

Effect of adaptation to alcohol and of age on voluntary consumption of alcohol by rats

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If an ethanol solution of more than about 6% concentration is the only fluid available to rats, their intake is at first low compared with that of water (Richter, 1953). But the amounts taken daily increase steadily up to a certain level. Thus it might be expected that rats that have first a period of free choice between alcohol and water and subsequently receive alcohol solution alone for some time would show a higher preference for alcohol when again presented with the choice. This supposition has been tested before, but the results are conflicting. Hausmann (1932) observed that, after 10 days' forced feeding with alcohol, the spontaneous alcohol intake of rats dropped to a low level when water was again accessible. After some days they began to drink a little alcohol, but not more than before the adaptation period. Richter (1957) obtained similar results with white laboratory rats, whereas wild rats drank more alcohol if previously adapted to it.

In our laboratory it has been observed that rats that have had 10% (v/v) ethanol as their sole drinking fluid for nearly a year drink relatively large amounts of alcohol when offered a choice. We have also noted that the rats' preference for alcohol increases with increasing age. The reports quoted above, and our own accidental observations, prompted two experiments on the relation between the age of rats, their previous experience of alcohol and their voluntary consumption of alcohol when given a free choice. The tolerance to the intoxicating effect of alcohol in a group of rats whose drinking suggested 'habituation' was compared with that of a group of non-habituated rats.

EXPERIMENTAL

The general technique in our auto-selection experiments has been described previously (Forsander, Kohonen & Suomalainen, 1958). The rats used were all of the laboratory stock. They were housed in metal cages measuring 235 × 195 × 175 mm and provided with grid floors. They were fed *ad lib.* on a laboratory stock ration, supplemented weekly with 5 g fresh cow's liver/rat. The positions of the drinking tubes in the cage were reversed at irregular intervals of a few days.

Expt 1. Ten female and ten male rats at the age of 90 days were given a free choice between pure water and 10% (v/v) ethanol in tap water. After 75 days, five animals of each sex were restricted to the alcohol solution alone for 61 days (restricted group), whereas the remaining ten animals continued to have free choice (self-selection group). Finally, all the animals were given the choice between alcohol and water for 20 days.

Expt 2. The animals used in this experiment were twenty male rats about 540 days old at the beginning of the experiment. They had not previously been used in any kind of experiment. Ten of these animals were restricted to 10% (v/v) ethanol as drinking fluid for 350 days (alcohol group), the other ten receiving only water during the same period (water group). After this time, both groups were allowed free choice, and their consumption of water and alcohol was observed for about 3 weeks. The 1st week was allowed for adjustment, and the values for the last 2 weeks were used to compare

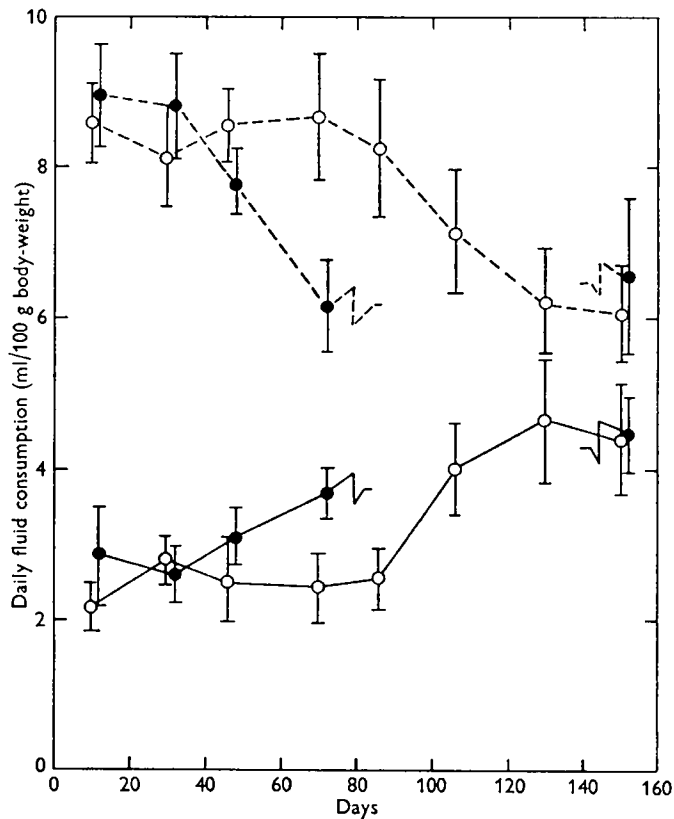


Fig. 1. Consumption of water (broken line) and 10% (v/v) ethanol (solid line) by two groups of ten rats aged 90 days at the beginning of the experiment. One group (○) was given free choice throughout, the other (●) was restricted to alcohol from the 75th to the 136th day of the experiment. Vertical bars show the standard errors of the means. Each point represents the mean consumption during a period of about 20 days.

the alcohol preferences of the two groups. At the end of the drinking experiment, any differences in tolerance to the intoxicating effect of alcohol between the alcohol and the water groups were measured by means of the tilted-plane test for alcohol intoxication developed by Arvola, Sammalisto & Wallgren (1958). The ethanol was administered intraperitoneally as a 10% (w/v) solution in saline, the dosage being 1.5 mg/g. The animals were tested at 15 min intervals for 2 h.

