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Ethanol Drinking by Rhesus Monkeys with Concurrent Access to Water[1]

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HENNINGFIELD, J. E. AND R. A. MEISCH. *Ethanol drinking by rhesus monkeys with concurrent access to water.* PHARMAC. BIOCHEM. BEHAV. **10**(5) 777–782, 1979.—Three monkeys were provided concurrent access to water and ethanol in concentrations of either 8, 16 or 32% (w/v) during daily 3-hr sessions. The monkeys were those for whom ethanol had been established as a reinforcer in an earlier study in which only ethanol or water was available. Ethanol was preferred to water at all concentrations and volume of ethanol consumed was inversely related to ethanol concentration. Quantity of ethanol (g/kg of body wt.) consumed remained relatively constant, and blood ethanol determinations confirmed that the monkeys were drinking ethanol. Water drinking occurred at negligible levels except by one monkey at 16 and 32% who followed ethanol drinking bouts by water bouts (chasers) in a manner similar to that reported in other studies. Two monkeys were also provided concurrent access to 8% ethanol and water during 23-hr daily sessions. Under these conditions, ethanol was consumed every few hours to the near exclusion of water. The significance of this study lies largely in its procedure; that is, the development and application of a concurrent water-ethanol preparation in which ethanol serves as a reinforcer for rhesus monkeys. This preparation should be useful in the evaluation of a wide range of factors suspected to control alcoholic drinking.

Ethanol Rhesus monkey Fixed-ratio Concurrent schedule Self-administration Physical dependence

FOLLOWING an appropriate conditioning history, aqueous ethanol serves as an orally effective reinforcer for rhesus monkeys [9,15]. These studies showed that despite the aversive taste of ethanol and other difficulties inherent to the oral preparation [18,28], e.g., leaking delivery systems and delayed onset of ethanol's effects, a monkey model of ethanol dependence, employing the oral route was a viable experimental possibility. Since earlier studies of ethanol drinking by animals have used the concurrent or water-ethanol choice procedure [22,25], the use of that procedure in the current oral preparation would facilitate evaluation of the findings. The concurrent procedure offers several other advantages over the single solution access experiment. First, it provides an unambiguous test of the reinforcing efficacy of ethanol—apart from any reinforcing properties due simply to its liquid character. Second, the concurrent procedure makes many experimental manipulations possible, such as the evaluation of behavioral and pharmacological procedures for their specific effects in controlling ethanol drinking.

In the present study, we used the monkey ethanol drinking preparation which has been described earlier [15]. However, a second liquid delivery system was added to each monkey's cage. Water and ethanol, in various concentrations, were concurrently available daily on alternating sides during three hour sessions. Additionally a brief experiment was conducted in which ethanol and water were nearly continuously available for ten consecutive days.

METHOD

Animals

Three young adult male rhesus monkeys *(Macaca mulatta)* whose free-feeding weights were 9.5 kg, M-A; 9.0 kg, M-C; 11.0 kg, M-T, were maintained at 9.4 kg, 7.7 kg, 9.3 kg, respectively, by adjusting their daily ration of Purina monkey chow. They were also fed one fresh fruit and one multiple vitamin pill each day. The monkeys had served in an earlier study [15] in which ethanol had been established as a reinforcer using a food-induced drinking procedure. Briefly, they were fed once per day during daily three hour sessions with water available. Under these conditions the monkeys developed a pattern of rapidly consuming all available food, then drinking 300 to 500 ml in one uninterrupted bout. Next, aqueous ethanol solutions were substituted for the water, and the concentration was gradually increased from 0.5 to 8% (w/v) across sessions. This procedure permitted the monkeys to gradually adapt to the taste of ethanol, and the behavior of ethanol-drinking was paired daily with ethanol's effects. When the monkeys were regularly drinking 100 to 200 ml of 8% ethanol, the food-induced drinking procedure

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was terminated, i.e., daily access to food was shifted from the 3-hr sessions to 1 hr following the sessions. Thereafter, sessions consisted simply of three hours access to either ethanol or water or both liquids, and the monkeys continued to drink ethanol in substantial quantities.

