the breaking point. This enhancement of performance was dose related, with the maximum

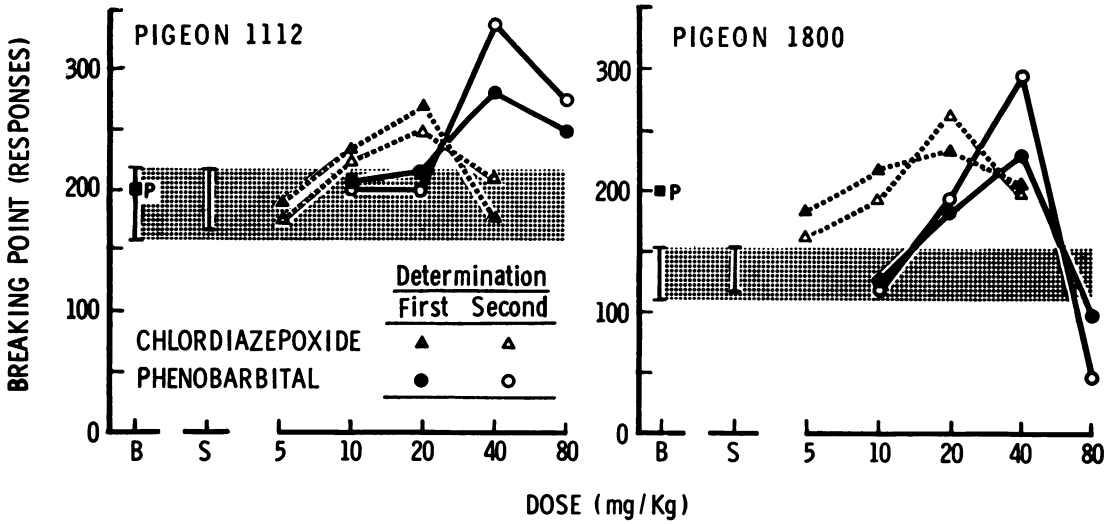

Fig. 1. Dose-effect curves for chlordiazepoxide and phenobarbital. Four doses of each drug were tested and there were two determinations of each dose with each subject. The breaking point refers to the number of responses in the last completed ratio of a session. The brackets and shaded area indicate the ranges of the breaking points for the baseline (B) and saline (S) sessions. The data points marked P represent the breaking points for the non-drug "probe" session, which was conducted after the subjects' body weights had been temporarily reduced from 80% to 70% of their free-feeding weights.

facilitation occurring at 20 mg/kg for chlordiazepoxide and at 40 mg/kg for phenobarbital. Note that the breaking point was increased by lower doses of both drugs when the baseline was relatively low (Pigeon 1800). At the largest dose of chlordiazepoxide (40 mg/kg), there was no effect on breaking point with Pigeon 1112, and less of a facilitating effect with Pigeon 1800, compared to the 20 mg/kg dose. At the largest dose of phenobarbital (80 mg/kg), there was less of a facilitating effect on breaking point with Pigeon 1112, compared to the 40 mg/kg dose, and a decrease in breaking point below baseline with Pigeon 1800. There were no systematic differences between the first and second determinations of the dose-effect curves for either drug.

The data points marked P in Figure 1 show the breaking points for the probe session that was conducted after drug testing when the subjects' body weights had been temporarily reduced to 70% of the free-feeding weights. The increased deprivation raised the breaking point above baseline only for the subject (1800) whose baseline range of breaking points was relatively low. The breaking point during the control session (not shown) was within the baseline range of variation for each subject, indicating that there was no effect of discontinuing the sessions for several days as long as the baseline deprivation was maintained.

Figure 2 shows the cumulative response records for Pigeon 1112 for a saline session and for the sessions in which the maximum facilitation of breaking point was obtained with each drug. Note that as the breaking point increased with the optimal dose of each drug, there was a decrease in the post-reinforcement pausing associated with the larger ratios. The high running rates of responding were not generally disrupted by the drugs; an exception can be seen in the middle record, where there is an instance of irregular responding. These effects were also detected with the other subject at the same doses.

Figure 3 shows the cumulative response records obtained during four consecutive daily sessions with Pigeon 1800, the focus being on the effects of the largest dose of phenobarbital (80 mg/kg; second determination). Although this dose resulted in a relatively low breaking point on the day that it was administered, the next day (a regular baseline session) the breaking point was well above the usual baseline range. The increased breaking point did not persist, however, as shown by the record obtained two days after drug administration. A similar sequence of effects was also observed

