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Consumption of Intoxicating Beverages by Rats and Mice Exhibiting High and Low Preferences for Ethanol

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YORK, J. L. *Consumption of intoxicating beverages by rats and mice exhibiting high and low preferences for ethanol.* PHARMAC. BIOCHEM. BEHAV. 15(2) 207–214, 1981.—Lines of rats selectively bred for alcohol consumption or avoidance (AA and ANA, ALKO, Finland) as well as inbred strains of mice (C57BL/6J and DBA/2J) and common female Wistar rats (Charles River) exhibiting high and low preferences for ethanol were tested under free-choice conditions for their consumption of solutions of ethanol (5, 10, or 15 g/100 ml tap water), sodium pentobarbital (0.19, 0.038, 0.076 g/100 ml tap water), and different beverages containing ethanol in the range of 8.1–9.6% (red and white wine, Scotch, ethanol in Hawaiian Punch). The Wistar rats and the mice classified as alcohol-preferring also tended to consume more of the pentobarbital solution than did alcohol-avoiding animals. Alcohol-nonaccepting (ANA) rats, however, consumed considerably more of all three pentobarbital solutions than did the alcohol-accepting (AA) rats. The intake of pentobarbital by the ANA rats and C57/BL/6J mice was in the range of 25–40 mg/kg/day, quantities that might be expected to produce pharmacological effects discriminable by those animals. The intake of ethanol by ANA rats was markedly elevated when the ethanol was contained in white wine or in punch.

Ethanol Pentobarbital Preference Rats Mice

THE factors that influence the kind and amount of alcoholic beverages consumed by people are considered to be complex and poorly understood [4,23]. The decision to consume or not to consume alcoholic beverages on any particular occasion may be influenced by a combination of biological, psychological, sociocultural, or situational factors [23]. Moreover, the availability of the preferred beverage may also determine whether or not amounts of ethanol sufficient to produce pharmacological effects are ingested.

Owing to the difficulties and limitations associated with the experimental study of the factors that influence alcohol consumption in man, methods have been sought for studying in the laboratory the factors that influence the consumption of alcoholic beverages by experimental animals. These studies are, unfortunately, limited by the questionable generality of the findings to the complex interplay of factors that influence alcohol consumption in man. An enduring problem has centered around the issue of whether or not laboratory animals that display high and low preferences for drinking solutions of ethanol are motivated by factors that bear a resemblance to those believed to operate in certain people displaying high and low preferences for ethanol. People are popularly believed (with some notable exceptions) to consume or avoid alcoholic beverages primarily because of a desire or aversion for the pharmacological effects produced by ethanol. However, it is not uncommon for individuals to develop specific preferences for particular types of alcohol beverages (e.g., beer, wine, or even a specific brand of distilled spirits). The availability of the favored drink may influence considerably the amount of ethanol consumed. The taste of the beverage is generally acknowledged as the primary factor determining choice of beverage, although the possibility that the onset and intensity of pharmacological effect obtained or the extent of hangover may also influence the choice of beverage is a relatively unexplored issue.

Particularly promising tools for researchers interested in studying the biological bases of alcohol preferences and aversions have been represented by strains of rats [11, 12, 21] and mice [24,25] in which inherited factors appear to play a primary role in alcohol selection or avoidance. The contribution of studies on these animals to the understanding of alcohol drinking behavior in man has yet to be convincingly argued. For instance, the role that taste versus desire for pharmacological effects plays in the oral self-selection of solutions of drugs has not been established. Moreover, the factors that limit ethanol intake in low-preferring strains are still only poorly understood. Some studies suggest that orosensory factors may play an important role [2, 26, 38]. Another proposed basis for the low self-selection of ethanol in alcohol-avoiding strains—the development of a taste aversion owing to untoward depressant effects of ethanol or rapid accumulation of toxic levels of acetaldehyde [8, 10, 20, 27, 28, 32–34]—has also been suggested to be a factor in governing drinking behavior in man [14,35].