RESULTS

Expt 1. The mean daily fluid intake of each individual has been calculated for periods of about 3 weeks, and these means were used for calculating group means. No difference between the sexes was observed, and the results obtained with males and females have been combined for each group and are presented graphically in Fig. 1. Calculations by Student's *t* test showed that both groups consumed less alcohol during the initial periods until the 60th day, compared with their consumption during the final period (days 136–156). In the restricted group, there appeared to be an increase in the proportion of alcohol consumed during days 55–75, but it was not statistically significant. In the self-selection group the increase occurred during days 95–115 and was significant. When the restricted group was given free choice again, the preference for alcohol was almost exactly the same in the two groups (40.0% in the self-selection group, 38.9% in the restricted group).

Table 1. *Mean values (with standard deviations) for daily consumption of water and of 10% ethanol during a 14-day period by two groups of ten male rats about 900 days old. The alcohol group had been restricted to 10% ethanol, the other to water, for 350 days before the period of observation*

	Fluid consumed (ml/100g body-weight)			Alcohol (% of total fluid consumption)
	Total	Water	Alcohol	
Alcohol group	7.1 ± 0.9	1.3 ± 0.6	5.8 ± 1.2	81.2 ± 11.3
Water group	6.4 ± 1.2	3.3 ± 1.2	3.2 ± 1.5	48.4 ± 21.2
Significance of difference between groups	<i>P</i> < 0.2	<i>P</i> < 0.001	<i>P</i> < 0.001	<i>P</i> < 0.001

Expt 2. The results of the self-selection experiment are shown in Table 1. There was a notable difference between the two groups in their preference for alcohol, those animals that had been restricted to alcohol drinking it almost to the exclusion of water. As suggested by the mean weights (425 ± 15 g for the alcohol group, 456 ± 12 g for the water group), nothing in the appearance of the rats suggested any difference in their physical condition.

The intoxication test indicated that there was no difference in alcohol tolerance between the groups. The mean values (with standard deviations) of the lowest values observed in the test (percentage of performance immediately before administration of alcohol) were 73.7 ± 8.0 for the alcohol group and 76.2 ± 5.7 for the water group, the means of all eight tests being 82.2 ± 5.5 and 84.3 ± 4.3, respectively.

DISCUSSION

Within a short time an animal is able to develop a metabolic tolerance for some new types of diet. After a few days, a rat given food high in fat has overcome the ketonuria initially produced (Wigglesworth, 1924). Rats have an absolute aversion from alcohol, since the fluid intake markedly decreases when alcohol is substituted for drinking water (Richter, 1953).

With free choice, the consumption of water is usually higher than that of the alcohol. However, this observation gives only a relative picture of the preference for alcohol rather than for water, not an absolute measure of the motivation to drink alcohol. Our experiments show that prolonged adaptation to alcohol—perhaps in combination with increased age—increased the preference for alcohol more than did the shorter adaptation. After nearly a year on 10% ethanol, rats had a preference for alcohol almost twice as high as others that had only had access to water for the same period. Adaptation to alcohol thus has only a slight effect on the animals' preference for it, and this effect appears slowly.

With the Skinner box technique, Myers & Carey (1961) observed an effect of adaptation to alcohol in a shorter time than we have found. Using alcohol solutions of various concentrations, they found that the threshold for preferring alcohol to water depended on the length of time the animals had been restricted to alcohol before the free choice.

In contrast to adaptation to alcohol, administration of butyrate has a rapid influence on the selection between alcohol and water (Forsander & Salaspuro, 1962). Even a single dose of butyrate, metabolizable in about a day, produces a marked increase in the alcohol consumption of rats. At the same time, an adaptation to the utilization of ketone bodies is developed. Alcohol and ketone bodies are oxidized by the same final metabolic stages. This may be the reason why adaptation to metabolism of ketone bodies also influences tolerance for alcohol (Forsander & Salaspuro, 1962). Curiously, alcohol itself does not have a similarly rapid effect on alcohol preference.

The initial consumption of alcohol solution by rats not accustomed to it was different for the young rats of Expt 1 and the old ones of Expt 2. The latter consumed much more alcohol relative to total fluid intake. It seems possible that both increasing age and prolonged consumption of alcohol contributed to the increased intake observed towards the end of Expt 1. As suggested by Forsander & Salaspuro (1962), it may be related to the ketone-body metabolism of the animals, since it is known that young rats are much more sensitive to a fat load than older ones (Wigglesworth, 1924).

The supposed metabolic adaptation in the long-term experiment was not paralleled by any increasing tolerance to the intoxicating effect of alcohol. In the simple functional test used, the performances of the two groups were almost identical. When intoxicating doses of alcohol have been administered a few times only, behavioural tolerance develops both in monkeys (Hogans, Moreno & Brodie, 1961) and in rats (Wallgren & Lindbohm, 1961; Wallgren & Savolainen, 1962). Because the pharmacological intoxicating effect of alcohol and alcohol metabolism are two quite separate phenomena, it is not surprising that differences exist between nervous tolerance and metabolic adaptation.

SUMMARY

1. The influence of adaptation to alcohol and of age on the free choice between alcohol (10%, v/v, ethanol) and water was examined in rats. Adaptation to alcohol was secured by restricting the animals to 10% alcohol for 350 or 61 days. The rats that consumed alcohol for 350 days were also tested by a simple functional test for tolerance to the intoxicating effect of alcohol.

2. Long-term restriction to alcohol solution increased the preference for alcohol.
3. Increased alcohol consumption after long-term adaptation was not paralleled by any increase in tolerance to the intoxicating effect of alcohol.
4. The age of the animals influenced the choice: the older the animals, the higher was their alcohol consumption.

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