

*THE EFFECTS OF DIAZEPAM AND TRIAZOLAM ON
REPEATED ACQUISITION AND PERFORMANCE OF
RESPONSE SEQUENCES WITH AN
OBSERVING RESPONSE*

WARREN K. BICKEL, STEPHEN T. HIGGINS, AND
JOHN R. HUGHES

UNIVERSITY OF VERMONT

Drugs often disrupt the acquisition of new response sequences at doses that fail to disrupt the performance of a previously acquired response sequence. This selective drug effect may result from differences in the control exerted by the stimuli presented after each response in the acquisition and performance sequences. To examine the function of these stimuli, an observing procedure was incorporated into a multiple schedule of repeated acquisition and performance of response sequences, in which stimulus presentations were contingent upon an observing response. Three experiments were conducted with humans. Experiment 1 compared responding with and without the observing contingency. No difference was found in the overall percentage of errors across the two conditions. Within the observing condition, observing behavior was maintained in the acquisition component as long as errors occurred, but was not maintained in the performance component. Experiment 2 examined whether a contingency that increased errors also would increase observing in both the acquisition and performance components. Specifically, reinforcer delivery in each component was contingent upon emitting 10 correct responses and one, two, or four errors. Observing responses increased in the acquisition component as the error requirement increased, whereas observing responses in the performance component increased only when the error requirement was four. Experiment 3 assessed the effects of diazepam (0, 7.5, 15, and 30 mg/70 kg, p.o.) and triazolam (0, 0.375, and 0.75 mg/70 kg, p.o.) on repeated acquisition and performance baselines with the observing contingency. Selective drug effects were obtained in this modified procedure; that is, the percentage of errors in the acquisition component increased at doses that failed to affect the percentage of errors in the performance components. Importantly, drug effects were selective, even though observing responses were not emitted in the performance component and, hence, the stimulus presentations did not occur in that component. These findings suggest that alternative explanations for these differential effects are needed; in that regard, a response-unit account of the selective drug effects is discussed.

Key words: repeated acquisition, response sequences, observing behavior, conjunctive schedule, diazepam, triazolam, conditioned reinforcement, key press, humans

In procedures involving the repeated acquisition of response sequences, reinforcer delivery is contingent on the acquisition of a new and predetermined sequence of responses (Boren, 1963; Thompson, 1973). During the acquisition of a sequence, each response typically produces a stimulus (i.e., response-dependent stimulus presentations); if the response is correct (i.e., part of the predetermined sequence), then a stimulus correlated with progression though the sequence is presented. If

the response is incorrect (i.e., not part of the predetermined sequence), then a stimulus paired with a timeout from reinforcement is presented. After sufficient training, response rates and the number of errors made in acquiring the sequence become stable, thereby providing a stable baseline of transition states upon which the effects of drugs or other variables may be examined (Thompson, 1973). The procedure also has been used in a two-component multiple schedule composed of an acquisition component, described above, and a performance component in which reinforcer delivery is contingent upon the occurrence of a previously acquired response sequence (Thompson & Moerschbaecher, 1979). The multiple-schedule procedure provides a baseline by which the acquisition of new behavior can be contrasted with the performance of previously acquired behavior (e.g., Barthalmus, Leander, & McMillan, 1978; Moersch-

This study was supported by National Institute on Drug Abuse Grants DA 05538, DA 04545, and Research Scientist Development Award (JRH) DA 00109. The authors thank Jonathan L. Katz for comments on an earlier draft of this manuscript and Charissa Weiland for her laboratory assistance. Send correspondence and reprint requests to Warren K. Bickel, Human Behavioral Pharmacology Laboratory, Department of Psychiatry, University of Vermont College of Medicine, 38 Fletcher Place, Burlington, Vermont 05401.

baecher, Thompson, & Winsauer, 1983; Penetar, 1985; Thompson & Moerschbaecher, 1979).

Responding in the acquisition component of the multiple-schedule procedure is usually more sensitive to the error-increasing effects of drugs than is responding in the performance component (Thompson & Moerschbaecher, 1979). Such selective effects have been reported with a variety of drugs and across several species (Barthalmus *et al.*, 1978; Bickel, Higgins, & Griffiths, 1989; Desjardins, Moerschbaecher, Thompson, & Thomas, 1982; Higgins, Bickel, O'Leary, & Yingling, 1987; Higgins, Woodward, & Henningfield, 1989; Thompson, 1975; Thompson & Moerschbaecher, 1979). The variables responsible for these drug effects are unknown. Response- and reinforcement-rate differences between the components have been shown not to contribute to the selective drug effects (Bickel *et al.*, 1989; Higgins, Bickel *et al.*, 1989). Another factor that may contribute to selective drug effects is the control exerted by stimuli presented after each response in the sequence (*i.e.*, the control exerted by the response-dependent stimulus presentations).

Several behavioral studies have assessed the effects of removing the response-dependent stimulus presentations. For example, removing the stimulus at a particular location in the sequence increased errors in the acquisition of the response immediately preceding and following the removed stimulus (Hursh, 1977). This disruption suggested that the stimulus functioned both as a conditioned reinforcer and as a discriminative stimulus (Hursh, 1977). Unfortunately, only the acquisition component was employed in that procedure, preventing examination of any differences in stimulus function across the acquisition and performance components. When acquisition and performance baselines have been examined under chained (*i.e.*, a stimulus presentation after each response) and tandem (*i.e.*, no stimulus presentation after each response) schedules with pigeons, fewer errors occurred in the chained than in the tandem schedule under both acquisition and performance conditions (*cf.* Harting & McMillan, 1976; Thompson, 1975; Thompson & Moerschbaecher, 1979). These studies showed that the presence or absence of these stimuli was correlated with the number of errors.

However, conflicting results have been reported. For example, removal of the response-dependent stimulus presentations after the acquisition of a sequence (*i.e.*, performance) did not alter accuracy of responding by pigeons or humans. These findings suggest that the response-dependent stimuli were not functionally related to accuracy with performance baselines (Deitz *et al.* 1987; Straub, Seidenberg, Bever, & Terrance, 1979). The reasons for this discrepancy are unknown.

One study has reported on the effects of drugs on the repeated acquisition and performance of response sequences under chained and tandem schedules with pigeons (Thompson, 1975). Under the chained schedules, chlordiazepoxide and phenobarbital increased errors in the acquisition component at doses that did not affect errors in the performance component. Under the tandem schedules, opposite results were obtained; drugs failed to increase errors in the acquisition component at doses that increased errors in the performance component. The presence or absence of the response-dependent stimuli appeared to determine the direction of the selective drug effects. However, these results should be interpreted with caution because the variability in tandem acquisition was considerably greater than in tandem performance; this may have obscured drug effects in the former condition. Thus, the relationship between the response-dependent stimulus presentations and selective drug effects in the procedures involving repeated acquisition and performance remains unclear.

The present experiments further assessed the function of the response-dependent stimulus presentations by incorporating an observing contingency into the repeated acquisition and performance procedure with human subjects. Observing behavior is maintained by the reinforcing effects of the stimuli that those responses produce (Dinsmoor, Flint, Smith, & Viemeister, 1969; Kelleher, Riddle, & Cook, 1962; Laties & Weiss, 1960). Given that the response-dependent stimulus presentations can function as reinforcers in the acquisition component (Hursh, 1977, discussed above), observing behavior may be maintained by those stimuli. Thus, by examining observing behavior under several different conditions, including conditions in which a drug is administered, differences in the function of the response-

dependent stimuli across the acquisition and performance component, if any, may be discerned.

EXPERIMENT 1

In this experiment, repeated acquisition and performance baselines were compared with and without an observing contingency to assess whether inclusion of an observing contingency altered the repeated acquisition and performance baselines.

METHOD

Subjects

Participants were 4 healthy males who provided written informed consent and lacked prior experience with the repeated acquisition procedure. Average age was 32 years (range, 22 to 44). Subjects participated as outpatients and received compensation at a rate of \$4.00 per hour of participation with additional monies contingent on responding in the repeated acquisition and performance procedure (\$0.05 per completed trial). Throughout the study, urine samples were collected and analyzed for the presence of amphetamine, barbiturates, cocaine, marijuana, and opioids. If drug use was detected, the test day was suspended until drug-free samples were submitted.

Setting and Apparatus

During sessions, subjects remained in a large room containing five experimental stations (brief visits to the restroom were permitted). Several subjects participated simultaneously and were instructed not to talk while in the experimental room.

Each experimental station was equipped with a Commodore® 64 microcomputer, a color video monitor (Panasonic DT1300), a three-key response panel and a numeric keypad (Cardco Cardkey). The computer controlled the experiment and recorded data. The response panel (4 cm by 5 cm by 25 cm) was custom-built, with the keys arranged in a row approximately 6 cm apart from each other. The "enter" key of the numeric keypad served as the observing key.

Procedure

Three-hour experimental test days were scheduled at approximately the same time twice weekly on Mondays and Thursdays or Tues-

days and Fridays. On test days, eight sessions of the repeated acquisition and performance procedures were conducted at approximately 20-min intervals. A session consisted of a single presentation of both the acquisition and performance components (see below). Each component ended after completion of 20 trials or after 5 min had elapsed, whichever occurred first. A new response sequence was to be acquired each session in the acquisition component, while the sequence remained the same in the performance component.

Multiple schedule with the observing contingency. Subjects performed under a multiple schedule of repeated acquisition and performance of response sequences (Desjardins et al., 1982; Higgins et al., 1987). The component in which the session began was counterbalanced across subjects. In each schedule component, subjects completed 10-response sequences using the left (L), center (C), and right (R) keys of the response panel. As illustrated in Figure 1, reinforcement delivery was contingent on depressing the keys in a predetermined order. The word "begin" was presented on the screen at the start of the sequence and remained there until the completion of the first response. In the illustrative response sequence shown in Figure 1, for example, the subject was required to depress the keys in the order of R, L, C, R, C, L, R, C, L, R. Correct responses moved the subject to the next position in the sequence. Incorrect responses returned the subject to the position in the sequence at which the error occurred. There were no scheduled stimulus presentations following responses on any of the three keys. Instead, stimulus presentations were contingent upon an observing response, that is, depressing the observing key. After each observing response, the stimulus "correct" or "wrong" was presented for 1 s in the center of the video screen. The stimulus that was presented depended on whether the most recent response to one of the three response keys was correct or incorrect. Completion of each sequence (i.e., trial) added one point to a running total displayed at the top of the screen and presented the word "begin" at the start of the next trial.

