ALCOHOL CONSUMPTION AND GUSTATORY HEDONIC PROFILES IN WISTAR-KYOTO HYPER- AND NORMOACTIVE RAT STRAINS

RAHARINORO RAZAFIMANALINA, PIERRE MORMÈDE and LYDIA VELLEY*

Génétique du Stress et Neurobiologie de l’Adaptation, INSERM-INRA, Institut François Magendie, Rue Camille Saint-Saëns, 33077 Bordeaux Cedex, France

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Abstract — The purpose of the present study was to compare the consummatory behaviour of rats of the Wistar-Kyoto Hyperactive (WKHA) strain, selected for their hyperactivity in a novel environment, with the normoactive Wistar-Kyoto (WKY) rats in three choice tasks: between water and increasing concentrations of saccharin, between water and increasing concentrations of quinine, and between water and a 10% (v/v) ethanol solution. The results of the present study show that: (1) WKHA rats exhibited a significantly higher acceptance of a 10% (v/v) alcohol solution than the normoactive control WKY rats when alcohol solution was the only available fluid; (2) WKHA rats also showed significantly larger alcohol intakes during the 15 days of choice between water and alcohol (WKY: 0.39 ± 0.05; WKHA: 1.72 ± 0.26 g/kg/day); (3) as frequently cited in the literature for other strains, the higher level of alcohol ingestion of WKHA rats was associated with a higher preference for saccharin; (4) no strain differences were observed in the water–quinine choice test. The discussion is mainly centred on the small alcohol consumption of the two strains, since the intake of WKHA rats is in the normal range for consumption of outbred strains, while the amount of alcohol consumption of WKY rats is very low and in the range of alcohol intake of non-preferring rat strains. It is concluded that the difference in alcohol consumption is mainly due to the low intake of the WKY rats and it is suggested that their different level of consumption might result from the particular behavioural profile of these rats.

INTRODUCTION

In a recent study (Razafimanalina et al., 1996), we showed that the higher alcohol preference of Roman High Avoidance (RHA) rats, as compared to their Roman Low Avoidance (RLA) counterparts, was related not only to a higher preference for saccharin-sweetened solutions versus tap water but, in certain conditions, to a preference for quinine-adulterated solutions. It has been reported frequently that the two lines, initially selected for their divergent active avoidance behaviour (Bignami, 1965), exhibit differences in emotionality and anxiety, RHA rats showing less emotion- and anxiety-related behaviours than their RLA counterparts. In particular, RHA rats also display higher locomotor activity than RLA rats in a novel environment (reviewed in Driscoll and Bättig, 1982). The difference in the gustatory hedonic profile between the two lines, together with differences found in their locomotor reactivity to novelty and in their emotionality, allowed us to formulate the hypothesis of a parallel with the human personality trait called 'sensation seeking' (Zuckerman, 1984), RHA rats being the higher 'sensation seekers'.

To verify this general hypothesis and, in particular, to establish whether higher locomotor reactivity to a novel environment, as well as higher gustatory preferences, could be associated to a greater tendency to consume alcohol, we decided to apply our experimental protocol to rats of the Wistar–Kyoto Hyperactive (WKHA) and the Wistar–Kyoto normoactive (WKY) strains.

With the objective of dissociating the hypertension and hyperactivity traits, which are both present in the SHR strain, the WKHA inbred strain has been selected from an F2 intercross between SHR and WKY strains for their high level of locomotor reactivity in a novel environment in activity cages and for low blood pressure. This strain has been inbred for over 20 generations (Hendley et al., 1986; Hendley and Ohlsson, 1991). Behavioural studies indicated that, like the
RHA rats, WKHA rats exhibited hyperactivity in an open-field test (Sagvolden et al., 1991), while displaying lower anxiety as measured using the elevated plus-maze test (Courvoisier et al., 1996).

MATERIALS AND METHODS

Subjects

Wistar–Kyoto Hyperactive rats were bred in our laboratory from progenitors kindly provided by E. D. Hendley (University of Vermont, USA). Wistar Kyoto rats, purchased from IFFA-CREDO (Lyon), served as controls. For this series of tests, rats were individually housed in wire cages in a temperature-regulated animal room (23°C) maintained on a 12 h light:12 h dark cycle (lights on at 07:00). At the beginning of testing, rats were 3 months old. Twenty rats (10 males and 10 females) of each strain were used. All behavioural tests were conducted in the home cages, during the light phase of the cycle. During 6 consecutive days before the beginning of choice tests, food and water were continuously available and body weight and water intake were recorded daily. Rats were then submitted successively to the three different choice tests, between water and increasing concentrations of saccharin, between water and increasing concentrations of quinine dihydrochloride: 1, 2, 10, 20, 50 and 100 μM. The protocol was the same as that used for the saccharin–water choice.

