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Effects Of Minimum-Interreinforcer Interval On Ethanol-Maintained Performance of Rats

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BEARDSLEY, P. M., G. A. LEMAIRE AND R. A. MEISCH. *Effects of minimum-interreinforcer interval on ethanol-maintained performance of rats.* PHARMACOL BIOCHEM BEHAV 19(5) 843–847, 1983.—Dipper cups filled with an 8% (w/v) ethanol solution were presented to Long-Evans hooded rats according to either a multiple Extinction *x* sec Fixed-Ratio 1 or a chain Differential-Reinforcement-of-Other-Behavior *x* sec Fixed-Ratio 1 schedule of reinforcement. The scheduled value of the extinction and differential-reinforcement-of-other-behavior components was varied to manipulate minimum-interreinforcer interval. Minimum-interreinforcer intervals from 0 sec (baseline condition of continuous reinforcement) to 480 sec were tested in an ascending series followed by a descending, retest series. Increasing the minimum-interreinforcer interval reduced the number of ethanol presentations obtained under both reinforcement schedules. These reductions were not due to ceiling effects imposed by the maximum number of possible deliveries obtainable within a session. The number of ethanol presentations obtained was always less than the maximum number permitted by the value of the minimum-interreinforcer interval. Thus, imposing minimum-interreinforcer intervals between drinking opportunities reduces the level of ethanol self-administration relative to continuous-access baseline conditions.

Ethanol Ethanol drinking Ethanol self-administration Ethanol as a reinforcer
Minimum-interreinforcer interval Chain DRO FR schedule Mult EXT FR schedule Lever press Rats

RATIO and interval schedules of reinforcement are the two fundamental methods of arranging deliveries of positive reinforcers [3]. In recent reviews it has been noted that although drug self-administration by animals under ratio schedules of reinforcement has been studied extensively, little attention has been given to interval schedules of drug reinforcement [7,9]. When interval schedules have been used to arrange drug deliveries, the drugs have usually been delivered via the intravenous or intramuscular routes [7,9]. Only a few studies involving interval reinforcement schedules have delivered drugs orally.

Interval reinforcement schedules enable the temporal control of drug availability and allow the study of the persistence of drug self-administration under intermittent access conditions. Previous studies with human subjects who had oral drug use histories have demonstrated that the minimum interreinforcer interval imposed by interval reinforcement schedules can be a critical determinant of oral drug self-administration [2, 4, 5, 6]. For example, incrementing the minimum-interdrink interval for ethanol [2] and for pentobarbital and diazepam [6] reduces oral self-administration of these drugs. Also, when drinks were spaced by a minimum interval of 60 min, 2/3 of the alcoholics on a closed hospital ward either abstained from drinking or eventually stopped drinking ethanol [4,5]. Research with rats has also demonstrated the potential importance of the minimum-interreinforcer interval. Increasing the duration of a fixed-interval schedule [FI] from 0 to 240 sec reduced the intake of 8% (w/v) ethanol by rats [1].

The purpose of the present experiment was to further examine the effects of minimum-interreinforcer interval imposed by interval reinforcement schedules on performance maintained by 8% (w/v) ethanol. In a previous study using rats drinking ethanol on FI schedules [1] the number of interreinforcement responses varied widely and may have acted along with the minimum-interreinforcer interval to control ethanol-maintained performance. Because minimum interreinforcer interval, per se, was the independent variable of interest in the present study, types of interval reinforcement schedules were used which were expected to minimize inter-

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reinforcement response occurrence. This experiment is the first in a series which examines temporal and response constraints on oral ethanol self-administration.

METHOD

Subjects

The subjects were ten experimentally naive male Long-Evans descent hooded rats (Blue Spruce Farms, Altamont, NY) approximately 120 days old at the beginning of the study. The rats were sorted into five pairs based on their similarity in free-feeding body weight. One member from each pair, selected randomly, was then assigned to the T-Group. The remaining rats composed the V-Group (the designations "T" and "V" were arbitrarily selected and are not abbreviations). The rats were maintained at 80% of their free feeding body weights and were individually housed in a continuously illuminated room regulated at 24°C. Water was always available in the rats' home cages except during the initial training period as noted below.