Apparatus

The monkeys were individually housed in stainless steel primate cages having three solid walls and one barred wall. On one solid wall of each cage were mounted two drinking devices (left and right side) with attendant stimulus lights. The drinking devices were automatic spouts which provided regulated delivery of approximately 0.5 ml when an appropriate lip-contact response was made. The apparatus has been described in detail in an earlier report [8]. Mounted 9 cm above each spout was a stimulus light which signalled water availability when illuminated, or ethanol availability when blinking at a rate of 10 hz. In addition, four stimulus lights (4.7 w) were mounted on a 3.5 cm radius from the center of the spout. The lights at the two and eight o'clock positions were green, and the lights at the four and ten o'clock positions were white. When ethanol was available, the green lights were illuminated by each lip-contact response; when water was available, the white lights were illuminated by each lip-contact response. Constant illumination was provided by overhead lights in the monkey's housing room. Experimental events were scheduled and recorded by equipment (Coulbourn Instruments, Inc.) located in an adjacent room.

Procedure

Concurrent water and ethanol drinking. Daily experimental sessions were 3 hr long; they were preceded by a 1-hr stimulus blackout and followed by a 2-hr stimulus blackout during which times data were recorded and solutions were changed. The monkeys were fed their daily food rations 1 hr following the sessions. Water was continuously available during the 18-hr intersession period which followed the 2-hr blackout. Intersession water was available on a fixed-ratio 1 (FR 1) schedule via one of the drinking spouts. Initially, during daily sessions, 8% ethanol was available on a FR 8 schedule (i.e., 8 lip-contact responses per 0.5 ml delivery), via the left spout, and water was available on a FR 8 schedule via the right spout. After 5 stable sessions of drinking were obtained, the side positions of water and ethanol were switched. When 5 stable sessions were obtained under these conditions, a procedure of daily alternation of the side position of 8% ethanol and water was begun. During intersession periods, water was always placed on the side which had delivered ethanol during the preceding session. When drinking had stabilized at 8%, the concentration was increased to 16%, and 16% and water were alternated from side to side each day. After drinking had stabilized, the concentration was increased to 32% and the procedure was repeated. Finally, 8% was retested.

Stability criteria throughout this entire experiment were 5 sessions in which no trend in drinking behavior was observed on a given side. Thus, when water-ethanol side positions were alternated each day, 10 consecutive sessions were required in which there was no trend in drinking on either side. Immediately following the last session of the 10-session series at each concentration, the monkeys were anesthetized with an intramuscular injection of ketamine HCl. The monkeys were then weighed, and 1 ml of blood was drawn from a saphenous vein, and blood ethanol levels (BEL) were determined by gas chromatography. Ethanol solutions were prepared 24 hr prior to sessions using 95% ethanol and tap water, and concentrations are expressed in grams percent (w/v). Ethanol and water were always presented to the monkeys at room temperature.

Continuous access to ethanol and water. After completion of the concentration manipulations, two monkeys (M-C and M-T) were run in 23-hr daily sessions, during which ethanol and water were continuously available. They were fed food and fruit each day during a 1 hr stimulus blackout, during which time data were recorded and solutions changed. Sessions were 23 hr long and provided continuous availability of 8% ethanol and water. Both solutions were presented on FR 8 schedules. Only 10 days of continuous access were provided. For the first 5 days, 8% ethanol was on the right side and water was on the left. During the second 5 days, water was on the right side and ethanol was on the left side. After 10 days, the monkeys were provided continuous access to water on FR 1 and closely observed for possible signs of the ethanol withdrawal syndrome as described in a report by Ellis and Pick [6].