In the acquisition component (paired with a red screen), a new 10-response sequence had to be acquired each session. The following criteria were used in the selection of sequences for the acquisition component: (a) the perfor-

Illustrative Response Sequence

Correct Response Keys: R, L, C, R, C, L, R, C, L, R

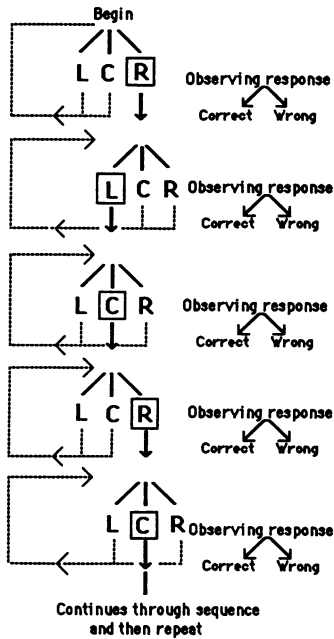


Fig. 1. The steps involved in moving through a typical 10-response sequence used in the study (after Higgins *et al.*, 1987). At the top are the 10 correct responses required on the response manipulandum. Correct responses advanced the subject to the next step in the sequence without presenting any stimuli. Incorrect responses returned the subject to the step in the 10-response sequence at which the error was made. An observing response resulted in a 1-s presentation of the word "correct" or "wrong." Each completed sequence added 1 point to a running total and returned the subject to the first step in the sequence.

performance sequence was never used in the acquisition component; (b) the first three responses in a sequence were never in a L, C, R order; (c) consecutive responses on the same key were never required within a sequence; (d) repetitions did not occur in any of the 10 positions in two consecutive acquisition sequences for an individual subject (e.g., if depressing C key was correct in the first link in the first sequence, then keys L or R would be the first link in the next sequence); and (e) subjects were not exposed to any sequence for more than one session. In the performance component of the multiple schedule (paired with a green screen), the 10-response sequence re-

mained the same throughout the experiment. The performance sequence was always to depress the keys in an order of C, L, R, L, R, C, L, R, C, L. The performance sequence had to be acquired initially under these same conditions.

Multiple schedule without the observing contingency. The repeated acquisition and performance procedure without the observing contingency was identical in all respects to the procedure with the observing contingency except that responses resulted in the immediate presentation of the words "correct" or "wrong" for 1 s (i.e., no observing response was required). Responses on the three-key response panel had no effect during the 1-s presentation of "correct" or "wrong."

Subjects were assigned randomly to start the study with or without the observing contingency. The alternate condition began when no increasing or decreasing trends in the percentage of errors were discernible during the preceding six sessions. Within-subject replications were then conducted.

Instructions. The following instructions were read to subjects immediately before their first session in each condition. These instructions were not available during sessions, but subjects could request that these instructions be reread before any session. Instructions in parentheses were read only before observing sessions.

This task involves you pressing three keys, left, center and right in a particular sequence. Press only one key at a time with your preferred hand. Every time you complete a sequence of 10 correct responses, the top counter advances.

The word "begin" will be presented at the beginning of the sequence. After you make your first response, (you must press the enter key on the numeric keypad to see if you were correct or wrong. When you press the enter key,) you will see the word "correct" on the screen if your response was correct. If you were wrong the word "wrong" will appear on the screen. (Whether you press the enter key to see whether you are correct or wrong is up to you. You may press that key as little or as much as you would like.) This will continue until the sequence of 10 correct responses is completed.

The green screen indicates a performance condition in which the sequence is the same from session to session. The red screen indicates a learning condition in which the sequence is different from session to session.

Press one of the keys when you are ready to begin.

Data Analysis

Number of responses on the observing key, overall rates of responding on the three response keys, overall errors, and within-session distribution of observing responses and errors were collected and analyzed separately for each component of the multiple schedule. Overall response rates in each schedule component were analyzed as responses per minute by dividing the total number of responses per schedule component by total time in that component minus stimulus presentation time. Errors were defined as responses on any response key other than the correct key and calculated as overall percentage of errors by dividing the total number of errors in the component by the total number of responses on the three response keys in that component and multiplying by 100.

RESULTS

The number of sessions per condition is displayed in Table 1.

Number of Responses per Session on the Observing Key

Responding on the observing key in the acquisition and performance components was replicable within subjects (Figure 2). (Of course, no observing responses were made in the no-observing condition.) With observing conditions in effect, observing responses ranged from 13 to 52 responses per session across subjects in the acquisition component. In the performance component, few or no observing responses were made, with responses ranging from zero to five responses per session across subjects.

Overall Percentage of Errors

The percentage of errors in the acquisition component was greater than in the performance component, and was comparable with and without the observing contingency (Figure 3). In the acquisition component, the percentage of errors ranged from 1.0% to 11.1% and 1.4% to 9.1% across subjects in the conditions with and without the observing contingency, respectively. In the performance component, the percentage of errors ranged from 0% to 3.9% and 0% to 4.6% across subjects in

Table 1
Number of sessions per condition.

Subject	Conditions					
	No obs	Obs	No obs	Obs	No obs	Obs
JL	41	59	12	55	—	—
GA	31	39	24	14	—	—
WK	—	27	15	22	12	14
PC	38	32	7	12	18	—

Note: Obs = observing contingency.

the conditions with and without the observing contingency, respectively.

Within-Session Distribution of Observing and Errors

Cumulative plots of observing responses and errors during three consecutive sessions from a representative subject show that observing responses and errors in the acquisition component generally covaried (Figure 4). Moreover, observing and errors decreased to a comparable extent during the session. Generally, neither observing nor errors occurred in the performance component.

Overall Response Rates

Overall rates of responding in the acquisition and performance components from the last six sessions of each condition were stable and replicable within subjects (Figure 5). However, response rates were generally lower in the no-observing condition than in the observing condition. For example, in the acquisition component, response rates ranged from 64.2 to 140.4 and from 43.4 to 54.1 responses per minute across subjects in the conditions with and without the observing contingency, respectively. In the performance component, response rates ranged from 121.1 to 243.6 and 44.1 to 51.5 responses per minute across subjects in the conditions with and without the observing contingency, respectively.

DISCUSSION

Adding an observing contingency did not affect the percentage of errors, but response rates were greater with than without the observing contingency. Response rates from the acquisition and performance components with the observing contingency were within the range of response rates reported previously with

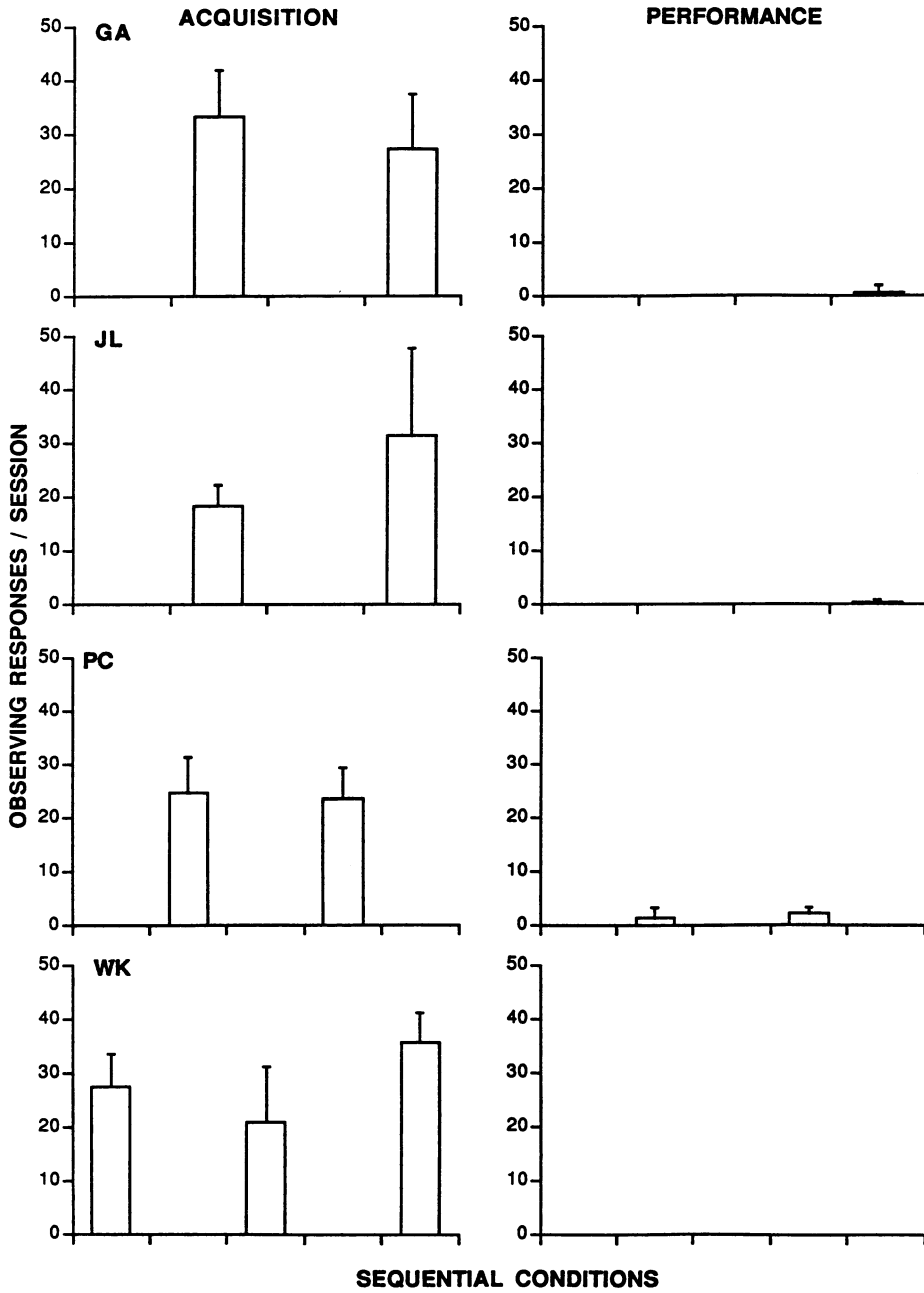


Fig. 2. Mean observing responses per session in the acquisition and performance components are shown for the last six sessions of the observing condition. The variability bar indicates the upper range.

