Reports from the Research Laboratories

of the

Department of Psychiatry

University of Minnesota

Effects of Substituting Ethanol Solutions for Water During Schedule-Induced Polydipsia: Initial Results

by

Richard A. Meisch, Richard J. Wahlstrom, and Roy W. Pickens

Report Number PR-70-1

April 3, 1970

EFFECTS OF SUBSTITUTING ETHANOL SOLUTIONS FOR WATER DURING SCHEDULE-INDUCED POLYDIPSIA: INITIAL RESULTS[1,2]

Richard A. Meisch[3], Richard J. Wahlstrom,

and Roy W. Pickens

PR-70-1

April 3, 1970

---

[1]This research was supported in part by U.S.P.H.S. grants MH-14112 and MH-15349 to the University of Minnesota.

[2]Portions of this data were presented at the Thirtieth Meeting of the Committee on Problems of Drug Dependence, National Academy of Sciences-National Research Council in February, 1968 in Indianapolis, Indiana, and also at the Ninth Annual Meeting of the Psychonomic Society in November, 1968 in St. Louis, Missouri.

[3]Life Insurance Medical Research Fellow.

Abstract

Ethanol self-administration by rats was obtained by substituting ethanol solutions for water during schedule-induced polydipsia. As the ethanol concentration was increased, there was a decrease in liquid responses, liquid reinforcements, and volume consumed. As the concentration was increased up to 8% (W/V), the quantity (milligrams) of ethanol intake also increased. The food baseline was decreased most at 8% (W/V) and progressively less so at concentrations above and below this value. When 4% (W/V) ethanol was presented a second time, liquid responding initially exceeded water control values. Schedule-induced polydipsia was suggested as a general technique for obtaining oral drug self-administration by animals.

INTRODUCTION

In 1961 Falk reported that when rats were placed on an intermittent schedule of food reinforcement and concurrently given access to water, they would drink up to one-half their body weight in water over a 3.17 hour period. He termed this phenomenon schedule-induced polydipsia and demonstrated that animals would respond (lever press) for water presentation (Falk, 1966).

Subsequently, Lester (1961) used Falk's polydipsia procedure to induce rats to self-administer 5.6% (W/V) ethanol; "intoxication" was produced in 3-hour test sessions with blood alcohol levels reaching 0.2 per cent. His results have since been replicated (Senter and Sinclair, 1967). However, following polydipsia training, Senter and Sinclair found no increase in ethanol solution consumed to total liquid intake.

Using the schedule-induced polydipsia procedure, Holman and Myers (1968) varied ethanol concentration and observed a decrease in the volume consumed with increases in drug concentration. Relative to intake levels measured in the absence of polydipsia, ethanol drinking increased during polydipsia only at concentrations below 8% (V/V). No change was noted in the number of food responses or reinforcements.

Meisch (1969b) obtained self-administration of sodium

pentobarbital solutions by substituting the drug solutions for water during the polydipsia procedure. Unlike the previous ethanol studies, liquid presentation was response contingent and the time course of changes in food and liquid responding was recorded. Presence of the drug solutions was found to produce significant changes in the food responding baseline.

The purpose of the present study was to determine the effects of ethanol substitution on liquid and food responding in the polydipsia procedure. In the study, time course values of several dependent variables were also recorded.

METHOD

Subjects: The subjects were two male Holtzman albino rats, Rat 270 and Rat 280, maintained at 428 and 480 grams, respectively, which were 80% of their free-feeding weights. They were approximately 250 days old at the beginning of the experiment and were individually housed in a temperature controlled, constantly illuminated room. Water was always available in the animals' home cages. Previously the animals had been subjects in another study utilizing schedule-induced polydipsia to obtain drug self-administration (Meisch, 1969b).

Apparatus: The apparatus was a standard operant conditioning chamber equipped with two levers, a food magazine, and a dipper for presenting liquid. The levers were separated by the reinforcement mechanisms, with the food magazine directly above the dipper. Each operation of the

food magazine produced a single 45 mg Noyes food pellet, and operation of the dipper made available 0.25 ml of liquid for 4 seconds. The operant conditioning chamber was housed in a ventilated sound-shielding enclosure. White masking noise was constantly present. Programming and data recording were automatic, by standard electromechanical equipment located in an adjacent room.

Procedure: Training was not necessary because of the animals' past experience (Meisch, 1969b). The animals were placed in the operant conditioning chamber at a regular starting time for six hours each day. Responding on the right lever delivered food on a VI 1 minute schedule. (On such a schedule a rat receives a food pellet on the average of one per minute, ranging from a few seconds to two minutes.) No stimulus indicated which lever press would be followed by a food pellet. Each response on the other lever produced liquid. At the end of the session the rats were given supplementary feedings in their home cage with Purina laboratory rat chow to maintain their weights at 80% of the free-feeding value.

During all sessions, the following dependent variables were recorded: (1) total liquid responses per session, (2) total liquid reinforcements per session, (3) total food responses per session, (4) total food reinforcements per session, and (5) total volume consumed per session. Responses and reinforcements for both food and liquid were also recorded

every 10 minutes by a 4-channel print-out counter. In addition, the temporal pattern of responding and reinforcement presentation was continuously recorded separately for food and liquid by cumulative recorders. Volume of liquid consumed was measured at the end of the first and sixth hours by subtracting the difference between the volume added to the reservoir and the volume remaining. All volumes were corrected for evaporation.

All the ethanol concentrations were prepared using absolute ethanol and tap water. The concentrations were expressed in terms of grams percent.

Experimental design: The ethanol concentrations presented and their order of presentation are listed in Table 1 for Rat 270 and in Table 2 for Rat 280. Each ethanol concentration was presented on the second day of a three-day sequence (Figure 1). On all three consecutive days the animals responded for food for all six hours. During the first hour on all three days water was also available. At the end of the first hour on all three days the liquid reservoir was exchanged. On the first and third days, a fresh water solution was substituted for the original water solution at the end of the first hour. On the second day, however, ethanol was substituted for water solution at the end of the first hour.

RESULTS

Principal findings: For both animals liquid responses,

DESIGN OF EXPERIMENT FOR INVESTIGATING WATER AND ETHANOL INTAKE DURING SCHEDULE-INDUCED POLYDIPSIA

	HOUR 1 (CONTROL)	HOURS 2-6 (EXPERIMENTAL)
DAY 1 (CONTROL)	FOOD REINFORCEMENT WITH WATER AVAILABLE	FOOD REINFORCEMENT WITH WATER AVAILABLE
DAY 2 (DRUG)	FOOD REINFORCEMENT WITH WATER AVAILABLE	FOOD REINFORCEMENT WITH ETHANOL AVAILABLE
DAY 3 (CONTROL)	FOOD REINFORCEMENT WITH WATER AVAILABLE	FOOD REINFORCEMENT WITH WATER AVAILABLE

Figure 1. Sequence of experimental conditions

Table 1

SESSION TOTAL VALUES OF THE DEPENDENT VARIABLES FOR RAT 270

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are not included. Each value is the sum for the entire 6 hour session including hour 1 on drug days when only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1. Volume consumed is given in milliliters.