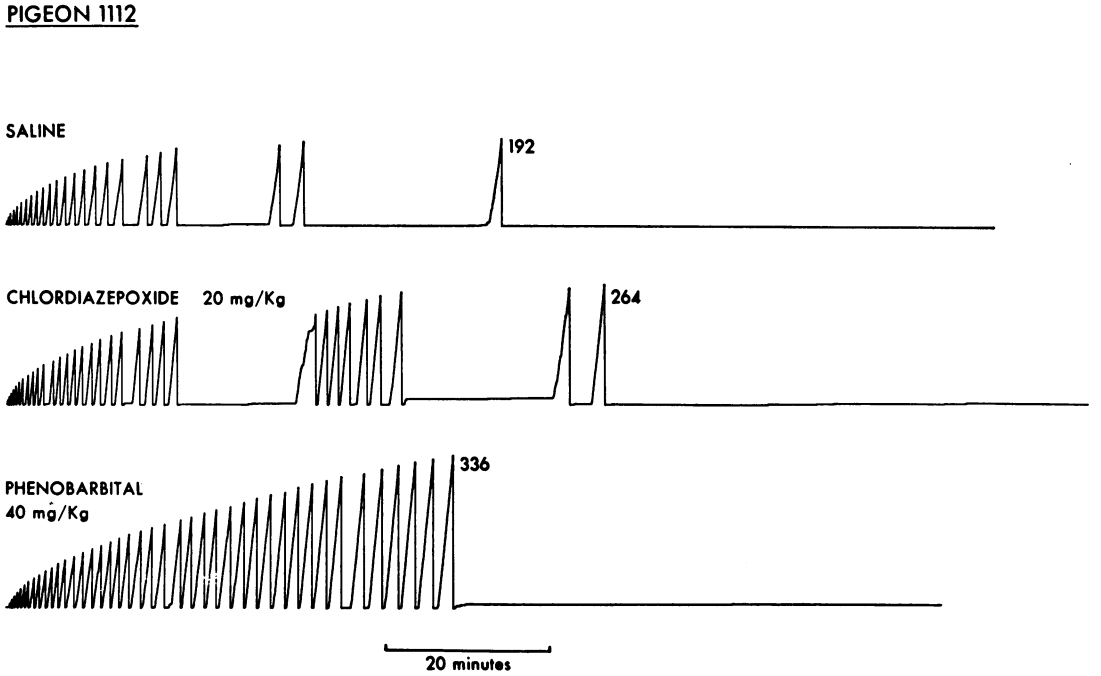

Fig. 2. Cumulative response records for Pigeon 1112 for a saline session and for the sessions in which the maximum facilitation of breaking point was obtained with each drug. The response pen reset after each reinforcement. Eight responses were required for the first reinforcement in each session, 16 responses for the second reinforcement, 24 responses for the third, *etc.* The number of responses in the last completed ratio (breaking point) is indicated for each session.

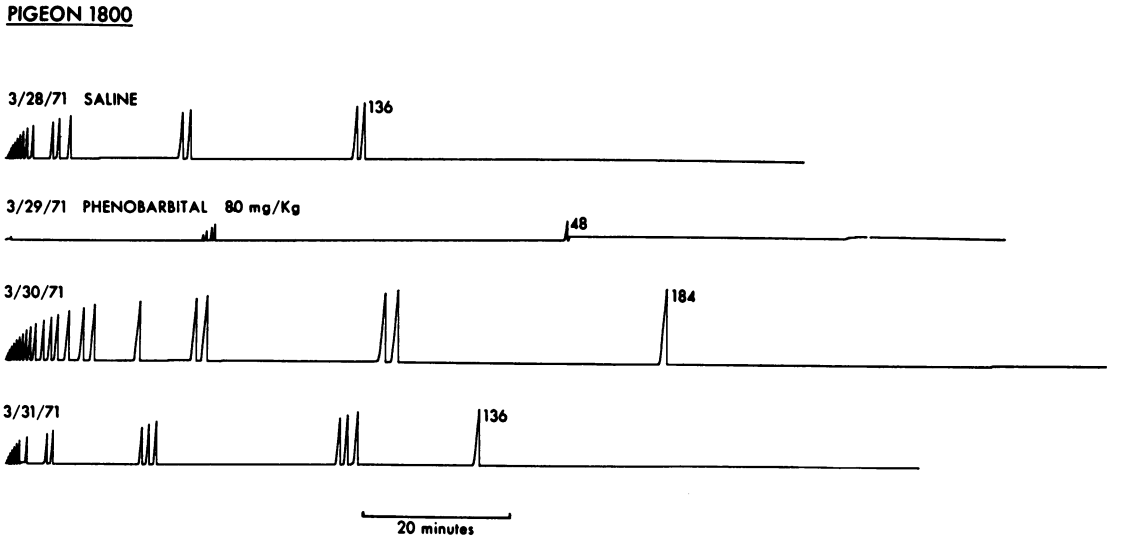

Fig. 3. Cumulative response records for Pigeon 1800 for four consecutive daily sessions: saline, phenobarbital (80 mg/kg), and the following two baseline sessions. The recording details are the same as in Figure 2.

after the first determination of the 80 mg/kg dose with Pigeon 1800. This set of conditions was the only exception to the general statement that the breaking points for all of the baseline sessions during drug testing were always within the ranges indicated in Figure 1.