repeated acquisition and performance base-lines in humans (Bickel *et al.*, 1989; Higgins *et al.*, 1987). Response rates from the acquisition and performance components without the observing contingency were consistently lower than those reported previously. Latency

to initiate a sequence (data not shown) was not different across conditions, suggesting that the lower response rates obtained in both components without the observing contingency were due to responding during the sequence. Perhaps the 1-s stimulus presentations, which

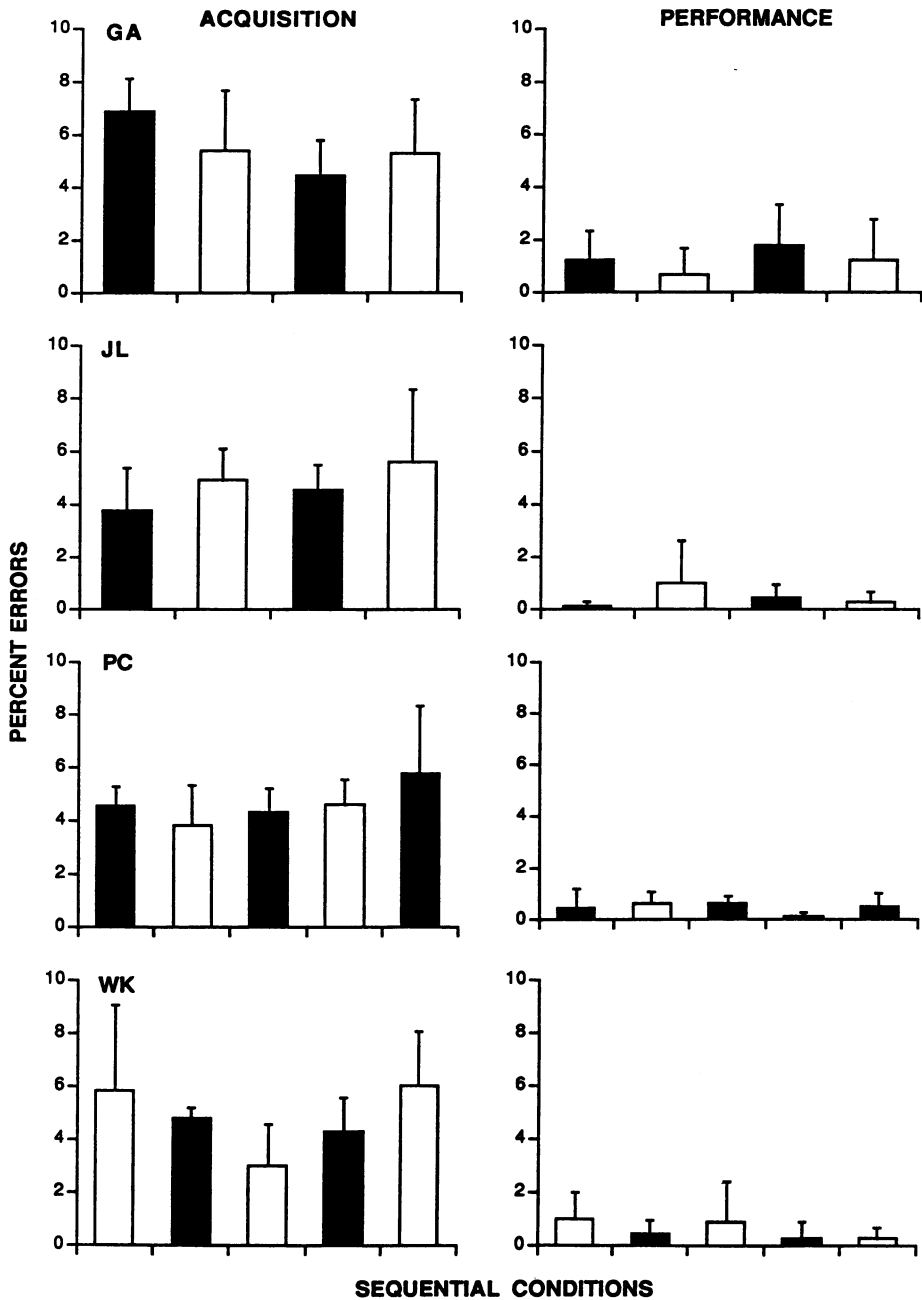


Fig. 3. Mean percentage of errors in the acquisition and performance components are shown for the last six sessions of each condition (i.e., no-observing or observing conditions). Filled bars indicate the no-observing condition, and unfilled bars indicate the observing condition. The variability bar indicates the upper range.

occurred after each response in the condition without the observing contingency, functioned as a brief timeout and suppressed rates of responding (Branch, Nicholson, & Dworkin, 1977; McMillan, 1967). Overall, the incor-

poration of the observing response, with the exception of response rate, did not substantially alter the repeated acquisition and performance baselines.

Observing in the acquisition component was

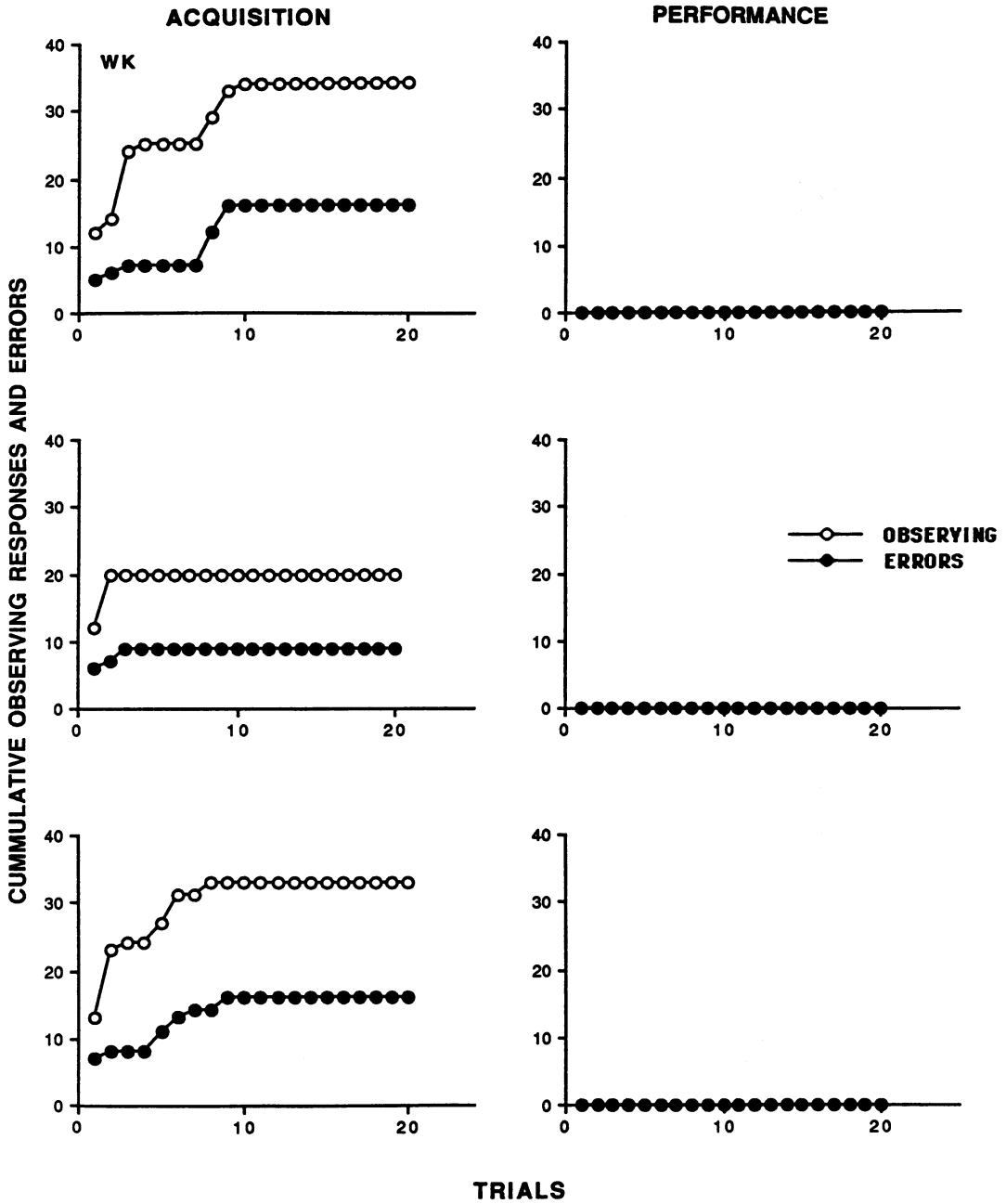


Fig. 4. Cumulative observing responses and errors in the acquisition component as a function of trials within a session from the first three consecutive sessions from the third exposure to the observing contingency for a single subject.

maintained as long as errors were made. Also, observing responses decreased during a session as errors decreased. In the performance component, the stimulus presentations did not maintain observing responses. However, given

the paucity of errors in the performance component, it is impossible to determine whether the relationship noted between errors and observing in the acquisition component also pertained to the performance component.