The present study was designed to shed light on the following issues: if the pharmacological effects of ethanol are

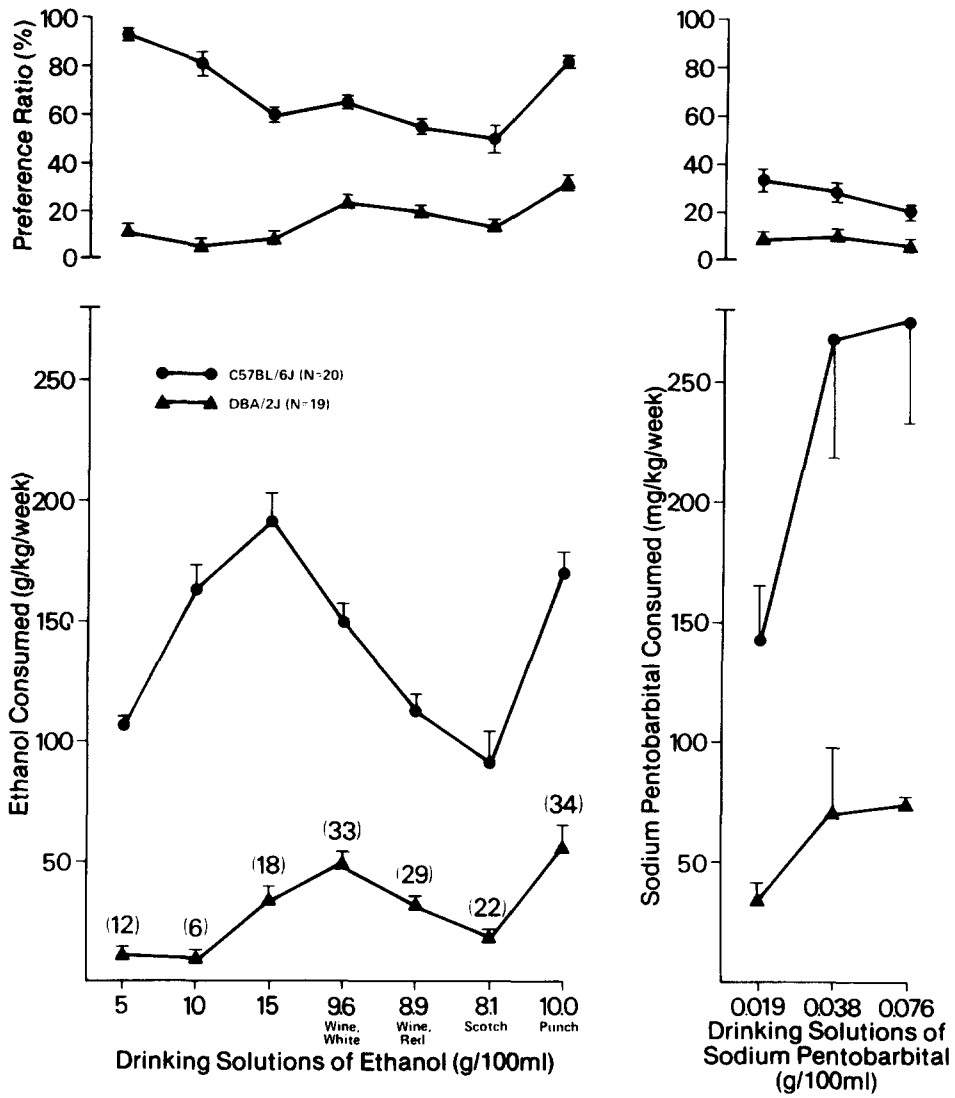

FIG. 1. Consumption of intoxicating beverages by selectively bred mice (Jackson Labs) exhibiting high (C57BL/6J) and low (DBA/2J) preferences for ethanol. Intoxicating beverages of various types (see abscissa) were presented to the animals under free-choice conditions with tap water available. The lower portion of the graph indicates grams (g, ethanol) or milligrams (mg, sodium pentobarbital) of drug consumed per kilogram of body weight (ordinate) for one-week test periods. The ratio (%) of ethanol consumed by DBA/2J mice to the quantity consumed by C57BL/6J mice is indicated in parentheses above the values for DBA/2J animals. The Preference Ratio (upper ordinate) indicates the percent of total fluid (drug + water) derived from the bottles containing drug. Brackets indicate the negative or positive component of one standard error of the mean.

aversive for those animals displaying low preferences for ethanol, then increasing the palatability of the solution by presenting different kinds of alcoholic beverages, some containing sugar, should not markedly influence their drug consumption; furthermore, if the desire or aversion for pharmacological effects is a primary factor, animals displaying innate preferences or aversions for ethanol should display similar preferences or aversions for other sedative agents that produce pharmacological effects similar to those produced by ethanol (e.g., sodium pentobarbital), providing the taste of the solutions is not a predominant factor.

