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Incremental Repeated Acquisition in the Rat: Acute Effects of Drugs[1]

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PAULE, M. G. AND D. E. McMILLAN. *Incremental repeated acquisition in the rat: Acute effects of drugs.* PHARMACOL BIOCHEM BEHAV 21(3) 431–439, 1984.—Rats lever pressed for food and learned new response sequences on three levers. At the beginning of each daily session, responses on only one of the levers produced food. After meeting criterion on one lever, the task was "incremented" so that sequential responses on two levers were required and so on up to five sequential responses. Each new required response was added in front of the previously performed sequence. Sequences of lever presses required to produce food changed each session. Following establishment of stable acquisition behavior, the acute effects of *d*-amphetamine (0.30–3.0 mg/kg), diazepam (0.125–4.0 mg/kg), morphine (0.30–10.0 mg/kg), pentobarbital (1.0–17.5 mg/kg), and chlorpromazine (0.10–3.0 mg/kg) were examined. All drugs decreased the number of response sequences completed in a dose-dependent fashion. Response rates generally decreased at or below those doses that caused an increase in errors. For *d*-amphetamine, the profound disruption of incremental repeated acquisition behavior was primarily due to drug-induced perserverative responding. Pentobarbital and chlorpromazine increased errors both when the sequence was incremented and within the sequence whereas diazepam only increased errors when the sequence was incremented. Morphine generally increased within sequence errors without affecting errors when the sequence was incremented.

Incremental repeated acquisition Learning *d*-Amphetamine Diazepam Morphine Pentobarbital Chlorpromazine Lever press Rats

SINCE Boren first described the use of repeated acquisition procedures for studying behavioral transition states (i.e., the acquisition of new behavior) in Rhesus monkeys [2,3], numerous investigators have used similar procedures for studying the effects of various schedule changes on acquisition in a variety of animal subjects, including pigeons [16,17], Patas monkeys [9], and rats [13]. Additionally, steady-state performance under such procedures has been used as a baseline for studying the effects of acute and chronic drug treatments [5, 8, 19, 20, 21, 22, 25] and chronic lead exposure [4].

Repeated acquisition procedures have also been developed as incremental tasks which require criterion performance of short response chains prior to the presentation of longer response chains [11, 12, 26, 27]. These studies have, however, utilized only primates as subjects. The present investigation was undertaken to develop an incremental repeated acquisition (IRA) procedure for use with rats and then to determine acute dose-response curves for *d*-amphetamine, diazepam, morphine, pentobarbital, and chlorpromazine. A primary concern of these studies was the development of a procedure that would reliably generate repeated acquisition data for at least three different response sequence lengths within each one-hour behavioral session.

METHOD

Subjects

Seven male Sprague-Dawley rats (Charles River), weighing approximately 400 grams at the start of the study served as subjects. Animals were maintained at 75–80% of their initial free-feeding weight by food reinforcers delivered during sessions and supplemental feeding with Purina® lab chow. All were housed individually with free access to water in their home cages. Their 12-hr light-dark cycle began at 0700 hours.

Apparatus

The test chamber was a two-lever Gerbrands rat chamber (Model G7105) housed in a sound-attenuating enclosure (Gerbrands Model G7210). The chamber was modified by the addition of a third lever and numerous lights arranged as shown in Fig. 1. Reinforcers (45 mg food pellets, P. J. Noyes Company, Lancaster, NH) were delivered by a Gerbrands Model D-1 pellet feeder. A sonalert, powered by 28 volts DC through 16,800 ohms was mounted on top of the testing chamber for presentation of auditory stimuli. The chamber was illuminated by two 28 volt houselights throughout the

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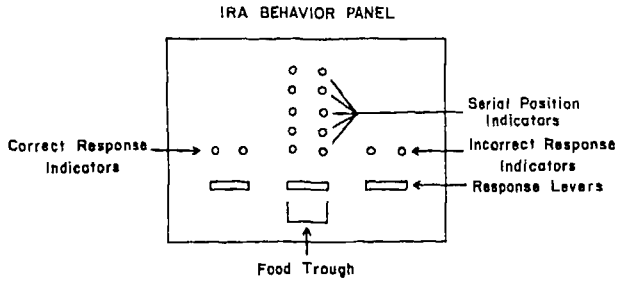

FIG. 1. Response panel, not to scale. Illumination of the first (bottom) set of serial position indicator lights (SPILS) indicated that only one correct response (i.e., a press on the 'correct' lever) was necessary for food reinforcement. Illumination of only the second set of serial position lights indicated that two more correct responses were necessary for reinforcer delivery, and so on up to five correct responses. SPILS extinguished with each response and the correct or incorrect response indicators were illuminated for one second. A tone was presented simultaneously with the illumination of the incorrect response indicators.

entire session and white noise was present continuously in the testing room. Electromechanical programming equipment and cumulative recorders were located in an adjacent room.

