VOLUNTARY ALCOHOL CONSUMPTION BY RATS FOLLOWING ADMINISTRATION OF GLUTAMINE

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A number of investigators (1, 2) have postulated the presence of unknown factors in natural materials which will decrease the voluntary alcohol consumption of experimental animals. Since Ravel *et al.* (3) have demonstrated that glutamine is effective in reversing the inhibition of growth of *Streptococcus faecalis* caused by the inclusion of small amounts of alcohol in the medium, it seemed desirable to carry out a preliminary study to determine the effects of glutamine on the voluntary consumption of alcohol by rats. This paper is a report of that study.

EXPERIMENTAL

Thirty Wistar rats (designated as the H strain in previous communications from this laboratory), fifteen male and fifteen female, at 6 months of age were kept in separate cages in a temperature-controlled room. Attached to each cage were two bottles, one containing tap water and the other 10 per cent alcohol. The bottles were emptied, washed, and refilled, and the positions of the bottles alternated every 2 to 5 days. The animals were fed Purina laboratory chow throughout the experiment. In order that each animal might serve as its own control, the quantity of alcohol consumed by each animal on the control diet was measured every 2 to 5 days for a period of 55 days.

From this group nineteen rats, seven male and twelve female, were then selected on the basis of their higher alcohol consumption for glutamine administration. Each animal was fed daily 100 mg. of glutamine mixed with ground laboratory chow for a period of 9 days, and measurements were made of the alcohol consumed.

The nineteen rats were then divided at random into two groups. During the following 17 day period, one group (four males and six females) continued to receive 100 mg. of glutamine orally each day, while those in the other group (three males and six females) were injected each day intraperitoneally with 50 mg. of glutamine dissolved in 1 ml. of 0.85 per cent sodium carbonate solution. The rats receiving glutamine orally were injected with

1 ml. of sodium carbonate solution. The alcohol consumed by each animal was measured as before.

TABLE I

Effect of Glutamine on Alcohol Consumption by Rats

Rat No.	Sex	Weight, gm.	Period before glutamine administration, 55 days	Period of glutamine administration			Period following glutamine administration, 63 days	Per cent change in alcohol consumption induced by glutamine administration
				1st 9 days, 100 mg. per rat per day, given orally	Next 17 days, 100 mg. per rat per day, given orally	Average consumption for 26 day period		
Average alcohol consumption (ml. per 100 gm. rat per day) for rats of Group I								
1	F.	233	0.84	0.14	0.21	0.18	0.69	−79
2	"	227	0.52	0.23	0.48	0.39	0.75	−25
4	"	201	0.89	1.02	0.92	0.95	1.05	+07
5	"	228	0.89	0.63	0.67	0.66	0.90	−26
6	"	203	0.32	0.40	0.32	0.35	0.52	+09
7	"	239	0.51	0.24	0.26	0.25	0.73	−51
17	M.	332	0.27	0.14	0.32	0.26	0.18	−04
18	"	388	0.41	0.06	0.06	0.06	0.21	−85
19	"	377	0.33	0.17	0.23	0.21	0.26	−36
27	"	393	0.27	0.05	0.13	0.12	0.21	−56
Mean.....			0.53	0.31	0.36	0.34	0.55	−35
Average alcohol consumption (ml. per 100 gm. rat per day) for rats of Group II								
8	F.	240	0.84	0.41	0.66*	0.58	0.30	−31
9	"	227	0.64	0.13	0.45*	0.33	0.89	−48
10	"	236	0.39	0.28	0.35*	0.33	0.74	−15
13	"	219	0.38	0.59	0.88*	0.78	0.98	+105
14	"	227	0.41	0.19	0.69*	0.51	0.60	+24
15	"	233	0.70	1.02	0.98*	0.99	0.89	+41
22	M.	363	0.34	0.37	0.38*	0.38	0.40	+12
24	"	408	0.42	0.12	0.05*	0.08	0.11	−81
30	"	365	0.38	0.15	0.32*	0.26	0.20	−32
Mean.....			0.50	0.36	0.53*	0.47	0.57	−03

* Glutamine (50 mg. per rat per day) intraperitoneally instead of orally.

At the end of the 17 day period, all the rats were returned to a pellet diet and their alcohol consumption was measured for an additional 63 days.

The average amount of alcohol consumed daily by each of the animals during each of the four periods is presented in Table I.

DISCUSSION

As can be seen from Table I, glutamine administered orally appears to be a relatively effective agent in decreasing the voluntary consumption of alcohol by rats. In the first group of rats the daily consumption was only 65 per cent as great during the 26 days of glutamine administration as during the previous control period. It is worth noting that, while one rat drank only 15 per cent as much and another only 21 per cent as much during the period, glutamine was almost wholly ineffective in reducing the alcohol consumption of three rats of this group. This is further evidence that in experimental animals individuality in metabolism exists (4), and is in confirmation of the genetotrophic concept (5, 6).

In this connection it may be pointed out that the nutritional status of the closely related compound glutamic acid has been in a state of confusion for a number of years. Investigators have repeatedly reported improvements in the intelligence level of mentally deficient children upon administration of glutamic acid, only to have other investigators report that no such improvement was observed. The fact that some mentally deficient individuals do show large gains as a result of glutamic acid therapy while others show no response at all probably is responsible, at least in part, for this confusion. Foale (7), for example, working with a group of mentally deficient children, found that the difference between the responses of the group on glutamic acid therapy and the control group was small; however, the "intelligence level" of some individuals on glutamic acid therapy showed fairly large gains (as much as eleven points), while none in the control group improved more than three points.

As with other nutritional supplements which have previously been found to reduce alcohol consumption in animals (8), the effect of glutamine does not persist long after its discontinuance. During the 63 day period following administration of glutamine, every animal in the first group except one returned to a higher rate of alcohol consumption than during the glutamine period.

The data on the second group of rats seem to indicate that glutamine is much less effective when injected than when fed orally. The animals of this group drank only 72 per cent as much alcohol when fed glutamine as during the control period, but when glutamine was injected the alcohol consumption returned to a level equivalent to that of the control period. The possibility of increased alcohol consumption due to a shock reaction from the injection was minimized by injecting the animals of the first group with an equivalent amount of sodium carbonate solution. The question arises as to whether glutamine must be transformed in the intestinal tract to some other agent in order to be effective.

Statistical analysis of the data presented in Table I reveals that, for all

nineteen rats taken as a group, the difference in mean alcohol consumption during the 9 day oral glutamine supplementation period as compared with the previous control period was significant at the 5 per cent confidence level ($P = 0.95$; $t = 2.15$). When the data were expressed as gm. of alcohol per rat per day and a similar statistical analysis was made, the difference was significant at the 1 per cent confidence level ($P = 0.99$; $t = 3.09$).

We now have similar experiments under way comparing the effects of glutamine, glutamic acid, and other nitrogen supplements on alcohol consumption. These results will be reported in a later paper.

SUMMARY

1. Glutamine fed at a level of 100 mg. daily caused a statistically significant lowering of the voluntary consumption of alcohol by rats.

2. Injected glutamine appeared to be relatively ineffective.

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