METHOD

Subjects

Lines of rats selectively bred for alcohol consumption and avoidance (AA and ANA, respectively, N=8–10 each, State Alcohol Monopoly, Finland) and inbred strains of mice (C57BL/6J and DBA/2J, N=20 and 19 each, Jackson Labs, Bar Harbor, ME) known to display high and low preferences, respectively, for drinking ethanol solutions were utilized. In addition, a group of 100 common, presumably genetically heterogeneous Wistar rats (Carworth Division of

Charles River, Wilmington, MA) were given ethanol-preference tests (10% w/v versus tap water for 7 days), and animals displaying high (N=6), middle (N=9), and low (N=6) preferences for ethanol were selected for further testing. All animals were female (5–11 months of age), were housed individually in clear polycarbonate cages (23 cm h × 25 cm w × 46 cm l for rats and 13 cm h × 18 cm w × 28 cm l for mice), and were allowed continuous access to Teklad 4% Rat and Mouse Diet.

Procedure

Preferences for drinking solutions were measured using a two-bottle, free-choice procedure in which one bottle containing normal tap water and a second bottle containing a solution for ethanol or pentobarbital were simultaneously presented to animals for 7-day periods. During the middle of the test period, positions of the bottles were switched to balance for position preferences. Bottles (1 pt) used for the rat preference tests were obtained from the Atco Corporation (Napa, CA) and were fitted with leak-resistant ball-point drinking tubes. For the mice, common mouse watering cylinders (100 ml) fitted with leak-resistant drinking tubes were used. The amount of fluid consumed over the 7-day period was determined by weighing the bottles before and after the 7-day test, and the amount of drug consumed per week in terms of grams of drug per kilogram of animal weight was then calculated on the basis of the density of the solution and the concentration of drug in solution. Preference Ratios (see figures) indicate the amount of fluid consumed from the drug bottle as a percent of the total fluid (drug bottle + water bottle) consumed over the 7-day test periods.

Test beverages containing ethanol were selected on the basis of expected differences in their palatability. Drugs employed were ethanol (99%, U.S. Industrial Chemicals Co., Tuscola, IL) mixed with tap water to make solutions of 5, 10, or 15% w/v or mixed with Hawaiian Punch (Very Berry, 11% sugar) to make a solution of 10% w/v; sodium pentobarbital (New England Nuclear, Boston, MA) dissolved in tap water to make a solution of 0.019, 0.038, or 0.076% w/v; Scotch (Chivas Regal) diluted with tap water to make a solution of 8.1% w/v ethanol; Carlo Rossi Rhine Wine (8.9% w/v, 3% sugar); Carlo Rossi Vin Rosé (8.9% w/v, 2.5% sugar); Carlo Rossi Burgandy (9.6% w/v, 1–2% sugar); and Reserve California Chablis (9.6% w/v, 1–2% sugar). The concentrations of drugs in solutions were verified by gas chromatographic analysis, when necessary. The percent reducing sugar concentration (g/100 ml) was estimated using Clinitest Reagent Tablets (Ames Company, Division of Miles Laboratories, Elkhart, IN), as sweetness is an important factor in determining palatability of drinking solutions. Concentrations of pentobarbital solutions were chosen on the basis of that drug possessing a potency nearly 100 times greater than that of ethanol in behavioral tests.

Each animal was tested with all of the solutions indicated for a particular group, generally in the order indicated in the illustrations. Order-of-presentation effects are confounded with treatment effects in this design, but were not believed to be critical in these measures, particularly inasmuch as several weeks were allowed to elapse between tests with pentobarbital and beverages containing ethanol. Statistical analyses were carried out by computer with the aid of a two-way analysis of variance for repeated measures programs (BMDP) developed by the University of California, Los Angeles. Only the data pertaining to the amount of ethanol consumed with reference to the body weights of subjects was analyzed for statistical significance.

RESULTS

For the selected lines of mice, both main effects were significant with regard to drinking solutions of ethanol (Fig. 1). As expected, C57BL/6J mice consumed more of all alcoholic beverages than did DBA/2J mice, $F(1,36)=563.27$; $p<0.0001$. The main effect of treatment (different solutions of ethanol) was also significant, $F(6,216)=27.49$; $p<0.0001$, and the group × treatment interaction was highly significant, $F(6,216=14.3$; $p<0.0001$, indicating that the effect of treatments on ethanol consumption was different for C57BL/6J and DBA/2J animals.