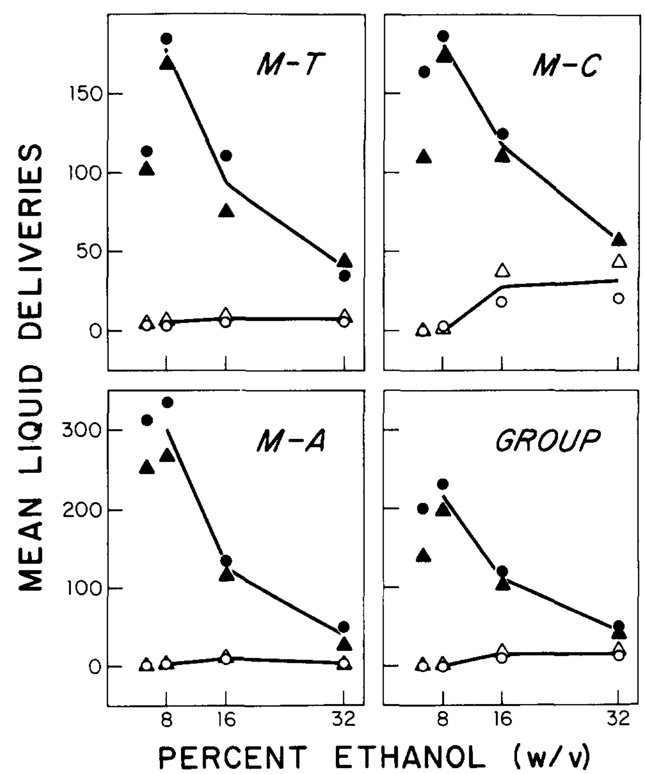

FIG. 1. Mean number of liquid deliveries per 3-hr session as a function of the ethanol concentration presented concurrently with water (n=5 on the individual graphs and n=15, 5 sessions × 3 monkeys, on the group graph). Circles indicate left side liquid deliveries, and triangles indicate right side liquid deliveries. Filled symbols indicate ethanol, and open symbols indicate water. The symbols displaced to the left of 8% are the 8% retest values. Standard errors of means are not graphed since nearly all points fall within the area occupied by the symbols.

TABLE 1

EFFECTS OF ETHANOL CONCENTRATION AND SIDE POSITION ON DEPENDENT VARIABLES*

% (w/v)	Side	Lip-Contact Responses	ml Consumed	g/kg 1st hr	g/kg 3 hr	BEL (mg%)
Monkey M-A						
8	L	2586(151.1)	169(9.3)	0.70(0.05)	1.38(0.06)	171
	R	2056(235.7)	133(9.6)	0.51(0.06)	1.08(0.09)	
16	L	1006(118.8)	61(6.7)	0.39(0.12)	1.05(0.12)	114
	R	878(110.3)	61(8.2)	0.37(0.12)	1.05(0.15)	
32	L	362(64.8)	25(3.8)	0.41(0.17)	0.87(0.12)	†
	R	200(26.8)	15(2.3)	0.15(0.08)	0.51(0.09)	
8	L	2366(94.5)	160(7.0)	0.67(0.08)	1.35(0.06)	129
RETEST	R	1983(124.1)	144(8.3)	0.66(0.03)	1.23(0.06)	
Monkey M-C						
8	L	1397(59.1)	98(4.2)	0.59(0.06)	1.05(0.03)	
	R	1321(91.7)	99(7.2)	0.57(0.06)	1.05(0.09)	100
16	L	941(36.2)	63(2.6)	0.71(0.05)	1.32(0.06)	126
	R	832(47.9)	52(3.3)	0.73(0.07)	1.11(0.06)	
32	L	429(21.4)	30(2.4)	0.93(0.05)	1.26(0.09)	
	R	434(34.0)	26(2.2)	0.63(0.07)	1.08(0.09)	124
8	L	1239(80.7)	87(4.9)	0.61(0.04)	0.90(0.06)	65
RETEST	R	841(32.9)	51(2.5)	0.39(0.05)	0.54(0.03)	
Monkey M-T						
8	L	1403(114.1)	94(4.7)	0.41(0.03)	0.81(0.03)	80
	R	1266(70.8)	93(6.9)	0.38(0.01)	0.81(0.06)	
16	L	810(80.9)	53(5.4)	0.36(0.10)	0.93(0.09)	
	R	550(47.3)	35(2.4)	0.36(0.05)	0.60(0.03)	†
32	L	261(33.7)	20(3.3)	0.58(0.04)	0.69(0.12)	
	R	312(60.7)	19(2.2)	0.39(0.08)	0.66(0.09)	24
8	L	1029(142.0)	64(7.3)	0.21(0.04)	0.57(0.06)	44
RETEST	R	957(118.5)	50(4.3)	0.14(0.04)	0.42(0.03)	

*Values, except BEL, (blood ethanol levels) are expressed as Mean ± SE of the last 5 stable sessions under each condition, e.g., 8% L. BEL was determined immediately following the last session under the condition indicated.

†These BEL's were lost by the gas chromatography laboratory which did the blood analyses.

