

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 diet⁸, 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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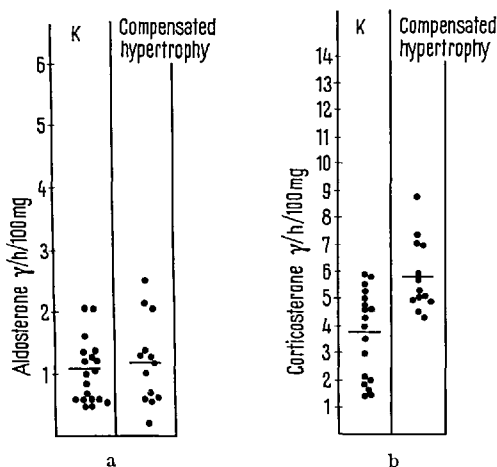
⁸ P. TEITELBAUM, J. comp. physiol. Psychol. 48, 156 (1955).

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 hyperfunction¹. Apart from morphological investigations, relatively few authors have examined the function of compensatory hypertrophic adrenals. In previous investigations², we have observed a moderate increase of the glyccorticoid (corticosterone) content of the adrenal venous blood. According to BOHUS, ENDRÖCZI, and LISSÁK³, 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 adrenals⁴.) The aim of the present experiments, carried out in rats, was to clarify this problem.

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 data¹, 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 GIROUD⁵, 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 system⁶ following the so-called purifying chromatography⁷. After isolating chromatography, the paper strips were developed with alkaline tetrazolium blue and the formazan patches due to steroid effect



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, $p < 0.02$.

¹ H. LANGENDORF and E. TONUTTI, *Ärzt. Forsch.* 3, 197 (1950).

² P. WEISZ, L. HORVÁTH, T. KÁDAS et al., *Acta physiol. Acad. Sci. Hung.* 5, 15, 259 (1959).

³ G. BOHUS, E. ENDRÖCZI, and K. LISSÁK, *Acta physiol.*, in press.

⁴ C. C. J. CARPENTER, J. O. DAVIS, J. E. HOLMAN, and C. R. AYERS, *J. clin. Invest.* 40, 196 (1961).

⁵ C. J. P. GIROUD, M. SAFFRAN, A. V. SCHALLY, J. STACHENKO, and E. H. VENNING, *Proc. Soc. exp. Biol. Med.* 92, 855 (1956).

⁶ I. E. BUSH, *Biochem. J.* 50, 370 (1952).

⁷ P. WEISZ and E. GLÁZ, *Med. exp.* 3, 264 (1960).

eluated with a mixture of ethyl-acetate:methanol (7:3). Concentrations were determined by Unicam Sp 500 spectrophotometer at 530 m μ wavelength. In every instance, at least 6 controls and 5 to 6 adrenals of unilaterally adrenalectomized rats were incubated together. The quantity of aldosterone is easily measurable in this way. Therefore, every point of the Figure illustrates the production of at least 5 adrenals. It is seen from the data of the Figure that, in accordance with literary data⁴, corticosterone production of compensatory hypertrophic adrenals shows a definite increase. On the other hand, production of aldosterone remains unchanged.

Although regulation of aldosterone production is, from many points of view, not yet entirely clarified, a regulation of humoral nature must certainly be considered, as shown in the first place by YANKOPOULOS' cross-circulation experiments⁸. The fact that in compensatory hypertrophy no increased aldosterone production was found, suggests that the regulating system of aldosterone production does not become mobilized by the effect of a 50% decrease. The increase of corticosterone production is

doubtless the consequence of endogenous ACTH hyperproduction. The present experimental findings are evidence against the aldosteronotrope role of ACTH.

Zusammenfassung. Die Aldosteronproduktion der kompensatorisch-hypertrophisierten Nebennieren wurde im Rattenexperiment untersucht. Die Corticosteronproduktion zeigte eine wesentliche Zunahme, dagegen blieben die Aldosteronwerte unverändert, was gegen eine ACTH-Regelung der Aldosteronsekretion spricht.

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March 25, 1963.

