Alteration of Relative Preference for Sugar and Saccharine Caused by Ventromedial Hypothalamic Lesions[1]

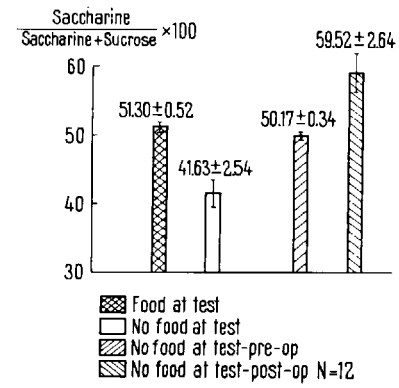
Destruction of the ventromedial hypothalamus induces hyperphagia in rats and mice. The demonstration that goldthioglucose, but not a variety of compounds in which gold is linked by a sulphur bridge to metabolites other than glucose, such as galactose, sorbitol, fatty acids, glycerol etc., selectively destroys cells in that area[2,3] has been taken as a confirmation of the postulated affinity for glucose of ventromedial cells regulating food intake[4]. Electron microscope studies have confirmed that goldthioglucose, but not other goldthio-compounds are in fact concentrated by such cells[5]. The sensitivity of this area for glucose, and the 'glucostatic' triggering of this function are also well illustrated by the demonstration of ANAND[6] that the electrical activity recorded from the ventromedial area is increased by hyperglycemia and decreased by hypoglycemia, with opposite changes being recorded in the lateral hypothalamus. Tissue removed from the hypothalami of fed monkeys shows greater oxygen and glucose uptake per unit of nucleic acid by the 'satiety' centers than by the 'feeding' centers of the hypothalamus, while the reverse situation obtained in tissues removed from fasted animals. Finally, the ventromedial area has also been shown to exercise a measure of control on gastric hunger contractions[7].

To test the possibility that destruction of the ventromedial hypothalamic area modifies differently the responses to sweet-tasting 'nutritive' (metabolic effect and taste) and non-nutritive (taste only) substances, preference tests with sucrose and saccharine were performed in normal rats and rats with hypothalamic lesions. Sucrose was chosen because this sugar, easily converted to glucose, is extremely sweet and hence the experiment could be conducted with low concentrations; this in turn meant that the metabolic state of animals would not be modified unduly by the variability in the small fraction (2% or so) of daily requirements ingested in the form of sucrose during the test.

Twelve adult female albino rats weighing 240–260 g were placed on a schedule of 1 h of water per day and *ad libitum* food (Purina Laboratory Chow) for 24 h. After daily intakes for each rat became stabilized and the weights remained at a constant level (approximately 90% of the original body weights) equal preference points for sucrose and saccharine solutions were determined for each rat by measuring volumes of solution ingested in a series of four-day tests. Specifically, 0.05 *M* sucrose was paired with various concentrations of saccharine each for four days of testing, alternating sides, to determine the amounts of saccharine ingested in approximately equal quantities to the sucrose solution. The saccharine solutions ranged from 0.003 *M* to 0.0035 *M*. After equal preference points for each rat had been determined for a four-day period, the rats were presented the same solutions during an additional four-day period, but had no food available during the hour test when the fluids were present. Volumes of standardized solutions ingested were measured. Only one of the rats failed to increase its volume of sucrose solution voluntarily ingested; the eleven others increased theirs with the maximum relative increase 29%. The corresponding group mean relative decrease of 9.67% of saccharine ingestion is significant at less than the 0.01 level of confidence. The change in means and the standard errors are shown on the left half of the Figure.

The rats were then allowed to 'rest' with food and water available for 24 h a day for 8 days, during which time the weights of the animals increased 30–62 g. Then the rats were placed on a daily schedule of 23 h of water deprivation with food available and 1 h of water and no food. When daily water intakes and weights reached a stable base line, the rats' equal acceptance values for 0.05 *M* sucrose and various saccharine solutions ranging from 0.0035 *M* to 0.004 *M* were determined. Electrolytic lesions of the ventromedial areas of the hypothalamus (the 'satiety' centers) were performed on each rat. Following the operation the rats were allowed food and water *ad libitum* for eight days to assess the success of the lesions before returning to the pre-operative deprivation regimen.

Following the induction of hypothalamic lesions a weight gain of 70–105 g was observed during the eight days following the operation; this was 2 to 3 times the weight gain of normal rats on *ad libitum* diets, and therefore, strong indication of the successful destruction of the ventromedial areas. Following the end of the experiment, histological check that these areas are in fact destroyed is conducted routinely. When the weights of the individual rats were reduced to the pre-operative level by reducing the food intake to one half the pre-operative level, the previously determined equally-preferred sucrose and saccharine solutions were presented to each rat for 1 h per day for four days with food not available during the preference test. Eleven out of 12 rats decreased the intake of sucrose solution ingested and increased the percentage intake of the saccharine solution by 0.5 to 27.0; one rat showed no change. The group mean increase of 9.35 of percentage of saccharine solution ingested is significant to the 0.01 level of confidence. These changes in means and the standard errors are shown on the right half of the Figure.