For C57BL/6J mice, the consumption of ethanol (g/kg/week) increased as the concentrations of ethanol in tap water was increased from 5 to 15% w/v (Fig. 1), a finding also reported by others [30,38]. In the case of the 10 and 15% w/v solutions, the intake of ethanol approached the estimated maximal metabolic rate for C57BL/6J mice (approximately 140 g/kg/week) [28]. About 80% of the total fluid requirements were obtained from the ethanol bottle in the case of the 10% ethanol preference test (Fig. 1, Preference Ratio). The presentation of different alcoholic beverages (white wine, red wine, ethanol in Hawaiian Punch) as well as 15% w/v ethanol increased the consumption of ethanol by DBA/2J mice as compared to their consumption of ethanol derived from 10% w/v ethanol in tap water. The C57BL/6J animals displayed decreases in ethanol consumption when red wine and Scotch were offered. Their consumption of ethanol derived from punch and white wine was very similar to their consumption of ethanol derived from 10% w/v ethanol in tap water. The ratio of the ethanol consumption (g/kg/week) for DBA/2J mice as compared to C57BL/6J mice (see Fig. 1, values in parentheses) was always greater when the drug was contained in some solution other than tap water (cf., 10% w/v ethanol).

For the same mice, further testing revealed that their preferences for drinking solutions of sodium pentobarbital paralleled their preferences for drinking ethanol solutions (Fig. 1), i.e., animals with high preferences for drinking ethanol solutions (C57BL/6J) displayed the highest preferences for drinking solutions of sodium pentobarbital, $F(1,36)=38.16$; $p<0.0001$, as compared to DBA/2J mice. Quantities of pentobarbital consumed by C57BL/6J animals ranged from approximately 20 mg/kg/day (0.019%) to approximately 40 mg/kg/day (0.076%). The main effect of varying the concentration of pentobarbital was significant across groups, $F(2,72)=4.84$; $p<0.01$. There was no significant interaction, $F(2,72)=1.62$; $p<0.2$. Thus, varying the concentrations of pentobarbital did not differentially affect drug consumption in C57BL/6J versus DBA/2J mice. Preference Ratios (Fig. 1) for pentobarbital solutions were low, probably owing to the considerable amount of drug and drug effect obtained from small quantities of solution.

Rats displaying low preferences for ethanol (ANA, Fig. 2) were found to increase markedly their ethanol consumption when presented with white wine or a solution of ethanol (10% w/v) in punch. The intake of ethanol from those solutions by ANA rats actually slightly surpassed the intake of ethanol by rats classified as alcohol-preferring (AA). Both groups (AA and ANA) derived from white wine and punch quantities of ethanol that approached their estimated capacity to metabolize that drug. When preferences were deter-