Ethanol intake. Rats were given water freely for 10 days and then the following choice procedure was used: first, the rats were given a 10% (v/v) ethanol solution for 2 days as the only fluid available; then, rats were presented with two bottles, one containing tap water and the other a 10% (v/v) ethanol solution. Fresh ethanol solution was prepared every day by dilution of 95% ethanol in tap water just before administration. Every day, at 08:30, the 24 h intakes of water and alcohol were recorded and the drinking bottles refilled. The choice test proceeded for 15 consecutive days. Animals were weighed every day and the bottle containing the alcohol solution was placed on a different side of the home cage every 3 days.

Statistical analysis

For the saccharin and quinine choice sessions, the results are expressed in ml of each fluid intake per kg body weight per 2 h. For alcohol, consumption was calculated in g of absolute alcohol per kg body weight per 24 h and also as a percentage of total daily fluid intake. Analysis of variance (ANOVA) for repeated measures with strain and sex as between-subject factors, Tukey’s HSD post-hoc t-test and Student’s t-test were used.

RESULTS

Body weight and water intake

A general estimate of rat body weight and water consumption over the period of behavioural testing was made by comparing the corresponding mean values of the four groups (male and female groups of each strain) recorded the day of their arrival in the experimental room, the day before the beginning of each test and the day before death.

The four groups of rats displayed different mean body weights during the time of the experiments. An ANOVA with two between-subject factors,
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Fig. 1. Saccharin solution intakes (in ml/kg/2 h) in male (left) and female (right) rats of the two strains for the seven tested concentrations (log scale).

Asterisks indicate significant differences between the two strains (Tukey’s t-test): *P < 0.05; **P < 0.01; ***P < 0.001. WKY, normoactive; WKHA, hyperactive.

Figure 1 summarizes the saccharin intakes (in ml/kg/2 h) of male (left) and female (right) rats of each strain. An ANOVA with two between-subject factors, strain and sex, and one within-subject factor, saccharin concentration (seven levels) showed significant strain (F_{1,36} = 14.4, P < 0.001) and sex (F_{1,36} = 44.7, P < 0.001) differences, without strain × sex interaction (F_{1,36} = 0.01, n.s.). Regarding the saccharin consumption of male rats, WKHA rats consumed significantly more sweetened solution than WKY rats (F_{1,18} = 11.4, P < 0.01). Tukey’s HSD t-test revealed that WKHA rats exhibited significantly higher saccharin intakes for 7.5, 25, and 50 mM concentrations. As in male rats, the female WKHA rats consumed more saccharin than their WKY counterparts (F_{1,18} = 5.1, P < 0.05), but the difference reached significance for the 50 mM concentration only (Tukey’s HSD t-test).

Concerning the concurrent water intakes expressed in ml/kg/2 h (data not shown), a global 2 × 2 × 7 ANOVA showed no strain difference (F_{1,36} = 0.05, n.s.), but a significant sex difference in favour of female rats (F_{1,36} = 24.8, P < 0.001).
Fig. 2. Daily intakes of a 10% (v/v) alcohol solution (in g of absolute ethanol/kg of body weight/24 h) as a function of rat strain and sex during the 2 days of forced consumption. Asterisks indicate a significant difference between the two strains (Student’s t-test): ***P < 0.001. Circles indicate significant difference between the sexes (Student’s t-test): **P < 0.01. WKY, normoactive; WKHA, hyperactive.

Quinine–water choice

No graphic representation is shown for the quinine–water choice test. All rats exhibited an increasing aversive response to quinine as its concentration increased. An overall ANOVA (strain × sex × concentration) for quinine consumption (ml/kg/2 h) showed no strain difference ($F_{1,36} = 2.1$, n.s.) but significant sex ($F_{1,36} = 23.0$, $P < 0.001$) and concentration ($F_{5,180} = 28.7$, $P < 0.001$) differences. The sex effect was due to the greater quinine intake of female rats of the lowest concentration (1 μM, $P < 0.05$) and the two highest concentrations (50 and 100 μM, $P < 0.01$ and $P < 0.001$ respectively). The overall ANOVA on concurrent water consumption showed a strain difference in favour of the WKHA rats ($F_{1,36} = 4.8$, $P < 0.05$) and a sex difference in favour of female rats ($F_{1,36} = 38.3$, $P < 0.001$).

