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Ethanol Reinforced Responding in the Rat: A Concurrent Analysis Using Sucrose as the Alternate Choice

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SAMSON, H. H., T. A. ROEHRS AND G. A. TOLLIVER. *Ethanol reinforced responding in the rat: A concurrent analysis using sucrose as the alternate choice.* PHARMAC. BIOCHEM. BEHAV. 17:(2) 333–339, 1982.—Rats were trained on a two lever concurrent schedule of reinforcement (Fixed Ratio 8 Fixed Ratio 8) with ethanol (5% v/v) and water as the two available fluids. After establishing baseline responding patterns, various concentrations of sucrose (0.05% to 5.0% w/v) were substituted for the water in an ascending series. When water was the alternative fluid, ethanol responding predominated. With increasing sucrose concentration, percent ethanol responding decreased. At sucrose concentrations between 1.00% and 1.25% approximately half of the total responses per session were for each substance. This change in relative responding for the two fluids occurred as a result of increased total responding and not as a result of decreased ethanol responses. When ethanol was paired with either a 3% or 5% sucrose concentration, ethanol responding decreased, with increased sucrose responding. However, when the number of responses required to obtain these sucrose solutions was greatly increased (Fixed Ratio 64), ethanol responding increased to levels of up to twice that of the water ethanol condition. This increased ethanol responding was found to remain in the following ethanol water session after the sucrose schedule manipulation.

Ethanol reinforced responding Concurrent schedules Sucrose Rats

OPERANT responding maintained by presentation of ethanol solutions has been well demonstrated in different animal species [1, 2, 8, 10, 13]. That ethanol is preferred to water in these self-administration procedures has been demonstrated by using a concurrent schedule in which both ethanol and water were simultaneously available [6, 7, 8, 9, 10]. Utilization of this concurrent schedule to examine ethanol's capability to maintain operant responding has led to the suggestion that the ratio of ethanol responding divided by total responding might provide a useful index of ethanol's reinforcing "efficacy" [12]. The stability of this index has been examined by manipulating body weight [10]; increasing the response requirement for ethanol presentation [12]; and by producing physical dependence upon ethanol [11]. While ethanol's efficacy was seen to be slightly altered as a result of the above manipulations, the ratio remained fairly stable at values from 0.8 to 1.0. This stability appeared to result from the almost exclusive responding for ethanol in all conditions, with very low responding of the other available fluid—water. Thus, even though some of the manipulations reduced total ethanol responding, the relative responding for ethanol in relation to water was not greatly affected.

In these previously reported concurrent studies, the animals were food but not water restricted, and thus the water clearly failed to produce much responding. We reasoned that a more appropriate test of ethanol's efficacy would result if responding levels for the two available fluids were similar. Under these conditions when various experimental manipulations occurred, changes in ethanol's efficacy could be more appropriately evaluated, in respect to response for the other available reinforcer. The present experiments were therefore performed using sucrose solutions instead of water as the alternative fluid to ethanol to determine if equal responding patterns could be obtained when both solutions were available concurrently.

EXPERIMENT 1

METHOD

Animals

Four male Long-Evans rats (90 days old), obtained from the Breeding Facility of the Department of Psychology of the University of Washington were used. They were individually housed in standard hanging cages in a multiple cage rack system. Water was available at all times except as specified

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below (see initial training procedure). Food was rationed daily until the rats reached 80% of their free-feeding body weight (free feeding body weight ranged from 375 g to 435 g). These weight levels were then maintained throughout the experiments, with daily food rations given after the 1-hr operant session. The animals were housed in a room with artificial lighting that was regulated on a 12 hr on/12 hr off cycle. The animals were run daily during the first half of the light cycle.

Apparatus

The two operant chambers and their enclosures used for this study have been described previously [10]. Briefly, each operant box had two levers and two liquid dipper dispensers (Ralph Gebrands Corp., Model #B-LH, Arlington, MA) mounted on the front wall. Responses on the right lever resulted in presentation of the dipper to the right of that lever, and responses on the left lever resulted in presentation of the dipper to the left of that lever. All dipper operations provided 3-sec access to the 0.1-ml dipper. The dippers' fluid reservoirs were partially covered to reduce evaporation. The fluid volumes in each reservoir were measured before and after each session with a graduated cylinder to determine fluid intake, with a correction for evaporation included. During a session, a small lamp (1 W) illuminated each chamber. An exhaust fan provided air circulation for the operant chamber which was housed inside a sound shielded outer chamber. The schedules were programmed with standard electromechanical and digital logic programming equipment.