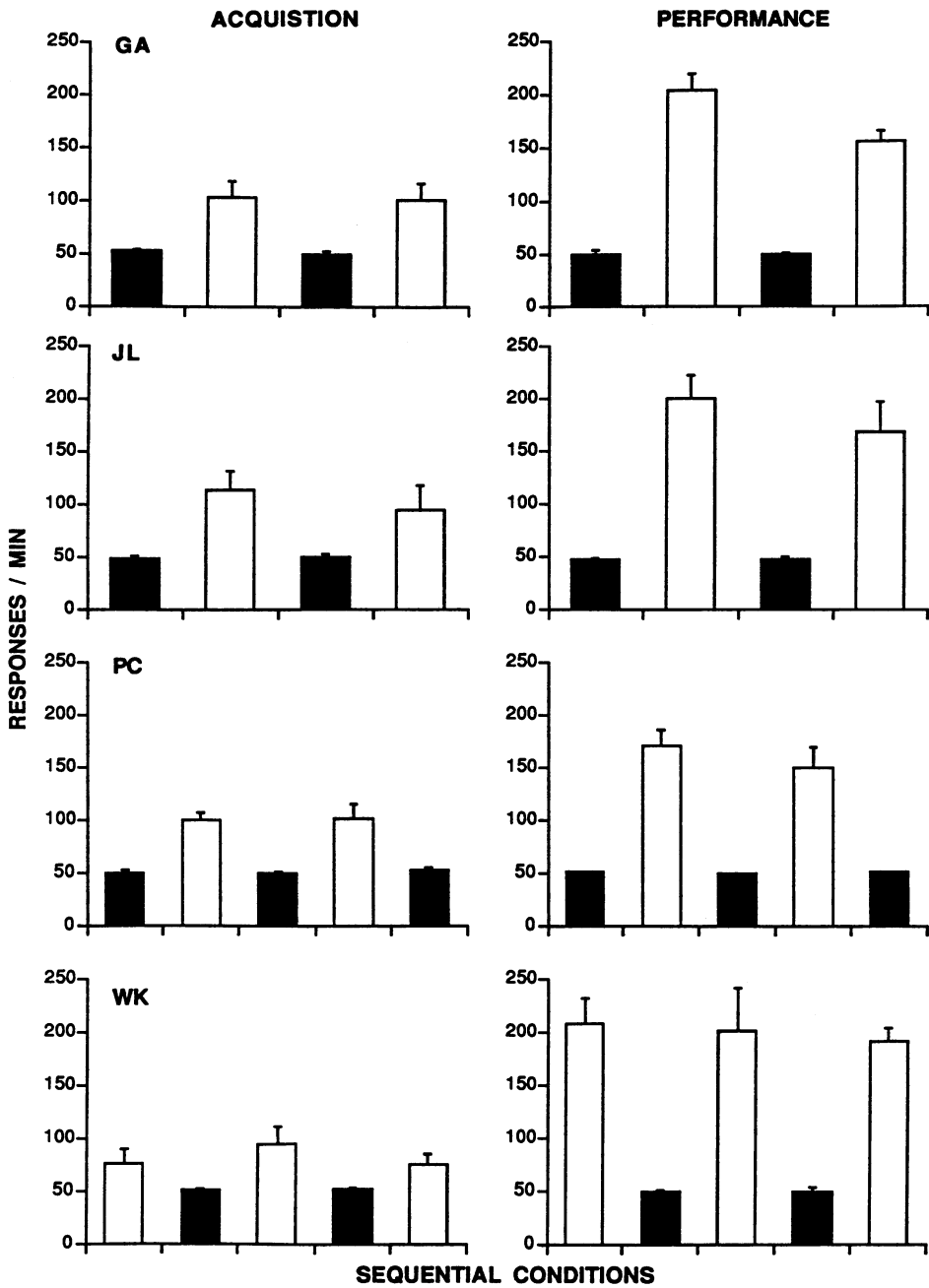


Fig. 5. Mean response rates in the acquisition and performance components of the last six sessions of each condition (i.e., no-observing and observing conditions). Filled bars indicate the no-observing condition, and unfilled bars indicate the observing condition. The variability bar indicates the upper range. Note that points overlap.

EXPERIMENT 2

Observing responses and errors were closely correlated in Experiment 1. If a relationship exists between these two responses, then the

absence of observing in the performance component may have been due simply to the absence of errors in that component. In Experiment 2, reinforcement was dependent on the

occurrence of "errors" in both the acquisition and performance components. If observing responses are functionally related to errors, then the production of errors should result in observing responses in both components.

METHOD

Subjects

Participants were 4 healthy adults (3 males and 1 female) with a mean age of 28 years (range, 22 to 44) who provided written informed consent. Subjects WK, GA, and PC had participated in Experiment 1; Subject VB lacked prior experience with the repeated acquisition and performance procedure. Subject earnings were the same as in Experiment 1.

Apparatus and Instructions

The apparatus and instructions were the same as in Experiment 1.

Procedure

Only the multiple schedule with the observing contingency was used in this study. The schedule of test days was the same as in Experiment 1. Once the percentages of errors became stable, the error contingency was introduced in the following manner. If the percentages of errors were stable across the first three of the eight sessions conducted each test day for both components, the error contingency was introduced for one randomly selected session between the fourth and seventh session inclusive. The error contingency was in place for only one trial in the selected session. Prior research indicated that errors typically were not made after the 10th trial in the acquisition component. Thus, the error contingency was introduced for one randomly selected trial between the 10th and 18th trial and was imposed on the same trial in both the acquisition and performance components. To show the number of errors and observing responses that typically occur in the absence of an error contingency, observing and error data from randomly selected trials that met the trial selection criteria (listed above) were used.

The error contingency required subjects to make one, two, or four errors and 10 correct responses to increment the counter on the video screen and to move to the next trial. The errors could be made at any point in the trial, making it a conjunctive schedule (Barrett, 1974; Herrnstein & Morse, 1958; Katz, 1983). An

observing response after an error resulted in a 1-s presentation of the word "wrong." If an error was made, the subjects remained at that position in the sequence until a correct response was completed. If the 10-response sequence was completed, then the subject remained at that position until the error contingency was satisfied or until the component timed out (e.g., 5 min). In general, each error requirement was imposed twice per subject in a random order. Due to experimenter error, Subject PC had the two-error requirement imposed on only one occasion. Subjects did not receive instructions about this contingency; the only instruction they received was the observing instruction given in Experiment 1.

RESULTS

In general, imposition of the error requirement had no effect on errors and observing other than in the trial in which it was imposed; overall responding on the multiple schedule was stable throughout this study. Figure 6 shows the number of errors and observing responses in the acquisition and performance components as a function of the error requirement for individual subjects. Under baseline conditions, errors and observing responses generally did not occur in the acquisition and performance components. In the acquisition component, the number of errors and observing responses generally increased as the error requirement increased with the two measures paralleling each other. In the performance component, increasing the error requirement generally increased the number of errors, similar to the effect seen in the acquisition component. Observing behavior, however, appeared less sensitive to this manipulation. For example, at the two-error requirement no observing responses were made in the performance component despite the occurrence of errors, and only zero to two observing responses occurred when the four-error requirement was imposed.

DISCUSSION

The introduction of the error requirement increased the number of errors in both components. Observing responses in the acquisition component increased as the error requirement increased, whereas observing responses increased to a more limited extent and only

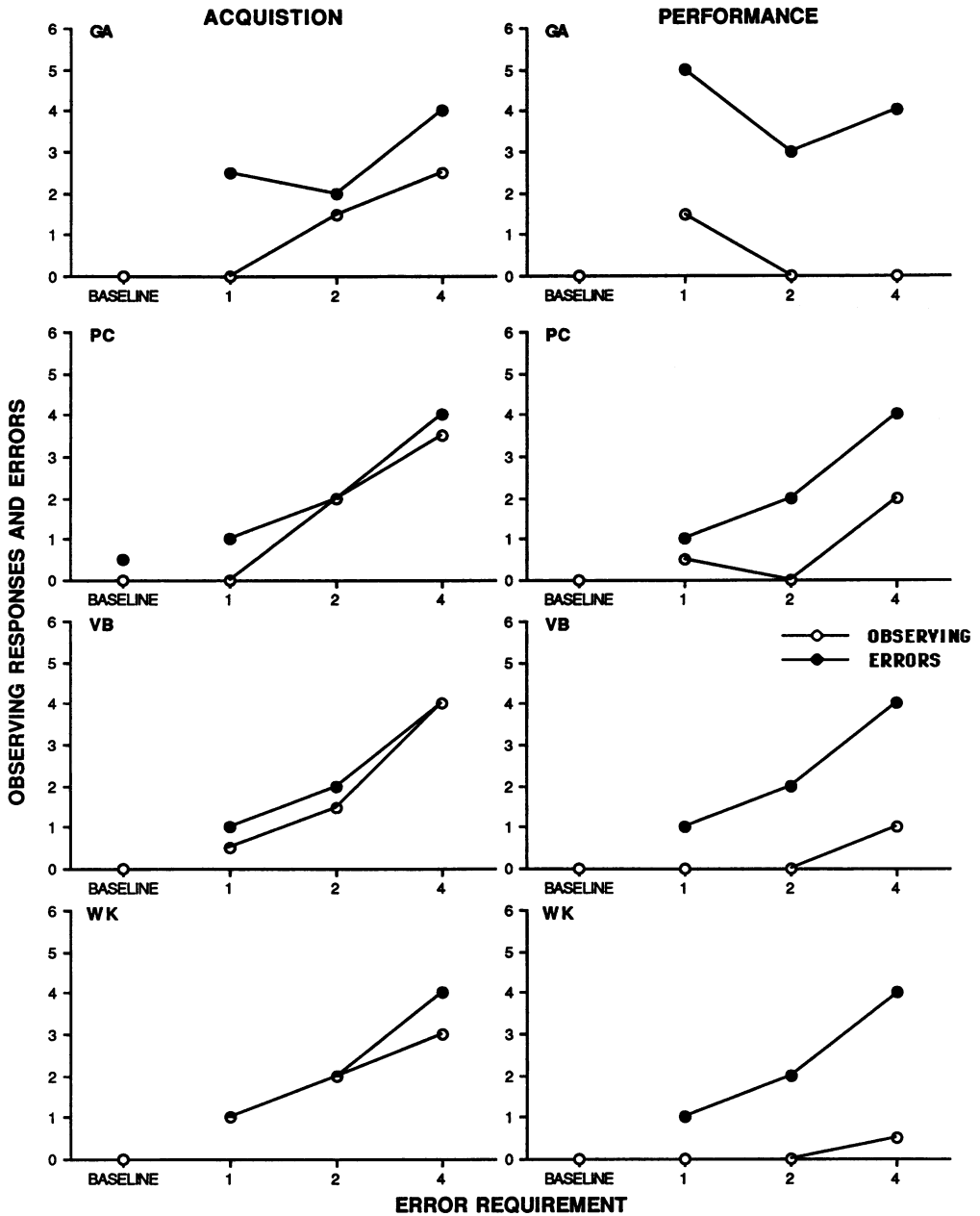


Fig. 6. Number of error and observing responses in the acquisition and performance components as a function of the "error" requirement. Data represent the mean of two observations.

when the maximum error requirement was imposed in the performance component. Of course, it is impossible to determine whether the error requirement increased errors and observing responses separately or if the error requirement increased errors that in turn increased observing responses. Nonetheless, these

findings support the observation from Experiment 1 that errors and observing are highly correlated in the acquisition component. These findings also suggest that observing in the acquisition component was more sensitive to this manipulation than was observing in the performance component.

