Pharmacology Biochemistry & Behavior, Vol. 17, pp. 111–117, 1982. Printed in the U.S.A.

Oral Ethanol Intake and Levels of Blood Alcohol in the Squirrel Monkey

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Received 26 September 1981

KAPLAN, J. N., M. B. HENNESSY AND R. A. HOWD. *Oral ethanol intake and levels of blood alcohol in the squirrel monkey*. PHARMAC. BIOCHEM. BEHAV. 17(1) 111–117, 1982.—Oral alcohol ingestion and blood alcohol levels were examined in adult female squirrel monkeys to assess the feasibility of using this primate as a model for fetal alcohol effects. In one experiment, alcohol intake was evaluated in nonpregnant animals under conditions in which the concentration of ethanol, length of ethanol exposure, and degree of liquid deprivation were varied. In another experiment blood alcohol levels were measured in pregnant animals of two subtypes that had been drinking ethanol. In a third experiment, time-dependent blood alcohol levels and behavior were evaluated in nonpregnant monkeys following intubation of specific doses of ethanol. Results showed that nonpregnant monkeys drank ethanol at concentrations of 5 to 10%, and that the amount of ethanol consumed was related to the concentration and length of time ethanol was available. When given access to a 5% ethanol solution, pregnant animals drank quantities that varied between individuals and subtypes, with maximum blood levels, measured up to 6 hr after presentation, ranging from 1 to 196 mg%. Intubation of ethanol resulted in blood alcohol levels and incoordination scores that were linearly related to dose, with maximum effects occurring 1 hr after administration. Elimination of ethanol from the blood at levels above 50 mg% occurred at a rate of about 35 mg%/hr, while the rate of clearance from the body was calculated to be approximately 250 mg/kg/hr.

Ethanol Oral ingestion Squirrel monkey Blood alcohol levels Pregnancy Behavior Oral intubation

UNLIKE humans, nonhuman primates generally will not ingest ethanol voluntarily above a concentration of 5–10%, even if attempts are made to mask its taste with fruit juices or other palatable solutions [1–4, 10]. This has posed a problem for research attempting to use nonhuman primates in studies of ethanol addiction based on drinking ethanol because of the difficulties in obtaining sufficiently high blood alcohol levels (BALs). Recently, certain behavioral techniques involving induced drinking in food-deprived animals have been used successfully with rhesus monkeys and baboons to get them to drink to intoxication [6–8]. But even though BALs in these studies were often over 200 mg%, and behavioral changes such as ataxia were noted, a state of ethanol dependency was never observed. Although nonhuman primates may not ingest quantities of ethanol sufficient to produce dependency, ingestion levels may be adequate for studying other potentially harmful effects, such as those reported to occur in the human fetus as a consequence of alcohol consumption during pregnancy [14].

Studies that have described oral ingestion of ethanol in nonhuman primates have been based entirely on Old World species—macaque monkeys, baboons, and apes—and in only a few cases have attempts been made to relate the amounts consumed to BALs [6–8]. The experiments reported here were undertaken to examine oral alcohol intake and BALs in a New World species, the squirrel monkey (*Saimiri sciureus*), in order to assess the feasibility of using this primate as a model for studying the effects of ethanol ingestion during pregnancy. Specifically, we investigated the effect of various schedules of ethanol presentation on consumption and the changes in BALs that occur during an oral intake regimen. In addition, changes over time in BALs following discrete specified doses of ethanol, and the relationship of BALs to behavioral signs of intoxication, were also examined.

EXPERIMENT 1

In this experiment oral ethanol intake was evaluated under conditions in which the concentration of ethanol, the length of ethanol exposure, and the degree of liquid deprivation were varied.

METHOD

Subjects

Subjects were 12 adult nonpregnant female squirrel monkeys of the Colombian subtype that had either been born in captivity or lived in captivity for several years. Five of the monkeys had had limited experience drinking a 5% ethanol solution approximately one year before the present experiment began.

Housing and Liquid Administration

Each monkey was housed alone in a cage 74×64×38 cm. Ethanol solutions (5 or 10% w/v) or water were administered in 950 ml glass bottles that hung inverted on the outside of the cage. Bottles were fitted with a 10 cm stainless steel sipper tube that protruded approximately 3 cm into the cage and contained a metal ball to reduce excess dripping. A fun-

nel leading into a 275 ml narrow mouth plastic bottle was fastened to the inside of the cage directly under the drinking tube to recover spillage that did occur.