Initial Procedure

The basic procedure has also been previously reported [10]. After the animals reached the 80% body weight level, they were placed on a daily 21.5-hr water deprivation schedule and trained to press the right lever (the left lever was removed from the box at this time) to obtain water reinforcement on a continuous reinforcement schedule (CRF). Daily operant sessions were 1-hr in duration. Following the session, the animal was fed its daily food ration and given 1.5-hr access to water.

When responding was well established, the animals were placed on a fixed ratio (FR) schedule, starting at 2 (FR2), and increased daily until a FR8 was attained. When response patterns were stable at FR8, the animals were presented with the left lever (the right now being removed), and stable responding for water on a CRF schedule established. FR responding was then instituted for the left lever using the same procedure described for the right lever. When stable FR8 responding occurred, the right lever was reintroduced and a concurrent FR8 FR8 with water available at both dippers was instituted. Over the next 20 sessions, the animals were checked for lever independence by increasing the FR requirement for one lever (i.e., right FR32, left FR8) (for rationale see [3]).

After independence had been demonstrated, water was again available ad lib in the home cage. Then the procedure previously used in our laboratory to establish responding for ethanol was employed [10]. This consisted of placing ethanol (5% v/v) in one reservoir, and water in the other, with both available on a concurrent FR8 FR8 schedule. At the start of each session, 5 g of the daily food ration were placed in the operant chamber. This was continued for the next 10–15 days, with the relative locations of ethanol and water alternated daily. Within 10–15 sessions, the animals were observed to follow ethanol from one lever to the other as it alternated between sessions. As well, responding for ethanol increased daily. When strong ethanol responding occurred, the total food ration was placed into the home cage after the daily operant session.

For the next four months, 3 of the animals (numbers 41, 42, and 45) were run five times per week, with ethanol and water as the available fluids on a FR8 FR8 concurrent schedule. The lever and reservoir for each fluid were alternated each session. The other animal (number 43) was exposed to the same ethanol-water, FR8 FR8 schedule for only one month prior to starting the experimental procedure.

Experimental Procedure

The last five days of the initial procedure were used as the original baseline responding level for water ethanol, FR8 FR8. The water was then replaced by 0.25% sucrose solution (w/v) (tap water was used as the solvent for all sucrose solutions) for the next seven days. The positions of the two solutions were alternated daily as before. The animals then received five days of water-ethanol, FR8 FR8 again before the next sucrose ethanol determination. Sucrose concentrations were incremented in each successive pairing by 0.25% steps for three of the four animals, and by 0.50% for the remaining animal. An ascending order was used, with five days at each sucrose concentration, always interspaced by five days of water ethanol pairing. The sucrose concentration was increased using this procedure until the ratio of ethanol responding to total responding (i.e., the efficacy index) was around 0.50. At all times the other available solution was paired with ethanol (5% v/v) on the FR8 FR8 concurrent schedule. Following the sucrose concentration that resulted in approximately equal responding for ethanol and sucrose, another five days of water-ethanol (FR8 FR8) was given. A 3% sucrose solution was then employed as the alternate fluid for five days, followed by another five days of water, and then five days with 5% sucrose.

The total number of responses on each lever, the total number of dipper operations, and the fluid reservoir change were measured for each session, with cumulative response records taken for selected sessions. Daily ethanol intakes in g/kg were calculated using the fluid changes corrected for evaporation.

RESULTS

Tabel 1 presents the mean daily water ethanol FR8 FR8 ethanol efficacy measures and ethanol intakes for the animals during the 1–4 months prior to the initiation of sucrose ethanol testing. Rats number 41, 42 and 45 developed a moderately stable efficacy score which changed by 10% or less over the last three months. It should be noted however that on any particular day, for a given individual, ethanol responding might fall below the 50% level. This was usually due to either very low responding, or to bar preferences that led to increased water responding on that day. Daily sessions intakes ranged from 0.2 to 1.2 g ethanol/kg body weight. These values are similar to those found in prior work [10, 11, 12].