Although no within-trial data are available to illustrate the distribution of errors and observing responses, informal observations across subjects showed a similar pattern. More specifically, the 10 correct responses were completed in both the acquisition and performance components. At this point, the computer did not indicate the completion of a chain (e.g., an increment of the point counter). Subjects then began to make errors; that is, they made a response on the three-button manipulanda. In the acquisition component, each error was usually followed by an observing response. In the performance component, no or few observing responses were made.

Importantly, this error contingency was imposed on an acquisition trial in which errors typically did not occur. At this point, responding in the acquisition and performance components was indistinguishable as measured by errors. In fact, this formal similarity has been the rationale for using behavior from the later portions of an acquisition session as the sole indicator of performance in some studies. However, the present study demonstrates that when behavior in the acquisition component is error free and appears performance-like, it is nonetheless more sensitive to some manipulations than behavior in the performance component; therefore, the two types of behavior should not be considered functionally equivalent.

EXPERIMENT 3

The results of Experiments 1 and 2 suggest that observing responses occur in the acquisition component when errors occur and that a similar effect occurs in performance, although to a lesser degree. In this experiment, two drugs (diazepam and triazolam) that have error-increasing effects (Bickel, Hughes, & Higgins, 1990) were administered to determine (a) whether selective drug effects would be obtained when the observing contingency was operating, (b) whether those selective drug effects would occur in the absence of observing behavior in the performance component, and (c) whether increased observing would be correlated with the error-increasing effects of the drugs.

First, the observing contingency may have altered the selective drug effects typically ob-

tained with the repeated acquisition and performance baselines. However, obtaining selective drug effects suggests that the observing contingency was unobtrusive. Second, if the stimuli were not observed in the performance component (i.e., observing responses did not occur) with selective drug effects still obtained, then the control exerted by those stimulus presentations could not have attenuated the sensitivity of responding in the performance component to those drug effects (cf. Thompson, 1975); that is, they would not have been present to have exerted any effect in that component. Third, if a functional relationship exists between errors and observing in both components, then increased observing should be observed to the extent that errors are observed.

Two benzodiazepines were studied. Diazepam and triazolam were selected because they have been studied previously in the repeated acquisition of response sequences by humans and therefore permit comparisons across studies (Bickel *et al.*, 1989, 1990; Desjardins *et al.*, 1982; Higgins *et al.*, 1987).

METHOD

Subjects and Apparatus

Participants were 7 healthy adults (4 males and 3 females) with a mean age of 28 years (range, 19 to 37) who provided written informed consent. Subject GA had participated in Experiments 1 and 2. The remaining subjects did not have prior experience with the repeated acquisition and performance procedure. Earnings were the same as in Experiments 1 and 2, and the apparatus was the same as in those experiments.

Procedure

Only the multiple schedule with the observing contingency was used in this study. The procedural aspects of the repeated acquisition and performance procedure with the observing contingency were identical to those described in Experiment 1 except that a test day consisted of five sessions; that is, a session was conducted before drug administration and again at 30, 60, 90, and 120 min after drug administration. The peak effect of both oral diazepam and triazolam on percentage of errors usually occurs 30 to 90 min after drug administration (Bickel *et al.*, 1989, 1990; Higgins *et al.*, 1987).

Drug administration. Three subjects (CM, GA, and CG) received diazepam, and 4 subjects (CA, DN, JT, and MT) received triazolam. Diazepam and triazolam were administered in two opaque capsules with lactose as filler under double-blind conditions. Placebo doses consisted of lactose only. Diazepam doses were 0 (placebo), 7.5, 15, and 30 mg/70 kg of body weight. Triazolam doses were 0 (placebo), 0.375, and 0.75 mg/70 kg of body weight. Each dose of diazepam and triazolam was tested on two and three occasions, respectively. For safety, a lower dose was always given before a higher dose during the first determination. After that, the dose order was determined randomly. The usual therapeutic doses of diazepam and triazolam are 10 mg and 0.25 mg, respectively (*Physicians Desk Reference*, 1991).

RESULTS

Number of Responses per Session on the Observing Key

Effects of diazepam and triazolam on observing responses per session are shown across a 2-hr time course in Figure 7. During placebo sessions, few observing responses were made under either schedule component, although more observing responses were made in the acquisition than in the performance component. For example, when placebo was administered, observing responses were usually stable in the acquisition component and ranged between 10 and 62 responses per session across all subjects, whereas in the performance component observing response rates ranged from zero to nine responses per session.

In the acquisition component, administration of the 15 and 30 mg/70 kg doses of diazepam and the 0.375 and 0.75 mg/70 kg doses of triazolam reliably increased observing responses above the range of control values for all subjects. In general, the 7.5 mg/70 kg dose of diazepam was not different from placebo. Onset of effects for both drugs was apparent at 30 or 60 min postdrug, with peak effects observed between 60 and 120 min postdrug. The duration of diazepam's effects was generally dose dependent, with the 30 mg/70 kg dose exerting a longer lasting effect than the 15 mg/70 kg dose. In general, triazolam did not produce reliable dose-related differences in the duration of effect.

In the performance component, observing responses were generally unaffected by any dose of diazepam or triazolam. The one exception was a slight increase in Subject CG's observing responses at the 7.5 mg/70 kg dose of diazepam 30 min after drug administration.

Overall Percentage of Errors

Effects of diazepam and triazolam on the overall percentage of errors are shown for individual subjects in Figure 8. During placebo conditions, relatively few errors were made in either schedule component, but errors were greater in the acquisition than in the performance component. For example, the percentage of errors across all subjects under placebo conditions ranged from 2% to 12% and 0% to 5% in the acquisition and performance components, respectively.

In the acquisition component, the 15 and 30 mg/70 kg diazepam doses and the 0.375 and 0.75 mg/70 kg triazolam doses generally increased errors above control levels for 2 of 3 and 3 of 4 subjects, respectively. The 15 mg/70 kg diazepam dose generally had no effects on Subject CG, and for Subject MT only the 0.75 mg/70 kg dose of triazolam increased errors. Onset of effect for both drugs in the acquisition component was apparent 30 to 60 min postdrug, with peak effects observed between 60 and 120 min for diazepam and between 30 and 60 min for triazolam. In general, the duration of these effects was dose dependent, with the 30 mg/70 kg dose of diazepam and the 0.75 mg/70 kg dose of triazolam exerting a greater duration effect than the 15 mg/70 kg dose of diazepam and the 0.375 mg/70 kg dose of triazolam.

In the performance component, overall percentage of errors was increased above control levels by the 30 mg/70 kg diazepam dose and by the 0.75 mg/70 kg triazolam dose. The 0.375 mg/70 kg triazolam dose increased the percentage of errors somewhat for Subjects DN and JN. In the performance component, onset of diazepam's effects was generally later than was seen in the acquisition component, whereas the onset of triazolam's effects in the performance component was comparable with that obtained in the acquisition component. Effects of both drugs in the performance component were generally shorter than in the acquisition component.