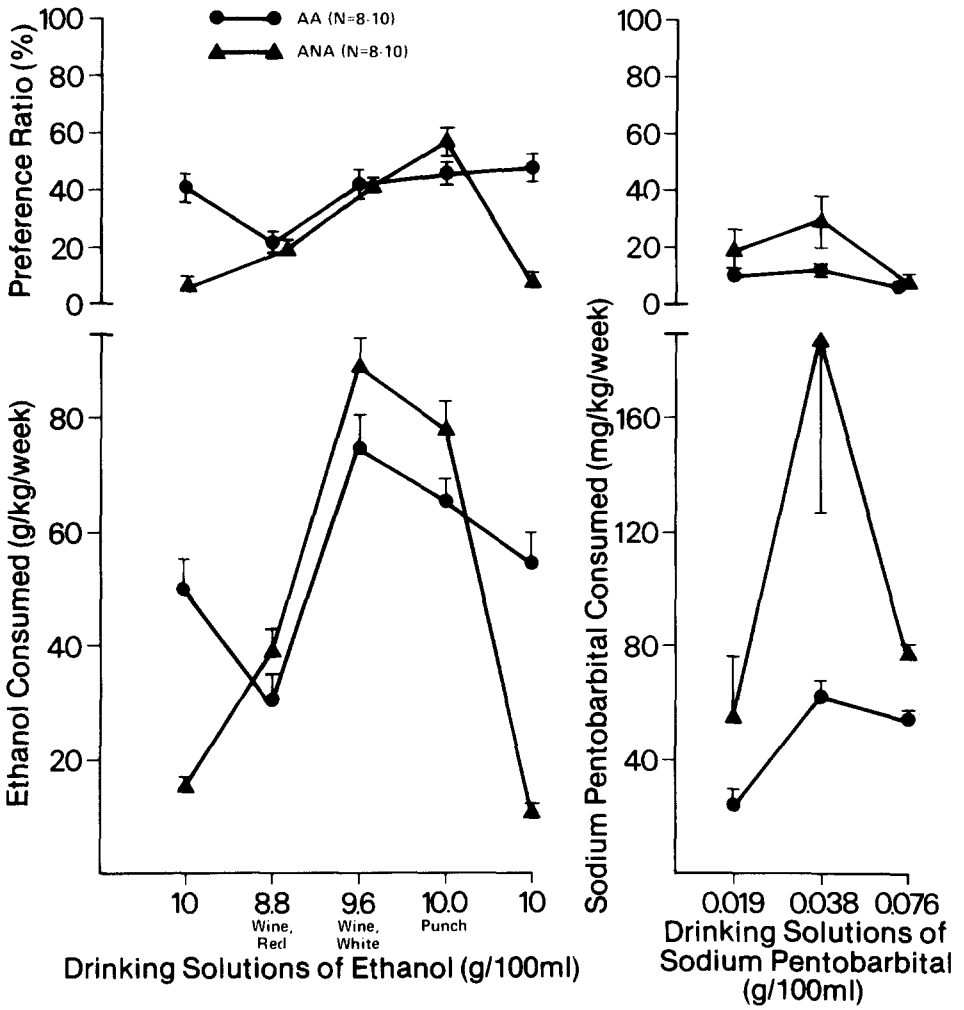

FIG. 2. Consumption of intoxicating beverages by selectively bred (Alko, Finland) alcohol-accepting (AA) and alcohol-nonaccepting (ANA) rats. Ordinate and abscissa as in Fig. 1.

mined by presenting 10% w/v ethanol in tap water, the intake of ethanol was in keeping with the traditional classifications for those animals. In contrast to C57BL/6J mice, AA rats obtained only about 40% of their fluid requirements from the bottle containing 10% ethanol (see Preference Ratios). The intake by ANA rats of sodium pentobarbital also surpassed the intake of that drug by AA rats for all three drinking solutions offered—with the greatest intakes (approximately 27 mg/kg/day) of drug occurring with the 0.038% solution of sodium pentobarbital, $F(1,15)=4.36$; $p<0.05$. The main effect of treatment (differing pentobarbital solutions) was also significant, $F(2,30)=6.11$; $p<0.005$. There was no significant group-by-treatment interaction.

Alcohol-preferring and alcohol-nonpreferring rats selected from a group of common Wistar rats displayed ethanol intakes similar to values observed in previous studies [41] and also roughly similar to those displayed by the Finnish rats (Fig. 3). The intake of sodium pentobarbital by those animals closely paralleled their ethanol preferences, with the greatest differences between groups observed at the 0.038% solutions and very little difference between groups with the 0.076% solution. Interestingly, even though the Wistar rats displayed slightly lower intakes of ethanol than did the AA rats, their preference ratios (cf., 10% w/v ethanol, Fig. 2) are much higher, owing to the generally lower total weekly fluid consumption by those animals (Table 1) as compared to the Finnish rats.

Table 1 summarizes the experimental design and presents important data not always reported in experiments on preference testing. The mean weight for each group of animals for each preference test is reported and indicates the general health status of the animals. In most cases, systematic changes in weights observed in succeeding preference tests indicate aging of the animals. The total volume of fluid consumed for each test period is reported and, when used in combination with the preference ratios, can be used to estimate the mean volume of fluid consumed from drug and water bottles. Thus, comparisons can be made with other studies in which volume of fluid is reported as the main dependent variable [30, 37, 39]. Furthermore, consistency in