The relation of ethanol efficacy scores to sucrose concentration is presented in Fig. 1. For every animal, as sucrose concentration increased, the relative responding for ethanol decreased. With sucrose concentrations between 1.0 and 1.5%, ethanol efficacy was approximately 50% for all animals. When sucrose concentrations were increased to 3

TABLE 1

DAILY SESSION ETHANOL EFFICACY SCORES AND INTAKES (g/kg)
(MONTHLY MEANS ± S.D.)

Animal Number		Month 1	2	3	4
41	Efficacy	0.91 ± 0.09	0.88 ± 0.12	0.80 ± 0.09	0.84 ± 0.11
	Intake	1.20 ± 0.20	0.75 ± 0.11	0.61 ± 0.20	0.79 ± 0.09
42	Efficacy	0.74 ± 0.12	0.82 ± 0.10	0.80 ± 0.22	0.90 ± 0.07
	Intake	0.58 ± 0.25	0.40 ± 0.12	0.66 ± 0.32	0.52 ± 0.03
43	Efficacy	—	—	—	0.57 ± 0.20
	Intake	—	—	—	0.22 ± 0.07
45	Efficacy	0.65 ± 0.22	0.73 ± 0.22	0.82 ± 0.16	0.72 ± 0.28
	Intake	0.56 ± 0.11	0.42 ± 0.06	0.36 ± 0.13	0.52 ± 0.15

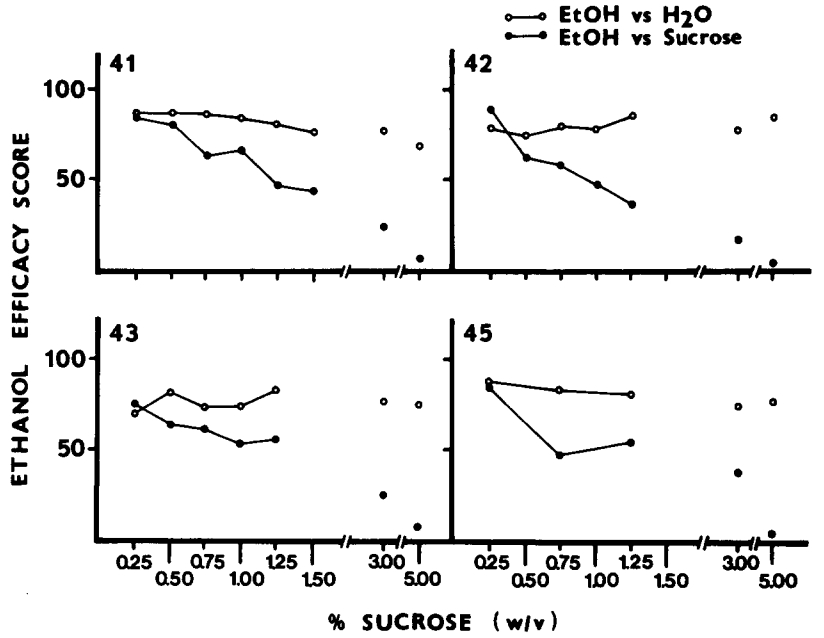

FIG. 1. Mean daily ethanol (5%) to total responding ratios (efficacy scores) on a concurrent schedule (FR8 FR8) with water or various % sucrose solutions as the other available substances. (Mean values based on 7 consecutive daily sessions.)

and 5%, the ethanol efficacy declined, with efficacy scores less than 10% when 5% sucrose was the alternate fluid. However, these decreases of ethanol efficacy as sucrose concentration increased were at the lower sucrose concentrations not a result of decreased ethanol responding, but rather due to an increase in total responding (Table 2). Only at the 3% and 5% sucrose comparison conditions did the number of ethanol reinforcements decline appreciably. Measurement of actual fluid consumed compared to number of dipper operations gave identical results, and thus only dipper operations are presented. Over the time period of sucrose presentations, the relation of ethanol to water responding was seen to change very little.

EXPERIMENT 2

In Experiment 1, altering the sucrose concentration in the concurrent pair, changed the responding for each substance. Thus, the composition of the alternate reinforcer appears to regulate the relative amount of responding for ethanol in the concurrent situation. Experiment 2 was designed to examine the effects of schedule manipulations in the same concurrent situation.