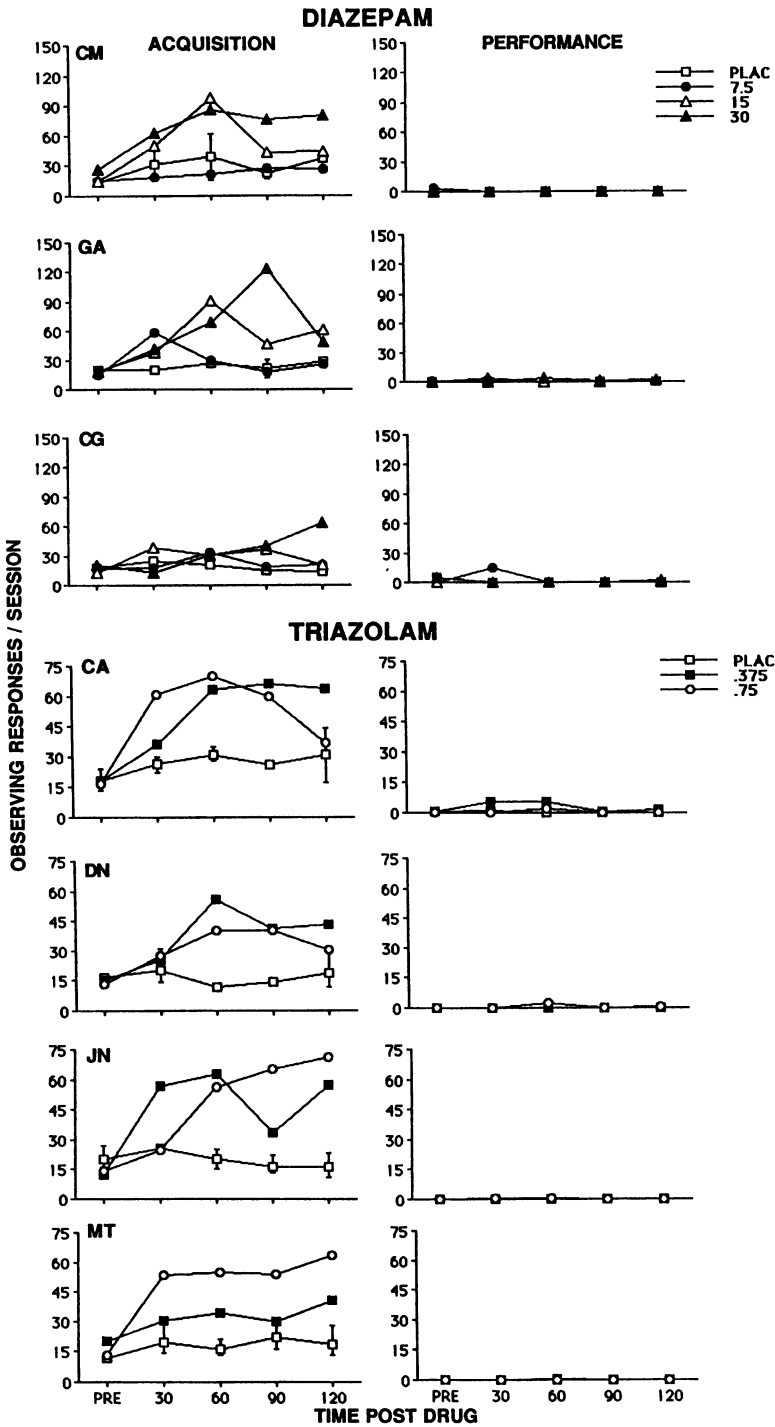


Fig. 7. Individual-subject data for the effects of diazepam and triazolam on overall observing response rate in the acquisition and performance components as a function of time after drug administration. The bars on placebo data represent the range of placebo values. Note that points overlap.

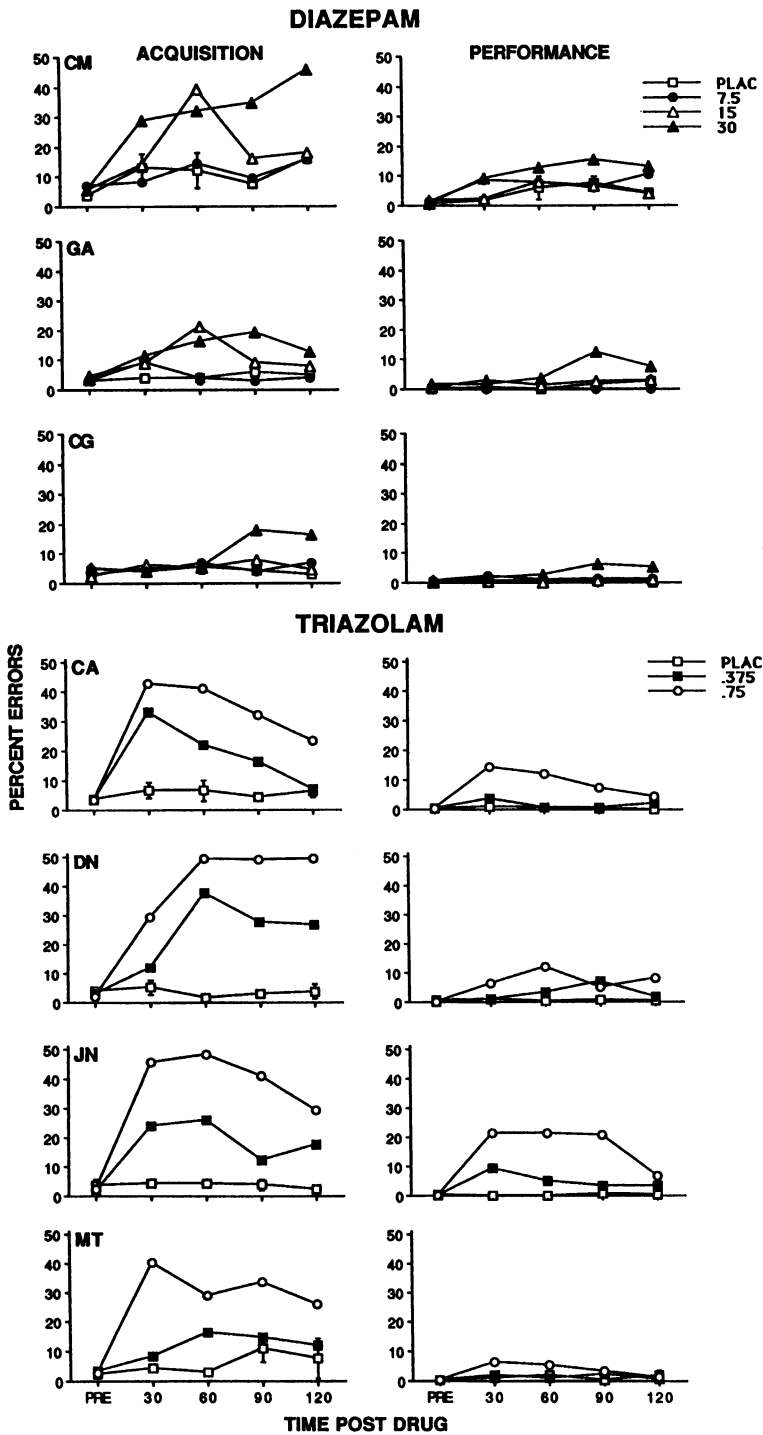


Fig. 8. Individual-subject data for the effects of diazepam and triazolam on overall percentage of errors in the acquisition and performance components as a function of time after drug administration. The bars on placebo data represent the range of placebo values.

Within-Session Distribution of Observing Responses and Percentage of Errors

The relationship between errors and observing responses can be discerned in Figure 9, which displays the cumulative number of observing responses and errors made by 2 subjects (1 each from each drug group) plotted as a function of trials within a session from both the acquisition and performance components. Overall, the cumulative observing responses and errors paralleled each other in the acquisition component; that is, as diazepam and triazolam increased errors there was a corresponding increase in observing responses. In the performance component, the highest dose of diazepam slightly increased the number of errors without increasing observing responses. This is shown even more dramatically at the 0.75 mg/70 kg triazolam dose, which produced more errors than diazepam in the performance component and a comparable number of errors to that obtained with that same dose in the acquisition component, but still without any increase in observing responses.

Overall Response Rate

Effects of diazepam and triazolam on response rate are shown for individual subjects in Figure 10. During placebo administration, responding generally was stable and ranged between 40 to 140 and 80 to 260 responses per minute in the acquisition and performance components, respectively, across subjects (Figure 10).

In the acquisition component, the 30 mg/70 kg dose of diazepam and the 0.05 mg/70 kg triazolam dose generally produced decreases in response rate for 2 of 3 and 4 of 4 subjects, respectively. The onset of drug effects usually occurred between 60 and 90 min postdrug for diazepam and 30 min postdrug for triazolam. For Subjects GA and CG, the rate-decreasing effects of 30 mg/70 kg diazepam returned to control levels by 120 min, whereas the rate-decreasing effects of the 0.75 mg/70 kg dose showed no evidence of dissipation.

In the performance component, the 30 mg/70 kg dose of diazepam and the 0.75 mg/70 kg dose of triazolam decreased response rates for 1 of 3 and 3 of 4 subjects, respectively. Diazepam at 30 mg/70 kg decreased response rates between 60 and 90 min postdrug for Subject GA. The effects of triazolam at 0.75 mg/

70 kg began between 30 and 60 min postdrug and continued to suppress rates throughout the 2-hr period.

DISCUSSION

The results of this experiment merit three observations. First, for some subjects, diazepam and triazolam increased errors in the acquisition component at doses that had no effect on responding in the performance component. Individual differences in the occurrence of selective drug effects are consistent with prior research on humans (Higgins *et al.*, 1987). These selective drug effects replicate previous research on the repeated acquisition of response sequences with benzodiazepines, and extend that finding to a novel repeated acquisition and performance baseline involving an observing response (Bickel *et al.*, 1990; Desjardins *et al.*, 1982; Higgins *et al.*, 1987; Thompson, 1973).

Second, selective drug effects occurred *without* the occurrence of observing responses in the performance component. Thus, in the performance component, the response-dependent stimulus presentations did not render behavior insensitive to selective drug effects because those stimuli were not present when selective drug effects were obtained. In fact, these findings may suggest that the stimuli dependent on observing responses generally were unrelated to the percentage of errors in the performance component. These results are consistent with previous research demonstrating that removal of these stimuli after the acquisition of a sequence (*i.e.*, performance) did not affect the percentage of errors (Deitz *et al.*, 1987; Straub *et al.*, 1979).

Third, as shown by the cumulative plots, errors and observing responses were correlated in the acquisition component at all triazolam doses but were not correlated in the performance component. This absence of observing responses in the performance component was evident even when a considerable number of errors were made. Thus, the relationship between errors and observing responses appears to be largely restricted to responding in the acquisition component.