Procedure

During initial training, a single response on any lever resulted in reinforcement. When IRA procedures were begun, one session per day five days per week, levers were randomly "deactivated" so that responses on only one lever produced food at the start (IRA1) of each session. Serial position indicator lights (see Fig. 1) were illuminated to indicate position in the required response sequence. Illumination of only the set of two lights closest to the pellet trough indicated that only one correct response was required for reinforcer delivery. After 40 responses on the correct lever, a one-minute time-out period was followed by the presentation of a two-lever sequence (IRA2). When 2 correct responses were required for reinforcer delivery, then only the second to the last set of serial position indicator lights (SPILS) was illuminated and so on up to illumination of the fifth set of lights when 5 correct responses were required (IRA5). Responding on a "correct" lever first resulted in a 1-sec illumination of the "correct response" indicator lights located to the left of the terminal SPILS (refer to Fig. 1), then the advancement of the SPILS one position. If the correct response was the last one required in a specified chain of responses, a food reinforcer was delivered immediately. After reinforcer delivery, a 5-sec post reinforcement timeout followed, during which all lights but the houselights were extinguished. The original SPILS appropriate for the given component (response sequence length) of the IRA session were then reilluminated. After the 40th errorless sequence (i.e., no errors made between the first and last elements of the required response sequence), a 1-min inter-component timeout followed, during which all but houselights were extinguished. At the end of this timeout, illumination of the SPILS signified a 1-lever increment in the required response sequence. This procedure was repeated until 40 errorless 5-element response sequences were completed, 60 minutes elapsed, or 5 min elapsed during which no responses were made.

Errors did not reset the response requirement back to the initial response of the particular IRA component in progress. Incorrect responses were followed by a 1-sec illumination of the incorrect response indicator lights (see Fig. 1) and operation of the sonalert.

All sessions began with the presentation of one-lever response sequences. The first required response in an incremented sequence was always different from the first response required in the previous component of the same session. After responding on the first correct lever of a two-response chain, subjects had only to respond on the lever that was the correct one in the preceding component, i.e., the one that was correct during illumination of the SPILS closest to the pellet delivery trough.

Different 5-lever response sequences were presented in a randomized manner and no two subjects were presented with the same sequence on any given day. Response sequences requiring successive responses on the same lever were not used and therefore a total of 48 different 5-lever response sequences were possible. No animal was scheduled to perform the same response sequence again for at least 48 sessions. Each animal was tested once daily at approximately the same time each day, Monday through Friday.

Drugs

d-Amphetamine sulfate and chlorpromazine hydrochloride (Smith, Kline and French, Philadelpha, PA), morphine sulfate (Mallinckrodt, Inc., St. Louis, MO), and sodium pentobarbital (Sigma Chemical Co., St. Louis, MO), were all dissolved in isotonic saline. Diazepam (Roche Products, Manati, Puerto Rico) was solubilized in 40% propylene glycol, 10% ethanol, and 50% isotonic saline.

Data Analysis—Percent Task Completed

Arbitrarily, completion of 40 errorless response sequences at each of the five possible response sequence lengths (IRA components) was designated as 100% task completion. For any given session, a "percent task completed" measure for each subject was defined as the actual number of errorless sequences completed per session divided by the total number of errorless response sequences possible per session (here the number possible was always 200). This quotient was then multiplied by 100 to yield a percent task completed value. This value is a direct measure of the response chain length completed by the subjects on a given day with values of 20, 40, and 60 percent corresponding to completion of one, two, and three-lever response chains, respectively. As the percent task completed value is a function of both response rates and response efficiencies, it could be altered by changes in either or both of these parameters provided that alterations in one parameter did not effectively oppose changes in the other. Where important changes in the percent task completed measure were noted, both response rate and efficiency data were examined to determine how specific drug treatments affected this measure of IRA performance.

Response Rates

Response rates were calculated as lever presses per second by dividing the total number of lever presses made in each component by the total running time (i.e., not including time-outs) of that component.