Session	Liquid Responses	Liquid Reinforcements	Volume Consumed	Food Responses	Food Reinforcements
Water (control)	3170	1930	135	15377	354
Ethanol 2%	1773	1302	111.5	9463	310
Water (control)	3342	2122	147.5	16191	353
Water (control)	3485	2158	160	15033	343
Ethanol 4%	1159	871	103	6129	228
Water (control)	3042	2164	175	15775	342
Water (control)	2453	1814	147.5	17547	341
Ethanol 1%	1738	1416	130	14327	316
Water (control)	1823	1559	125	16133	325
Water (control)	1949	1568	137.5	20970	334
Ethanol 8%	502	410	72	5594	152
Water (control)	1580	1323	135	20469	345
Water (control)	1525	1199	130	27425	351
Empty	503	410	25	23324	337
Water (control)	1122	968	127.5	27991	347
Ethanol 16%	397	333	46	6974	216
Water (control)	1254	1007	125	30588	348
Water (control)	1325	1070	110	32087	353
Ethanol 32%	388	304	33	23582	318
Water (control)	1171	977	125	28714	350
Water (control)	1071	863	105	27345	350
Ethanol 0.5%	1171	922	125	24832	343
Water (control)	1086	899	120	29975	337
Water (control)	1072	866	120	31208	340
Ethanol 64%	350	277	26	29890	336
Water (control)	1289	1024	126	26953	337

Table 2

SESSION TOTAL VALUES OF THE DEPENDENT VARIABLES FOR RAT 280

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are not included. Each value is the sum for the entire 6 hour session including hour 1 on drug days when only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1. Volume consumed is given in milliliters.

	Liquid Responses	Liquid Reinforcements	Volume Consumed	Food Responses	Food Reinforcements
Water (control)	1266	1190	170	5321	327
Ethanol 0.5%	1400	1336	160	5384	324
Water (control)	1194	1163	167.5	5053	320
Water (control)	1510	1383	160	5257	324
Ethanol 1%	1523	1439	155	5002	331
Water (control)	1407	1363	177.5	4434	321
Water (control)	1721	1605	165	5043	333
Ethanol 2%	1461	1327	154	4141	327
Water (control)	1496	1364	155	4798	332
Water (control)	1214	1075	140	5067	333
Ethanol 4%	739	692	93	3321	264
Water (control)	1201	1010	140	5296	335
Water (control)	1044	969	135	4128	330
Empty	954	890	30	4376	327
Water (control)	1353	1178	155	4035	327
Water (control)	1338	1234	145	4311	330
Ethanol 8%	522	478	72	3068	243
Water (control)	1340	1170	155	3715	325
Water (control)	1196	1115	140	4327	332
Ethanol 16%	462	437	73.5	3873	311
Water (control)	1206	1081	140	4205	326

liquid reinforcements, and volume consumed were an inverse function of ethanol concentration. Food responses and reinforcements were decreased most at 8% and progressively less at concentrations above and below this value. When 4% ethanol was presented a second time, liquid responses immediately increased to a level above water control values and remained elevated for at least 20 minutes.

Total session values: Liquid reinforcements and volume consumed at each ethanol concentration are illustrated in Figure 2 for Rat 270 and in Figure 3 for Rat 280. The values are also listed in Table 1 for Rat 270 and in Table 2 for Rat 280. Volumes of ethanol consumed are presented in Tables 3 and 4 for Rats 270 and 280, respectively.

Starting at 1% for Rat 270 and at 0.5% for Rat 280 there were systematic decreases in volume consumed with increases in ethanol concentration. Up to 8% the quantity of intake (mg/kg/hr) increased for Rat 270 (Table 3). With further concentration increases, the quantity consumed decreased (Table 3). The quantity of ethanol consumed by Rat 280 increased as a direct function of ethanol concentration (Table 3).

Ethanol reinforcements and volume consumed had the same rank order between concentrations of 1% to 64% for Rat 270 (Table 1) and between concentrations of 1% to 8% for Rat 280 (Table 2).

Over a period of weeks when the concentrations were

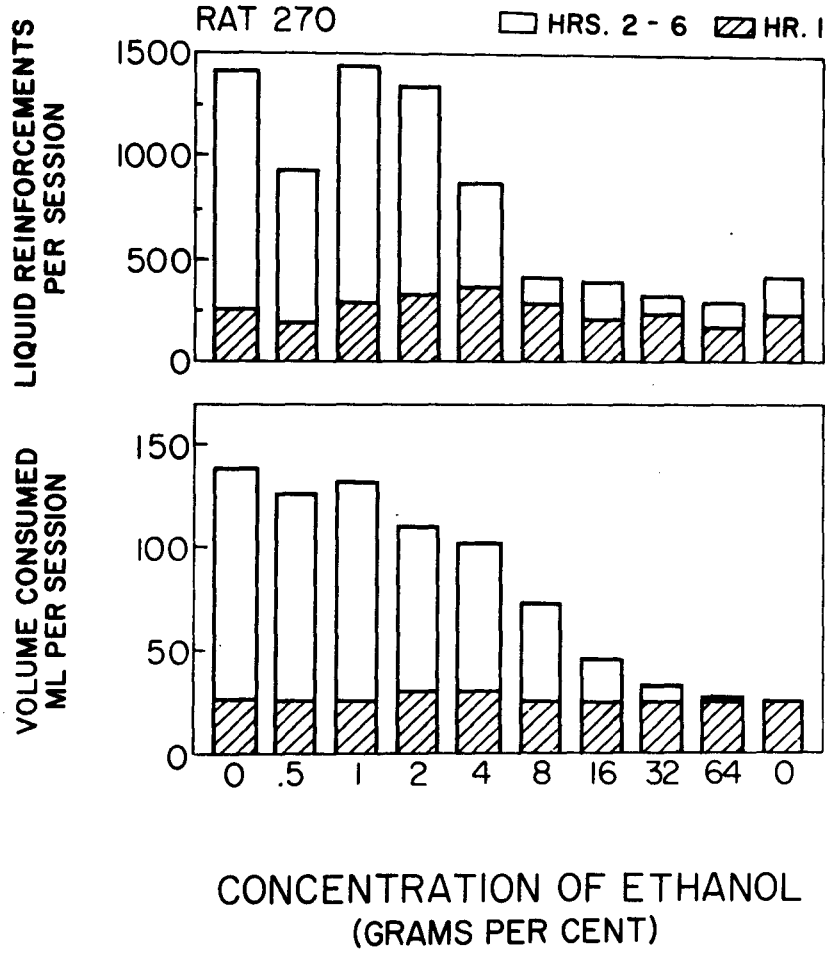

Figure 2. Effect of ethanol concentration on liquid reinforcements and volume consumed. The columns labeled zero on the left represent the average value for the 17 water control sessions listed in Table 1. Other columns each represent results from a single session. The zero columns on the right indicate the results for the session when the liquid reservoir was left empty after the first hour. The striped portion at the bottom of each bar shows the value for the first hour when only water was available.