METHOD

Animals and Apparatus

Three of the four animals that were used in Experiment 1

TABLE 2

AVERAGE NUMBER OF DIPPER OPERATIONS AND ETHANOL INTAKE (g/kg) PER DAILY SESSION (MEAN OF 7 CONSECUTIVE SESSIONS)

Concurrent Pair Animal Number	Water	Ethanol (g/kg)	Sucrose	Ethanol (g/kg)	Water	Ethanol (g/kg)	Sucrose	Ethanol (g/kg)
			0.25				0.50	
41	10	61 (0.79)	12	69 (1.02)	9	53 (0.79)	10	53 (0.76)
42	6	36 (0.52)	3	22 (0.33)	10	28 (0.40)	22	31 (0.46)
43	8	22 (0.22)	8	26 (0.27)	9	38 (0.37)	12	24 (0.27)
45	5	37 (0.52)	5	32 (0.46)	—	—	—	—
			0.75				1.00	
41	9	54 (0.69)	27	44 (0.66)	8	49 (0.71)	22	45 (0.63)
42	10	41 (0.63)	34	48 (0.75)	14	56 (0.78)	35	30 (0.43)
43	7	19 (0.18)	17	25 (0.24)	10	27 (0.29)	19	22 (0.22)
45	5	29 (0.42)	29	23 (0.31)	—	—	—	—
			1.25				1.50	
41	8	39 (0.55)	32	29 (0.43)	9	30 (0.45)	38	31 (0.44)
42	8	46 (0.70)	78	42 (0.63)	—	—	—	—
43	6	32 (0.34)	21	27 (0.26)	—	—	—	—
45	6	27 (0.39)	18	24 (0.34)	—	—	—	—
			3.0				5.0	
41	12	45 (0.73)	106	29 (0.41)	18	40 (0.69)	178	16 (0.22)
42	12	57 (0.81)	101	22 (0.35)	10	61 (0.86)	338	12 (0.16)
43	7	28 (0.30)	50	17 (0.17)	5	16 (0.16)	120	12 (0.12)
45	4	15 (0.22)	16	10 (0.13)	6	20 (0.32)	268	12 (0.18)

continued into Experiment 2. One animal (number 41) was discontinued due to a respiratory illness. The animals were maintained at their 80% body weight level by restricted food as in Experiment 1. Water was available in the home cage at all times, and housing and lighting were identical to Experiment 1.

Procedure

Immediately following the end of Experiment One, the animals were returned to the ethanol-water concurrent (FR8 FR8) schedule for up to two weeks in order to redetermine and stabilize baseline ethanol responding. As in the previous experiment, the relative positions of the fluids were alternated each day. All sessions were again 1 hr.

Five to eight daily sessions with ethanol and 5% sucrose available on the concurrent schedule (FR8 FR8) were then given, followed by five to eight sessions of ethanol and 5% sucrose in which the ethanol remained at FR8, but the sucrose response requirement was increased to FR64. Following this schedule manipulation, a second 5 to 8 sessions of ethanol and sucrose (FR8 FR8) was given. After this last ethanol-sucrose test, another 5 to 8 sessions of ethanol-water (FR8 FR8) was run to redetermine ethanol water baseline responding.

To further examine the effect of schedule manipulations, two additional sequences of five to eight sessions each were then conducted with sucrose and water as the two concurrently available fluids. For the first sequence, 3% sucrose and water were available on a FR8 FR8 schedule. During the second sequence, the schedule requirement for sucrose was increased to FR64, with that for water remaining at FR8.

RESULTS

Figure 2 presents the results for reinforcements presented and efficacy scores. All animals had essentially identical changes with the various schedule manipulations. When ethanol was paired with water, ethanol responding predominated with ethanol efficacy scores ranging from 0.60 to 0.90. When sucrose was paired with either ethanol or water on the FR8 FR8 concurrent schedule, sucrose responding predominated with sucrose efficacy scores ranging from 0.85 to 1.00.