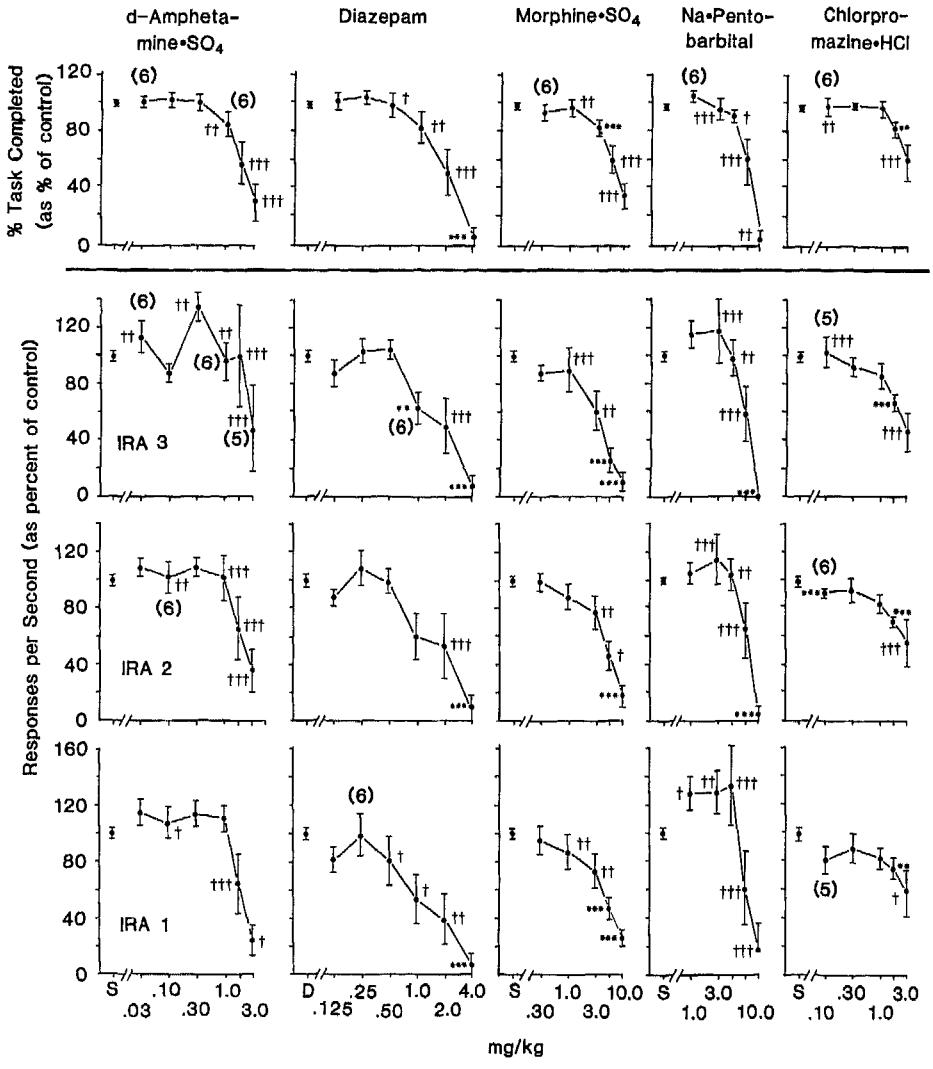

FIG. 2. Percent IRA task completed and responses per second expressed as percent of control values. Control data were obtained from 21 to 60 observations in 7 animals (6 for chlorpromazine) after appropriate vehicle (S-saline, D=diazepam diluent) injections and are shown here bracketed by their standard errors. Drug data are means plus and minus standard errors from single observations in 7 animals (6 for chlorpromazine) unless otherwise indicated (n). For two-tailed *t*-tests: *=$p<0.01$, **=$p<0.005$; and ***=$p<0.001$. For the F-test analysis of variance: †=$p<0.01$, ††=$p<0.005$, and †††=$p<0.001$. Significance shown is measured against control (vehicle injection) data.

Response Efficiencies

Response efficiencies for each response sequence length were determined by dividing the total number of correct responses by the total number of responses and multiplying the quotient by 100. Response efficiencies were calculated only if criterion performance (40 errorless sequences) was attained for a given component.

Errors Within Sequences

Errors within sequences are defined as those incorrect lever presses occurring after "entry" into a response chain (i.e., after the first correct response of the chain) but before reinforcer delivery (the last correct response). There can be no within sequence errors for sequences consisting of only one response.

Errors Between Sequences

Errors between sequences are defined as those errors occurring prior to the first correct response of a required sequence. These errors can thus occur at the start of a component or after reinforcer delivery during that component.

Dose-Response Curves

All drugs and vehicles were injected IP in volumes of 1.0 ml/kg 15 min prior to the start of each session. Behavior sessions were scheduled once a day and drugs were administered only on Tuesdays and Fridays with doses randomized. Drug vehicle injections were made on Tuesdays, Thursdays and/or Fridays. Dose response curves were obtained for one drug at a time in the following order: *d*-amphetamine sulfate,