RESULTS

Concurrent Water and Ethanol Drinking

Figure 1 shows that mean ethanol deliveries exceeded mean water deliveries at all concentrations and on both the left and the right sides. Figure 1 also shows that as concentration increased, number of liquid deliveries decreased, producing a relatively stable level of ethanol intake (g/kg/session). Specifically, at 8, 16, 32 and 8% R, mean ethanol intake (n=30, 3 monkeys × 10 sessions) was 1.03, 1.01, 0.85, and 0.84 g/kg body weight/3-hr session, respectively. Number of lip-contact responses and volume of solution consumed (ml) were also inversely related to ethanol concentration (Table 1). Blood ethanol levels (Table 1) confirm that the monkeys were drinking the ethanol and these values vary directly with the mean quantities consumed. Intermittent monitoring of the monkeys via closed circuit television revealed that the solutions were not spilled and that the drinking devices were correctly operated by mouth and not by hand. Visual observations also revealed that the little behavioral impairment followed ethanol drinking. That is, the monkeys were somewhat sedated and slow to respond to stimulus change (e.g., an experimenter entering the room) but they were not ataxic or grossly uncoordinated. A clear and consistent side preference for ethanol drinking was shown (Fig. 1) as left-side ethanol deliveries exceeded right-side ethanol deliveries at nearly all test points. No comparable side preference was shown for water drinking.

Ethanol drinking occurred in a negatively accelerated temporal pattern across the session, and this is most clearly shown by the cumulative records (Fig. 2). Most drinking occurred at the start of the session, then occasional smaller bouts occurred over the rest of the session. Similarly, Table 1 shows that nearly one-half of session ethanol intake oc-

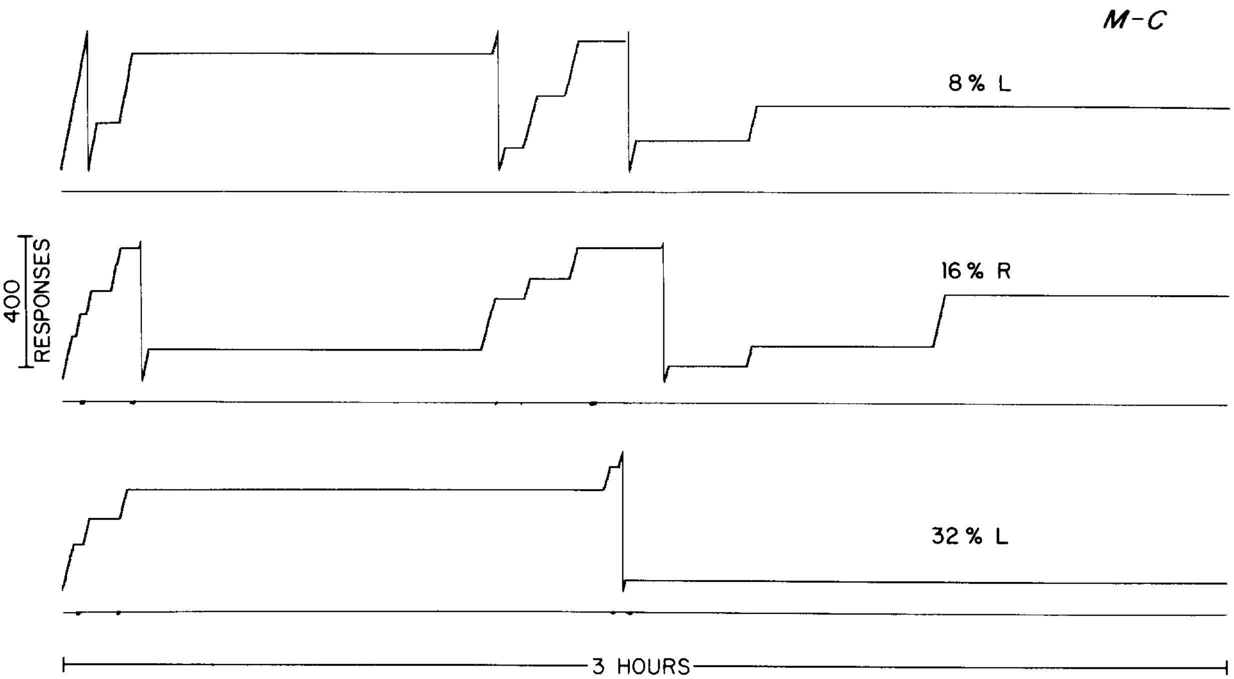

FIG. 2. Characteristic daily patterns of drinking by Monkey M-C are illustrated by these cumulative records. Liquid deliveries (approximately 0.5 ml) are indicated by slash marks. The upper record at each concentration shows cumulative ethanol lip-contact responses and deliveries, and the lower record shows water deliveries over time. The patterns of ethanol drinking are representative of the other monkeys in this experiment.