Forced alcohol consumption

Figure 2 summarizes, for male and female rats of each strain, the consumption during two consecutive days of 10% (v/v) solution of alcohol (g of absolute ethanol/kg body weight/24 h) when it was the only fluid available. An overall strain × sex × repetition ANOVA showed significant strain ($F_{1,36} = 64.1$, $P < 0.001$), sex ($F_{1,36} = 14.6$, $P < 0.001$) and repetition ($F_{1,36} = 4.5$, $P < 0.05$) differences. The daily alcohol consumption of WKHA rats was always superior to the consumption of WKY rats, although the difference did not reach significance the first day with male rats. Moreover, on the first day the alcohol intake of the WKHA female rats was significantly superior to the consumption of the male WKHA rats, and on the second day the WKY female rats drank more alcohol than the male rats of the same strain.

During forced alcohol consumption, all animals decreased their daily fluid intakes. WKY showed a significantly larger decrease than did WKHA rats (54.4 ± 2.8 and 34.3 ± 2.4%, respectively; $F_{1,36} = 29.2$, $P < 0.001$). No difference was observed between male and female rats in this decrease of daily fluid intake.

Alcohol–water choice

Figure 3 shows the strain differences in alcohol consumption (g of absolute ethanol/kg body
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weight/24 h) during the 15-day choice test. An overall strain x sex x days ANOVA on alcohol intake showed that WKHA rats drank significantly more alcohol than WKY rats \( (F_{1,36} = 23.4, P < 0.001) \). Tukey’s HSD test indicated that, throughout the test, WKHA rats ingested significantly higher amounts of alcohol than did the WKY rats. No sex difference was observed but a significant repetition effect \( (F_{14,504} = 2.3, P < 0.01) \) occurred, WKHA rats increasing their intake during the 15 days of testing.

The same analysis on concurrent water intake showed no strain effect \( (F_{1,36} = 2.0, \text{n.s.}) \), but significant sex \( (F_{1,36} = 23.7, P < 0.001) \) and repetition \( (F_{14,504} = 27.9, P < 0.001) \) effects. As usual, female rats consumed significantly more water per unit body weight than did males, and all rats drank high amounts of water on the first 3 days of choice testing, presumably to compensate for the decrease in daily fluid intake during the 2 days of forced alcohol consumption.

Expressing alcohol consumption as a percentage of total fluid intake showed a comparable and significant strain difference \( (F_{1,36} = 25.7, P < 0.001) \) with no sex effect. The mean percentage alcohol intakes over the 15-day choice test were: 5.1 ± 0.7% for WKY strain, 20.3 ± 3% for WKHA strain, 14.1 ± 3.2% for male rats and 11.3 ± 2.2% for female rats.

DISCUSSION

The purpose of the present study, by comparing WKHA and WKY rat strains, was to search for possible relationships between alcohol consumption on the one hand and locomotor reactivity as well as gustatory preference and aversion on the other. The main observations can be summarized as follows: (1) WKHA rats consumed more alcohol than the WKY rats; (2) WKHA rats also consumed more saccharin than their WKY counterparts; (3) no strain difference was observed for quinine intake. Each of these results will be briefly discussed.

Before discussing the main results, it is noteworthy that most studies of alcohol consumption have been conducted on male animals, but, when both sexes were included, females were often found to consume more alcohol than males (Li and Lumeng, 1984; Adams et al., 1991; Adams, 1995). In the present study, sex differences were observed in favour of female rats in saccharin and in forced alcohol intake tests when the consumption was related to body weight. No sex difference was found for the alcohol free-choice test, irrespective of the method used to express alcohol consumption (i.e. g/kg/day or % of total fluid intake).