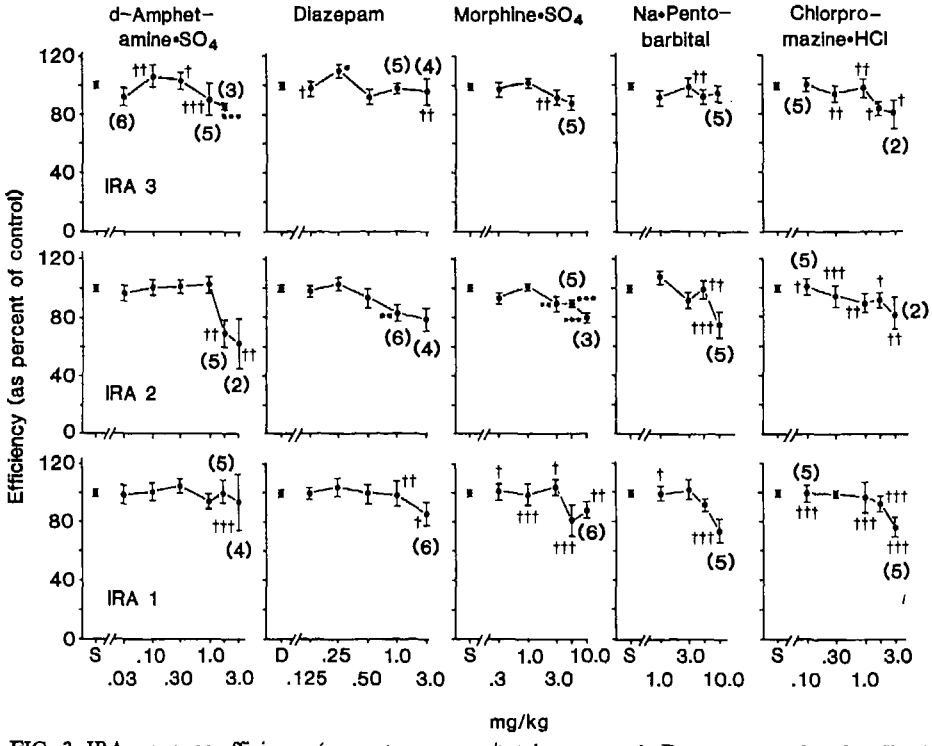

FIG. 3. IRA response efficiency (correct responses/total responses). Data expressed as for Fig. 2.

diazepam, morphine sulfate, sodium pentobarbital, chlorpromazine hydrochloride. Each dose-response study was followed by a minimum of one week during which animals received no injections or vehicle only. Vehicle control data are represented by averages plus and minus standard errors of observations for all seven animals (except for chlorpromazine data, where six animals were used and where otherwise noted). Drug data are presented as means plus and minus standard errors obtained for each dose of drug given once to all seven animals (six for chlorpromazine).

RESULTS AND DISCUSSION

Percent task completed data and response rate data for the first three components of the IRA schedules expressed as percentages of control values are shown in Fig. 2. Without exception, control response rates increased as the response chain length increased as indicated in Table 1 where control response rates for the *d*-amphetamine dose-response curve are shown. However, as the required response chain length increased, the proportion of time spent lever pressing increased while the opposite was true for time to initiate the first response (i.e., response latency). Once initiated, lever pressing proceeded relatively evenly and quickly and overall rates of responding increased as the chain length was increased. Note that as response chain lengths increased, the variability of control response rates remained constant (Fig. 2). Thus, drug effects on performance of response sequences of different lengths could be examined without complications resulting from changes in variability.

Response rate data (Fig. 2) indicate that doses of drugs causing decreases in the percent task completed also caused decreases in response rates during at least one of the IRA components shown. Such observations suggest that response rate suppression was an important determinant of the percent IRA task completed.

TABLE 1

CONTROL RESPONSE RATES (RESPONSES PER SECOND) OBTAINED DURING DETERMINATION OF *d*-AMPHETAMINE DOSE-RESPONSE CURVES

	mean*	±S.D.	n
IRA1	0.46	0.21	7
IRA2	0.60	0.18	7
IRA3	0.78	0.25	7

*Averages are of means from 7 observations in each animal.

Animals capable of completing one and two-lever response sequences often did not complete longer response sequences after receiving *d*-amphetamine because of the induction of perseverative responding (especially at doses of 1.75 mg/kg—not shown—and 3.0 mg/kg—Fig. 4) and an associated decrease in response efficiency (Fig. 3). Drug-induced perseverative responding has also been noted in pigeons during chronic cocaine administration [23] but despite several investigations on the effects of *d*-amphetamine in repeated acquisition schedules, the lack of other reports of perseveration induced by this compound is puzzling.

The lower doses of 0.10 and 0.30 mg/kg *d*-amphetamine significantly increased efficiency during the IRA3 component only (Fig. 3). This effect was not correlated with drug effects on response rates (Fig. 2) for this component when no

