Decreased tolerance of hypothalamic hyperphagics to quinine in drinking water[1]

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Thirsty hypothalamic hyperphagic rats are less willing than normals to drink water containing quinine. This finding makes tenuous the inference, which has been made by other investigators, that hypothalamic hyperphagics' unwillingness to eat quinine adulterated food implies that their hunger drive is low.

It is well established that animals with bilateral lesions in the ventromedial hypothalamus over-eat and so become obese if they are allowed ad libitum access to food (Hetherington & Ranson, 1942). Since lesions of the lateral hypothalamus cause anorexia which is unalleviated by ventromedial lesions, and since stimulation of the lateral area elicits feeding behavior in satiated animals (Miller, 1960), it has been suggested (Anand & Brobeck, 1951; Brobeck, 1960) that the ventromedial hypothalamic area exerts an inhibitory influence on lateral "feeding centers" in the normal, satiated animal. The hyperphagia resulting from ventromedial lesions, then, presumably reflects the unbridled action of the lateral "feeding centers" and seems to imply tonically voracious hunger.

Miller, Bailey, & Stevenson (1950), however, have demonstrated that hypothalamic hyperphagic rats are less willing than normal rats to do work or to overcome obstacles to obtain food; in particular they will not eat food made bitter by the addition of quinine. Thus, while measures of food consumption indicate that hunger in ventromedially lesioned rats is increased, other measures indicate that it is reduced. More recently, Graff & Stellar (1962) have presented some evidence suggesting that hyperphagia can occur with very little of the finikiness discovered by Miller et al. Their paradox, then, might be fully resolved if it were additionally shown that hyperphagic rats' unwillingness to overcome obstacles on the way to food is a manifestation of some general dysfunction which is not particularly related to hunger at all. It is shown here that hyperphagics, who are unwilling to eat food made somewhat bitter by quinine, are also unwilling to drink quinine-bitter water to relieve thirst.

Method

Successful hypothalamic hyperphagia was induced in 11 female Sprague-Dawley rats averaging 263 gm body weight at the time of operation by placing bilateral electrolytic lesions in the ventromedial hypothalamus; 11 unoperated animals from the same population served as controls.

Number 1840 (Anchor brand, taper point) stainless steel needles insulated except for 1/2 mm at the tip were lowered stereotaxically to coordinates (deGroot, 1959, system) 5.0 mm anterior to and 1.5 mm dorsal to the inter-aural line at 0.5 mm on either side of the midline to serve as anodes for production of lesions which were effected by passage of a 1.2 ma current for 30 sec. between stereotaxic ear bars and anode.

After at least two weeks of recovery from the operation, the rats' ad lib Purina chow intake and weight gain were measured for a five day period; hyperphagics were selected by the criterion that they should eat at least 5.0 gm per day more than any control rat. Hyperphagics consumed 47.1 gm per day; normals consumed 19.3 gm per day. Hyperphagics gained 8.21 gm per day; normals gained 0.64 gm per day.

It was necessary to equate the groups' food consumption during water intake measurements to avoid artifacts resulting from differential food intake, but the groups were not equated for body weight. Animals had ad lib water but no food from 9:00 a.m. to 7:00 p.m. daily. At 7:00 p.m. water was removed and each rat given 10 gm Purina chow, an amount which would be entirely consumed during several hours even without water. At 10:00 p.m. a test solution either of tap water or quinine hydrochloride in tap water was introduced and left until 9:00 a.m. the following morning, at which time the

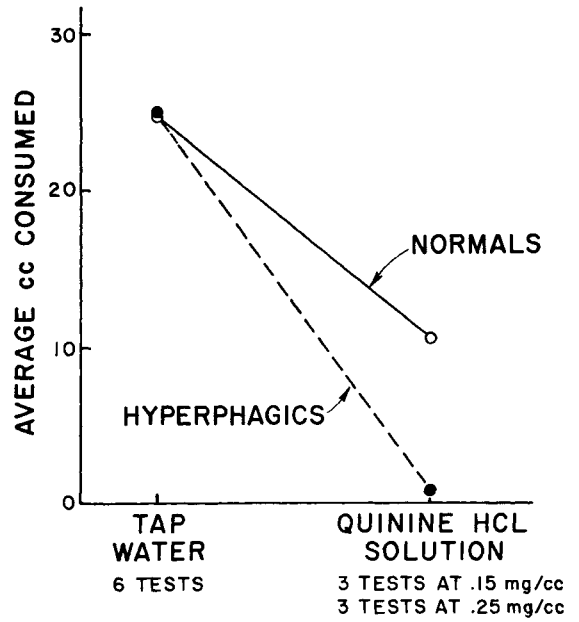

Fig. 1. Tap water and quinine water consumption of normal and hypothalamic hyperphagic rats.