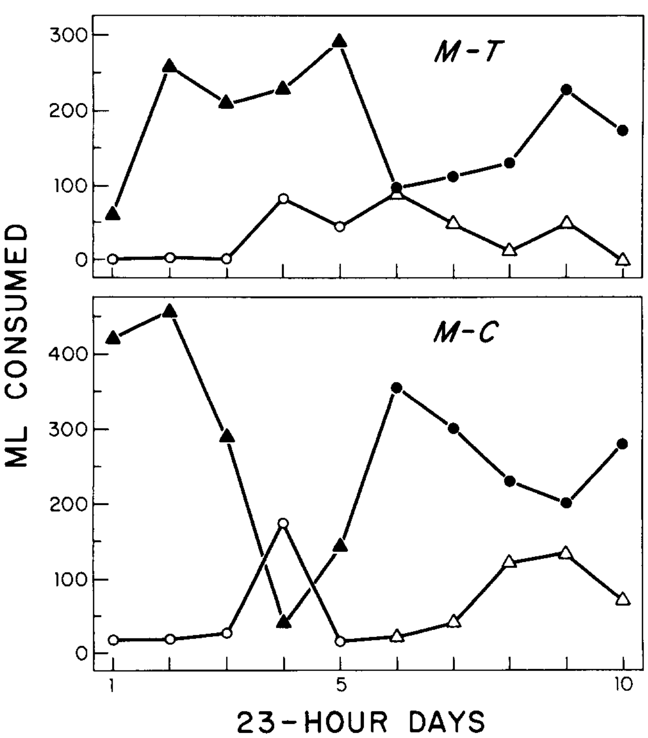

FIG. 3. Milliliters consumed under FR 8 schedules during the 10 consecutive 23-hr daily sessions run under these conditions. Circles indicate left side liquid deliveries, and triangles indicate right side liquid deliveries. Filled symbols indicate 8% (w/v) ethanol, and open symbols indicate water.

curred during the first hour of the three-hour sessions. The cumulative records (Fig. 2) also show the characteristic fixed-ratio patterns of responding: response rates were high and constant, and ethanol drinking bouts were occasionally followed by pauses.

At 8% ethanol for M-C, and at all concentrations for the other monkeys, water consumption was less than 5 ml per session, and this drinking did not show any consistent pattern across sessions. However, as the concentration was increased to 16 and 32%, M-C drank 13 and 14 ml (mean values, n=10), respectively. Moreover, as illustrated in the cumulative records (Fig. 2), M-C regularly drank water immediately following ethanol drinking bouts, and water drinking was roughly proportional to ethanol concentration and amount of ethanol drinking in a given bout. Specifically at 8, 16, 32, and 8% R, mean number of water deliveries accounted for 0.2, 19.7, 37.2, and 0.5%, respectively, of the total number of liquid deliveries per session. Monkeys M-A and M-T displayed no such trend in water drinking.

Continuous Access to Ethanol and Water

When both water and 8% ethanol were available 23 hr per day on FR 8 schedules, ethanol drinking generally exceeded water drinking (Fig. 3). However, Fig. 3 also shows that daily ethanol drinking was quite variable, sometimes occurring at lower rates than water drinking, and occasionally occurring to the near exclusion of water drinking. For each monkey, total daily liquid intake remained relatively stable since ethanol drinking and water drinking were inversely related. Daily ethanol intake by the monkeys was as follows: 3.15 g/kg/23 hr, M-C, right side; 3.12 g/kg/23 hr, M-C, left side; 1.38 g/kg/23 hr, M-T, right side; and 1.84 g/kg/23 hr, M-T, left side.

On days of higher rate ethanol drinking, e.g., sessions 2–5 for M-T and 6–10 for M-C, ethanol drinking occurred in discrete bouts every few hours of the 23 hr session. This pattern was in contrast to that observed on low intake days, e.g., sessions 4 and 5 for M-C, in which little drinking of any kind occurred overnight (Note that although the experimental room was constantly lighted, the monkeys' activity levels followed a normal diurnal pattern which may have been maintained by the daily feedings and activity of experimenters).