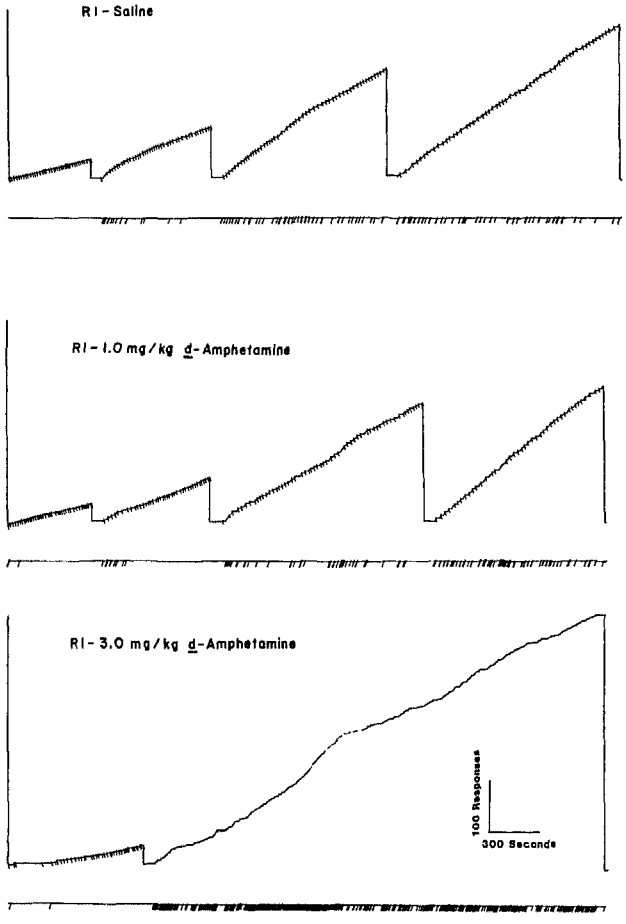

FIG. 4. Cumulative records of IRA tasks for animal R-1 after Saline, 1.0 and 3.0 mg/kg *d*-amphetamine sulfate. Each lever press stepped the pen and downward hash marks occurred with the delivery of each reinforcer (upper traces). The event pen was operated with each incorrect press (lower traces). The pen reset when criterion (40 errorless sequences) had been reached (i.e., after each IRA component). Note that perseverative responding (many consecutive errors) was incipient at 1.0 mg/kg and fully developed after 3.0 mg/kg.

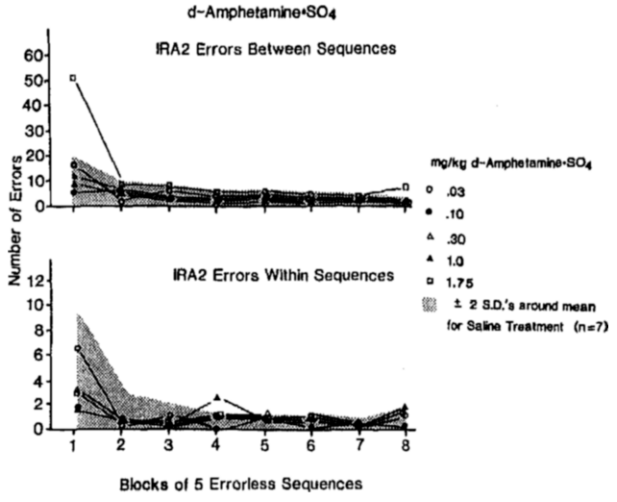

FIG. 5. Errors within and between sequences after *d*-amphetamine sulfate. Control data (shaded area represents 95% confidence interval) were calculated from seven mean observations and drug data are means of single observations from five animals.

change was noted after 0.10 mg/kg and an increase occurred after 0.3 mg/kg. This effect of *d*-amphetamine was noted only for IRA3, and therefore may reflect an interaction of response sequence length (task difficulty) and drug effect, or it may be related to the time course of *d*-amphetamine's action.

d-Amphetamine decreased response rates during all components at doses of 1.75 mg/kg and greater. The rate decreases noted after treatment with these higher doses of *d*-amphetamine have been shown for pigeons [5, 20, 24] and Patas monkeys [10,27] under repeated acquisition procedures; however, 0.30 mg/kg *d*-amphetamine increased rates in our rats. This increase in rate was significant only for the three-lever component. This finding may reflect an interaction of drug effect and response chain length, and/or baseline response rate, or the time course of *d*-amphetamine's action. Amphetamine-induced response rate increases have also been noted in pigeons [5,24] and rats [13,14] performing repeated acquisition tasks.

d-Amphetamine doses of 1.75 mg/kg and higher produced perseverative responding and between sequence errors increased dramatically (almost 500%) early in the two-lever component, Fig. 5. This behavior disappeared completely after the completion of the first five errorless sequences. Errors within sequences were essentially unaffected by treatment (Fig. 5) with *d*-amphetamine indicating that stimulus control over responding during the last element (perseverated lever) of the response sequence remained intact. It is doubtful that the *d*-amphetamine-induced perseverative responding is a reflection of alterations in components of acquisition mechanisms in the rat. Rather, it is likely that perseverative responding is incompatible with the expression of acquisition.

The finding that *d*-amphetamine did not decrease IRA2 errors in our rats is in agreement with the reported effects of *d*-amphetamine on repeated acquisition performance in pigeons [8, 18, 20, 24], monkeys [9,25], and rats [13,14]. Under some conditions in pigeons, however, certain doses of *d*-amphetamine have been reported to decrease errors in repeated acquisition performance [5]. Analysis of data for the longer (IRA3) response sequences (with higher rates of baseline errors) show similar error decreases in the present study as noted by the increase in efficiency after 0.10 and 0.30 mg/kg mentioned previously. Unfortunately, response rate suppression and/or perseverative responding prevented the study of longer response chains in this paradigm.