Drinking Conditions

All monkeys were examined in seven conditions in which water or an ethanol solution was administered in the drinking bottles at specific periods of the day. Standard rations of monkey biscuits were provided twice each day, at 0700 and 1600 hr. However, since the monkeys generally did not consume all of the biscuits supplied at each meal, food was essentially continuously available. Each drinking condition was administered for 6 consecutive days and immediately followed the previous condition. A description of the conditions, in the order in which they were imposed, is presented below.

Condition I	water continuously available
Condition II	5% ethanol from 0900–1600 hr; water from 1600–0700 hr; no fluid from 0700–0900 hr
Condition III	5% ethanol from 0900–1600 hr; water from 1600–1700 hr; no fluid from 1700–1900 hr
Condition IV	5% ethanol from 0900–1600 hr; no fluid from 1600–0900 hr
Condition V	5% ethanol continuously available
Condition VI	10% ethanol from 0900–1600 hr; water from 1600–1700 hr; no fluid from 1700–0900 hr
Condition VII	10% ethanol continuously available

Ethanol solutions were diluted from 95% stock solution (U. S. Industrial Chemicals Co.) and were mixed with one of four fruit-flavored drinks favored by our monkeys (orange-flavored Tang, cherry-flavored Kool Aid, grape-flavored Kool Aid, and Hawaiian Punch; all diluted according to label instructions) on each of the six days of administration. Previous tests in our laboratory had shown that, in general, these different fruit drinks were preferred equally by our monkeys, although specific preferences were shown by some individuals. Different flavors were used in this experiment so that no one flavor would be associated with any aversive effects of ethanol. The four flavors were rotated over the six sessions so that each was given at least once per condition and that the two that were given twice varied randomly. Ethanol solutions were typically prepared the day before they were given to the monkeys and were refrigerated between the time they were prepared and the time they were administered. The ethanol solution or water given to the monkeys was weighed before and after each session in which it was presented, and the amount of spillage was deducted from the difference to provide the value for ingested fluid. The amount of evaporation in the bottles containing spilled material was considered negligible since the funnel made a tight fit with the narrow opening in the bottle. When ethanol or water was available on a continuous basis, bottles were weighed and filled twice a day, once at 0900 hr and once at 1600 hr. Body weights were obtained on the animals after the last session of each condition.

RESULTS AND DISCUSSION

The average daily amount of ethanol (g/kg body weight) ingested differed significantly among the different conditions, as measured by a repeated measures Analysis of Variance (ANOVA, $p<0.01$, Fig. 1a). The amount of ethanol ingested in each of the two conditions in which ethanol was provided on a continuous basis (Conditions V and VII) was significantly greater (all $ps<0.01$, Newman-Keuls) than in any of the other conditions in which alcohol was provided for 7 hr daily (Conditions II, III, IV, VI). Moreover, when ethanol was continuously available, the amount ingested at a concentration of 10% (Condition VII), was greater than that ingested at 5% (Condition V; $p<0.01$, Newman-Keuls). All the conditions involving ethanol presentation for 7 hr daily produced statistically equivalent levels of ethanol intake.

The total amount of liquid consumed also differed over conditions ($p<0.01$, ANOVA) and, in general, depended on the availability of water (Fig. 1b). Continuous access to water (Condition I) produced the greatest intake and differed statistically from all other conditions except for Condition II in which 5% ethanol was given for 7 hr, followed by 15 hr of water (I vs III, IV, V, VII, $ps<0.01$; I vs VI, $p<0.05$, Newman-Keuls). The three conditions in which water was given for either 1 or 15 hr following 7 hr of ethanol availability (Conditions II, III, and VI), did not differ statistically in terms of the total amount of liquid intake, although as can be seen in Fig. 1b, 15 hr of access to water did produce numerically greater total intake. Particularly interesting in this regard was the finding that the monkeys consumed approximately twice as much water in the one hour interval following 10% ethanol availability as they did in the same period following 5% ethanol availability (Condition VI vs Condition III, $p<0.001$, t-test). Also interesting was the result that continuous access to a 5% ethanol solution produced comparable levels of fluid intake to the two conditions in which water was given in addition to 7 hr of access to 5% ethanol.

A comparison of the 5% and 10% concentrations of ethanol that were used showed that the monkeys drank significantly less of the 10% solution under comparable conditions of availability (i.e., Conditions V vs VII and III vs VI, both $ps<0.01$, t-test). However, even though a lower overall intake of the 10% solution occurred, the amount of ethanol ingested was greater at the 10% concentration when continuous access to ethanol was provided (see above).

