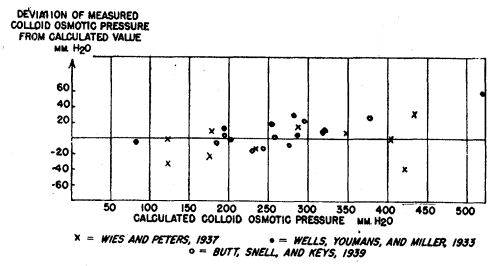

FIG. 1.

bivalent ions from the derivation of (6), (7), and (8). It is obvious that serum sodium varies in the same direction as does $[HCO_3^-] + [Cl^-]$ (or Y).

Taking the partial derivative of P with respect to Y in (8), it is found that

$$\partial P/\partial Y = T[2 - \{\sqrt{Y/(Y+Z)} + \sqrt{(Y+Z)/Y}\}]. \quad (10)$$

It is obvious that $\partial P/\partial Y$ is always negative. In other words, an increase in Y always produces a decrease in P, and a decrease in Y always produces an increase in P.

It is to be noted then that, with all other factors remaining constant, a fall in serum sodium produces a rise in serum colloid osmotic pressure (Fig. 2). This is an

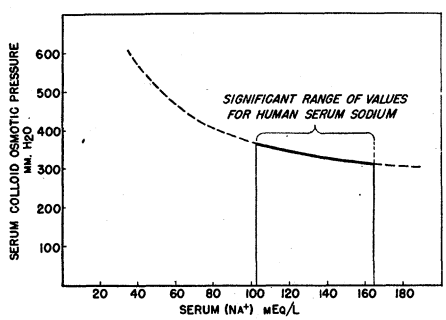

FIG. 2.

observation not previously emphasized and is a consequence of the Donnan equilibrium; it is discussed in more detail elsewhere (*11*). It is interesting in this connection that oral administration of isotonic sodium chloride has been shown to produce a fall in serum colloid osmotic pressure (*13*).

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Decreased "Hunger" but Increased Food Intake Resulting from Hypothalamic Lesions[1]

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A marked increase in food intake, hypothalamic hyperphagia, regularly follows bilateral lesions in the region of the ventromedian nuclei of the hypothalamus. There is no corresponding increase in energy output; the result is obesity. These effects have been produced experimentally in the rat, cat, dog, and monkey; they have been observed as one of the effects of basal brain tumors in man (Froelich's syndrome, or dystrophia adiposogenitalis), and of spontaneous degeneration of the ventromedian nuclei in the mouse.

The literature relating to this problem has been summarized elsewhere (*1, 6*), but since effects of lesions in this area are not generally known they will be listed briefly here. In the rat the diurnal cycle of food intake disappears, being replaced by a relatively constant level. Resection of most of the stomach does not appreciably reduce the hyperphagia. The increased food intake and rapid weight gain (dynamic phase) are not indefinitely maintained; a weight plateau is reached in about 2 months, with food intake gradually falling to a more normal level (static phase). However, after fasting to normal weight, these animals will again show a hyperphagia on return to an ad libitum diet.

Discrete bilateral electrolytic lesions made with the Horsley-Clarke stereotaxic instrument have ruled out direct involvement of the pituitary. In the rat these lesions also cause a marked upset in water balance, as demonstrated by delay in release of water loads, low ratio of water to food intake, and increased renal tubular reabsorption. An increased serum sodium in these animals suggests that a chronic state of relative

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dehydration results from an inadequate intake of water, "hypothalamic hypodipsia" (7). Rage is more easily evoked in the cat and the rat, and gonadal atrophy usually occurs, but these effects do not always accompany obesity and may follow lesions of other hypothalamic areas that do not produce obesity.

The purpose of the present study was to determine whether the marked increase in food intake produced by this lesion is accompanied by increased performance in a variety of behavioral tasks motivated by hunger. Different tests were used in order to reduce the possibility that the operation affected the particular function employed as a measure of motivation rather than the motivation itself.