A dose of 0.25 mg/kg diazepam significantly increased response efficiency during the three-lever component (Fig. 3). This increase was not as great during shorter response chains suggesting that performance of the longer response chains was more sensitive to the effects of diazepam than were the shorter response sequences or that the peak time for the error-decreasing effects of diazepam occurred during performance of this component. As the variability of control data were almost identical for the one and three-lever components, it is unlikely that the drug effect was dependent upon response variability. Enhancement of repeated acquisition performance by the chronic administration of ben-

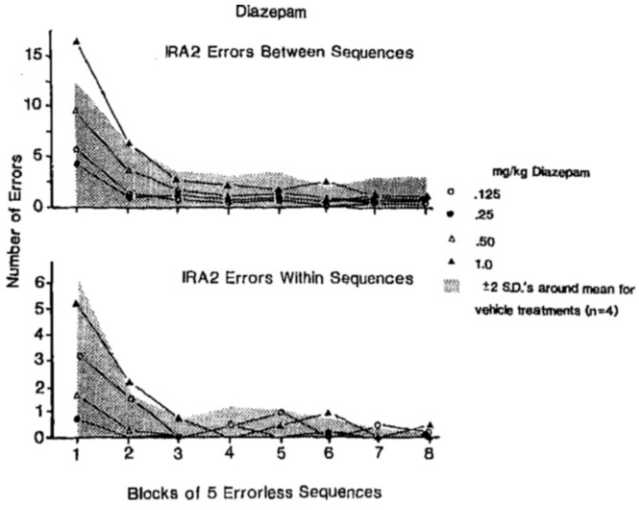

FIG. 6. Errors within and between sequences after diazepam. Control data (shaded area represents 95% confidence interval) were calculated from four mean observations and drug data are means of single observations from six animals.

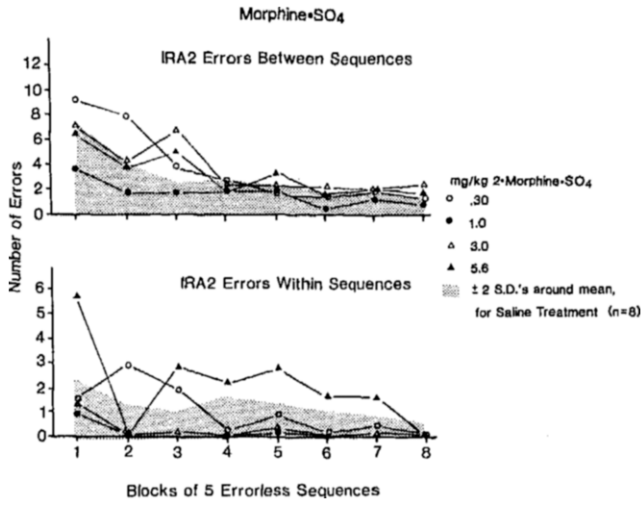

FIG. 7. Errors within and between sequences after morphine sulfate. Control data (shaded area represents 95% confidence interval) were calculated from 8 mean observations and drug data are means of single observations from six animals.

zodiazepines has been reported previously in the epileptic baboon [11,27]. Enhancement of repeated acquisition behavior after acute benzodiazepine treatment has, however, not yet been reported; only decreases in efficiency have been observed in pigeons [1, 18, 19, 21]. The doses used in the pigeon studies were generally greater than 1.0 mg/kg and were thus greater than the dose causing an improvement in the performance of our rats. Pieper [12] noted that benzodiazepines had little or no affect on repeated acquisition performance at doses below those causing motor deficits and this observation is consistent with those of the present study.

Decreases in IRA2 errors were not detected at any dose of diazepam (Fig. 6). The very low baseline error rate may have made detection of error decreases impossible. At 1.0 mg/kg, errors between sequences were selectively increased for the early portions of the component, Fig. 6. This increase was much less than that for *d*-amphetamine and was not accompanied by perseverative responding. This finding suggests that diazepam, at doses high enough to disrupt repeated acquisition behavior, decreases the ability of animals to acquire new response sequences. Performance of already acquired responses was not affected (no changes in within-sequence errors, Fig. 6). As response rates were also significantly decreased at this dose, it is possible that this rate difference may have influenced acquisition. However, as similar rate decreases were not accompanied by similar selective increases in between sequence errors after other drugs (i.e., morphine, 5.6 mg/kg, Figs. 2 and 7, and pentobarbital 5.6 mg/kg, Figs. 2 and 8) it is unlikely that the rate decrease alone was responsible for the noted increase in errors made during the acquisition of a new response.

Morphine (3.0 mg/kg) caused greater decreases in response rates (Fig. 2) than efficiencies (Fig. 3). Thus, the decrease in the percent task completed measure (Fig. 2) noted after morphine was due primarily to its rate-suppressing effects. This finding parallels that observed in Patas monkeys performing repeated acquisition tasks of conditioned discriminations [10]. In that study, it was demonstrated that morphine produced dose-related decreases in response rates while not affecting accuracy of discrimination.