Although the amount of food the animals consumed during the different conditions (which might account in part for differences in liquid intake) was not measured, changes in body weight were not significantly different at the end of the experiment compared to the beginning (mean at end=669 g, mean at beginning=687 g), suggesting that food consumption was not particularly altered over the course of the experiment.

The results of this experiment are of practical importance since the goal of most studies concerned with oral ingestion is to maximize ethanol consumption while at the same time minimizing any secondary effects that might either risk the animals' health or limit interpretation of results. For example, although the greatest amount of ethanol was consumed by animals that were given continuous access to a 10% ethanol solution, the low level of total fluid intake that occurred at this concentration might have deleterious effects if administered on a chronic basis. Clearly, the advantages and disadvantages of using different concentrations of ethanol as well as the need for supplementary periods of access to water should be considered carefully in planning experiments involving ethanol ingestion.

EXPERIMENT 2

As a first step in investigating the effects of alcohol expo-

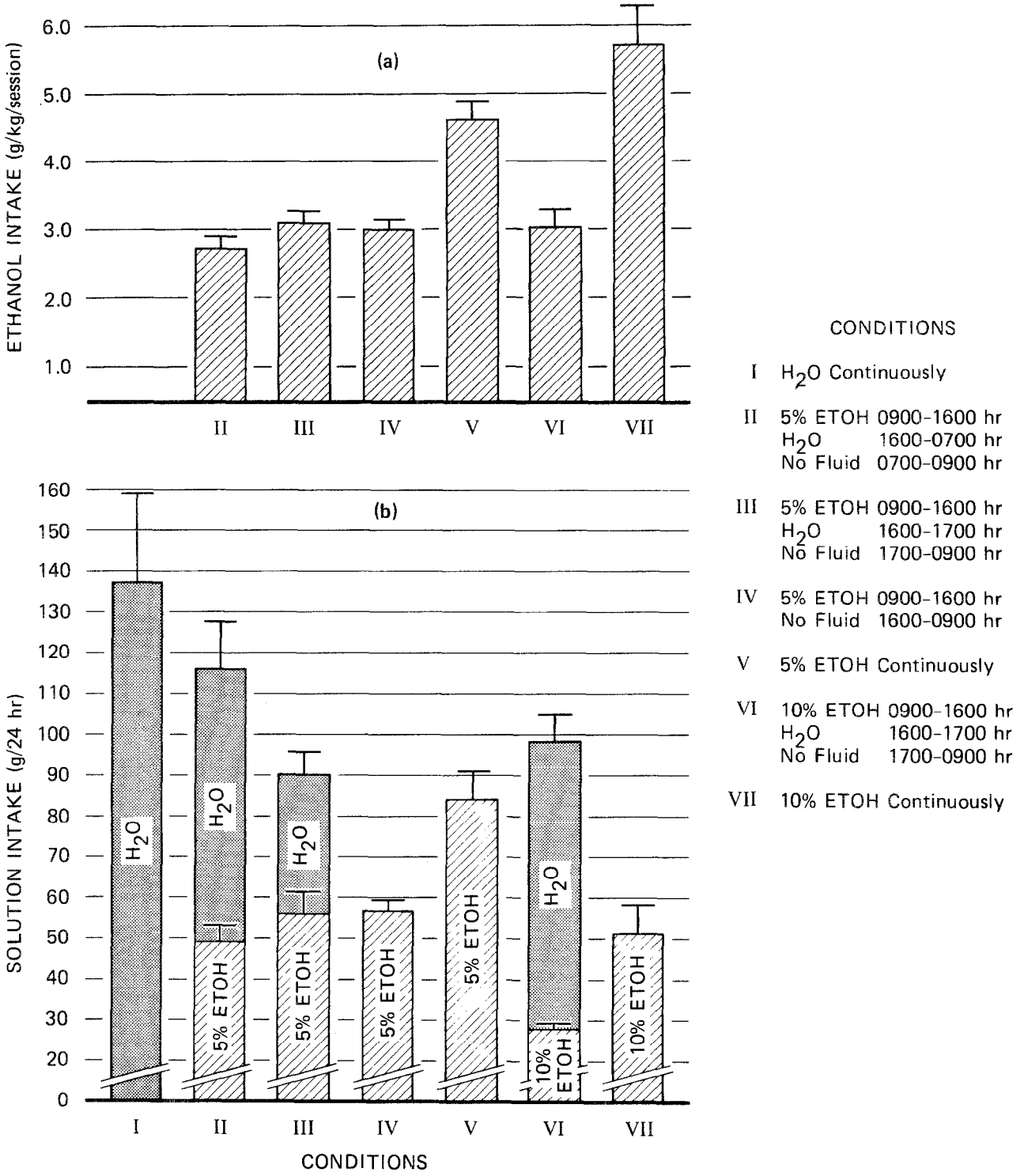

FIG. 1. Mean scores and standard errors for amount of ethanol consumed (a), and ingested amounts of 5% and 10% (w/v) ethanol solutions and water (b), under various schedules of ethanol and water availability.

sure *in utero* on pre and postnatal development, the present experiment was conducted to examine BALs that occur during ethanol ingestion in pregnant monkeys at various intervals following ethanol presentation.

METHOD

Subjects

Subjects were 20 adult wildborn female squirrel monkeys from our breeding colony, 13 of which were of the Colombian type and 7 of which were of the Bolivian type. All had lived in captivity for several years. None had participated in Experiment 1 and only a few had limited experience drinking ethanol prior to this experiment. Pregnancies were generally detected by the fourth week of gestation by a urine bioassay test that measured changes in mouse uterine weight [13], and ethanol administration began within the week following detection. The normal gestation period for the squirrel monkey is approximately 22 weeks [13].

Ethanol Administration and Blood Sampling