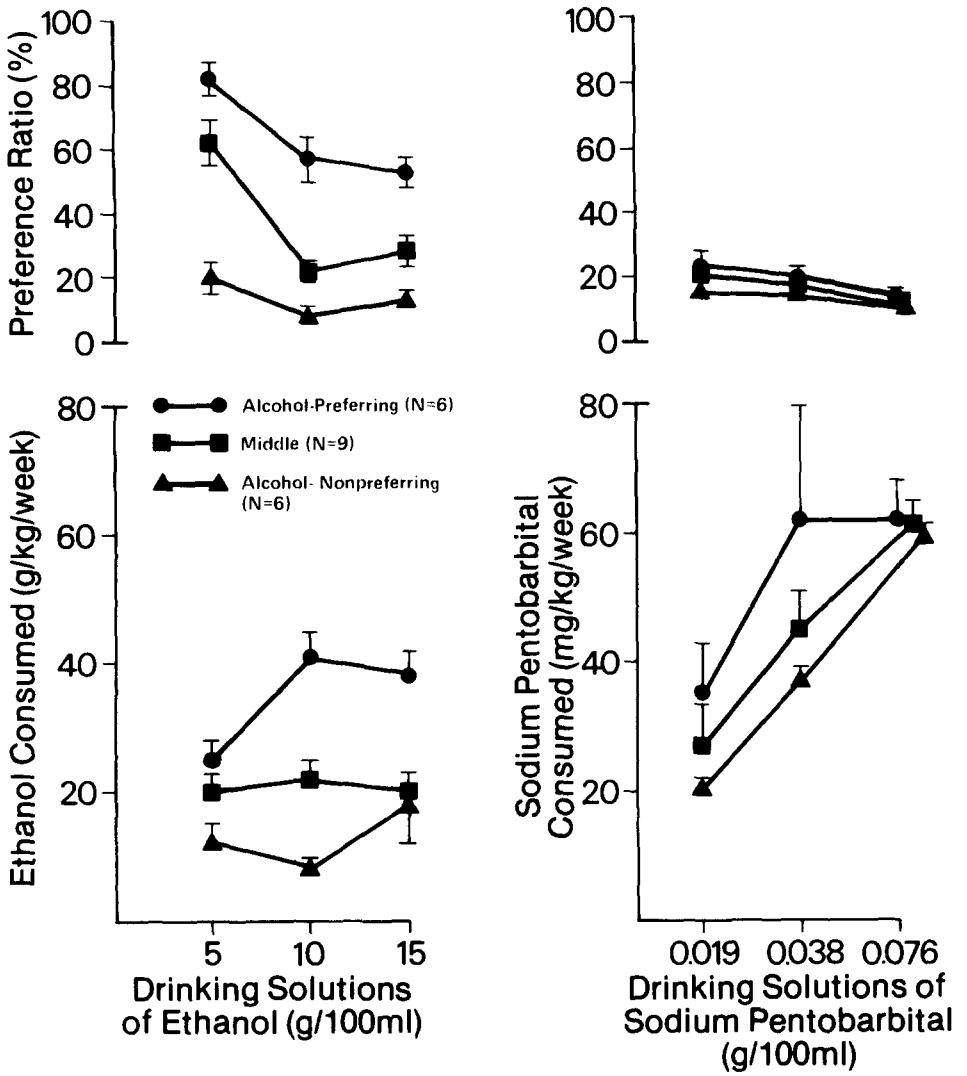

FIG. 3. Consumption of intoxicating beverages by commercially supplied Wistar rats (Charles River). Animals were classified as alcohol-preferring, middle, or alcohol-nonpreferring on the basis of prior preference tests with 10% w/v ethanol solutions. Ordinate and abscissa as in Fig. 1.

the fluid consumption data minimizes the fear the extraneous factors, such as excessive undetected leakage, may have contributed to the observations.

DISCUSSION

The findings of the present experiment may shed light on the hypothesis that the pharmacological effects of ethanol are aversive to animals displaying low preferences for drinking solutions of ethanol in tap water. For instance, the distinction between "alcohol-preferring" mice and "alcohol-nonpreferring" mice was found to be less pronounced when alcoholic beverages in the form of wine or punch were offered as test solutions. The intake of ethanol by DBA/2J mice increased to nearly one-third the value for C57BL/6J animals when ethanol (10% w/v) was contained in punch, as compared to only 6% of the value for C57BL/6J mice when 10% ethanol in tap water was the test solution (see Fig. 1). Inasmuch as wine and punch contain 2–3% and 10% sugar, respectively, these findings are in harmony with the observation by Rodgers [29,30] that the intake of ethanol by C57BL/10J and DBA/2J mice can be increased by the addition of sucrose (16% w/v) in test beverages.

Of more interest, however, is the possibility that the amounts of ethanol derived by DBA/2J mice from test solutions of white wine and punch (7–8 g ethanol/kg body weight/day) produced pharmacological effects that were discriminable (yet, seemingly, not aversive) to those animals. Under free-choice conditions, such as those prevailing throughout the present experiment, fluid consumption is expected to be spaced throughout the 12-hour darkness cycle, with peak blood levels of ethanol achieved approximately midway through that period [9,16]. We have no direct evidence from gross observations of these animals that pharmacological effects were experienced at any time during the present study. However, it seems unlikely that the quantities of ethanol imbibed by DBA/2J mice in white wine and punch did not produce either direct pharmacological effects or ef-

TABLE 1

TOTAL WEEKLY FLUID CONSUMPTION (ml ± SEM) AND BODY WEIGHTS (g ± SEM, IN PARENTHESES)