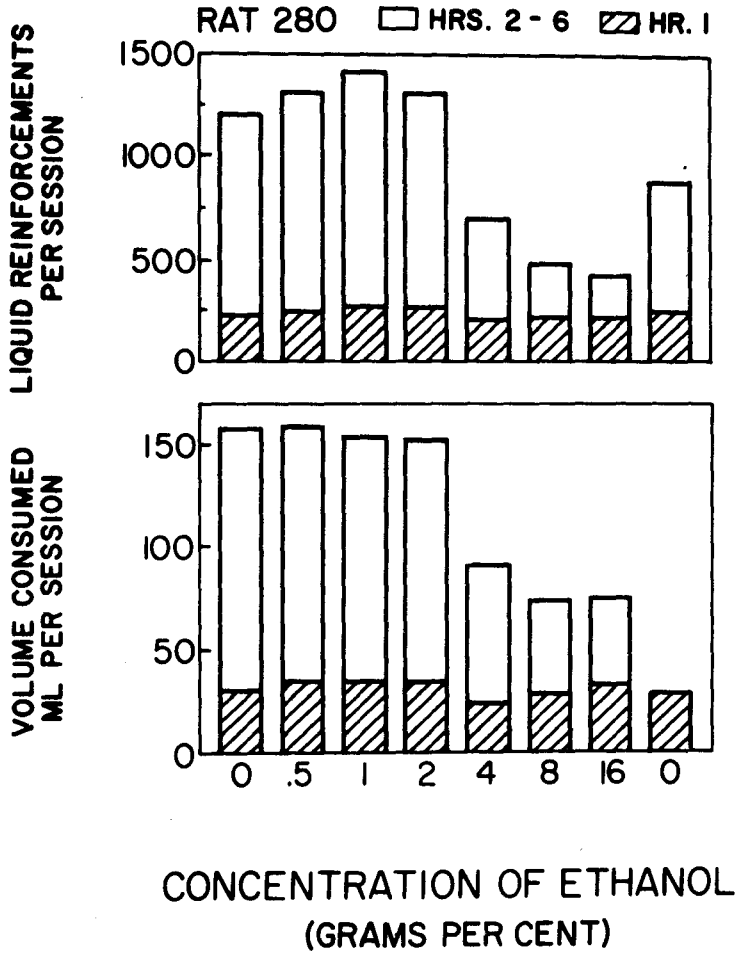

Figure 3. Effect of ethanol concentration on liquid reinforcements and volume consumed. The columns labeled zero on the left represent the average value for the 14 control sessions listed in Table 2. Other columns each represent results from a single session. The zero columns on the right indicate the results for the session when the liquid reservoir was left empty after the first hour. The striped portion at the bottom of each bar shows the value for the first hour when only water was available.

Table 3

ETHANOL INTAKE OF RAT 270

The concentration is in grams percent by weight. The volume specified is the number of milliliters of ethanol solution consumed in 5 hours. The volume per unit of body weight is in terms of milliliters of ethanol solution per 100 grams of body weight per hour, and the quantity per unit of body weight is the milligrams of absolute ethanol consumed per 100 grams of body weight per hour.

Concentration	Volume	Volume/Body Wt.	Quantity/Body Wt.
0.5	100	4.67	23.4
1	105	4.90	49.0
2	81.5	3.80	76.0
4	73	3.41	136.4
8	47	2.19	175.2
16	21	0.98	156.8
32	8	0.37	118.4
64	0	0	0

Table 4

ETHANOL INTAKE OF RAT 280

The concentration is in grams percent by weight. The volume specified is the number of milliliters of ethanol solution consumed in 5 hours. The volume per unit of body weight is in terms of milliliters of ethanol solution per 100 grams of body weight per hour, and the quantity per unit of body weight is the milligrams of absolute ethanol consumed per 100 grams of body weight per hour.

Concentration	Volume	Volume/Body Wt.	Quantity/Body Wt.
0.5	125	5.20	26.0
1	120	5.00	50.0
2	119	4.95	99.0
4	68	2.83	113.2
8	42	1.75	140.0
16	41	1.70	272.0

presented there was a progressive decrease in Rat 270's water responses, and at the same time there was a progressive increase in food responses (Table 1). As the water responses decreased, the number emitted became closer in value to the number of water reinforcements (Table 1). Rat 280's water responding remained more constant between sessions, and its water responses tended to approximate closer the number of water reinforcements (Table 2). For each animal water control values were similar for days immediately before and after a given drug day.

Food responses and reinforcements at each ethanol concentration are shown in Figure 4 for Rat 270 and in Figure 5 for Rat 280. The values of these dependent variables are also presented in Tables 1 and 2 for Rats 270 and 280, respectively.

For both food responses and food reinforcements the largest decrease occurred at 8%. Above and below 8% the decreases were systematically smaller in magnitude.

Values for food reinforcements remained relatively constant across water control sessions (Tables 1 and 2). However, as mentioned above, Rat 270's food responses increased across sessions (Table 1) while Rat 280's slightly decreased (Table 2).

Time course: Time course values of liquid reinforcements, food responses, and food reinforcements are illustrated in Figure 6 for Rat 270 and in Figure 7 for Rat 280. The values

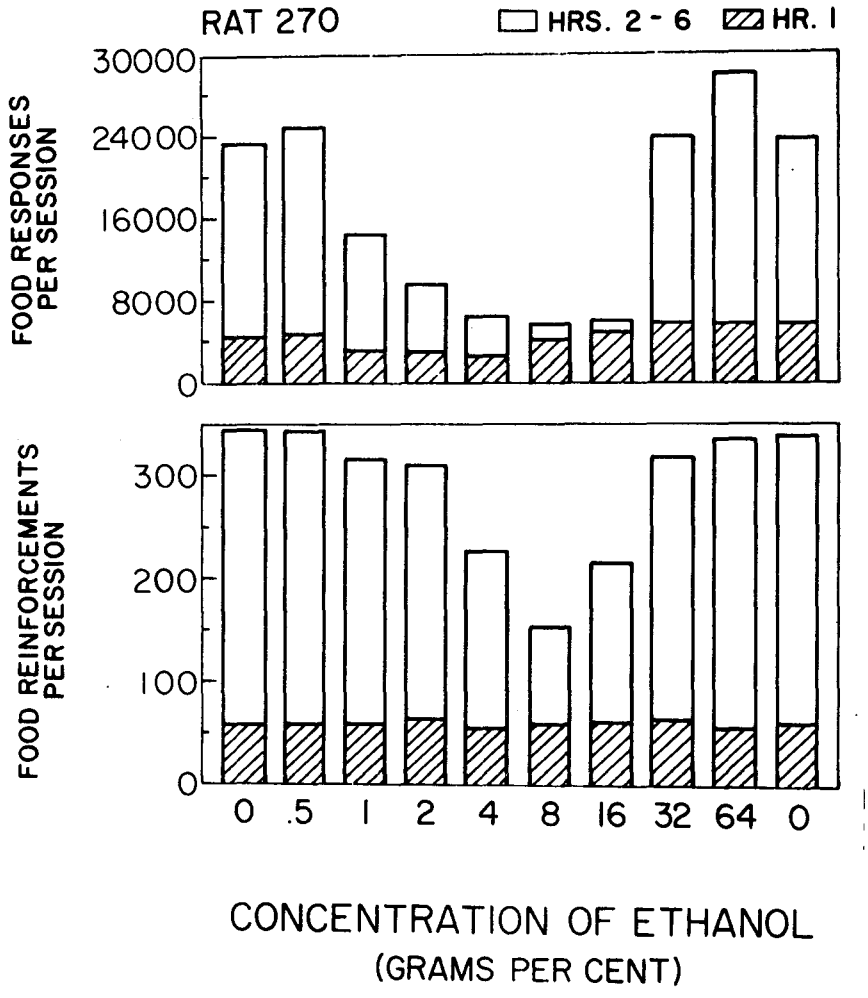

Figure 4. Effect of ethanol concentration on food responses and reinforcements. The columns labeled zero on the left represent the average value for the 17 control sessions listed in Table 1. Other columns each represent results from a single session. The zero columns on the right indicate the results for the session when the liquid reservoir was left empty after the first hour. The striped portion at the bottom of each bar shows the value for the first hour when only water was available.