⁸ N. A. YANKOPOULOS, J. O. DAVIS, B. KLIMAN, and R. E. PETERSON, *J. clin. Invest.* 38, 1278 (1959).

Food Intake Patterns from Weaning to Adulthood in Male and Female Rats with Hypothalamic Lesions¹

The classical studies of HETHERINGTON and RANSON²⁻⁵, of BROBECK^{6,7}, and ANAND and BROBECK^{8,9} described the role of the hypothalamus in the control of food intake; these findings were confirmed by numerous workers¹⁰.

Aside from a study by KENNEDY¹¹, who investigated the effect of ventromedial lesions on food intake in weanling rats, these studies were conducted in adult rats. In contrast, however, studies of food intake pattern in rats that had lesions placed in various parts of the hypothalamus shortly after weaning are not known to this author.

The rats reported here were used initially for a study concerning the effect of hypothalamic lesions on growth. The present note deals with the food intake pattern observed in these animals from the time of operation (25 days of age) to the age of 98 days. Charles River rats of both sexes received bilateral electrolytic lesions using a modified Horsley-Clarke stereotaxic instrument. All rats were housed in individual cages in a room, kept at 24°C which was successively light and dark for 12 h periods. A synthetic diet, which yielded 4.2 Cal/g, and water were available *ad libitum*. Food intake was measured either for three consecutive days weekly or for four consecutive days every two weeks. Variations in the size of the groups as well as in the periods of measurement occur because some animals were used for experiments other than described in this note.

(A) *Food Intake Pattern of Male Rats with Hypothalamic Lesions Compared to Intact Controls.* The only group with a consistently lower food intake throughout the entire period of this investigation is that with lesions in the area of the dorsomedial nuclei (Group 5M, Table I). In none of the other groups was there a significant difference from the control values before the ninth week of life (sixth week post-operative). Food intake diminished temporarily in rats with lesions in the supraoptic area insufficient to produce diabetes insipidus (Group 2M). But ablations in both the ventromedial area (Group 3M) and lesions in the region of the mammillary-dorsal premammillary nuclei (Group 7M) were associated with significantly increased food ingestion at comparable ages. This finding

correlates with puberty (50–60 days¹²). It is noteworthy that rats with ventromedial lesions did not display the extreme degree of hyperphagia which is so characteristic for older animals with ablations in this structure^{3,6,7}. Furthermore, lesions in the mammillary-dorsal premammillary area (Group 7M) were associated with continued hyperphagia in the post-pubertal period.

(B) *Food Intake Pattern of Female Rats with Hypothalamic Lesions versus Intact Controls.* In female rats with lesions in the region of the supraoptic nuclei a slight, but significant, hyperphagia occurred during the tenth week of life (Group 2F, Table II); in male rats this had transpired during the ninth week. On the other hand, lesions in the area of the dorsomedial nuclei (Group 5F) did not cause the hypophagia shown by male rats with similar lesions. Ablations involving the mammillary-dorsal premammillary nuclei of females (Group 7F) resulted, as in the males, in increased food intake which appeared during the tenth week of life. Rats with lesions in the

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³ A. W. HETHERINGTON, *Amer. J. Physiol.* 133, 326 (1941).

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⁵ A. W. HETHERINGTON and S. W. RANSON, *J. comp. Neurol.* 76, 475 (1942).

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⁷ J. R. BROBECK, *Physiol. Rev.* 26, 541 (1946).

⁸ B. K. ANAND and J. R. BROBECK, *Proc. Soc. exp. Biol. Med.* 77, 323 (1951).

⁹ B. K. ANAND and J. R. BROBECK, *Yale J. Biol. Med.* 24, 123 (1951).

¹⁰ B. K. ANAND, *Physiol. Rev.* 41, 677 (1961).

¹¹ G. C. KENNEDY, *J. Endocrinol.* 16, 9 (1957).

¹² E. C. GREENE, in E. J. FARRIS and J. Q. GRIFFITH *The Rat in Laboratory Investigation* (Eds., J. B. Lippincott, Philadelphia 1949), 2nd Edition.