As pregnancies were detected monkeys were removed from their breeding pens and housed individually as in Experiment 1. Ethanol was administered at a concentration of 5% (w/v) and was mixed with the same fruit drinks used in Experiment 1. The ethanol-fruit-drink mixture was presented in bottles on a daily basis for 6 hr each day beginning at approximately 0900 hr. Water was continuously available during nonalcohol periods and food was always available.

Blood sampling began three weeks after the monkeys had been drinking ethanol on this schedule. Blood was collected from each monkey at 0, 2, 4 and 6 hr following ethanol presentation. Samples were obtained on two days, separated by a 14–18 day interval, during which the monkeys continued to receive ethanol in the usual manner. For half of the monkeys, blood was collected at 0 and 4 hr following ethanol presentation on the first sampling day, and at 2 and 6 hr following ethanol presentation on the second day. For the remaining monkeys this order was reversed. Each animal's bottle was weighed at the beginning and end of each 6 hr session to determine the amount of ethanol solution it had consumed.

Blood was obtained from the thigh by making a small, x-shaped incision with a scalpel blade and withdrawing 50–100 μl in a heparinized microhematocrit capillary tube. Blood flow was induced by massaging the area just before and after the incision was made. In most cases, the second sample collected on the same day was obtained by simply removing the scab that had formed over the initial incision.

Blood Alcohol Analysis

Analyses were performed by gas-liquid chromatography. Immediately following blood collection, the blood was centrifuged for 10 min in an IEC model B microcapillary centrifuge. Duplicate injections of one to two μl of serum were made on a 4 mm ID by 1.8 m glass column packed with Porapak Q, in a Hewlett Packard 5750B gas chromatograph. The temperatures of the injection port, column, and flame ionization detector were 170°C, 200°C, and 260°C, respectively. Helium was used as the carrier gas, at a flow rate of 20 ml/min. The minimum detectable amount of ethanol (retention time 2 min) was about 10 ng, corresponding to less than 1 mg% blood alcohol under these assay conditions. Serum proteins would occasionally clog the needle of the injection syringe, which was cleaned by burning out the residue. The alcohol content of serum was calculated by peak height vs standards of 95% ethanol in water. The relative deviation of the duplicate serum injections from their mean was 4 to 5%.