Apparatus

Five identical sound-attenuated commercial operant-conditioning chambers (Lehigh Valley Electronics) were equipped with two levers and a solenoid driven liquid dipper. The levers were symmetrically centered on the front panel and were separated by an inactivated food magazine. The dipper cup was situated in an opening in the panel located to the right of the magazine. Three colored jewel lights were located above each lever. A 4.76 W white light was located 3.2 cm above the hole in the panel where the dipper was located. A 2.80 W house light was centered at the top of the front panel. The speaker of a Sonalert (Sonalert, 2900 Hz, Mallory and Co.) was located immediately below the house light. Reinforced lever presses resulted in the refilling of the dipper cup with 0.11 ml liquid. During refilling, the dipper cup was lowered into a reservoir and then returned to the up-available position. Simultaneous with the dipper cup refilling operation was a 0.8 sec sounding of the Sonalert and illumination of the white light above the dipper-panel opening. White masking noise was constantly present, and an exhaust fan provided ventilation.

Programming and data recording were automatically controlled by standard electromechanical equipment in an adjacent room. The temporal patterns of responses and dipper presentations were continuously recorded by cumulative recorders and by counters that printed out every 5 minutes.

Procedure

Daily 3-hr sessions were conducted throughout the experiment. All schedule requirements pertained to presses of the right lever. Presses on the left lever had no programmed consequence but were recorded. Initially, the rats were induced to lever press for water on a fixed-ratio 1 (FR 1) schedule of reinforcement by depriving them of water at their home cages and by feeding them their daily maintenance allotment of Purina Laboratory Chow in their operant chambers. Following two consecutive sessions of water reinforcement, water bottles were restored to the home cages and access to 2, 4, and 8% (w/v) ethanol was made available for 2, 4, and 6 sessions, respectively, with daily maintenance food provided during experimental sessions. Subsequently, in-session feedings were discontinued, and food was given to the rats only in their home cages following each session. Different schedules of liquid access were then arranged for each group. When the white house light was illuminated, the first lever press produced a delivery of ethanol or water by the dipper (i.e., a one-response fixed-ratio schedule, FR 1). After each dipper presentation, the white house light was turned off and the jewel lights were illuminated for x sec (T-Group) or until the rats ceased pressing the lever for x sec (V-Group). Using the terminology of Ferster and Skinner [3], the schedule for the T-Group is referred to as a multiple Extinction x sec Fixed Ratio 1 (i.e., mult EXT x sec FR 1) and the schedule for the V-Group as a chain Differential-Reinforcement-of-Other-Behavior x sec Fixed Ratio 1 (i.e., chain DRO x sec FR 1). Different schedules of reinforcement were used with the T- and V-Groups to insure a constant interval between drinking opportunities (with the mult EXT x sec FR 1 schedule in the T-Group) or to insure a constant interval without a lever press preceding drinking opportunities (with the chain DRO x sec FR 1 schedule in the V-Group).

Tests at EXT and DRO component durations of 0 (baseline). 7.5, 15, 30, 60, 120, 240, and 480 sec were followed by retests at 240, 120, 60, 30, 15, 7.5, and 0 sec, in that order. If a rat obtained, on the average, 20 or fewer ethanol presentations at a particular duration, longer durations were not tested. This criterion was used to prevent extinction of ethanol responding which would have necessitated retraining during the test series. Rats T-1, T-2, V-1 and V-5 obtained 20 or fewer ethanol presentations at 240 sec and subsequently were not tested at 480 sec. Following completion of the 0-sec retest condition, water was made the available liquid at a duration of 0 sec. Except for the baseline 0-sec test condition, in which the rats were maintained for 10 consecutive stable sessions, changes from one condition to the next were made following five consecutive sessions in which there were no systematic increases or decreases in the number of dipper presentations.

The solutions, expressed in grams percent (w/v), were prepared using 95% (v/v) ethanol in tap water. The solutions were prepared at least 20 hr before use and were kept in stoppered flasks at room temperature. The volume consumed was measured at the end of each session by subtracting the volume remaining from the volume added to the reservoir, corrected for evaporation. Because the volume measured by this method was sometimes greater than the product of dipper-cup size (0.11 ml) and the number of dipper presentations, this product was used for all calculations of volume consumption.

RESULTS

Increasing the EXT (Fig. 1) and DRO (Fig. 2) component durations resulted in progressive decreases in the number of dipper presentations obtained. When exceptions to this relationship occurred, they usually occurred at the shorter durations. Group mean number of presentations obtained during the retest conditions usually exceeded the number obtained during the corresponding test conditions. When water was made available at 0 sec, presentations were infrequent and fewer in number than those obtained at 0 sec when 8% ethanol was available.