When ethanol availability was discontinued, water consumption immediately increased to normal daily levels for these monkeys, i.e., a mean (n=5) of 214 ml for M-C and 434 ml for M-T. The monkeys became somewhat hyperexcitable for about 2 days following removal of ethanol but no clear signs of the ethanol withdrawal syndrome were observed.

DISCUSSION

The present study demonstrates a preparation that should lend itself to general application in studies of ethanol drinking by nonhuman primates. The concurrent water-ethanol procedure has enjoyed widespread use in earlier studies of ethanol drinking, but in most of those studies, high ethanol concentrations were neither preferred to water, nor consumed in intoxicating quantities (see reviews [13, 22, 25, 28]). In primate studies from our laboratory (e.g. [9]), ethanol was consumed in intoxicating quantities, but the concurrent water-ethanol procedure was not used.

The main finding of the present study was the clear demonstration of preference for ethanol over water when both liquids were equally available. This finding is consistent with that of studies using food (e.g. [5]) and other drugs (e.g. [11]) in which reinforcing efficacy is derived from preference. This finding is also interesting since most other studies of ethanol-water drinking by monkeys have demonstrated a strong aversion to the taste of ethanol which is highly resistant to modification (e.g. [20,21]). The current findings are consistent with those of a similar study from this laboratory in which rats preferred ethanol, in concentrations of 8 to 32%, over water [14]. In addition, the findings are consistent with earlier primate studies from this laboratory in which across-session exposure to water and ethanol resulted in more drinking of ethanol than of water. The effects of ethanol concentration manipulations are not unlike those of earlier monkey and rat studies in which volume of solution consumed has been shown to be inversely related to ethanol concentration [9, 14, 17, 25]. That is, volume consumed is greatest at 8% and least at 32%. In these studies, this relationship has resulted in relatively small changes in total intake of ethanol (g/kg) as a function of concentration when these changes are compared to the 4-fold increase in ethanol concentration. That this relationship is not simply an artifact of the taste properties of ethanol is indicated by the similar relationship which occurred when the volume of 8% ethanol delivered to rats was varied over a 5-fold range [7]. The negative acceleration of ethanol drinking (Fig. 2) during the 3-hr sessions is similar to that observed when ethanol served as an orally effective reinforcer for rats [7, 14, 17] and monkeys [9,15], and as an intravenously effective reinforcer for rats [24], and monkeys [27]. In addition, similar patterns of drug self-administration occur when monkeys have intravenous access to barbiturates [26] and opiates [10].

In the current study, ethanol was always preferred to water, and ethanol concentration had no effect on water drinking by Monkeys M-A and M-T. However, water-drinking by Monkey M-C was directly related to ethanol concentration and this monkey consistently followed drinking bouts of 16 and 32% ethanol with smaller drinking bouts of water (chasers). That the change in water drinking did not simply reflect a nonspecific shift in the water baseline is indicated by the similar amounts of water consumed at both 8% and the 8% retest (Fig. 1). The possibility that this was not an anomolous finding is suggested by an earlier study [20] in which a similar pattern of ethanol-water drinking occurred under a complex paradigm of schedule-induced drinking by rhesus monkeys. In addition, a similar phenomenon was observed in a human subject who obtained concentrations of ethanol ranging from 8 to 32% (w/v) in 5 ml quantities (Henningfield and Griffiths, Unpublished observations).

The blood ethanol determinations confirm the observations that the monkeys were actually drinking the ethanol solutions. This confirmation is necessitated by earlier reports describing the various behaviors that rhesus monkeys may develop in which drinking response requirements are achieved but little ethanol is consumed (e.g. [21]). Since blood ethanol levels reflect temporal pattern of drinking, gastric load, and ethanol concentration, as well as quantity consumed, it was not expected that blood levels would provide a reliable quantitative measure of amount consumed. However, the blood ethanol data were relatively orderly and this may reflect the fact that the monkeys were food deprived and that the drinking patterns were similar from day to day.