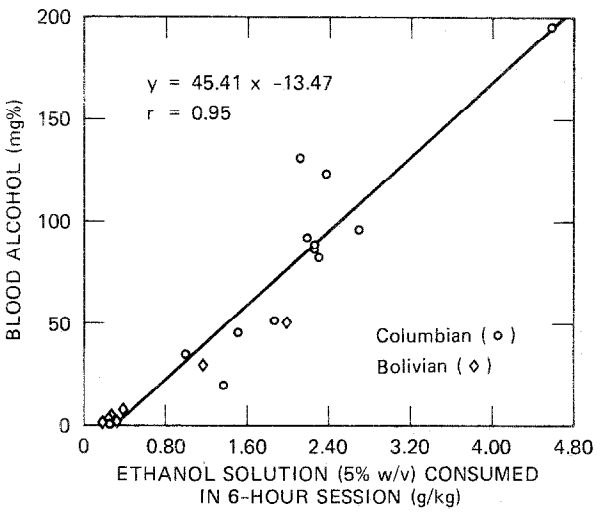

FIG. 2. Linear regression showing the estimated relationship of ethanol ingestion to blood alcohol level (BAL) in two subtypes of squirrel monkey. Each point represents the highest BAL obtained on each monkey over two sessions in which blood was collected, and the amount of ethanol solution consumed in that session. In one session blood was collected at 0 and 4 and in the other session at 2 and 6 hr following ethanol presentation.

Results and Discussion

There was a large amount of individual variation in the amount of ethanol consumed during the 6-hr period ethanol was available. BALs at the various intervals following ethanol presentation revealed a wide variation in the time course of drinking. Mean levels at the 2, 4 and 6 hr time points were similar, as shown by ANOVA, averaging approximately 60 mg%. Virtually no ethanol was found in the blood at the 0 hr time point, indicating that practically all of the ethanol had been eliminated since the end of the previous day's consumption. Maximum BALs for individual animals ranged from 1 to 196 mg%, reflecting the variation in the time course and amount of ethanol consumed.

In order to obtain an estimate of the relationship between ethanol consumption and BAL, the highest individual BAL obtained for each monkey was correlated with the amount of ethanol solution consumed in the session in which that BAL was obtained. A significant correlation was obtained on these data ($r=.95$, Pearson product-moment coefficient, $p<0.001$), showing that animals that drank more ethanol solution had clearly higher BALs (Fig. 2). It was also found that Colombian animals drank significantly more ethanol than Bolivian animals ($p<0.01$, t-test).

Taken together, these data are of interest in several respects. First, they show that pregnant squirrel monkeys will drink a 5% ethanol solution to about the same extent as nonpregnant animals (i.e., those used in Experiment 1) even without any fluid deprivation, and that the resulting concentrations of blood alcohol can reach levels which have been

found to produce fetal abnormalities both in man and certain nonprimate species [14]. Second, the results suggest that monkeys of Colombian origin would be better subjects than those of Bolivian origin for oral ingestion studies because of their apparent greater acceptance of ethanol. Third, because of the clear linear relationship between BAL and the amount of ethanol solution consumed, fairly accurate estimates of BAL can be made on the basis of intake values.

One caveat suggested by this experiment for future studies of fetal effects concerns the variable ingestion levels of ethanol which occurred among different monkeys. The amount of solution consumed in a 6-hr session ranged from 4 to 77 g and 0 to 34 g for Colombian and Bolivian animals, respectively, although individual monkeys were very consistent from day to day in the amounts of ethanol solution they consumed. Because of such inter-animal variability, investigators of fetal effects would do well to consider the correlation of ingestion levels and/or BALs with the degree of obtained deficits.

EXPERIMENT 3

This experiment was conducted to assess the effect of specific doses of ethanol on BALs and the change in BALs over time, and to examine the relationship between BALs and behavior. Due to the difficulty of specifying doses with an oral ingestion procedure, such as that used in Experiments 1 and 2, ethanol was given by means of oral intubation.

METHOD

Subjects

Subjects were 49 adult nonpregnant female monkeys from our colony (25 Colombian, 24 Bolivian), 9 of which had participated in Experiment 2 approximately six months earlier. The remaining animals had not been exposed to ethanol prior to this experiment. All of the animals had lived in captivity for several years. The animals were divided into four groups balanced by subtype, each of which received a different dose of ethanol.

Ethanol Administration and Blood Collection

Monkeys were housed individually as in the first two experiments. Ethanol, at a concentration of 20% (w/v) mixed with orange-flavored Tang, was administered to the monkeys by means of oral intubation using an 18 ga×15 cm curved stainless-steel intubation tube on a 10 ml syringe. Monkeys received a single dose of ethanol at 0.5, 1.0, 1.5 or 2.0 g/kg body weight at 0900 hr. Blood was collected using the procedures employed in Experiment 2, at 1, 2, 4 and 6 hr following intubation. Food was removed from the monkeys' cages shortly before ethanol administration and was withheld for the subsequent 6 hr period; water remained available continuously. Each test session consisted of testing approximately one animal of each of the two subtypes at each dose level.