In parallel with the number of dipper presentations obtained, ethanol intake (mean mg ethanol/kg body weight /3-hr session) decreased with increasing EXT and DRO durations. The combined mean ethanol intake of the T and V rats ranged from 330.4 mg ethanol (at 480 sec) to 2715.8 mg ethanol (at

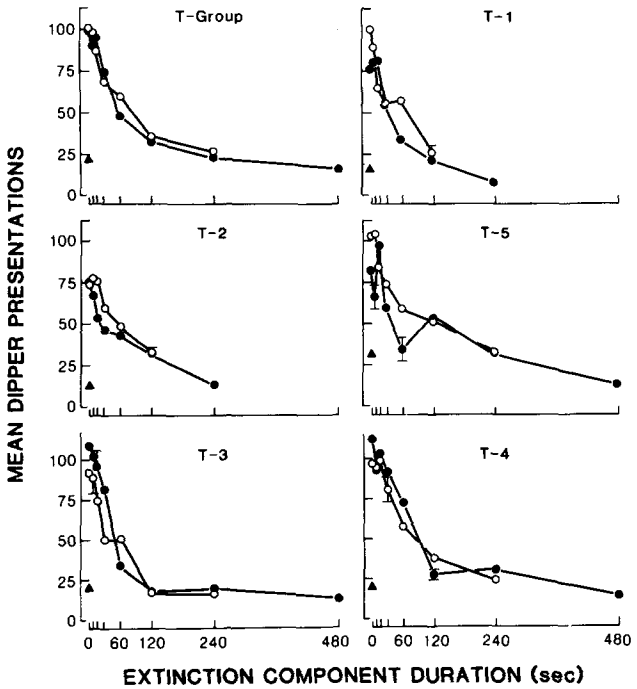

FIG. 1. Mean dipper presentations obtained by the T-Group and individual T-rats as a function of EXT component duration. Filled circles: ascending, 8% ethanol test values. Unfilled circles: descending, 8% ethanol retest values. Filled triangles: water control values. Except for the 0-sec 8% test value, each point within individual subject frames represents the mean of five consecutive sessions. Absence of a data point indicates that the rat failed to meet criterion performance during a preceding condition and was not subsequently tested at longer intervals. The 0-sec 8% test value represents the mean of 10 consecutive sessions. Brackets indicate the standard errors of the mean. Brackets are plotted only for standard errors that exceeded 10% of the mean. Points in the group graph represent the mean of available subject means (N=5; except for 480 sec, N=3)..

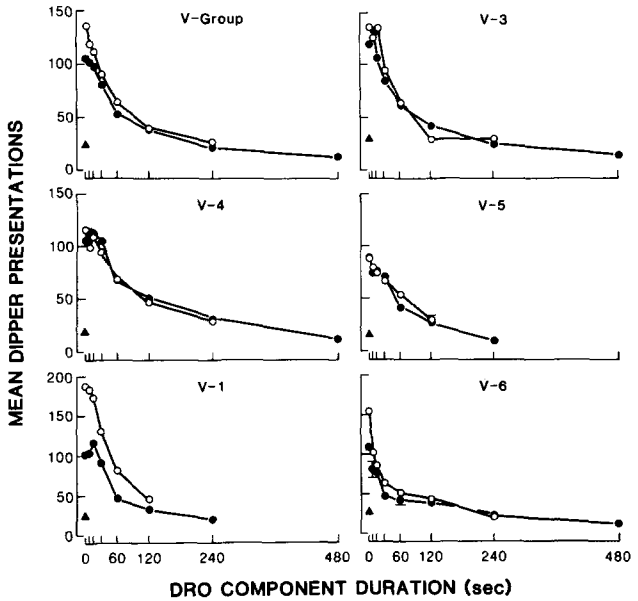

FIG. 2. Mean dipper presentations obtained by the V-Group and individual V-rats as a function of DRO component duration. Filled circles: ascending, 8% ethanol test values. Unfilled circles: descending, 8% ethanol retest values. Filled triangles: water control values Except for the 0-sec 8% test value, each point within individual subject frames represents the mean of five consecutive sessions Absence of a data point indicates that the rat failed to meet criterion performance during a preceding condition and was not subsequently tested at longer intervals. The 0-sec 8% test value represents the mean of 10 consecutive sessions. Brackets indicate the standard errors of the mean. Brackets are plotted only for standard errors that exceed 10% of the mean. Points in the group graph represent the mean of available subject means (N=5; except for 480 sec, N=3).

the 0-sec retest condition)/kg body weight/3-hr session. Up through minimum-interreinforcer intervals of 60 sec, most rats consumed ethanol in amounts exceeding 300 mg/kg body weight/hr, the rate at which rats metabolize ethanol [10].