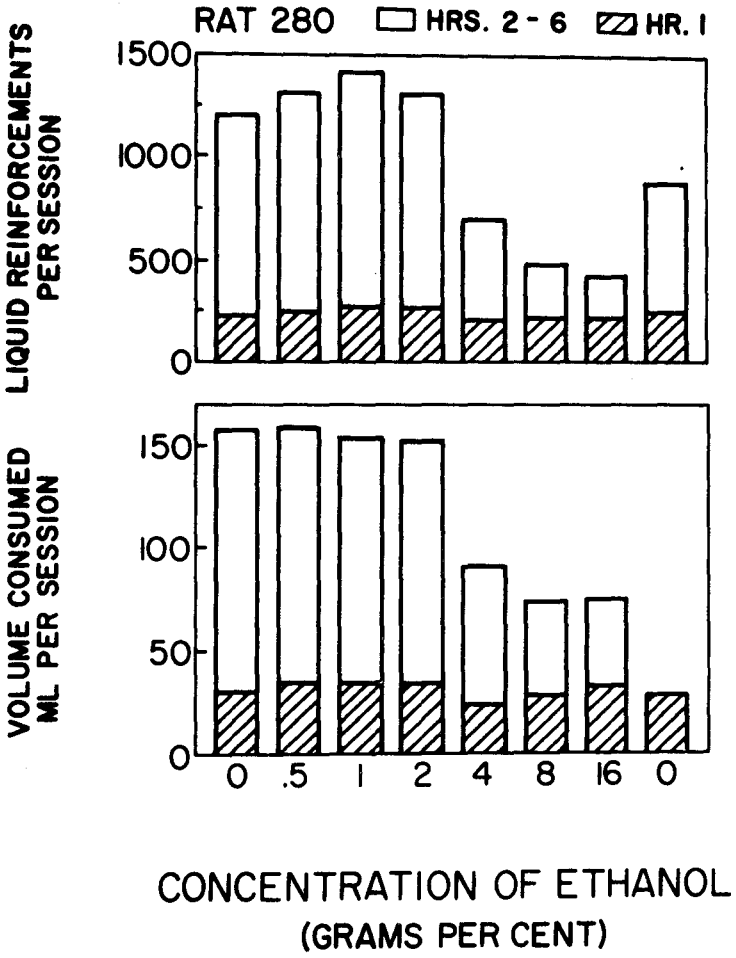

Figure 5. Effect of ethanol concentration on food responses and reinforcements. The columns labeled zero on the left represent the average value for the 14 control sessions listed in Table 2. Other columns each represent results from a single session. The zero columns on the right indicate the results for the session when the liquid reservoir was left empty after the first hour. The striped portion at the bottom of each bar shows the value for the first hour when only water was available.

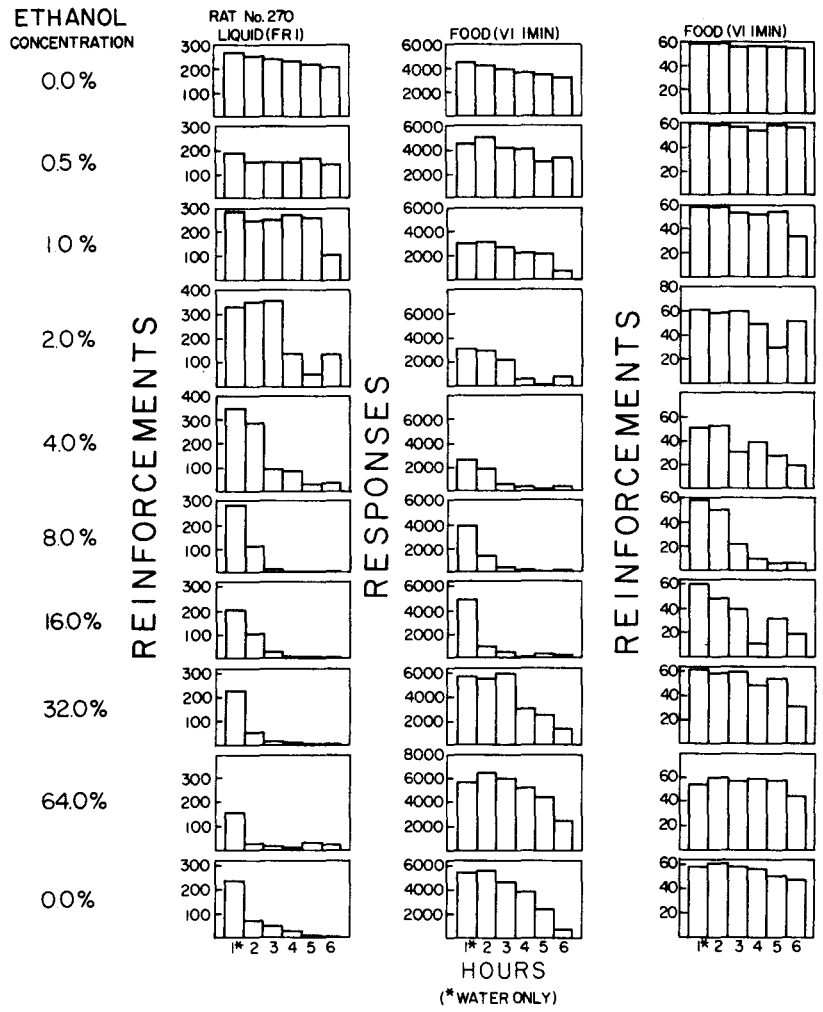

Figure 6. Time course of the effect of ethanol concentration on liquid reinforcements, food responses and food reinforcements. The zero percent row at the top of the figure represents the average values for the 17 control sessions listed in Tables 5, 7, and 9. Other rows each represent results from a single session. The zero percent row at the bottom shows the results for the session when the liquid reservoir was left empty after the first hour.

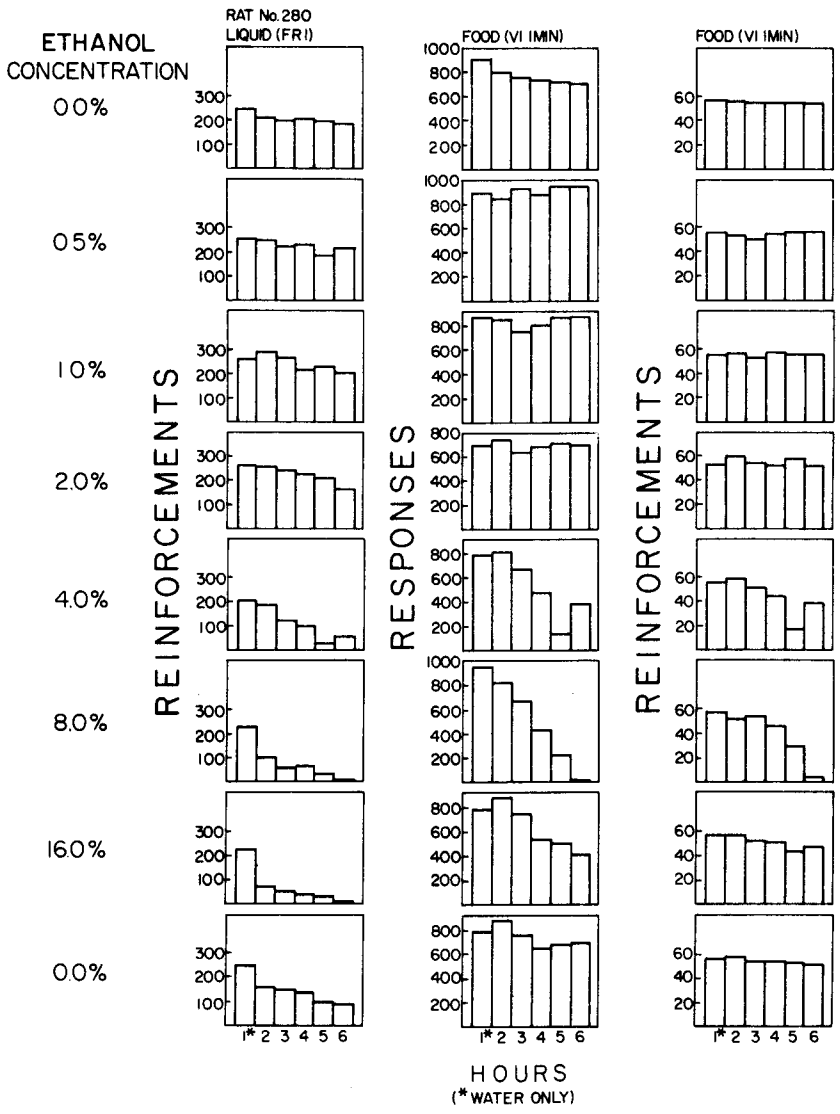

Figure 7. Time course of the effect of ethanol concentration on liquid reinforcements, food responses and food reinforcements. The zero percent row at the top of the figure represents the average values for the 14 control sessions listed in Tables 6, 8, and 10. Other rows each represent results from a single session. The zero percent column at the bottom shows the results for the session when the liquid reservoir was left empty after the first hour.

of these dependent variables are also specified as a function of session hour in Tables 5-10.