	Water	Water + 5% Etoh	Water + 10% Etoh	Water + 15% Etoh	Water + Pentobarb (0.019%)	Water + Pentobarb (0.038%)	Water + Pentobarb (0.076%)	Water + Wine (White)	Water + Wine (Red)	Water + Scotch	Water + Punch
C57BL (N=20)	36.8 ± 0.9 (18.5 ± 0.23)	42.2 ± 1.7 (19.3 ± 0.27)	39.1 ± 2.4 (19.7 ± 0.30)	41.8 ± 1.6 (20.4 ± 0.33)	47.2 ± 3.1 (20.8 ± 0.30)	51.0 ± 3.2 (21.3 ± 0.25)	53.0 ± 3.6 (21.4 ± 0.26)	56.5 ± 4.8 (21.9 ± 0.27)	51.0 ± 1.6 (22.4 ± 0.28)	48.0 ± 3.0 (22.4 ± 0.27)	46.3 ± 2.2 (22.9 ± 0.28)
DBA/2J (N=19)	33.5 ± 1.2 (19.3 ± 0.37)	43.5 ± 1.4 (19.9 ± 0.35)	42.8 ± 1.5 (20.5 ± 0.35)	49.6 ± 1.4 (20.9 ± 0.36)	45.2 ± 1.5 (21.4 ± 0.36)	43.1 ± 1.7 (21.7 ± 0.36)	42.8 ± 1.9 (21.9 ± 0.41)	48.2 ± 2.2 (21.9 ± 0.27)	44.6 ± 2.5 (21.9 ± 0.27)	44.2 ± 2.0 (22.0 ± 0.30)	37.9 ± 2.6 (21.7 ± 0.47)
AA (N=8-10)	———	———	307.5 ± 12.0 (196.3 ± 2.1)	———	270.0 ± 10.9 (206.8 ± 2.3)	296.0 ± 11.0 (204.9 ± 2.1)	273.5 ± 10.5 (207.4 ± 2.2)	442.6 ± 14.2 (210.0 ± 6.1)	311.5 ± 10.8 217.6 ± 2.5)	———	288.6 ± 17.0 (210.0 ± 6.1)
ANA (N=8-10)	———	———	323.1 ± 12.4 (175.4 ± 3.0)	———	259.6 ± 7.2 (180.9 ± 3.0)	292.2 ± 9.7 (176.7 ± 3.4)	261.0 ± 9.5 (181.9 ± 3.0)	387.7 ± 11.9 (162.0 ± 4.1)	327.6 ± 16.1 (168.1 ± 3.2)	———	220.0 ± 15.7 (162.0 ± 4.1)
High Alcohol (N=6)	———	194.3 ± 18.8 (305.0 ± 7.2)	187.5 ± 12.2 (292.8 ± 6.3)	150.7 ± 10.0 (307.8 ± 7.7)	187.6 ± 17.2 (296.3 ± 6.4)	192.3 ± 8.5 (299.3 ± 6.6)	189.5 ± 9.5 301.5 ± 6.9)	———	———	———	———
Middle (N=9)	———	197.4 ± 8.3 (320.0 ± 5.8)	201.4 ± 10.5 (303.8 ± 5.3)	166.3 ± 5.3 (323.4 ± 5.9)	216.4 ± 9.6 (307.6 ± 5.3)	209.3 ± 9.9 (312.1 ± 4.9)	200.6 ± 8.0 (314.3 ± 5.4)	———	———	———	———
Low Alcohol (N=6)	———	176.2 ± 13.3 (316.0 ± 13.2)	198.8 ± 15.3 (299.2 ± 9.6)	165.4 ± 11.1 (318.6 ± 13.0)	207.0 ± 15.4 (303.6 ± 10.8)	195.2 ± 12.8 (308.4 ± 11.5)	192.8 ± 12.7 (311.6 ± 11.7)	———	———	———	———

fects due to the production of acetaldehyde, a substance believed to be aversive to DBA/2J mice and to be a factor limiting the consumption of ethanol in mice [32]. Blood ethanol levels in the neighborhood of 15 mg/100 ml have been reported to be discriminable by laboratory rats [40].

In ANA rats, the presentation of ethanol in white wine or punch dramatically increased their ethanol consumption to a level higher than that observed for AA rats. In fact, the intake of ethanol from punch and white wine approximated the estimated capacity of those animals to metabolize ethanol [8]. In those instances, even more so than with the DBA/2J mice, it seems highly unlikely that either direct or indirect pharmacological effects were not experienced by the strain classified as alcohol-nonpreferring. The reason why such animals were presumably willing to experience those effects as derived from wine or punch, but not from solutions of ethanol in tap water, must be related to the content of other substances contributing to the flavor or nutrient value of those beverages. However, the important point for the purpose of the present study is that any untoward pharmacological effects (possibly from acetaldehyde, although blood levels of this agent were not measured) were seemingly of minor importance as compared to other effects related perhaps to the taste or nutrient value of those beverages. Interestingly, white wine and punch were the two solutions containing the greatest concentrations of sugar (3% and 11%, respectively). These findings seem not to be in harmony with the report that AA and ANA rats maintain their high-preference and low-preference status when presented with ethanol solutions sweetened with saccharine [11], but do lend credence to the notion that a low threshold of aversion to solutions of ethanol in tap water may have been inadvertently bred into ANA rats [38]. Of course, sugar and saccharine are equivalent neither in taste nor nutrient value. The possibility must also be considered that other substances in white wine or punch may have masked the taste of ethanol for ANA rats in the present study.