The WKHA rats, selected for their phenotype of locomotor hyperactivity, exhibited a significantly higher level of acceptance of a 10% alcohol solution than their normoactive WKY counterparts, when alcohol was the only fluid available, as well as a 4-fold greater alcohol intake during the 15 days of free choice between water and alcohol, irrespective of the manner used to express alcohol consumption. However, alcohol consumption by both strains was quite modest (WKY rats: 0.39 ± 0.05 g/kg/day; WKHA rats: 1.72 ± 0.26 g/kg/day), as compared to consumption observed in strains selected for alcohol preference or acceptance, which were found to reach \( \geq 5 \) g/kg/day in comparable conditions (Rezvani et al., 1995). Moreover, the mean daily alcohol consumption of WKHA rats was even lower than that of RHA rats recorded in our previous study, although Roman lines were not selected on the basis of alcohol acceptance or preference (Razafimanalina et al., 1996). It is noteworthy that the daily alcohol intake of WKHA rats was about the same as the daily alcohol consumption recorded in outbred strains such as Wistar rats, whose average alcohol intake is 2 g/kg/day (Samson and Chappelle, 1995; Samson et al., 1996).

Although the present data do not allow the exclusion of some relationship between locomotor hyperactivity and alcohol consumption in WKHA rats, such a relationship appears unlikely, given that alcohol intake of these rats is not different from that of outbred strains. Moreover, the published data concerning the relationship between alcohol drinking and locomotor activity are conflicting. Positive correlation was reported between these two behavioural parameters (Li et al., 1979; Badishtov et al., 1995; Stewart et al., 1996; Razafimanalina et al., 1996). However, opposite findings have also been reported (Erikson, 1972; Fahlke et al., 1993). Results are also confusing when a correlation is sought within the same strain (Bisaga and Kostowski, 1993; Samson and Chappelle, 1995). Given the number
of factors implicated in the regulation of locomotor activity, it is not surprising that there is no consistent relationship between this complex behaviour and alcohol intake. A second possibility to explain our observations is to assume that the difference in alcohol intake between the two strains results from the subnormal intake of the WKY rats (0.39 ± 0.05 g/kg/day), the value of which is clearly inferior, for example, to that of RLA rats (1 g/kg/day) during the 15 days of free choice (Razafimanalina et al., 1996). WKY rats have often been characterized as a ‘low preference’ strain control (Cannon and Carrell, 1987). These animals have been considered as being hyper-emotional (Paré, 1989a,b,c). In addition, when tested in the elevated plus-maze, the scores reflecting anxiety are higher for WKY rats as compared to Fischer-344 and Wistar rats (Paré, 1992). When the elevated plus-maze test was used in our laboratory, WKY rats exhibited a higher level of anxiety-related behaviours than WKHA rats (Courvoisier et al., 1996) or a number of other rat strains (Ramos et al., 1997). Lastly, the same authors (Courvoisier et al., 1996) showed that WKHA rats display less anxiety and lower neuroendocrine responses to stressful challenge. Given these different data, it can be suspected that the low alcohol consumption of WKY rats is related to their behavioural profile, in particular their higher anxiety- and stress-related behaviours. Although this suggestion is in conflict with the ‘tension-reduction’ hypothesis (Cappell and Herman, 1972), it cannot be excluded at present. However, given that the daily alcohol intake of the WKY rats did not vary throughout the 15 days of testing it is unlikely that this low consumption results from some emotional deficit such as freezing or neophobic reactions, but rather suggests some post-ingestive metabolic problems.

The second aspect of our results concerns the gustatory profile of the WKHA strain. In agreement with other data, the higher alcohol consumption of these rats is positively associated with higher ingestion of saccharin (Gosnell and Krahn, 1992; Overstreet et al., 1993; Bell et al., 1994; Razafimanalina et al., 1996). It has been suggested that this association is caused by the implication of a common reinforcement mechanism thought to involve opioid release (Sinclair et al., 1992).

Concerning the consumption of quinine solutions, we found no strain differences and consequently no association with saccharin preference and with ethanol intake. These results differ from those obtained with Roman lines (Razafimanalina et al., 1996), where the RHA rats actually preferred the 2, 10 and 20 uM quinine solutions to water. This paradoxical appetitive response to normally aversive solutions substantiates the ‘sensation-seeking’ hypothesis (Zuckerman, 1984). On the contrary, in the present experiment, the aversive responses of the two strains were identical, neither strain showing any quinine preference whatever the concentration tested. This last result, together with the low alcohol intakes in both strains, clearly indicates that even if the ‘sensation-seeking’ hypothesis can be applied to the case of Roman lines, it cannot explain the present results. In conclusion, the propensity to drink alcohol could be associated with different behavioural parameters, depending on the strain or the line studied.

REFERENCES


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