volume which had been consumed was recorded. Plain tap water and quinine water test days were alternated; solutions of 0.15 mg and 0.25 mg of quinine per cc of water gave similar results which were pooled.

Results and Discussion

The results are given as Fig. 1. Thirsty hyperphagics and normals drink the same amount of tap water, but hyperphagics drink very little quinine water compared to normal controls.[2]

The percent decrement in consumption due to adding quinine to the drinking water was computed for each rat and a t test done to compare the groups; $t = 6.26$ with 20 degrees of freedom ($p < .001$).

Thus, hyperphagics will tolerate quinine in neither food nor water.

It is often observed that ventromedial rats are sluggish (Hetherington & Ranson, 1942) and "hyperemotional" (Anand & Brobeck, 1951; Hetherington & Ranson, 1942); these symptoms, as well as lack of tolerance for bad taste, may be non drive-specific dysfunctions which are produced in addition to (but independently of) increased hunger. In any case the present results further emphasize that ventromedially lesioned rats are abnormal in many ways and not only in their regulation of food intake.

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Notes

1. The work reported here was done at Yale University during the tenure of a National Science Foundation Predoctoral Fellowship. It was supported by Grant M647 from the National Institute of Mental Health, United States Public Health Service. The writer wishes to thank Professor Neal E. Miller for helpful suggestions.

2. The present lack of a between-group difference in tap water consumption should be compared with results reported in Stevenson et al (1950).

Comment on Jacobson et al *by David J. Barker*

Jacobson et al (1966) report data from an experiment in which RNA from rats rewarded for choosing one or the other side of a two-choice apparatus was injected into naive rats, whose side "preferences" in the apparatus were then measured. Table 1 of their data shows "preferences" of test animals as indexed by their "predominant" choices on 25 test trials, regardless of the strength of "preference." The authors, however, do not make explicit what they mean by a predominant choice. Examination of Table 1 shows that of the 42 test rats, 29 chose the alternative to which their donor rats had been trained (a + d diagonal). Referring now to Table 2, the distribution of scores of the test rats, it is clear that these 29 rats must have come from the upper half of the distribution which includes the scores from 13 to 21. Thus, one would assume that the definition of a "predominant" choice was selecting the alternative to which the donor had been trained 13 or more times out of 25. Under the assumption that the injection of RNA from a donor rat into a recipient rat did *not* influence the recipient's choices, that its choices were random, the probability of 13 or more choices of the donor-trained alternative out of 25 is quite high ($p = .50$). Thus, while the fact that 29 out of 42 rats showed a "preference" for the side to which their donor had been trained is statistically significant ($p = .01$), it is highly likely that many of these "preferences" were random choices, and not due to the injection of RNA. If the criterion for "predominant" choice had been 14 out of 25 instead of 13 out of 25, the number of rats choosing the alternative to which their donor had been trained would have been 21 out of 42, a result which is not significant ($p = .50$). It would seem that in such an important and controversial research area, a more conservative definition of "predominant" choice should have been adopted, with strength of preference taken into account. This seems especially important in view of the fact that Gross & Carey (1965) twice failed to replicate the Babich et al (1965) study of the transfer of a response by injection of RNA.

The authors conclude from their results that "... specific training given to donor rats was a determinant of the subsequent choices of recipient rats." This strong conclusion does not follow from the results presented. All that a significantly large Chi square implies, in this case, is a lack of independence between "preference of injected rats" and "side to which donor was trained." It does not indicate that one determined the other. A quote from Hays (1963) may be appropriate here: "Given a large enough sample size, the chances are very good that the psychologist can demonstrate the association of any two qualitative attributes via a Chi square test."

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For Reply to David J. Barker see page 334.