The monkeys in the current study drank less ethanol per body weight (g/kg) than the monkeys in an earlier study from this laboratory [9]. Blood ethanol levels also reflected this difference. In the earlier study, the monkeys usually obtained 2 to 3 g/kg and achieved blood levels over 200 mg%. The lower levels of ethanol intake in the current study could have resulted from concurrent water drinking supplanting ethanol drinking. However, with the exception of Monkey M-C at 16 and 32% ethanol, only trivial volumes of water (<5 ml) were consumed during the 3-hr sessions. A more likely factor is one which has received considerable attention in our laboratory, viz., level of food deprivation. It has been noted that the amount of ethanol and other drugs consumed in drug self-administration studies is directly related to the level of food deprivation [2, 3, 4, 12, 16, 17]. The consistent finding in these studies is that increasing the level of food deprivation increases the amount of drug consumed. In the earlier reported study in which higher levels of ethanol intake were observed, the monkeys were at about 80% of their free-feeding body weights and weighed an average of 5.8 kg (n=3). The current animals were at 85%, M-T; 86%, M-C; and 99%, M-A, and weighed an average of 8.8 kg. While such an across-experiment comparison is certainly limited in explanatory power, the observed relationship is worth noting since it is consistent with a well established body of data.

When both ethanol and water were available 23 hr per day, ethanol consumption was greater than that which occurred during 3-hr daily sessions and was usually greater than water consumption. Also, the wide day to day fluctuation in ethanol drinking under these conditions contrasted to the very regular performance of monkeys during 3-hr sessions. Similar findings were also reported when monkeys who self-administered ethanol intravenously were provided access to ethanol under either 3 or 24-hr daily sessions [27]. The day to day performance revealed in Fig. 3 is also similar to that of monkeys who self-administered ethanol intragastrically [1] and humans who drank ethanol under experimental conditions [19]. Daily ethanol intake was less than the 4 to 8 g/kg which is known to produce physical dependence in rhesus monkeys [6,23], and accordingly, the monkeys did not show clear signs of physiological dependence when ethanol was removed. However, the monkeys were unusually aggressive and hyperexcitable, and it is possible that longer exposure to ethanol, perhaps at a greater level of food-deprivation would yield physiologically dependent monkeys. The monkeys displayed tolerance to ethanol insofar as they rarely became ataxic to the degree observed when they first began drinking ethanol in similar quantities.

The findings of this study support the notion that, with an appropriate conditioning history, rhesus monkeys can serve as viable models of alcoholic drinking. The basic findings were consistent with those obtained in earlier monkey studies employing oral, intravenous and intragastric routes of administration [1, 9, 15, 27, 28], but in this study ethanol and water were concurrently available and ethanol was the preferred liquid. The advantages of an oral preparation over intravenous and intragastric preparations include the closer approximation of the oral model to the human phenomenon of alcoholism, and the absence of technical problems associated with the use of catheters.