The following tests were used: rate of bar pressing reinforced by food at 5-min intervals, speed of running down a short alley to secure food, strength of pull exerted during temporary restraint on the way to food, amount of electric shock required to prevent approach to food, amount eaten when a weighted lid has to be lifted to get food, and amount eaten in spite of a bitter taste when quinine was mixed with the food. Because performance on these tests is known to increase with food deprivation (up to reasonable limits), it is assumed that they are behavioral measures of "hunger." Positive results on these measures would indicate that this lesion increases a general hunger drive, negative ones would suggest that it maintains hunger at a relatively constant low level or that it interferes with the mechanism of stopping eating.

Twenty-two hungry male albino rats of the Sprague-Dawley strain, weighing approximately 350 g, were first trained to press a bar to secure a small pellet of food. During the latter part of the training the food reinforcement was at 5-min intervals—that is, the food-delivering mechanism was reset every 5 min. Under these conditions rats respond at a steady rate, which increases progressively with the length of food deprivation up to 4 or more days (5). The animals were also thoroughly trained to wear a little harness and run down a short alley, at the end of which they pressed back a small metal shield to secure food. In this type of situation, the speed of running, strength of pull when temporarily restrained (2, 3), and amount of electric shock required to keep the animal from the goal (4) have been found to increase with food deprivation, and hence presumably with hunger.

After the preliminary training, the animals were divided in two matched groups: (a) 10 controls, 5 of which were anesthetized and had their skulls opened with a drill to simulate an operation; and (b) 12 animals that received bilateral lesions approximately 1 mm in diameter in the regions of ventromedian nuclei of the hypothalamus. The lesions were made with the Horsley-Clarke stereotaxic instrument. The coordinates used were those previously found to produce lesions in or near the lateral aspect of the ventromedian nuclei of rats of the same strain and size. The electrodes were insulated except at the tip, the current used was 2 ma for 15 sec. One of the operated animals died, 11 recovered to apparently good health. All animals were allowed food ad libitum except during the various tests.

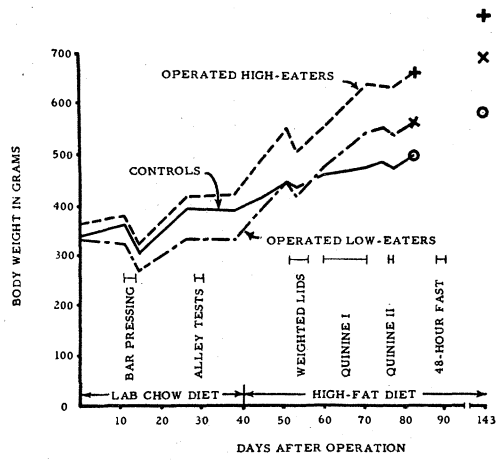

FIG. 1. Weights of different groups of rats when various tests were administered. During the first three types of tests, one of the operated subgroups was heavier and the other lighter than the unoperated controls. After the introduction of the high-fat diet, both operated groups gained more rapidly than the controls, so that by the end of the experiment even the Operated Low-Eaters were heavier than the controls.

Placed on a diet of dry, ground lab chow, 4 of the operated animals (to be called *Operated High-Eaters*) ate 30%–85% more than the average of the controls; 7 (*Operated Low-Eaters*) ate approximately the same or less than the controls. When a high-fat synthetic diet[2] was introduced on the 40th day after operation, the average food intake of the Operated Low-Eaters went above that of the controls, the difference being statistically significant ($p < .01$). These effects are reflected in the weight curves in Fig. 1, which also shows how long after the operation each type of test was given. It can be seen that during the bar-pressing and alley tests, the average weight of the Operated High-Eaters was above, whereas that of the Operated Low-Eaters was below, that of the unoperated controls. This gives us a way of ruling out the effects of weight on the test performance of the operated animals. After the high-fat diet was introduced, the weights of the operated animals increased markedly, so that even the Operated Low-Eaters became heavier than the controls ($p < .01$).