As the concentration was increased, there was an earlier and more profound decrease in liquid reinforcements. When only water was present, the average number of water reinforcements decreased each hour for Rat 270 (Figure 6). A similar pattern occurred with Rat 280 (Figure 7).

Decreases in food responses and food reinforcements covaried (Figures 6 and 7). The earliest and greatest decreases were at 8% and progressively smaller decreases occurred at higher and lower values. When only water was present, the average number of food responses decreased with each successive hour (Figures 6 and 7). Food reinforcements for Rat 280 decreased in the same manner. A less orderly but similar time trend was apparent with food reinforcements for Rat 270 (Figure 6). Control values for days immediately preceding and succeeding a particular drug day were usually very similar (Tables 5-10). When there were large differences within a pair of control values, they usually occurred toward the end of a session.

Second (II) presentation of 4% ethanol: The session total values for the first (I) and second (II) presentation of 4% ethanol are given in Table 11. The liquid response time course values for the 30 minutes preceding and succeeding the introduction of ethanol are presented in Table 12. In Figures 8 and 9 are cumulative response records for Rat 270

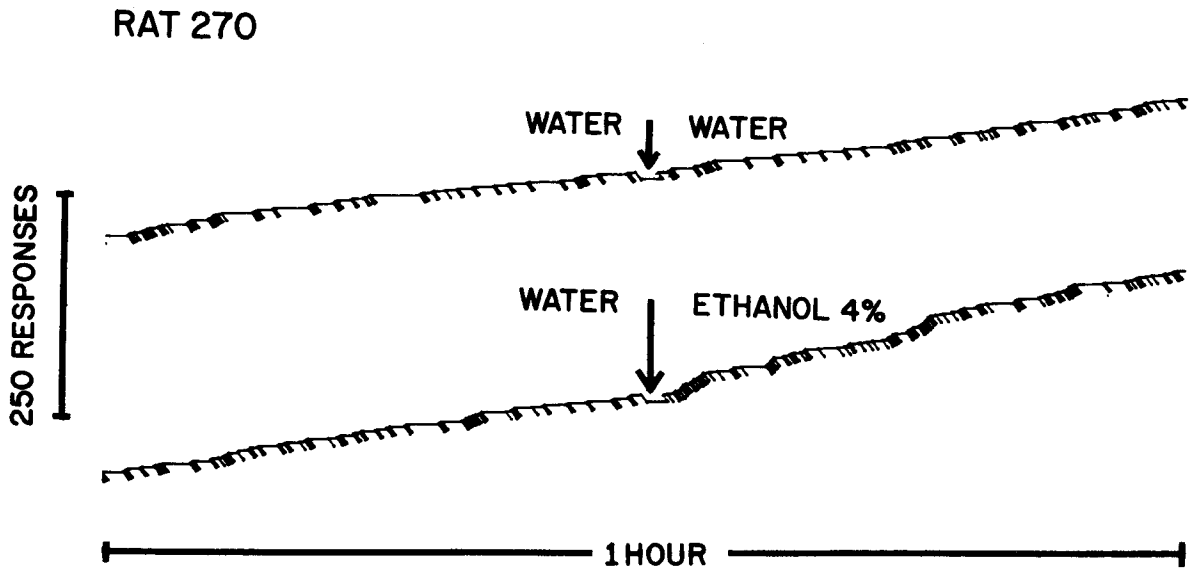

Figure 8. Cumulative response records for Rat 270 illustrating the effect on liquid responding of substituting 4% ethanol for water. The arrows indicate when the liquid in the reservoir was changed. The upper record is from a control session on the day immediately preceding the drug session. The time course values are tabulated in Table 12.

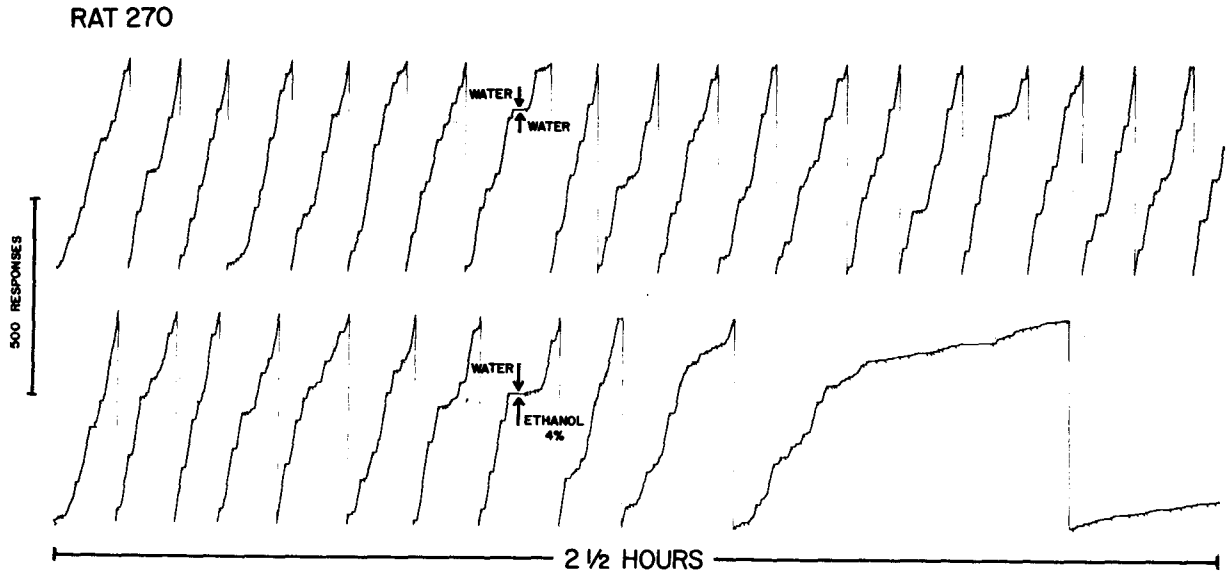

Figure 9. Cumulative response records for Rat 270 illustrating the effect on food responding of substituting 4% ethanol for water. The arrows indicate when the liquid in the reservoir was changed. The upper record is from a control session on the day immediately preceding the drug day. The session total values are in Table 11.