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REFERENCES

1. Altshuler, H., S. Weaver and P. Phillips. Intragastric self administration of psychoactive drugs by the rhesus monkey. *Life Sci.* **17:** 883–890, 1975.
2. Beardsley, P., G. Lemaire and R. A. Meisch. Ethanol reinforced behavior in rats with concurrent access to food and water. *Psychopharmacology* **59:** 7–11, 1978.
3. Carroll, M. E., C. P. France and R. A. Meisch. Food deprivation increases oral and intravenous etonitazene intake in rats. *Science* In press.
4. Carroll, M. E. and R. A. Meisch. Effects of food deprivation on etonitazene consumption in rats. *Pharmac. Biochem. Behav.* **10:** 155–159, 1979.
5. Catania, A. C. Concurrent performances: A baseline for the study of reinforcement magnitude. *J. exp. Analysis. Behav.* **6:** 299–300, 1963.
6. Ellis, F. W. and J. R. Pick. Experimentally induced ethanol dependence in rhesus monkeys. *J. Pharmac. exp. Ther.* **175:** 88–93, 1970.
7. Henningfield, J. E. and R. A. Meisch. Ethanol-reinforced responding and intake as a function of volume per reinforcement. *Pharmac. Biochem. Behav.* **3:** 437–441, 1975.
8. Henningfield, J. E. and R. A. Meisch. Drinking device for rhesus monkeys. *Pharmac. Biochem. Behav.* **4:** 609–610, 1976.
9. Henningfield, J. E. and R. A. Meisch. Ethanol drinking by rhesus monkeys as a function of concentration. *Psychopharmacology* **57:** 133–136, 1978.
10. Hoffmeister, F. and U. U. Schlichting. Reinforcing properties of some opiates and opioids in rhesus monkeys with histories of cocaine and codeine self-administration. *Psychopharmacologia* **23:** 220–227, 1972.
11. Johanson, C. E. and C. R. Schuster. A choice procedure for drug reinforcers: Cocaine and methylphenidate in the rhesus monkey. *J. Pharmac. exp. Ther.* **193:** 676–688, 1975.
12. Lang, W. J., A. A. Latiff, A. McQueen and G. Singer. Self administration of nicotine with and without a food delivery schedule. *Pharmac. Biochem. Behav.* **7:** 65–70, 1977.
13. Meisch, R. A. Ethanol self-administration: Infrahuman studies. In: *Advances in Behavioral Pharmacology*, edited by T. Thompson and P. B. Dews. New York: Academic, 1977, pp. 35–84.
14. Meisch, R. A. and P. Beardsley. Ethanol as a reinforcer for rats: Effects of concurrent access to water and alternate positions of water and ethanol. *Psychopharmacologia* **43:** 19–23, 1975.
15. Meisch, R. A. and J. E. Henningfield. Drinking of ethanol by rhesus monkeys: Experimental strategies for establishing ethanol as a reinforcer. In: *Alcohol Intoxication and Withdrawal: Experimental Studies*, III b, edited by M. M. Gross. New York: Plenum, 1977, pp. 443–463.
16. Meisch, R. A. and P. J. Kliner. Etonitazene as a reinforcer for rats: Increased etonitazene reinforced behavior due to food deprivation. *Psychopharmacology*, 1979, in press.
17. Meisch, R. A. and T. Thompson. Ethanol intake as a function of concentration during food deprivation and satiation. *Pharmac. Biochem. Behav.* **2:** 589–596, 1974.
18. Mello, N. K. A review of methods to induce alcohol addiction in animals. *Pharmac. Biochem. Behav.* **1:** 89–101, 1973.
19. Mello, N. K. and J. H. Mendelson. Experimentally induced intoxication in alcoholics: A comparison between programmed and spontaneous drinking. *J. Pharmac. exp. Ther.* **173:** 101–116, 1970.
20. Mello, N. K. and J. H. Mendelson. Evaluation of a polydipsia technique to induce alcohol consumption in monkeys. *Physiol. Behav.* **7:** 827–836, 1971.
21. Mello, N. K. and J. H. Mendelson. The effects of drinking to avoid shock on alcohol intake in primates. In: *Biological Aspects of Alcohol*, edited by M. K. Roach, W. M. McIsaac and P. J. Creaven. Austin: University of Texas, 1971, pp. 313–340.
22. Myers, R. D. and W. L. Veale. The determinants of alcohol preference in animals. In: *The Biology of Alcoholism, Vol. II*, edited by B. Kissin and H. Begleiter. New York: Plenum, 1971, pp. 131–168.
23. Pieper, W. A. and M. J. Skeen. Development of functional tolerance to ethanol in rhesus monkeys using an oral acceptance technique. *Life Sci.* **11:** 989–997, 1972.
24. Smith, S. G., T. E. Werner and W. M. Davis. Comparison between intravenous and intragastric alcohol self-administration. *Physiol. Psychol.* **4:** 91–93, 1976.
25. Wallgren, H. and H. Barry, III. *Actions of Alcohol, III, Chronic and Clinical Aspects*. Amsterdam: Elsevier, 1970.
26. Winger, G. D., M. L. Stitzer and J. H. Woods. Barbiturate-reinforced responding in rhesus monkeys: Comparisons of drugs with different durations of action. *J. Pharmacol. exp. Ther.* **195:** 505–514, 1975.
27. Winger, G. D. and J. H. Woods. The reinforcing property of ethanol in the rhesus monkey: Initiation, maintenance and termination of intravenous ethanol-reinforced responding. *Ann. N.Y. Acad. Sci.* **215:** 162–175, 1973.
28. Woods, J. H. and G. D. Winger. A critique of methods for inducing ethanol self-intoxication in animals. In: *Recent Advances in Studies on Alcoholism*, edited by N. K. Mello and J. H. Mendelson. Washington, D.C.: U.S. Government Printing Office, 1971, pp. 413–436.