DISCUSSION

The present research indicated that the breaking-point technique is a way of assessing the behavioral effects of drugs in a free-operant situation without reference to rate of

responding. The breaking point of pigeons' progressive-ratio performance was increased substantially by the administration of chlordiazepoxide and phenobarbital. One interpretation of the enhanced performance is that the drugs increased the pigeons' "motivation" to work. Since previous research (*e.g.*, Bainbridge, 1968) has shown that both drugs can increase food intake of rats in their home cages, it is not unreasonable to argue that the enhanced progressive-ratio performance of the pigeons occurred because the food maintaining the performance was more reinforcing under the drug conditions. Dews (1956) suggested that if a drug affects food-reinforced responding by modifying the deprivation conditions ("hunger," "appetite," *etc.*), then the effect of the drug should be mimicked by manipulation of the deprivation conditions by other means. This was the rationale for the deprivation probe that followed drug testing in the present experiment. When the pigeons' body weights were reduced from 80% to 70% of their free-feeding weights by increasing the food deprivation, the breaking point did increase for one of the subjects (1800), but the amount of increase was relatively small compared to the maximum effects seen with both drugs (Figure 1). Of course, the possibility remains that the maximum drug effects could have been mimicked if the body weights had been reduced even more. Nevertheless, on the basis of the present data, the strongest statement that can be made supporting the above "motivational" interpretation is that it may account for some, but not all, of the drug-induced enhancement of performance.

Another interpretation of the enhanced performance with chlordiazepoxide and phenobarbital involves the properties of the progressive-ratio schedule itself. During the 60 days of baseline training, the most noticeable transition that occurred before the pigeons' breaking points stabilized was the development of long post-reinforcement pauses at the larger ratios. If rats, with a similar training history, are given the opportunity to escape from the progressive-ratio schedule by responding on a separate timeout lever, they will do so at the larger ratios, and typically the escape responses occur during the post-reinforcement pauses (Gaines, Thompson, and Woods, 1964). Taken together, these observations suggest that the post-reinforcement pauses that develop during exposure to a progressive-ratio schedule represent suppressed behavior, and that the suppression occurs because the larger ratios have aversive properties (*cf.* Scheckel, 1970; Thompson, 1965). It is well known that the "minor tranquilizers", such as chlordiazepoxide and phenobarbital, may increase previously suppressed behavior in a variety of aversive situations (Kelleher and Morse, 1968; Margules and Stein, 1967). Accordingly, the shortening of the post-reinforcement pauses found in the present experiment with chlordiazepoxide and phenobarbital could mean that the progressive-ratio schedule was less aversive. Moreover, since the criterion for the breaking point was usually reached by the occurrence of a long post-reinforcement pause, this interpretation could also account for the increased breaking point found under the drug conditions. The same interpretation may apply to a related situation involving fixed-ratio reinforcement. Morse (1962) found that amobarbital increased responding under a large fixed ratio by reducing the post-reinforcement pause, whereas responding under a small fixed ratio was not enhanced.

A simpler interpretation of the drug-induced increase in breaking point could also be made. According to the "law of initial value" (Wilder, 1967), the response of a test system is a function of the initial value of the system. Applied to the present data, this law could account for the increased breaking point at a given dose by the drug-induced shortening of post-reinforcement pauses that were initially long. It could also account for the finding that the magnitude of the increase above baseline was consistently greater across the dose range of both drugs when the baseline range of breaking points was relatively low (compare subjects in Figure 1). This finding is consistent with previous research using a fixed-ratio baseline, in which the relative increase in responding produced by pentobarbital was found to be inversely related to the baseline levels of responding (Waller and Morse, 1963).

The decrease in breaking point below baseline on the day when the largest dose of phenobarbital (80 mg/kg) was administered to Pigeon 1800 (Figures 1 and 3) is not difficult to explain. This subject could barely stand and showed other obvious signs of ataxia, although it is noteworthy that when responding did oc-

cur, the rate was high and usually not disrupted (Figure 3). Perhaps even more interesting was the "rebound" effect on the next day when the breaking point was well above the usual baseline range. One interpretation of this effect is that phenobarbital, whose long action is well known, was still present but exerting an effect roughly equivalent to that obtained with the 20 mg/kg dose (compare Figures 1 and 3). This interpretation can also account for the absence of a "rebound" effect in the case of Pigeon 1112, since there was no effect on breaking point with this subject at the 20 mg/kg dose of phenobarbital (Figure 1).

The present results again reemphasize the similarities between the effects of chlordiazepoxide and phenobarbital. Inverted U-shaped dose-effect curves were obtained with both drugs, the only consistent difference being that the facilitating effects of chlordiazepoxide were found at lower doses than with phenobarbital (Figure 1). The present results are consistent with a recent review of the "sedatives and minor tranquilizers" (Irwin, 1968), which concluded that the major differences between the effects of the barbiturates (*e.g.*, phenobarbital) and the benzodiazepines (*e.g.*, chlordiazepoxide) are quantitative rather than qualitative.

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