Table 5

TIME COURSE VALUES OF LIQUID REINFORCEMENTS FOR RAT 270

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	353	346	332	343	327	280
Ethanol 2%	328	348	357	132	50	133
Water (control)	377	354	384	347	335	344
Water (control)	372	375	384	383	349	334
Ethanol 4%	351	286	90	87	33	38
Water (control)	394	368	350	319	297	296
Water (control)	334	301	301	304	304	302
Ethanol 1%	287	251	255	271	258	102
Water (control)	281	296	318	310	267	112
Water (control)	341	273	260	222	236	236
Ethanol 8%	284	111	13	2	0	0
Water (control)	259	224	206	214	187	232
Water (control)	248	226	210	198	169	162
Empty	239	71	52	24	17	10
Water (control)	175	166	165	161	154	146
Ethanol 16%	201	102	26	4	4	1
Water (control)	206	186	161	140	169	149
Water (control)	239	195	180	161	151	163
Ethanol 32%	224	50	17	15	0	0
Water (control)	201	192	157	158	144	131
Water (control)	168	139	141	130	161	129
Ethanol 0.5%	182	148	148	151	157	142
Water (control)	168	165	163	139	137	136
Water (control)	176	148	151	139	115	147
Ethanol 64%	158	24	20	16	33	32
Water (control)	203	168	182	164	158	163

Table 6

TIME COURSE VALUES OF LIQUID REINFORCEMENTS FOR RAT 280

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	231	229	180	191	163	196
Ethanol 0.5%	248	247	223	227	183	216
Water (control)	192	182	218	217	198	171
Water (control)	281	242	233	218	215	212
Ethanol 1%	257	286	261	218	222	204
Water (control)	233	231	219	260	203	227
Water (control)	318	232	264	286	289	248
Ethanol 2%	258	255	239	223	203	158
Water (control)	288	253	226	238	191	171
Water (control)	211	168	187	164	183	190
Ethanol 4%	207	183	121	105	26	59
Water (control)	205	234	155	160	131	132
Water (control)	204	201	134	148	158	143
Empty	251	162	148	138	102	96
Water (control)	219	161	170	185	219	226
Water (control)	249	236	182	207	193	196
Ethanol 8%	224	99	63	64	32	1
Water (control)	273	223	214	147	182	137
Water (control)	224	173	210	204	162	151
Ethanol 16%	223	76	53	38	35	12
Water (control)	220	201	193	158	178	140

Table 7

TIME COURSE VALUES OF FOOD RESPONSES FOR RAT 270

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	2680	2624	2443	2526	2708	2399
Ethanol 2%	2927	2803	2201	659	119	757
Water (control)	3140	2950	2326	2473	2748	2560
Water (control)	3072	2700	2273	2456	2221	2304
Ethanol 4%	2682	1919	557	472	220	278
Water (control)	3035	2749	2490	2589	2634	2280
Water (control)	3315	3088	2875	3003	2729	2550
Ethanol 1%	3111	3181	2714	2376	2300	650
Water (control)	3356	3172	3295	2861	2631	826
Water (control)	3740	3497	3462	3664	3156	3444
Ethanol 8%	3922	1293	315	27	12	27
Water (control)	4756	4309	3031	3196	2450	2783
Water (control)	5042	5145	4850	4454	4154	3784
Empty	5599	5727	4722	3910	2407	963
Water (control)	4489	5285	5208	4594	4001	4404
Ethanol 16%	4820	974	465	100	356	255
Water (control)	6027	5120	5424	4254	4705	5050
Water (control)	6022	5551	5465	4739	5189	5120
Ethanol 32%	5555	5465	5918	3038	2405	1211
Water (control)	5147	5180	4824	4824	4590	4156
Water (control)	5447	4742	4938	4651	3985	3618
Ethanol 0.5%	4531	5084	4285	4160	3225	3536
Water (control)	6031	5579	5000	4778	4342	4240
Water (control)	5736	5472	5117	5007	5409	4462
Ethanol 64%	5518	6513	5814	5066	4452	2533
Water (control)	5022	5077	4619	4289	4232	3704

Table 8

TIME COURSE VALUES OF FOOD RESPONSES FOR RAT 280

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	978	927	871	781	918	846
Ethanol 0.5%	889	835	922	854	939	940
Water (control)	1048	983	890	754	703	669
Water (control)	1084	894	904	824	732	816
Ethanol 1%	870	848	769	797	859	866
Water (control)	794	820	834	706	668	611
Water (control)	1008	1004	793	843	721	681
Ethanol 2%	690	744	621	680	715	696
Water (control)	1005	850	809	755	637	743
Water (control)	912	929	900	800	802	726
Ethanol 4%	793	828	671	480	157	389
Water (control)	1018	780	890	818	928	860
Water (control)	775	714	636	627	659	723
Empty	776	872	727	651	663	672
Water (control)	863	622	596	614	636	701
Water (control)	814	698	671	673	696	758
Ethanol 8%	949	816	667	427	210	14
Water (control)	864	653	622	512	545	518
Water (control)	725	701	717	740	713	726
Ethanol 16%	789	875	748	524	499	436
Water (control)	843	752	693	669	655	592

Table 9

TIME COURSE VALUES OF FOOD REINFORCEMENTS FOR RAT 270

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	63	60	58	58	58	57
Ethanol 2%	61	59	60	48	30	52
Water (control)	61	59	58	57	59	59
Water (control)	60	56	56	58	56	57
Ethanol 4%	54	56	31	39	27	21
Water (control)	57	57	56	61	55	56
Water (control)	56	60	57	57	56	55
Ethanol 1%	58	58	55	54	56	35
Water (control)	59	60	54	54	62	36
Water (control)	57	57	52	56	60	52
Ethanol 8%	59	48	24	9	6	6
Water (control)	61	60	57	57	51	59
Water (control)	62	59	58	57	57	58
Empty	59	61	58	57	54	48
Water (control)	56	61	57	56	58	58
Ethanol 16%	60	47	40	13	36	20
Water (control)	57	62	58	56	56	58
Water (control)	59	63	56	58	59	58
Ethanol 32%	61	59	60	49	54	35
Water (control)	59	59	58	61	56	57
Water (control)	58	60	58	59	58	57
Ethanol 0.5%	59	58	57	55	58	56
Water (control)	58	56	54	57	55	57
Water (control)	57	59	55	56	55	57
Ethanol 64%	56	59	58	59	58	46
Water (control)	60	55	55	57	55	55

Table 10

TIME COURSE VALUES OF FOOD REINFORCEMENTS FOR RAT 280

The data are tabulated chronologically with the first experimental session listed at the top. Sessions disrupted by equipment malfunctions are omitted. On experimental days during hour 1 only water was present. The row labeled "empty" is for the session when the liquid resevoir was left empty after hour 1.

	Hours					
	1	2	3	4	5	6
Water (control)	57	59	54	53	52	52
Ethanol 0.5%	55	53	50	54	55	56
Water (control)	54	56	53	52	53	53
Water (control)	55	52	54	54	55	54
Ethanol 1%	55	56	53	57	55	55
Water (control)	54	56	53	55	52	51
Water (control)	57	54	55	55	57	55
Ethanol 2%	53	59	54	53	57	51
Water (control)	55	56	56	54	55	56
Water (control)	56	55	57	55	53	57
Ethanol 4%	56	58	51	44	17	38
Water (control)	59	58	53	55	55	55
Water (control)	55	56	56	54	53	55
Empty	56	57	54	54	53	53
Water (control)	56	55	54	55	53	54
Water (control)	55	58	53	53	57	53
Ethanol 8%	57	53	54	46	30	3
Water (control)	57	55	54	53	54	52
Water (control)	59	55	55	55	54	54
Ethanol 16%	57	57	53	52	43	48
Water (control)	56	53	55	55	52	54

illustrating the effect on liquid and food responding, respectively, of substituting 4% ethanol for water.

The second time 4% ethanol was given to each animal, there was an immediate increase in the liquid response rate (Table 12; Figure 8). With Rat 280 but not with Rat 270 a similar increase occurred the first time this concentration was presented (Table 12; Figure 8). When the liquid response rate did increase following ethanol introduction, the rate was highest during the first ten-minute period and decreased successively during the next two ten-minute periods (Table 12). This pattern of an increase above the hour 1 control level followed by subsequent systematic decreases was not observed on control days (Table 12).

With the second presentation Rat 270 but not 280 exhibited an earlier decrease in food responding as well as a greater decrease in total session food responding relative to control levels (Figure 9, Table 11).