The other hypothesis addressed in the present study concerns whether there is a general appreciation or aversion for an intoxication state by animals exhibiting high or low preferences for ethanol. If ethanol intake is governed primarily by a desire or aversion for the direct pharmacological effects of that drug, then similar patterns of drug intake should be observed in preference tests with drugs that produce effects similar to those produced by ethanol, providing some other aspect of the drug solution, such as taste or food value, does not have a predominant influence. Pentobarbital and ethanol produce similar effects in many respects: the acute intoxication states produced by the two drugs are almost indistinguishable [3, 6, 7, 17]; cross tolerance and dependence develop to a considerable extent between these two drugs [15,19], and the discriminative stimuli produced by the two classes of drugs are very similar under some conditions [1]. It might be expected, then, that animals that appreciate the pharmacological effects of ethanol would also appreciate the effects produced by pentobarbital. This expectation was, in fact, realized in the observations made on the mice (Fig. 1) and commercially supplied rats (Fig. 3). The C57BL/6J mice consumed quantities of pentobarbital in the neighborhood of 40 mg of drug per kg of body weight per day, quantities that would be expected to have pharmacological effects noticeable to those animals (40 mg/kg of sodium pentobarbital administered intraperitoneally produces hypnosis in rats and mice) even though the drug would have been consumed throughout the entire 12-hour darkness feeding cycle. Commercially supplied Wistar rats classified as alcohol-

preferring consumed in the neighborhood of 9 mg/kg of drug per day. That dose, if given orally in one administration, would produce effects probably only slightly noticeable to the animals.

An unexpected finding was that animals selectively bred for their low alcohol preferences (ANA) consumed more of all three pentobarbital solutions than did their alcohol-preferring counterparts (AA). Significant quantities of the drug were consumed by the ANA rats with the 0.038% solution (i.e., approximately 25 mg/kg per day). Surprisingly, AA rats did not consume amounts of pentobarbital likely to produce noticeable pharmacological effects. Thus, our observations of these animals do not support the notion of a general desire or aversion for depressant pharmacological effects in AA and ANA rats, respectively.

The findings reported here raise many questions that should be addressed in future studies. Blood levels of ethanol and pentobarbital should be measured for all test conditions for which animals are expected to experience pharmacological effects to determine if, in fact, those levels are high enough to produce effects discriminable to the animals. Those measurements should, ideally, be accompanied by an assessment of behavioral effects, perhaps motor impairment, also taken at a time when peak blood levels of drug are expected. Evidence regarding the strictly reinforcing properties of ethanol, pentobarbital, and other drugs in the absence of taste variables can be obtained by the use of intravenous or intragastric self-administration procedures, although difficulties have been reported in persuading common laboratory rats to self-administer ethanol intravenously (Dr. James R. Weeks, personal communication).

The role that innate sensitivity (responsiveness) to drug effects plays in the self-selection of those drugs under free-choice conditions remains unclear. The C57BL/6J mice have been reported to be less impaired by ethanol than are the DBA/2Js [20, 28, 33, 34], but are reported to be more impaired by pentobarbital than are DBA/2Js [28,36]. The accumulation of acetaldehyde in DBA/2J animals is also believed to be a factor limiting their intake of ethanol [32]. Pentobarbital is not known to produce a toxic metabolite, yet DBA/2Js still seemingly prefer not to imbibe pharmacologically active amounts of that drug. Thus, C57BL/6Js display a general desire, and DBA/2Js an aversion, for depressant drug effects. Their appetite for morphine solutions [13,37] and for propylene glycol [18,33] is consistent with this notion. Yet, those preferences seem not to be systematically related to innate responsiveness to the effects of those agents. Although AA rats have been reported to be less affected by ethanol than are ANA rats [27], we found no difference between the groups in a measure of motor impairment produced by ethanol [42]; yet, ANA animals were less affected by a range of doses of sodium pentobarbital in the same test. Using a different measure of motor impairment, Malila [22] has demonstrated that AA rats are less affected by barbital than are ANA animals. Thus, with regard also to AA and ANA animals, no definitive statement can be made at this time relating drug self-selection to the extent of impairment produced in those two subgroups.

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