When the sucrose response requirement was increased to FR64, the number of alternate fluid reinforcements delivered increased. When ethanol was the alternative fluid, significant increases in ethanol reinforcements were observed in all animals. This occurred when this condition is compared either to the first water-ethanol (FR8 FR8) condition or to either of the ethanol-sucrose (FR8 FR8) conditions. In two of the three animals, twice as many ethanol reinforcements occurred compared to the first water-ethanol pairing. When water was present as the alternative fluid with sucrose, and the sucrose response requirement was FR64, much smaller

TABLE 3

MEAN DAILY ETHANOL INTAKES (g ETHANOL/kg BODY WEIGHT) FOR EACH CONCURRENT SCHEDULE (MEAN OF 5 CONSECUTIVE DAILY SESSIONS)

Animal Number	H_2O FR8/EtOH FR8	Suc FR8/EtOH FR8	Suc FR64/EtOH FR8	Suc FR8/EtOH FR8	H_2O FR8/EtOH FR8
42	0.86	0.16	1.15	0.08	1.36
43	0.16	0.12	0.40	0.09	0.33
45	0.32	0.18	0.56	0.12	0.47

increases in the number of water reinforcements delivered was observed. Table 3 shows the increase in actual ethanol consumed as a result of the schedule manipulation.

Figure 3 presents the cumulative records for one animal (number 43) across the various conditions. Similar results occurred for the remaining two animals. Ethanol responding from the initial water ethanol condition (11/16/80) compared to that occurring after the schedule manipulation (12/9/80) was markedly increased. When sucrose was available on the equal FR schedule (11/23/80 and 12/1/80), the animal spent a majority of the session responding for sucrose. However, when the response requirement for sucrose was increased to FR64, sucrose responding decreased over the next five sessions coupled with a marked increase in ethanol responding.

The difference between ethanol and water reinforcement during concurrent pairing with sucrose on the FR8 FR64 schedule can be seen by the difference in change in responding for sucrose (i.e., sucrose efficacy; Fig. 2). When ethanol was the alternative fluid sucrose efficacy dropped to between 0.10 and 0.20. When water was the alternative sucrose efficacy declined only to 0.60–0.80. This difference is not due to differences in sucrose responding, but rather by marked increases in ethanol responding compared to the small changes in water responding.

Post-hoc analysis (a one way analysis of variance) [4], using the daily scores in each condition for each animal, revealed that all three animals had significant increases in the number of ethanol reinforcements delivered when comparing the first ethanol water FR8 FR8 condition to the ethanol sucrose FR8 FR64 condition (number 42: $F(1,10)=7.36$, $p<0.05$; number 43: $F(1,10)=26.34$, $p<0.01$; number 45: $F(1,13)=9.16$, $p<0.01$). Interestingly, when comparing the second ethanol water FR8 FR8 condition to the first ethanol water FR8 FR8 condition, a significant increase in the number of ethanol reinforcements received also occurred (number 41: $F(1,12)=17.43$, $p<0.01$; number 43: $F(1,12)=9.83$, $p>0.01$; number 45: $F(1,12)=9.89$, $p<0.01$). No significant differences were found between the ethanol sucrose FR8 FR64 condition and the second water ethanol FR8 FR8 condition.

GENERAL DISCUSSION

The first experiment shows that ethanol's efficacy score can be manipulated depending on the solution concurrently available. For all animals, ethanol efficacy decreased as sucrose concentration increased. It was possible to manipulate the concentration of sucrose such that approximately half of the responses were on the lever associated with ethanol, and half on the lever associated with sucrose. At this point,