Behavior

Behavioral observations were made on each animal from behind 1-way glass immediately preceding the collection of a blood sample. At the onset of each of four 30-sec periods, spaced at 120-sec intervals, the monkey's location in its cage was noted. During the 30-sec periods, the frequencies of vocalization, movement between the left and right halves of the cage, and manipulation of objects (e.g., food container, water bottle) were recorded. Ratings were also made of each animal's state of alertness and coordination. At the beginning of each 30-sec period, alertness was measured by recording whether an animal appeared alert, resting (motionless and inattentive to environment), or unconscious. Coordination was measured at the end of the observation session and consisted of rating the animal's responses to being handed a preferred food (marshmallow) on a scale of 1 to 4 (1=coordinated, rapid response; 2=appearing somewhat slow in responding or slightly unbalanced; 3=definitely slow in responding or very unbalanced; 4=no response).

RESULTS AND DISCUSSION

A number of the monkeys regurgitated shortly after receiving ethanol and the number increased with increasing dosage. Consequently, only those animals that did not regurgitate were included in the analysis of BAL at different doses. However, all of the animals were used for comparing behavior with BALs since the actual dosage of ethanol delivered was not of concern in these calculations.

Changes in BALs over time were evaluated for five Bolivian and four Colombian animals at both the 0.5 and 1.0 g/kg doses, and two Colombian animals and one Bolivian animal at the 1.5 and 2.0 g/kg doses, respectively. An ANOVA comparing BALs for the two subtypes showed that they did not differ with respect to changes over time at either the 0.5 or 1.0 g/kg dose, and therefore more complete analyses of BALs were performed irrespective of subtype.

BALs were lincarly related to dose, indicating accurate dosing and reproducible absorption. Maximum levels were obtained at 1 hr following intubation and were 37, 92, 181 and 225 mg% for the 0.5, 1.0, 1.5 and 2.0 g/kg doses, respectively. Figure 3 illustrates BAL vs dose at 1 and 2 hours after the administration of ethanol, where most of the levels were still high enough to be in the quasi-linear portion of the elimination curve (i.e., above about 50 mg%, see below). The Y intercept of these lines corresponds to the amount of alcohol eliminated and unabsorbed in the 1 or 2 hr before blood samples were taken. The mean absolute mg%/hr ($^{35}/_{1} + {}^{60}/_{2}$ = 32.5 mg%/hr) is about the same as the alcohol elimination rate calculated from the means of the rate of decline of BAL in each monkey.

The alcohol elimination curves shown in Fig. 4 are fitted under the simplifying assumption of linear (zero-order) elimination above 50 mg%. The mean slope of the elimination lines of all animals (at BALs above 50 mg%) was 35±3 (SE; n=9) mg%/hr, representing the approximate rate of alcohol elimination. The mean slope of points between 50 mg% and the lower limit of assay sensitivity was calculated to be 23±2 (SE) mg%/hr and differed significantly from the slope at levels above 50 mg% ($p<0.05$, t-test). Elimination rates in individual monkeys varied from 22 to 46 mg%/hr at BALs above 50 mg%. The mean rate of elimination was as rapid from 1 to 2 hr as from 2 to 4 hr (at levels above 50 mg%), indicating that alcohol was essentially completely absorbed within the first hour.

Using the extrapolation back to 0 hr (T_0) of the elimination data for BALs above 50 mg% (Fig. 4), the volume of distribution (V_D) was obtained for each monkey where V_D = Dose ÷ BAL at T_0. The mean V_D of alcohol in these monkeys was 71.5±4.4% (SE) of body mass, which is consistent with the known distribution of alcohol with total body water.

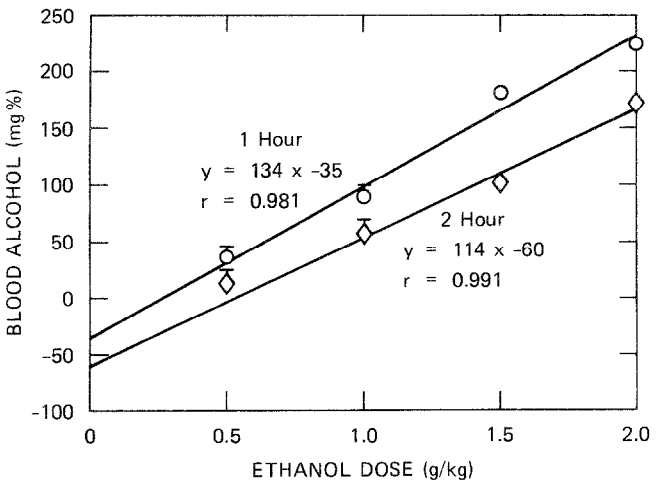

FIG. 3. Dose vs BALs at 1 and 2 hr after oral intubation of 20% (w/v) ethanol solution. From the low to the high dose, n=9, 9, 2, 1. Linear regression lines and formulas are given. The points for 0.5 g/kg were excluded from the linear regression calculation since these were below 50 mg% (see text). Standard error scores are provided only for points where n>2.