Absence of liquid after hour 1: The effect of leaving the liquid reservoir empty after the first hour is shown by the column on the far right in Figures 2-5. The session total and time course results are presented in Tables 1, 2 and 5-10, respectively.

Even though no liquid was present after hour 1, Rat 280 emitted a substantial number of liquid responses (Table 2).

Table 11

SESSION TOTAL VALUES: COMPARISON OF THE FIRST (I) AND SECOND (II) PRESENTATION OF 4% ETHANOL

	Session	Liquid Responses	Liquid Reinforcements	Volume Consumed	Food Responses	Food Reinforcements
Rat 270 I	Water	3485	2158	160	15033	343
	Ethanol 4%	1159	871	103	6129	228
	Water	3042	2164	175	15775	342
Rat 270 II	Water	990	851	120	25015	339
	Ethanol 4%	482	399	60	6661	192
	Water	1008	860	132	27496	335
Rat 280 I	Water	1214	1075	140	5067	333
	Ethanol 4%	739	692	93	3321	264
	Water	1201	1010	140	5296	335
Rat 280 II	Water	958	854	136	3014	322
	Ethanol 4%	568	529	97	2650	268
	Water	870	733	119	2721	318

TABLE 12

TIME COURSE OF LIQUID REINFORCEMENTS IN 10 MINUTE INTERVALS: COMPARISON OF THE FIRST (I) AND SECOND (II) PRESENTATION OF 4% ETHANOL

"P" is an abbreviation for "presentation." The first row of each pair contains values from the control day immediately before the experimental day. The 10 minute intervals are from the 30 minute periods preceding and succeeding the end of hour 1.

		Minutes				Minutes		
Rat Number	P	Liquid	30-20	20-10	10-0	Liquid	0-10	10-20	20-30
Rat 270	I	Water	63	68	59	Water	67	62	64
		Water	53	56	65	Ethanol	61	51	48
	II	Water	30	19	21	Water	23	27	28
		Water	27	25	24	Ethanol	40	35	31
Rat 280	I	Water	34	21	40	Water	23	30	27
		Water	35	28	30	Ethanol	45	40	24
	II	Water	18	20	18	Water	29	26	27
		Water	22	24	24	Ethanol	43	36	21

Rat 270 also continued to respond in the absence of liquid (Table 1). Both animals emitted fewer responses with each succeeding hour (Tables 5 and 6).

Leaving the reservoir empty did not decrease Rat 280's food responses or food reinforcements (Table 2). Rat 270 exhibited a slight decrease in food responses, but its food reinforcements were within the control range (Table 1).

Hour 1 values: The values of the dependent variables for hour 1 are listed in the left hand column of Tables 5-10. On both drug and control days only water was present during hour 1, and the values of the dependent variables did not systematically differ.

DISCUSSION

In the present study the volume of ethanol solution consumed decreased with concentration increases. A similar relation between intake volume and ethanol concentration during schedule-induced polydipsia was reported by Holman and Myers (1968). In other ethanol schedule-induced polydipsia studies, ethanol concentration was not varied (Lester, 1961; Senter and Sinclair, 1967). In the absence of polydipsia, rats also drink smaller volumes with ethanol concentration increases (Hausmann, 1932; Myers and Carey, 1961; Myers and Holman, 1967; Rick and Wilson, 1966; Clay, 1964; Mendelson and Mello, 1964).

As the ethanol concentration increased Rat 280 increased its intake in terms of milligrams of absolute ethanol consumed.

Rat 270 increased its quantity of absolute ethanol intake until 8% was reached with further concentration increases accompanied by successive decreases in intake.

Subsequent research has confirmed the pattern found with Rat 280. Ethanol intake increases, in terms of milligrams of absolute ethanol consumed, with concentration increases during concurrent food reinforcement (i.e., schedule-induced polydipsia) and during concurrent food extinction (Meisch, 1970). The same relation between ethanol intake and concentration was observed in the total absence of food reinforcement (Meisch, et al., 1970). The aberrant trend of Rat 270's intake at 16% and 32% may be attributed to the shift in the water baseline toward lower water intake.

Holman and Myers (1968) observed maximum quantity of intake at 11% (V/V) with less intake occurring at concentrations above or below this value. Since the intake was not specified in relation to body weight, comparisons of specific values cannot be made with the results reported here. In the absence of polydipsia, quantity of ethanol intake increased with the concentration in one study (Holman and Myers, 1968) and did not exhibit a systematic relation to ethanol concentration in another study (Mendelson and Mello, 1964).

By repeatedly presenting a series of ascending ethanol concentrations with water concurrently available Veale and Myers (1969) found that:

> "The preference reached levels not previously reported (Lester, 1966) unless alcohol was injected directly into the brain (Myers, 1963). During the seventh sequence some rats drank as much as 20 ml of the 20% concentration, which for a 500g rat is approximately equivalent to 6.0 g/kg."

Six grams per kilogram per day equals 25 mg/100g/hr, and in the present study this level of intake was exceeded at all concentrations except 0.5%.

Ethanol intake in relation to body weight has been measured under different experimental conditions using the technique of two-liquid option. When intake at the same concentrations is compared, the quantities consumed in this study are greater than those reported in other studies using rats. Specifically, greater quantities were consumed in this study than were observed (1) in "big consumers" in a general rat population (Forsander, 1966), (2) in different strains of rats on different diets (Williams, et al., 1950), (3) during various vitamin deficiencies (Beerstecher, et al., 1951) or during iodine deficiency (Maenpaa and Forsander, 1966), (4) after treatment with diuretic drugs (Erickson, 1967) or carbon tetrachloride (Sirnes, 1953), (5) after restriction to ethanol (Wallgren and Forsander, 1963), (6) after gondectomy (Schadewald, et al., 1953), or (7) in rats genetically selected for ethanol drinking (Erickson, 1968). Consequently, it may be concluded that substituting ethanol for water during schedule-induced polydipsia resulted in greater ethanol intake than previously reported.

In the present study liquid reinforcements and volume

consumed were found to covary. Thus, the temporal distribution of liquid reinforcements can be used to measure the time course of liquid intake.

At the beginning of the series of ethanol concentration presentations, Rat 270's liquid responses greatly exceeded liquid reinforcements. This discrepancy became smaller with subsequent sessions and was also smaller with Rat 280. It was possible for liquid responses to exceed liquid reinforcements since responses could occur after the liquid dipper had been activated by a preceding response. Responses occurring while the dipper was activated, however, had no programmed consequence.

In other ethanol schedule-induced polydipsia studies, liquid presentation was not contingent upon a lever press but was available in a drinking bottle (Lester, 1961; Senter and Sinclair, 1967; Holman and Myers, 1968). Consequently, in these studies liquid responses and reinforcements were not reported.

Maximum decreases in the food baseline occurred at 8% and successively smaller decreases were observed at concentrations above and below this value. When sodium pentobarbital instead of ethanol was present, decreased as well as increased food responding was observed (Meisch, 1969b). The pattern of decreases observed when ethanol is present has been confirmed (Meisch, 1970). The importance of these decreases is that they indicate quantitatively and objectively that the ethanol consumed during polydipsia

has an influence on the animal's behavior.

In other ethanol schedule-induced polydipsia studies either no change has been observed in the food baseline (Holman and Myers, 1968) or results of the food baseline have not been reported (Sentar and Sinclair, 1967). In one study (Lester, 1961) one animal's food responding was initially found to decrease with increases in the blood ethanol levels. However, results for water control responding were not reported.

The reason for the systematic drift across sessions in Rat 270's food baseline is not known. However, long term cyclic fluctuations in variable-interval responding have been previously noted (Sidman, 1960).