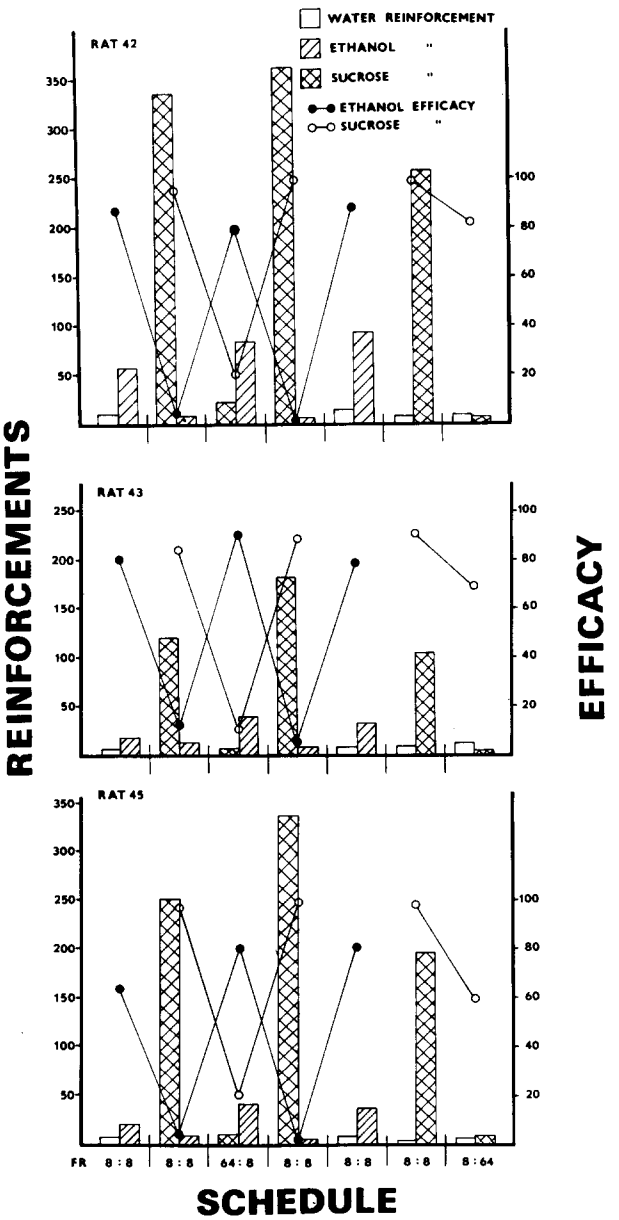

FIG. 2. Mean number of reinforcements presented and efficacy scores (number of substance responses/total responses) on concurrent schedules which vary both the available substances and FR requirements. (Means based on 5 consecutive daily sessions.)