At 0.30 mg/kg, a dose not causing response rate suppression, morphine increased both within and between sequence errors at IRA2 (Fig. 7). These data would suggest that morphine disrupted both the acquisition of new response sequences and the performance of previously acquired response sequences. Unfortunately, this effect was not dose-related. At 5.6 mg/kg, errors within sequences were selectively affected by morphine, remaining elevated throughout most of the two-lever component (Fig. 7). Such data would suggest that at this dose, performance of previously acquired response chains was disrupted while the acquisition of new responses was relatively unaffected. The pattern of error disruption obtained after morphine is clearly different from those seen after either *d*-amphetamine or diazepam (Figs. 5 and 6).

Pentobarbital at 1.0 mg/kg increased the percent IRA task completed (Fig. 2) with the increase being statistically significant at the 0.05 level (two tailed students *t*-test not shown). This increase in the percent task completed measure was primarily due to the increased response rates noted at this dose of pentobarbital. It should be noted, however, that during the IRA2 component, 1.0 mg/kg pentobarbital also significantly increased response efficiency ($p<0.025$, two tailed *t*-test, not shown) which also helped increase the percent task completed measure. Acute administration of pentobarbital has not been reported to increase the efficiency of repeated acquisition behavior. The efficiency of IRA behaviors has, however, been reported to increase during the chronic administration of pentobarbital [26,27].

Efficiency of performance at IRA1 and IRA2 was decreased by 5.6 mg/kg pentobarbital (Fig. 3). This disruption of efficiency was absent during the IRA3 component. These data may reflect rapid (within-session) development of tolerance to this effect of pentobarbital or they may indicate that the time course of the drug effect influenced the results. The amount of time from the beginning of IRA1 to the completion of IRA3 was generally about 30 minutes, therefore, it

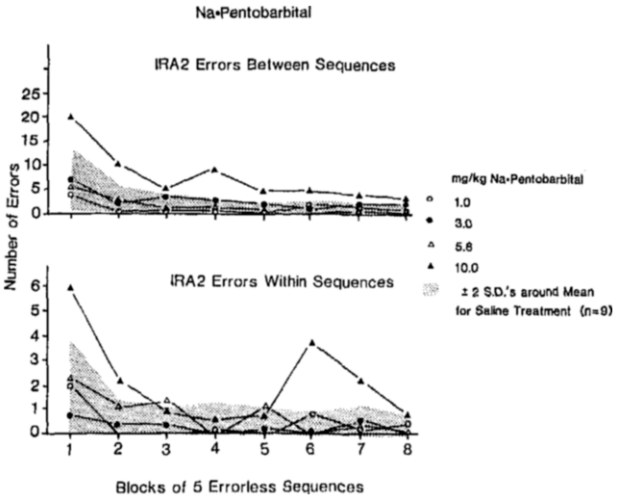

FIG. 8. Errors within and between sequences after sodium pentobarbital. Control data (shaded area represents 95% confidence interval) were calculated from nine mean observations and drug data are means of single observations from five animals.

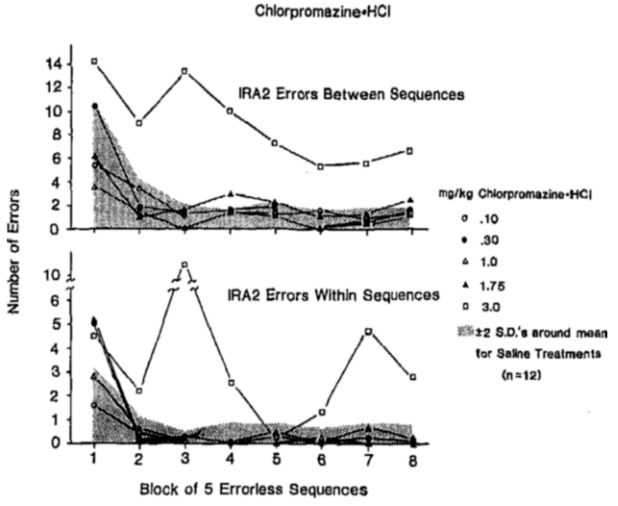

FIG. 9. Errors within and between sequences after chlorpromazine hydrochloride. Control data (shaded area represents 95% confidence interval) were calculated from 12 mean observations and drug data are means of single observations from six animals.

is likely that changing levels of drug would influence this observation. A similar effect was noted after 10.0 mg/kg pentobarbital in that efficiencies for the one and two-lever components were decreased more than those for the three-lever component. This 10.0 mg/kg dose produced considerable response rate suppression during all three IRA components. These data show that at doses that decreased response rates, efficiency was not affected (IRA3) and again suggest that IRA efficiency is not functionally tied to response rate.