The time course values of liquid reinforcements were related to total session values in that as the concentration was increased, there was both a greater decrease in total session values and an earlier and more profound decrease in the time course values. Time course measurements were possible because liquid presentation was contingent upon a lever press, and thus the occurrence of responses and reinforcements could be repeatedly recorded during experimental sessions.

The time course and total session values of food responses and reinforcements varied together, and at concentrations where the total session values were decreased the most, there were also earlier and greater decreases in

the time course values. These findings for liquid and food responding have been confirmed in a subsequent study (Meisch, 1970).

Lester (1961) presented time course changes for one animal when ethanol was available. However, water control results were not given. In other studies (Senter and Sinclair, 1967; Holman and Myers, 1968) time course results were not reported.

Recording of the time course values of the dependent variables is important for these values may change as a function of drug experience even in the absence of session total changes. Also, recording of time course values permits study of the time changes of one dependent variable in relation to time changes of other dependent variables.

The second time 4% ethanol was presented both rats exhibited an orderly increase in the rate of ethanol responding that exceeded water control levels. This is evidence for ethanol serving as a reinforcer. This finding was confirmed for these animals by studying their rate of ethanol responding during food extinction for concentrations up to 32% (Meisch, 1969a). In all cases volume consumed and liquid responding for ethanol exceeded water control values. These results were replicated with additional animals (Meisch, 1970).

Rat 270 increased its rate of ethanol responding the second time 4% ethanol was presented relative to the first

presentation. Also, its rate of food responding decreased faster during the second presentation. In contrast, Rat 280, did not increase its rate of ethanol responding, and its food baseline did not decrease faster. For both animals water control values remained stable or decreased, thus ruling out the possibility that changes in ethanol responding were due to a shift in the liquid baseline. Subsequent research has confirmed these findings. Ethanol responding increased with experience if the initial values did not significantly exceed water control values, and food responding decreased significantly faster when ethanol responding significantly increased (Meisch, 1970).

Leaving the liquid reservoir empty after hour 1 did not affect the food baseline values. Thus, changes in the food baseline that were found with high ethanol concentrations cannot be attributed to liquid deprivation, i.e., the low or absent liquid intake that occurred when these concentrations were present.

The absence of systematic differences between the hour 1 control values on ethanol and water days rules out the possibility that results on experimental days were a function of aberrant first hour values.

Schedule-induced polydipsia possesses a number of advantages as a procedure for obtaining oral drug self--administration by animals. Rats rapidly acquire the constant

rate variable-interval pattern of food responding as well as the polydipsic drinking. Within several weeks the values of the dependent variables stabilize. In this study and in a previous (Meisch, 1969b) and subsequent one (Meisch, 1970), drug self-administration was immediately obtained by simply substituting a drug solution for water. Consumption of large liquid volumes permits the use of low nonaversive drug concentrations. Failure to find an increase in drug intake with experience cannot be attributed to lack of drug experience for the high level of liquid intake results in consumption of the drug solution.

By permitting access to water early in the session, later intake of the drug solution is optional in that the animal is not liquid deprived and in that presence of liquid is not necessary for orderly food responding. Also, drug intake is optional in that drinking is not necessary for shock avoidance or food reinforcement.

Drug presentation may be made contingent upon a lever press (Meisch, 1969b), and thus the time course of drug responding can be recorded and schedule factors studied. Subsequent increases in drug intake may be investigated by comparing across successive sessions the time course of responding. Changes in the food baseline permit measurement continuous over time of behavioral changes produced by the self-administered drug. Animals other than rats can be used, for schedule-induced polydipsia has been observed in

monkeys (Schuster and Woods, 1966) and pigeons (Shanab and Peterson, 1969).

REFERENCES

Beerstecher, E., Reed, J. G., Brown, W. D., and Berry, L. J. The effects of single vitamin deficiencies on the consumption of alcohol by white rats. University of Texas Publication No. 5109, 1951, 115-138.

Clay, M. L. Conditions affecting voluntary alcohol consumption in rats. Quarterly Journal of Studies in Alcohol, 1964, 25, 36-55.

Eriksson, K. Effect of two diuretic drugs on liquid consumption and free choice of alcohol in albino rats. Nature, 1967, 213, 316-317.

Eriksson, K. Genetic selection for voluntary alcohol consumption in the albino rat. Science, 1968, 159, 739-741.

Falk, J. L. Production of polydipsia in normal rats by an intermittent food schedule. Science, 1961, 133, 195-196.

Falk, J. L. The motivational properties of schedule-induced polydipsia. Journal of the Experimental Analysis of Behavior, 1966, 9, 19-25.

Forsander, O. A. Metabolism of rats as related to voluntary alcohol consumption. Psychosomatic Medicine, 1966, 28, 521-528.

Hausmann, M. F. The behavior of albino rats in choosing food and stimulants. Journal of Comparative Psychology, 1932, 13, 279-309.

Holman, R. B. and Myers, R. D. Ethanol consumption under conditions of psychogenic polydipsia. Physiology and Behavior, 1968, 3, 369-371.

Lester, D. Self-maintenance of intoxication in the rat. Quarterly Journal of Studies in Alcohol, 1961, 22, 223-231.

Maenpaa, P. and Forsander, O. A. Influence of iodine deficiency on free choice between alcohol and water in rats. Quarterly Journal of Studies in Alcohol, 1966, 27, 596-503.

Meisch, R. Increased rate of ethanol self-administration as a function of experience. Reports from the Research Laboratories, Department of Psychiatry, University of Minnesota, No. PR-69-3, March 1969a.

Meisch, R. A. Self-administration of pentobarbital by means of schedule-induced polydipsia. Psychonomic Science, 1969b, 16, 16-17.

Meisch, R. A. Self-administration of ethanol by the rat. Ph.D. thesis. University of Minnesota, 1970.

Meisch, R., Anderson, W. W., and Thompson, T. Water deprivation, food deprivation, and reinforcement schedule determinants of oral ethanol self-administration by rats. Minutes of the Meeting of the Committee on Problems of Drug Dependence, NAS-NRC, Washington, D.C., 1970.

Mendelson, J. H. and Mello, N. K. Ethanol and whiskey drinking patterns in rats under free-choice and forced-choice conditions. Quarterly Journal of Studies in Alcohol, 1964, 25, 1-25.

Myers, R. D. and Carey, R. Preference factors in experimental alcoholism. Science, 1961, 134, 469-470.

Myers, R. D. and Holman, R. B. Failure of stress of electric shock to increase ethanol intake in rats. Quarterly Journal of Studies in Alcohol, 1967, 28, 132-137.

Rick, J. T. and Wilson, C. W. M. Alcohol preference in the rat: Its relationship to total fluid consumption. Quarterly Journal of Studies in Alcohol, 1966, 27, 447-458.

Schadewald, M., Emerson, G. A., Moore, W. T., and Moore, B. M. Voluntary preference for alcohol of white rats after gonadectomy. Federation Proceedings, 1953, 12, 364-365.

Schuster, C. R. and Woods, J. H. Schedule-induced polydipsia in the rhesus monkey. Psychological Reports, 1966, 19, 823-828.

Senter, R. J. and Sinclair, J. D. Self-maintenance of intoxication in the rat: A modified replication. Psychonomic Science, 1967, 9, 291-292.

Shanab, M. E. and Peterson, J. L. Polydipsia in the pigeon. Psychonomic Science, 1969, 15, 51-52.

Sidman, M. Tactics of Scientific Research. Basic Books, Inc., New York, 1960.

Sirnes, T. B. Voluntary consumption of alcohol in rats with cirrhosis of the liver. A preliminary report. Quarterly Journal of Studies in Alcohol, 1953, 14, 3-18.

Veale, L. and Myers, R. Increased alcohol preference in rats following repeated exposures to alcohol. Psychopharmacologia, 1969, 15, 361-372.