The number of dipper presentations obtained was not determined by the maximum number of possible dipper presentations imposed by the value of the EXT and DRO components. Figure 3 shows the percent of possible dipper presentations obtained at each duration for the two groups (test and retest conditions combined). Subjects never obtained all of the possible dipper presentations available at any duration. However, the mean percent of possible dipper presentations obtained increased as duration increased.

The rats failed to maintain baseline numbers of dipper presentations when the scheduled minimum-interreinforcer interval permitted them to do so (i.e., when the duration was 60 sec or less). This can be seen in Fig. 3. The dotted lines in Fig. 3 depict 0-sec baseline presentations as a proportion of (i.e., percentage of) the maximum number obtainable at durations 60 sec and less. When the data points fall below this dotted line the rats were not obtaining baseline numbers of ethanol deliveries even though numbers equal to or greater than baseline were obtainable. Note that the data points representing the percent of obtained dipper presentations always fall below these dotted lines.

The mean number of lever presses emitted per dipper presentation did not systematically vary with DRO component duration. The V-Group mean number of lever presses per presentation was close to unity during most conditions, and never exceeded 2.0 per presentation. However, for the T-Group the mean number of lever presses per dipper presentation showed moderate increases followed by decreases between EXT values of 0 and 240 sec. Nevertheless, mean T-Group response output never exceeded 3.0 responses per presentation. For both groups, mean responses per presentation were usually less during the retest phase than the test phase at identical durations.

Sample cumulative records at each condition for rat V-6 (Fig. 4) show that ethanol presentations occurred in bursts, with the largest burst occurring at the beginning of each session. Unreinforced ethanol responses (lever presses occurring during the DRO components) were infrequent. When water was available at a schedule duration of 0 sec, few dipper presentations occurred.

DISCUSSION

Increases in minimum-interreinforcer interval resulted in

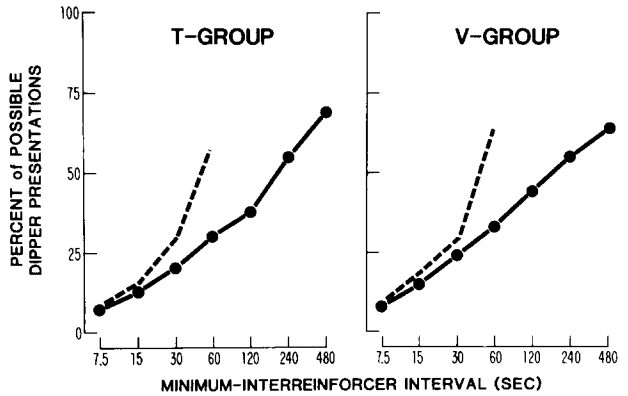

FIG. 3. Mean percent of possible dipper presentations obtained by the T-Group and V-Group as a function of minimum-interreinforcer interval. Each filled circle represents the group mean of the test and retest values. Data points depicted by the filled circles were determined by dividing the actually obtained mean number of dipper presentations by the maximum number potentially obtainable within a 3-hr session and then mulitplying this quotient by 100. The maximum number of obtainable presentations was determined by dividing the session duration (10800 sec) by the minimum-interreinforcer interval adjusted for dipper recycling time (i.e., adjusted by adding 0.8 sec to the minimum-interreinforcer interval). The dotted lines represent the mean number of presentations obtained during the 0-sec test and retest conditions expressed as the percent of available presentations. For example, the T-Group averaged 100.5 dipper presentation at 0 sec. At 60 sec, 177 dipper presentations were obtainable in a 3-hr session. In order to obtain 100.5 presentations (i.e., the average baseline number) the T-Group needed to obtain 57% of the 177 dipper presentations that were available at 60 sec.

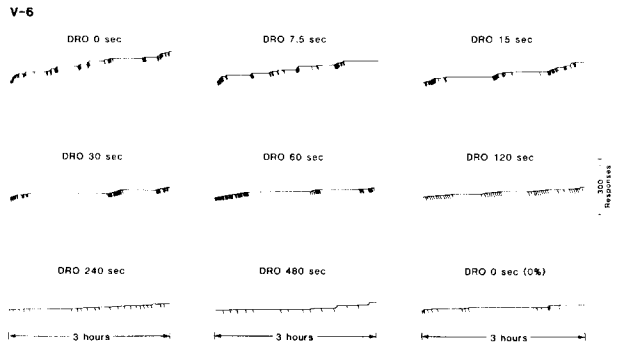

FIG. 4. Sample cumulative records of rat V-6's performance under each DRO component duration tested with 8% ethanol and under the water control condition. Vertical steps in the pen indicate lever presses. Pen pips represent dipper presentations. The resolution of these cumulative records prevents accurate counting of individual presentations at short durations because multiple consecutive presentations are depicted as single, thickened pen pips. Records from V-6 were selected because its mean number of dipper presentations was, overall, closest to the group mean number.