The effect of pentobarbital on IRA2 within and between sequence errors (Fig. 8) was different than that for *d*-amphetamine, diazepam and morphine. Both error types were essentially unaffected at doses less than 10.0 mg/kg, but at that dose between-sequence errors were elevated. Errors within-sequence were also elevated albeit erratically. The data suggest that the acquisition of a new response was decreased for the duration of the IRA2 component. At no time were between sequence errors at levels obtained during control observations. Performance of previously acquired response sequences was disrupted early in the component but this effect disappeared during the middle portion of the component where within sequence errors returned to levels noted during control observations.

Others have reported that in pigeons performing under repeated acquisition schedules, response rates were increased after administration of relatively low doses of barbiturates [5,19]. Response rate increases were also noted in our rats after the 1.0, 3.0 and 5.6 mg/kg doses of pentobarbital (Fig. 2). Performance efficiency (IRA2, Fig. 3), was decreased at a dose (5.6 mg/kg) lower than that necessary to depress response rates. Efficiencies of the shorter response sequences were affected at doses not affecting efficiency at IRA3.

Chlorpromazine decreased both efficiency and response rates. These findings are similar to those reported for baboons performing incremental repeated acquisition tasks during chronic chlorpromazine administration [15], where response rates were depressed at the same doses that decreased efficiencies. Our data show, however, that chlorpromazine significantly decreased IRA efficiencies at doses (0.30 and 1.0 mg/kg) that do not significantly decrease response rates (Figs. 2 and 3, IRA2 and IRA3). In pigeons, response rates are decreased by doses of chlorpromazine lower than those necessary to decrease accuracy of repeated acquisition performance [18,24].

The effects of chlorpromazine on within and between sequence errors (Fig. 9) resemble those of pentobarbital. Errors between sequences remained elevated for the entire two-lever response-sequence after 3.0 mg/kg. This effect was not as large as that noted after 10 mg/kg pentobarbital but it appeared to change very little over the entire course of the two-lever component. These data suggest that chlorpromazine also decreases the acquisition of new lever responses in the rat. Performance of previously acquired response sequences was also altered by chlorpromazine administration in much the same manner as that noted after pentobarbital treatment. At 3.0 mg/kg chlorpromazine, erratic increases in within sequence errors were observed over most of the two-lever chain where values resembling control data were noted only occasionally.

SUMMARY

The current investigation showed that the "incremental" repeated acquisition procedure for rats can be used as a baseline to study drug effects on the acquisition of new behaviors. By requiring animals to meet a criterion for specific response sequences before they are presented with longer chains that are presumed to be more difficult, drug effects on both acquisition of new responses and performance of previously acquired responses can be studied in the same behavioral session. Additionally, the different components of the IRA procedure generate different baseline values while maintaining very similar variabilities. These aspects of performance under IRA schedules are important, as numerous investigators have shown that drug effects often depend upon the variability and/or magnitude of baseline values [1, 4, 5, 7, 20].

Responding in the earlier components (shorter response chains) of the schedule may serve as a control for responding in the longer response chains. If subjects successfully complete the initial IRA component, it may be assumed that the sensory, motor, and motivational systems necessary for maintenance of lever pressing behavior in this schedule are intact. Drug-induced changes in behavior during longer response sequences (if different from those observed for shorter chains) would then likely reflect the interactions of task difficulty (and/or decreased stimulus control over such behaviors) and drug treatment. Such interactions have, in fact, been quite apparent in studies of chronic anticonvulsant treatment in baboons [11]. The drug studies reported here indicate (except for chlorpromazine) that rates of responding under this schedule are generally affected at or below those doses that affect the number of errors made in performing position sequences.

It appears that chlorpromazine and pentobarbital disrupt IRA errors similarly, although their effects on response rates vary. Both drugs increased between sequence errors and within sequence errors. The relatively non-specific nature of the deficits produced by these agents suggests that they decreased stimulus control over responding in this schedule. Such results are similar to those found with promazine and pentobarbital in pigeons [6] where these agents also were shown to decrease stimulus control of responding. Response rate suppression by these agents could not have accounted for the increased errors noted in the current investigation as similar rate suppression by the other agents studied did not yield similar increases in errors. *d*-Amphetamine had essentially no effect on IRA accuracy at doses that did not induce preseverative responding. The observation of *d*-amphetamine-induced perseverative responding in this schedule suggests that care must be taken in the interpretation of repeated acquisition data, as the induction of behaviors incompatible with those being studied may lead one to erroneously conclude that specific "learning" behaviors are disrupted, when in fact, other explanations are more likely. Additionally, administration of *d*-amphetamine to animals responding under the IRA schedule may be a useful model to study perseverative behavior. Diazepam decreased the acquisition of new behaviors (increased between sequence errors) without affecting performance of previously acquired responses (within sequence errors).

Morphine, at relatively low doses (0.3 to 3.0 mg/kg), had mixed effects on IRA errors. The higher dose of 5.6 mg/kg, however, rather selectively decreased the performance of previously acquired responses (increased within sequence errors) without affecting the acquisition of a new response (no change in between sequence errors). Thus, agents from different pharmacological classes differentially affect processes involved in the expression of the acquisition of response sequences.

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