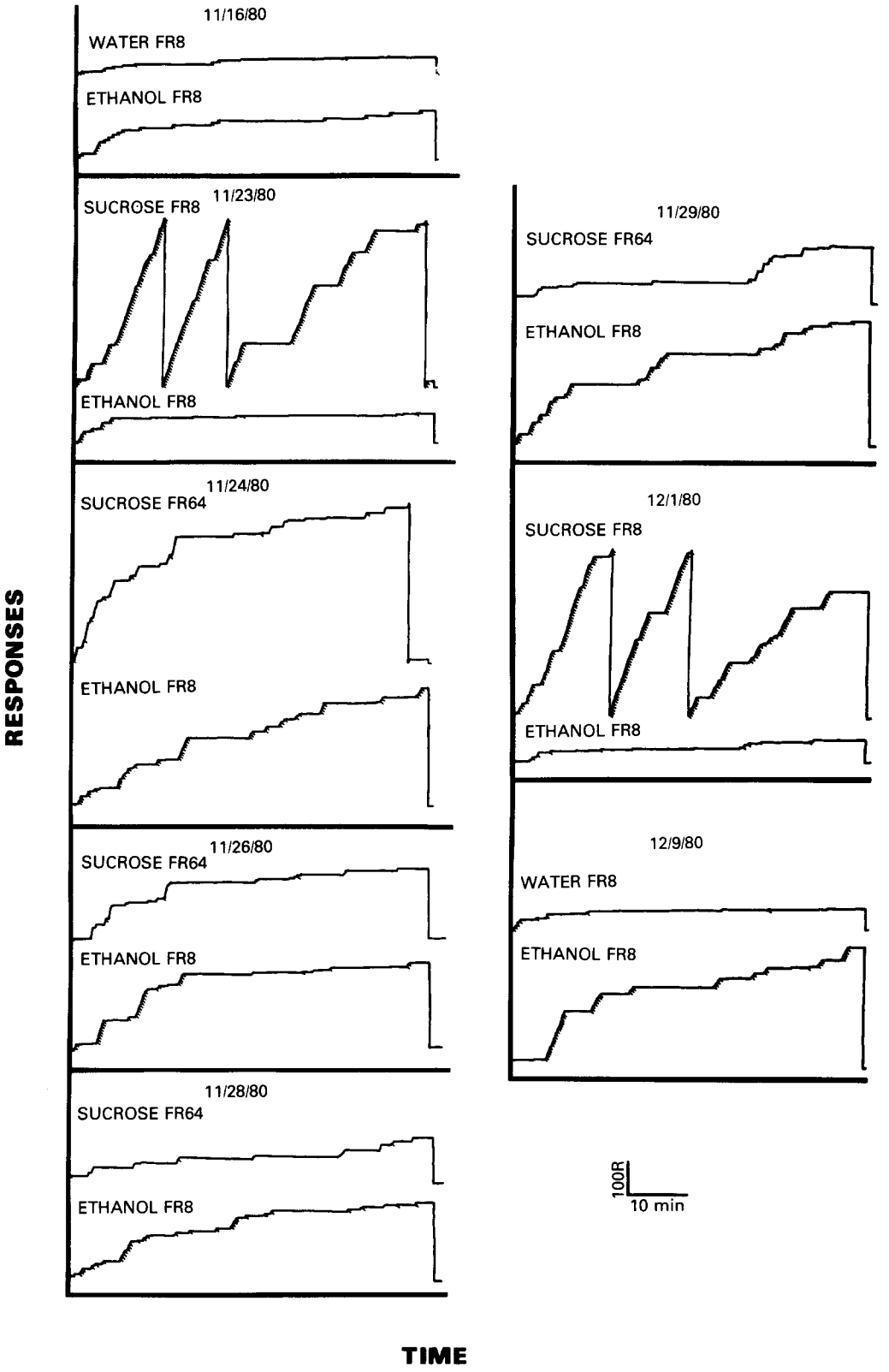

FIG. 3. Cumulative response records for Rat 43 during the concurrent manipulation as described in Experiment 2. Fluid available and FR requirement are above each response record. Pen deflections indicate dipper operations.

where ethanol's efficacy score was 0.50, the actual number of responses for ethanol when compared to water baseline levels, did not differ. Rather, responding for the alternative substance had increased, thus lowering ethanol's efficacy score. Not until the sucrose concentration reached 3% or 5% did ethanol responding, and thus the number of ethanol reinforcements, decrease.It is clear that an efficacy value measured in this way for a particular substance is dependent not only upon its own reinforcing properties, but also upon the reinforcing qualities of other available substances. When both substances are of equal reinforcing capacity, and response contingencies are such that both can be obtained without behavioral incompatability, additional total responding occurs. When the reinforcing capacity of one greatly exceeds the other, then no or limited responding for the lesser reinforcer occurs. Thus, when ethanol and water were concurrently available, ethanol responses were predominant and there was little water responding. This occurred even though the ethanol response rate was not high enough to result in behavioral incompatability. That this is the case can be observed when ethanol and 1.25% sucrose are concurrently available. Total responding during this condition was approximately twice that of the water ethanol situation, with ethanol responding levels unchanged.

The results of the second experiment found that not only the reinforcing properties of the two available substances but also the contingencies of reinforcement for each can alter the response patterns. When the contingency for the more preferred substance (5% sucrose) was dramatically increased (i.e., from FR8 to FR64) a marked increase in responding for the other available substance (5% ethanol) occurred. This increase in alternate substance responding was not found however, when ethanol and water were paired with the ethanol response requirement increased [10], or when sucrose and water were paired and the sucrose response requirement increased (Experiment 2). This would indicate that the reinforcer properties and the reinforcing contingencies are not independent.

Because the efficacy value of ethanol can be shown to change with changes in the other reinforcer available (Experiment 1), it may be better to use the terminology of choice rather than efficacy when using the concurrent procedure to assess oral intake of drugs. While the concept of reinforcer efficacy may be applicable to concurrent performance for different drug dosages [5], these experiments would seem to suggest that ethanol's efficacy is not really measured by this procedure. Even though we have in prior work shown the stability of the efficacy measure [10, 11, 12], the results in those papers could be interpreted using preference terms as easily. If this is done, then the connotations of efficacy and related pharmacological effects of ethanol, which in these experiments cannot be dissociated from substance preference, would be avoided.

It is tempting to speculate that the rats were "driven to drink" when the response requirement for sucrose was greatly increased. However, until other reinforcers besides ethanol or water are compared with sucrose under similar conditions, it is impossible to determine if the increased ethanol intake was associated with its pharmacological properties or was rather a result of the interaction of any two preferred reinforcers and their contingencies of reinforcement. However, one interesting effect that could imply a pharmacological explanation was the maintained increase in ethanol responding observed in the ethanol/water pairing that followed the sucrose/ethanol schedule manipulation in Experiment 2. Whether this increase represents a true change in the reinforcing properties of ethanol or a behavioral contrast effect that would occur for any similar set of reinforcers remains to be determined.

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