decreases in both ethanol deliveries and ethanol intake. An inverse relationship between minimum-interreinforcer interval and ethanol intake has been similarly found with humans [2] and with Sprague-Dawley rats [1]. The present data systematically extend this relationship to include additional schedules of reinforcement (mult EXT x sec FR 1 and chain DRO x sec FR 1).

The decreases in ethanol deliveries that occurred with increases in minimum-interreinforcer interval were not due to the rats obtaining the maximum number of deliveries permitted at a particular condition (Fig. 3). Up through minimum-interreinforcer intervals of 60 sec the rats could have obtained as many ethanol presentations as they had obtained during baseline continuous reinforcement conditions (i.e., at 0-sec), but did not. At durations 120 sec and greater, the scheduled minimum-interreinforcer intervals did establish maximum limits of dipper presentations which were less than the average numbers obtained during baseline conditions. At these intervals, nevertheless, the rats did not obtain the maximum number of deliveries which would have, in effect, produced ethanol intake levels closest to those maintained during baseline conditions. Thus, when minimum-interreinforcer intervals were imposed between drinking opportunities, levels of ethanol intake were reduced below both baseline and scheduled-ceiling levels. When minimum-interreinforcer intervals have been imposed between drug ingestions using human subjects, similar reductions below baseline levels of drug self-administration have occurred [2, 4, 5, 6].

One potential mechanism through which increases in minimum-interreinforcer interval could have acted to reduce the number of ethanol deliveries below baseline and scheduled-ceiling levels is suggested by the patterns of ethanol intake. At short durations, ethanol drinking occurred in bursts (e.g., see Fig. 4). However, when progressively longer minimum-interreinforcer intervals were imposed between ethanol deliveries, drinking in bursts was prevented. Perhaps ethanol is weakened as a reinforcer if bursts of drinking are prevented because, as a result, the local level of obtainable pharmacological effect is reduced. Other responsible mechanisms may have been less specific to ethanol and general to all reinforcers. For example, increasing the minimum-interreinforcer interval reduces the density of reinforcement. When the density of food reinforcement is reduced the relative strength of responding maintained by food is reduced [8]. Perhaps increasing the minimum-interreinforcer interval weakens responding maintained by ethanol because the reinforcement density is reduced. An experiment that could help clarify these hypotheses would be to test a range of ethanol concentrations across a range of minimum-interreinforcer intervals.

Anderson and Thompson examined the behavior of rats drinking 8% w/v ethanol on FI schedules ranging from 0 to 240 sec during 5-hr experimental sessions [1]. The contingencies of FI schedules are similar to the contingencies of the schedules used for the T and V rats in that minimum intervals are imposed between reinforcer deliveries. Comparisons between Anderson and Thompson's study and the present study must be qualified because session duration (5 hr vs. 3 hr) and dipper cup size (0.25 ml vs. 0.11 ml) were different. However, certain similarities do appear. Firstly, ethanol drinking occurred in bursts at short interval durations and became progressively distributed within individual sessions at longer interval durations. Secondly, ethanol intake during continuous reinforcement conditions (i.e., at 0 sec) was similar. The rats of both studies averaged approximately 2.5 g ethanol/kg body weight/session at 0 sec (note that the estimate of intake for Anderson and Thompson's

rats is derived by obtaining volumes of ethanol consumed from Fig. 6 [1] and then converting to intake expressions based on the weights of the individual rats; estimate of intake for the T and the V rats was obtained by averaging the intake for all rats during the 0-sec Test and Retest conditions). Thirdly, and most importantly, in both studies as the minimum-interreinforcer interval was increased, the number of ethanol deliveries decreased to below baseline (0 sec) and scheduled-ceiling levels. Differences do occur between the two studies in that when tested at identical durations above 0 sec (at 60, 120, and 240 sec), Anderson and Thompson's rats had higher ethanol intakes per session. It is unknown whether the higher ethanol intakes obtained in the Anderson and Thompson study [1] reflect their use of longer session durations and larger dipper cup sizes or whether it also involves other factors such as their use of FI schedules and the higher rates of lever pressing generated by these schedules.

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