The absence of a relationship between errors and observing responses in the performance component appears somewhat inconsistent with the relationship between errors

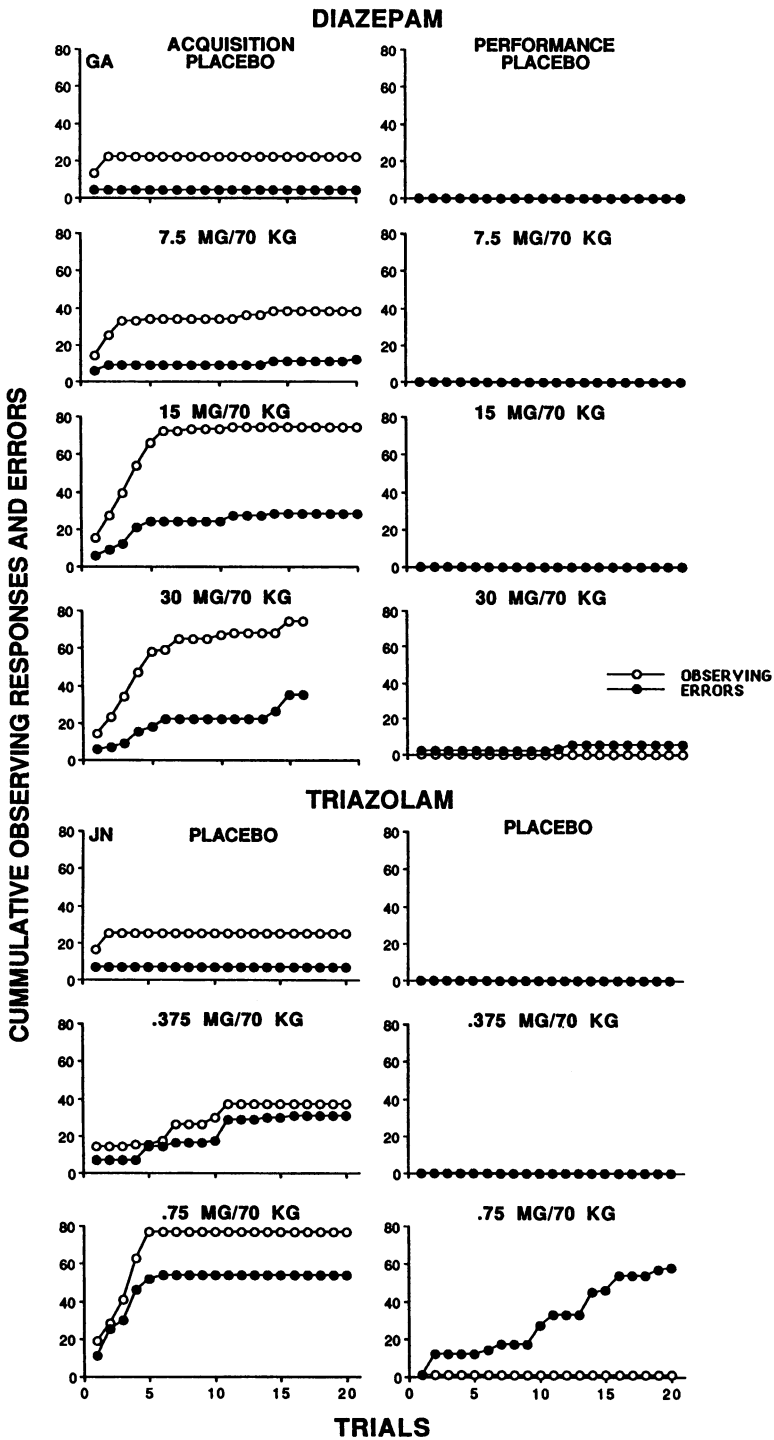


Fig. 9. Cumulative observing responses and errors in the acquisition and performance components as a function of trials within a session. These data were taken 1 hr after administration of diazepam and triazolam.

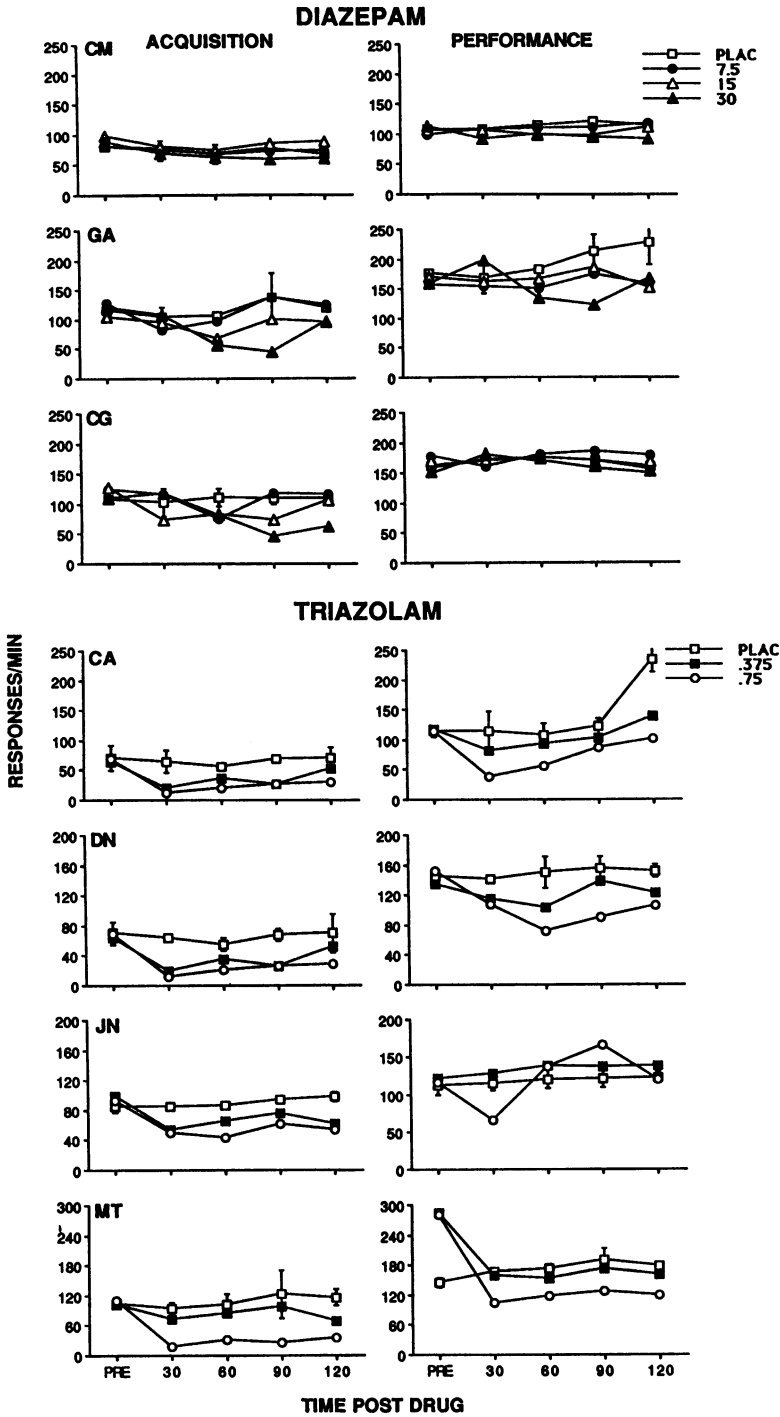


Fig. 10. Individual-subject data for the effects of diazepam and triazolam on overall response rate in the acquisition and performance components as a function of time after drug administration. The bars on placebo data represent the range of placebo values.

and observing responses seen in that component in Experiment 2. In Experiment 2 imposition of the largest error requirement increased observing responses. Perhaps errors produced via contingencies have different effects than errors produced via drug administration. Future research will be necessary to discern the relevant factors.

GENERAL DISCUSSION

The present experiments, by using an observing procedure, were designed to ascertain the function, if any, of the response-produced stimuli presented in a procedure involving the repeated acquisition and performance of response sequences. More specifically, we wanted to find out whether those stimuli played a role in the selective drug effects observed across the acquisition and performance components. In general, the observing contingency was successful in identifying the conditions under which observing was maintained; that is, the results from the three experiments consistently demonstrated that observing was maintained in the acquisition component. In that component, errors and observing responses were well correlated. The results were inconsistent concerning whether observing responses were maintained in the performance component; that is, the observing responses in the performance component occurred to a limited extent when a contingency for errors was imposed, but did not occur in the presence of drug-induced errors.

Our observation that errors are related to observing responses in the acquisition component is consistent with prior findings (D'Amato, Etkin, & Fazzaro, 1968). In that study, monkeys could observe stimuli required for correct performance on multiple discriminations (see Dinsmoor, 1983, for a discussion of this study). During acquisition, the number of observing responses increased as the percentage of correct responses increased and then decreased when the percentage of correct responses reached asymptote. This is consistent with our findings that observing responses increased and then decreased during acquisition of the response sequence. Moreover, D'Amato et al. (1968) reported that reversal of the discrimination or placement of the discrimination

in extinction increased observing behavior (see also Premack & Collier, 1966). In the present study, increases in errors in the acquisition component via a contingency or drug administration increased observing. Considered together, this occurrence of observing responses in the presence of errors suggests that a functional relationship exists between errors and observing in the acquisition component.

Interestingly, the use of an observing contingency with the repeated acquisition of behavioral sequence procedure results in steady states of transition for observing. Observing is stable in that approximately the same number of observing responses occur across sessions. However, observing is in transition in that observing responses as reflected in the cumulative plots first increase and then decrease within a session. These procedures may provide a useful experimental arrangement for the study of observing behavior and conditioned reinforcement because both increases and decreases in observing can be reliably obtained and the variables responsible for that transition may then be subjected to an experimental analysis.

The present results show that the response-dependent stimulus presentations in the performance component do not contribute to selective drug effects because those stimuli were not observed when selective drug effects occurred. This finding, in conjunction with our previous research, indicates that neither the response-produced stimuli nor reinforcement- and response-rate differences between the components are the determinants of the selective drug effects (Bickel et al., 1989; Higgins, Bickel, et al., 1989). Identifying the specific mechanism that accounts for selective drug effects will require future studies examining control exerted by other variables that may be present (e.g., stimuli correlated with the multiple schedule), as well as error rates and patterning.

Another consideration in accounting for the selective drug effects across the two components may be that responding in the performance component functions as a unit, whereas responding in the acquisition component represents the formation of a unit. Criteria proposed for the identification of a behavioral unit include that the unit (a) be reinforceable as if it were a single response (Branch, 1977; Marr,

1979), (b) have cohesiveness and integrity and consequently not be susceptible to disruption (Marr, 1979; cf. Schwartz, 1981), and (c) not depend on exteroceptive stimuli for within-unit responding (Kelleher, 1966; Marr, 1979). Behavior in the performance component generally meets these criteria. First, behavior in performance has been reinforced as a unit according to an FR schedule of reinforcement (second-order schedule) (Thompson & Moerschbaecher, 1979). Second, behavior in the performance component is more resistant to disruption by drugs or programmed error contingencies than is behavior in the acquisition component (e.g., Experiments 2 and 3 of this study; Bickel *et al.*, 1989; Higgins *et al.*, 1987; Higgins, Bickel, *et al.*, 1989; Schwartz, 1981). Third, as shown in the present study, behavior in the performance component does not require exteroceptive stimuli for within-unit responding.