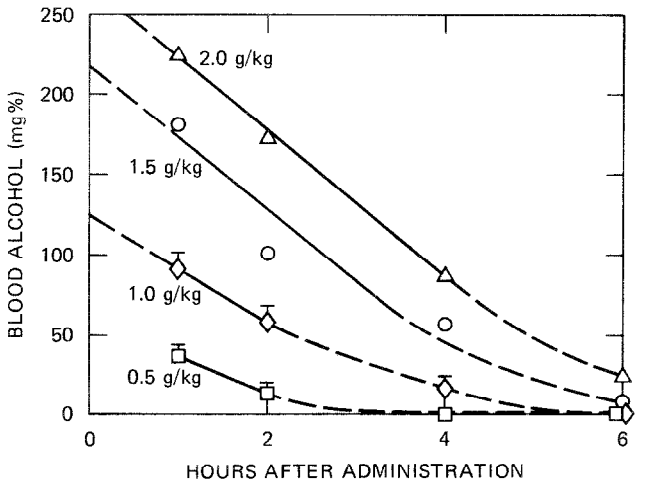

FIG. 4. BALs after oral intubation of various doses of 20% (w/v) ethanol; 0.5 g/kg, n=9; 1.0 g/kg, n=9; 1.5 g/kg, n=2; 2.0 g/kg, n=1. The lines are arbitrarily drawn to correspond to assumptions of linear elimination of alcohol above 50 mg%, and a decreasing rate thereafter. Extrapolation of linear elimination lines back to 0 hours allows calculation of alcohol distribution volume (see text). Standard error scores are provided only for points where n>2.

The total body clearance rate for alcohol is the rate of elimination from blood × V_D × body weight, or 0.35 mg/ml/hr × 0.715 × 666 g (mean weight of monkeys) = 167 mg/monkey/hr = 250 mg/kg/hr.

No differences were observed between the two subtypes in their behavioral reactions following ethanol administration. For monkeys of both subtypes, increased BALs were significantly associated with a lack of coordination (r=.67, $p<0.001$; Fig. 5). None of the other behavioral measures were found to be significantly associated with BALs. Thus, it appears that alcohol in the range of BALs observed here does not affect these other behaviors, at least not to the extent that effects can be observed in such relatively brief observation periods.

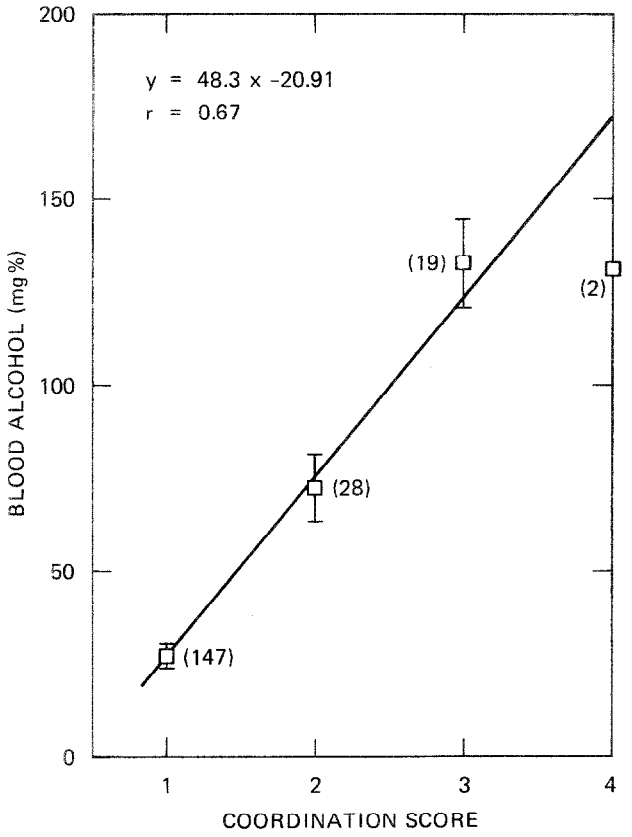

FIG. 5. Relationship of BAL to physical coordination. Each subject was rated on its coordination in reaching for a miniature marshmallow immediately before blood was collected at 1, 2, 4 and 6 hr following oral intubation of a 20% (w/v) ethanol solution. Scores of 1 to 4 represent decreasing degrees of coordination, and each point represents the mean BAL obtained at each rating. The number of times each rating was made is shown in parentheses. Standard error scores are provided only for points where n>2.