Volume of saccharine solution: Volume of saccharine and sucrose solutions ingested in 1 h tests in the presence or absence of food for normal rats and in the absence of food for rats before and after ventro-medial hypothalamic lesions. Figures and brackets are means ± standard errors.

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The first part of the experiment thus indicates that in the absence of food, normal rats showed a greater degree of preference for sucrose solution than they had in the presence of food. To equate voluntary consumption of saccharine and sugar solutions under 'fed' conditions, it is necessary to increase the sweetness of the saccharine solution over what sufficed in the presence of food; this suggests that in the absence of food, sugar preference is based on two elements, one due to taste and the other to the metabolic effects of sugar ingestion.

A similar conclusion can be derived from the observations made on hypothalamic animals. The destruction of the ventromedial 'satiety' area causes hyperphagia and, in the presence of enough food, obesity. In the present experiments, the operated rats are deprived on two accounts. On the one hand, they had been reduced by food restriction to their pre-operation weight, a practice which invariably tends to make animals ravenous. On the other hand, the availability of fluid for only 1 h tends to maintain this deprived state. Such animals could well be expected to increase their intake of the nutritive sucrose solution in the preference test. That they do not respond positively to the sucrose solution as do rats with normal hypothalami—their relative intake of sucrose in fact decreases—suggests that the nutritive or metabolic component of the preference for sugar has been decreased or eliminated by the operation. The alternative interpretation is that ventromedial lesions introduce a modification of peripheral taste function which affects in different fashion perception of sweetness in sugar and in saccharine solutions. While it is true that hyperphagic animals are hyperactive to positive and negative qualities of the diet[8], such a differential reaction to two sweet agents seems to us highly unlikely.

Résumé. Lorsque l'on détermine le pourcentage de choix de solutions de saccharine et de sucre chez le rat, on trouve que la préférence pour le sucre est diminuée quand les animaux ont accès à leur nourriture pendant le test. La destruction de la région ventromédiale hypothalamique diminue aussi la préférence relative pour le sucre. Ces résultats confirment l'idée que l'un des facteurs de la préférence pour le sucre dépend de l'intégrité de la fonction des récepteurs hypothalamiques.

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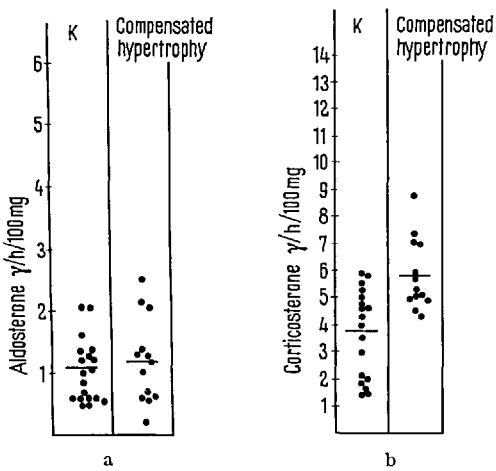
Aldosterone Production of Compensated Hypertrophic Adrenals

It is a known fact that, after removal of one of the adrenals, the other shows quite soon, already in one to two days: a compensatory hypertrophy. The histological pattern also suggests hyperfunction[1]. Apart from morphological investigations, relatively few authors have examined the function of compensatory hypertrophic adrenals. In previous investigations[2], we have observed a moderate increase of the glycocorticoid (corticosterone) content of the adrenal venous blood. According to BOHUS, ENDRÖCZI, and LISSÁK[3], the *in vitro* corticosterone production of the surviving adrenal portions increase in male rats. No literary data could be found as to the aldosterone production of adrenals displaying compensatory hypertrophy. (Literary data refer to transplanted adrenals[4].) The aim of the present experiments, carried out in rats, was to clarify this problem.



Figs. a and b illustrate aldosterone and corticosterone production in surviving adrenal portions of control animals and after compensatory hypertrophy. No significant change is seen in aldosterone production; corticosterone production is increasing, $p < 0.02$.

The left adrenal of male rats of identical breed, weighing 80 to 130 g each, was removed in ether narcosis. Aldosterone production was investigated 5 days later when, according to literary data[1], definite compensatory hypertrophy could be observed. For the purpose of the examination of aldosterone production, the animals were decapitated; the adrenals were immediately removed, cut into four parts and, according to GIROUD[5], incubated in a Krebs-Ringer-bicarbonate-solution containing 200 mg% glucose at 38°C temperature. After an initial incubation of half an hour, the incubation solution was changed and aldosterone and corticosterone production of the adrenals characterized by the steroid content of a further period lasting 2 h. At the end of incubation, the incubation solution was shaken with chloroform and the chloroform vacuum distilled at +45°C. The dry residue was treated on Whatman No. 1 filter paper strip with isolating chromatography in Bush B 5 system[6] following the so-called purifying chromatography[7]. After isolating chromatography, the paper strips were developed with alkaline tetrazolium blue and the formazan patches due to steroid effect

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