Responding in the acquisition component, in contrast, does not meet these criteria for a behavioral unit. For example, responding in the acquisition component is relatively sensitive to the disruptive effects of drugs and other events (e.g., Experiments 2 and 3). Perhaps more importantly, responding in the acquisition component is dependent upon the brief exteroceptive stimuli for within-unit responding (e.g., Experiment 1).

This behavioral-unit analysis suggests that an established unit may be more difficult to disrupt than a unit in development. Such an interpretation may set the occasion for more refined questions about the nature of the selective drug effects and the differences between schedule components. For example, when does behavior in acquisition become a unit and function as responding in the performance component? Results from Experiment 2 suggest that the cessation of errors is not sufficient to indicate that responding in acquisition is performance-like. In that experiment, the introduction of an error requirement at a point at which errors did not occur resulted in considerably more observing responses in the acquisition component than in the performance component. Perhaps formation of the performance unit proceeds through at least three phases. In Phase 1, the sequence is acquired (i.e., within-session error reduction occurs). In this phase, responding begins to conform to the contingencies. In Phase 2, errors have

ceased and yet responding is not fully performance-like. Perhaps in this second phase, responding in acquisition represents a series of conditional discriminations (e.g., Snodgrass & McMillan, 1989). Phase 3 is the point at which the behavior becomes fully performance-like; that is, it functions as a single behavioral unit.

This phase analysis suggests that a detailed characterization of the development of the response sequence in the acquisition component is needed. For example, drug effects typically occur early in the session, suggesting that sensitivity to drug effects differs in the development of a sequence. Observing could be used as a marker to show when behavior becomes performance-like and, thus, may provide a means to investigate drug effects during the development of a behavioral unit.

Finally, several lines of evidence suggest the applicability of our results to nonhumans. First, in the present study, response-produced stimuli were not required to maintain accurate responding in the performance component, similar to prior results obtained with pigeons (Straub *et al.*, 1979). Second, the stimuli in the acquisition component have been shown to function as conditioned reinforcers for monkeys (Hursh, 1977), consistent with the present findings. Third, drug effects on the repeated acquisition and performance of response sequences in pigeons and monkeys are consistent with findings in humans for a variety of compounds (e.g., Barthalmus *et al.*, 1978; Bickel *et al.*, 1989, 1990; Higgins *et al.*, 1987, 1989; Higgins & Stitzer, 1990; Penetar, 1985; Thompson, 1973; Thompson & Moerschbaecher, 1979). Thus, the preponderance of studies supports the generality of findings across human and nonhuman responding under repeated acquisition and performance baselines and suggests that the findings from the present study may be relevant to nonhuman responding under comparable baselines.

REFERENCES

- Barrett, J. E. (1974). Conjunctive schedules of reinforcement: I. Rate-dependent effects of pentobarbital and *d*-amphetamine. *Journal of the Experimental Analysis of Behavior*, *22*, 561-573.
- Barthalmus, G. T., Leander, J. D., & McMillan, D. E. (1978). Combined effects of ethanol and diazepam on performance and acquisition of serial position sequences by pigeons. *Psychopharmacology*, *59*, 101-102.
- Bickel, W. K., Higgins, S. T., & Griffiths, R. R. (1989).

- Repeated diazepam administration: Effects on the acquisition and performance of response chains in humans. *Journal of the Experimental Analysis of Behavior*, **52**, 47-56.
- Bickel, W. K., Hughes, J. R., & Higgins, S. T. (1990). Human behavioral pharmacology of benzodiazepines: Effects on the acquisition and performance of response chains. *Drug Development Research*, **20**, 53-65.
- Boren, J. J. (1963). The repeated acquisition of new behavioral chains. *American Psychologist*, **18**, 421. (Abstract)
- Branch, M. N. (1977). On the role of "memory" in the analysis of behavior. *Journal of the Experimental Analysis of Behavior*, **28**, 171-179.
- Branch, M. N., Nicholson, G., & Dworkin, S. I. (1977). Punishment-specific effects of pentobarbital: Dependency on the type of punisher. *Journal of the Experimental Analysis of Behavior*, **28**, 285-293.
- D'Amato, M. R., Etkin, M., & Fazzaro, J. (1968). Cue-producing behavior in the capuchin monkey during reversal, extinction, acquisition, and overtraining. *Journal of the Experimental Analysis of Behavior*, **11**, 425-433.
- Deitz, S. M., Gaydos, G. R., Lawrence, A. D., Quinn, P. C., Brasher, L. D., & Frederick, L. D. (1987). Feedback effects on sequential ordering in humans. *Journal of the Experimental Analysis of Behavior*, **48**, 209-220.
- Desjardins, P. J., Moerschbaecher, J. M., Thompson, D. M., & Thomas, J. R. (1982). Intravenous diazepam in humans: Effects on acquisition and performance of response chains. *Pharmacology Biochemistry and Behavior*, **17**, 1055-1059.
- Dinsmoor, J. A. (1983). Observing and conditioned reinforcement. *Behavioral and Brain Sciences*, **6**, 693-728. (Includes commentary)
- Dinsmoor, J. A., Flint, G. A., Smith, R. F., & Viemeister, N. F. (1969). Differential reinforcing effects of stimuli associated with the presence or absence of a schedule of punishment. In D. P. Hendry (Ed.), *Conditioned reinforcement* (pp. 357-384). Homewood, IL: Dorsey Press.
- Harting, J., & McMillan, D. E. (1976). Effects of pentobarbital and *d*-amphetamine on the repeated acquisition of response sequences by pigeons. *Psychopharmacology*, **49**, 245-248.
- Herrnstein, R. J., & Morse, W. H. (1958). A conjunctive schedule of reinforcement. *Journal of the Experimental Analysis of Behavior*, **1**, 15-24.
- Higgins, S. T., Bickel, W. K., O'Leary, D. K., & Yingling, J. (1987). Acute effects of ethanol and diazepam on the acquisition and performance of response sequences in humans. *Journal of Pharmacology and Experimental Therapeutics*, **243**, 1-8.
- Higgins, S. T., Bickel, W. K., Rush, C. R., Hughes, J. R., Pepper, S. L., & Lynn, M. (1989). Comparable rates of responding and reinforcement do not eliminate the differential effects of ethanol on response chain acquisition and performance. *Psychological Record*, **39**, 583-595.
- Higgins, S. T., & Stitzer, M. L. (1990). Comparison of the effects of secobarbital and diazepam on the repeated acquisition of response sequences in humans. *Drug Development Research*, **20**, 43-52.
- Higgins, S. T., Woodward, B. M., & Henningfield, J. E. (1989). Effects of atropine on the repeated acquisition and performance of response sequences in humans. *Journal of the Experimental Analysis of Behavior*, **51**, 5-15.
- Hursh, S. R. (1977). The conditioned reinforcement of repeated acquisition. *Journal of the Experimental Analysis of Behavior*, **27**, 315-326.
- Katz, J. L. (1983). Effects of drugs on stimulus control of behavior: II. Degree of stimulus control as a determinant of effect. *Journal of Pharmacology and Experimental Therapeutics*, **226**, 756-763.
- Kelleher, R. T. (1966). Chaining and conditioned reinforcement. In W. K. Honig (Ed.), *Operant behavior: Areas of research and application* (pp. 160-212). New York: Appleton-Century-Crofts.
- Kelleher, R. T., Riddle, W. C., & Cook, L. (1962). Observing responses in pigeons. *Journal of the Experimental Analysis of Behavior*, **5**, 3-13.
- Laties, V. G., & Weiss, B. (1960). Human observing behavior after signal detection. *Journal of the Experimental Analysis of Behavior*, **3**, 27-33.
- Marr, M. J. (1979). Second-order schedules and the generation of unitary response sequences. In M. D. Zeiler & P. Harzem (Eds.), *Advances in analysis of behaviour: Vol 1. Reinforcement and the organization of behaviour* (pp. 223-260). Chichester, England: Wiley.
- McMillan, D. E. (1967). A comparison of the punishing effects of response-produced shock and response-produced time out. *Journal of the Experimental Analysis of Behavior*, **10**, 439-449.
- Moerschbaecher, J. M., Thompson, D. M., & Winsauer, P. J. (1983). Effects of heroin, methadone, LAAM and cyclazocine on acquisition and performance of response sequences in monkeys. *Pharmacology Biochemistry and Behavior*, **19**, 701-710.
- Penetar, D. M. (1985). The effects of atropine, benactyzine, and physostigmine on a repeated acquisition baseline in monkeys. *Psychopharmacology*, **87**, 69-76.
- Physicians desk reference*. (1991). Oradell, NJ: Medical Economics Data.
- Premack, D., & Collier, G. (1966). Duration of looking and number of brief looks as dependent variables. *Psychonomic Science*, **4**, 81-82.
- Schwartz, B. (1981). Reinforcement creates behavioral units. *Behaviour Analysis Letters*, **1**, 33-41.
- Snodgrass, S. H., & McMillan, D. E. (1989). Repeated acquisition of behavioral chains: Response sequences or conditional discriminations? *Journal of the Experimental Analysis of Behavior*, **51**, 233-241.
- Straub, R. O., Seidenberg, M. S., Bever, T. G., & Terrace, H. S. (1979). Serial learning in the pigeon. *Journal of the Experimental Analysis of Behavior*, **32**, 137-148.
- Thompson, D. M. (1973). Repeated acquisition as a behavioral base line for studying drug effects. *Journal of Pharmacology and Experimental Therapeutics*, **184**, 506-514.
- Thompson, D. M. (1975). Repeated acquisition of response sequences: Stimulus control and drugs. *Journal of the Experimental Analysis of Behavior*, **23**, 429-436.
- Thompson, D. M., & Moerschbaecher, J. M. (1979). Drug effect on repeated acquisition. In T. Thompson & P. B. Dews (Eds.), *Advances in behavioral pharmacology* (Vol. 2, pp. 229-259). New York: Academic Press.