Bar pressing. On the 11th day after the operation the animals were thoroughly satiated on ground lab chow moistened with water and then immediately put in with the bar for a 20-min period. The number of times they pressed the bar was recorded. The same test was repeated at various intervals (up to 96 hr) during the fast. With the technique of periodic reinforcement, the amount of food each animal received (0.2 g per test) was negligible. The results are presented in Fig. 2. Immediately after satiation both operated groups pressed the bar less frequently to get food than did the controls.

[2] The high-fat synthetic diet yielded 5.8 cal/g, of which 60% was from fat, 20% from carbohydrates, and 20% from protein. It contained adequate amounts of all known accessory food factors required by the rat, including 4% by weight of a salt mixture.

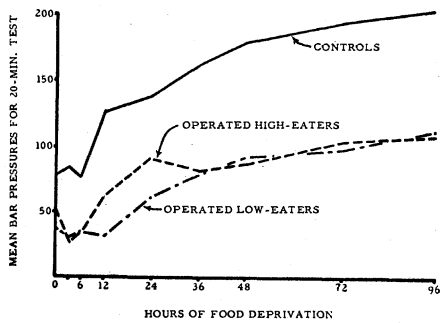

FIG. 2. Effect of hypothalamic lesions on the rate of bar pressing after various intervals of food deprivation. The rate of bar pressing (reinforced at 5-min intervals) increases with hours of food deprivation; the performance of both operated subgroups is poorer than that of the control rats. (Since one of the Operated Low-Eaters had a total score that was more than 12 S.D. above the mean of the rest of the operated group, his scores are omitted from this graph. They were, respectively: 141, 120, 123, 180, 220, 252, 229, 287, and 220. This is the only type of test on which this animal's scores were significantly different from those of the other operated animals.)

The rate of bar pressing by all groups increased with hours of food deprivation, but the increase of both operated groups was less than that of the controls. At each of the 9 points on the curve, the inferiority of the operated animals is highly significant statistically ($p < .01$).

Alley tests. On the 29th day after the operation the animals were satiated again and immediately afterward given 4 test trials in the alley without wearing harnesses. The average speed of the operated animals was slower than that of the controls, but the difference was not statistically reliable. After 72 hr of fasting the animals were given 2 additional trials with harness in the alley. Again the operated animals ran more slowly than the controls; this time the difference was fairly reliable ($p < .05$). Next their strength of pull was measured when they were temporarily restrained on the way to the food. The control animals pulled harder than the operated animals, and the difference was statistically significant ($p < .01$). Finally, the animals were given tests during which they received increasingly strong shocks from the metal shield covering the food. On the average the operated animals were stopped by lower values of shock than the controls, but the difference was not statistically significant.

Weighted lids. From the 40th day after the operation to the end of the study the animals were kept on a high-fat synthetic diet. On the 46th day light, hinged lids, concealing the food but easy to operate, were put on the food dishes in each rat's home cage. After 6 days of learning to operate the lids, a 75-g weight was put on the outer edge of the lid for half of both operated and control animals. After 3 days of testing, the weights were shifted for 3 days to the lids of the dishes of the animals in the other half of each group. Without weights on the lids, the operated animals ate more than the controls, the daily means being 21.2 and 16.3 g ($p < .01$). With weights on the lids, the total intake of both groups was reduced, and the direction of the difference between them was reversed, the daily means being 3.3 g for operated and 10.8 g for controls ($p < .01$).

Quinine tests. In order to impose an entirely different type of "resistance" to eating, the lids were removed and the high-fat diet gradually made bitter by progressively adding more quinine to it each day from the 61st to the 70th day after operation. While the concentration of quinine was still relatively weak, the operated animals ate reliably more than the controls, the daily means being 26.4 and 15.1 g, respectively ($p < .01$). Increasing amounts of quinine decreased the intake until, by the 70th day, when the proportion was 1,024 mg of quinine per 100 g, the daily means were down to 2.8 and 8.8 g for the operated and control animals, respectively ($p < .01$). The use of this different kind of "resistance" to eating had again reversed the relative food intakes.