GENERAL DISCUSSION

The results of these experiments show that the squirrel monkey, like other primates, will drink ethanol at concentrations of 5 to 10%, and that the amount of ethanol consumed at such concentrations, along with resulting BALs, are a function of both concentration and the length of time ethanol is available. The greatest amount of ethanol consumed in the present study occurred at a concentration of 10% and when ethanol solution was available on a continuous basis. Continuous access to a 5% ethanol solution produced a significantly lower intake of ethanol, although the amount of total alcohol solution ingested was greater.

Access to ethanol for 7 hr daily produced significantly lower levels of ethanol ingestion than did continuous access. Moreover, different degrees of liquid deprivation before such limited periods of ethanol availability had a negligible effect on levels of ethanol intake.

These results suggest that experiments with squirrel monkeys involving oral ingestion of ethanol over a long period of time, and which require intake levels of at least 3 g/day (i.e., approximately 4.5 g/kg), would probably have the most success by using a 5% solution as the only source of liquid and providing it on a continuous basis. The relatively low volume of fluid consumed at a concentration of 10% would likely produce severe dehydration and a concomitant reduction in food consumption if ethanol were the only liquid available to drink. Whether long-term administration of 5% ethanol as the only available liquid would eventually produce a state of poor health (since total volume consumed is approximately 60% of daily water intake) cannot be answered by the present study. All of the animals appeared healthy and lost minimal amounts of weight during the 6-day drinking periods that were imposed in Experiment 1. On the basis of the results obtained in Experiments 2 and 3, it would be expected that monkeys which consumed an average of about 3 g/day of ethanol (which would occur with continuous access to a 5% ethanol solution in Colombian monkeys) would achieve BALs of over 150 mg% at some point in the day. This level would be sufficient to affect behavior and may produce other deleterious effects, such as fetal anomalies when administered during pregnancy [14].

The total body clearance rate for alcohol which we have calculated for female squirrel monkeys to be approximately 250 mg/kg/hr, is in line with that of other species, considering the small body mass of these monkeys [9,15]. Wallgren and Barry [15] have summarized clearance data for several species, reporting, for instance, rates of 100 mg/kg/hr in man, 130 in dogs, 300 in rats, and 550 in mice. Pieper and Skeen [11] have reported ethanol clearance rates of 160 and 220 mg/kg/hr in rhesus monkeys and young chimpanzees, respectively.

Alcohol elimination rate has been traditionally claimed to be linear (zero order) at high doses, due to saturation of metabolic enzymes, and asymptotic (first order) at low levels, about 9 to 23 mg% in non-primate species [5,15]. More recent data indicate elimination processes may be somewhat more complex [11,12]. Salaspuro and Lieber [12], for example, found two apparently linear phases, with a break at around 50 mg% in baboons; the rate above 50 mg% appeared to be increased by chronic alcohol consumption. The squirrel monkeys in the present study had much less prior alcohol exposure than the baboons of Salaspuro and Lieber, so that an increase in metabolism at high levels seems unlikely. However, the blood sampling in our study was not frequent enough to distinguish between two linear elimination phases, vs a high-level, zero-order plus low-level, first-order process, although a decrease in rate at levels below about 50 mg% is evident.

Although no differences were found in the present study either in metabolism or the behavioral effects of ethanol for the two subtypes of squirrel monkeys that were used, animals of the Colombian type drank substantially more ethanol than animals of the Bolivian type. The reason for this difference is not apparent, but investigators planning to use oral ingestion procedures with squirrel monkeys should take these results into consideration in designing their experiments.

ACKNOWLEDGEMENTS

This research was supported by NIH Grant No. AA03827 awarded by the National Institute on Alcohol Abuse and Alcoholism. We wish to thank Kathy Hagen and Thomas Steeger for their technical assistance throughout all of the experiments.

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