After 6 days' recovery on a bland, high-fat diet, all animals were returned to the 1,024 mg of quinine per 100-g diet mixture, and at various times, up to 48 hr after introduction of the bitter mixture, cumulative measures were taken of the total amount eaten. The results, compared with similar measures taken on bland food 9 days later, are presented in Fig. 3. It can be seen that under all conditions the eating continued at a reasonably regular rate, as indicated by the fact that the curves roughly approximate linearity. The rate of food consumption is greater for the bland than for the bitter mixture; with the bland mixture it is greater for the operated animals than for the controls, and with the bitter mixture this difference is reversed. All these differences are highly reliable ($p < .01$).

Forty-eight-hr fast. As a supplement to the behavioral tests, the effects of a 48-hr fast on subsequent food consumption were determined for various intervals up to 24 hr. On the 89th day after operation, food was taken away from all animals and then restored after 48 hr. Whereas before the fast the operated animals had been eating more than the controls, afterwards this difference was reversed during the period of observation ($p < .01$).

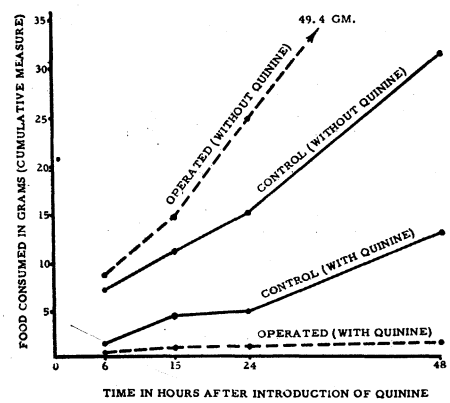

FIG. 3. Effect of a bitter taste on the food intake of rats with hypothalamic lesions. With a bland mixture of synthetic high-fat diet the cumulative curves show a higher food intake for the operated animals than for the controls; with a bitter mixture (1,024 mg of quinine/100 g) the food intakes of both groups are reduced, and the direction of the difference between them is reversed.

It should be noted that the operated animals were all considerably heavier than the controls by the time this fast was given.

In all the behavioral tests the operated animals performed more poorly than the controls, and in most instances the differences were clearly significant statistically. Because of the consistent results with such a variety of tests, it seems more plausible to assume that the operation interfered with hunger than to assume that it had specific effects on the different functions involved in each of the various tests.

While they were on a diet of ground lab chow, some of the operated rats ate consistently more than the controls, whereas others ate somewhat less. The performances of both operated groups were highly similar on the behavioral tests; both of them were poorer than the controls. The fact that one of the operated subgroups was heavier and the other lighter than the controls rules out the factor of body weight as an explanation for their inferior performance.

When placed on a high-fat diet, both operated groups ate consistently more than the controls in all ad libitum situations throughout the experiment. The reduced intake of the Operated Low-Eater subgroup on the less-well-liked ground lab chow diet seems to be analogous to the poorer performance of the operated animals on the behavioral tests.

One interpretation of the results of this study is that the hypothalamic lesions cause the mechanism regulating hunger to "stick" at a relatively constant low level. This explanation would not be sufficient by itself, however, to account for the poor performance of the operated animals on bar pressing immediately after satiation. Another interpretation would be that the lesions interfere seriously with the mechanism of stopping eating and somewhat less seriously with the mechanism of hunger. Whatever the final explanation may be, the striking fact is that the measures of the amount of food eaten in ad libitum situations yielded results opposite to those of the tests where some form of work had to be done or "resistance" overcome. This suggests caution in drawing inferences about "drive" from consummatory behavior in both psychological and psychiatric studies.

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Comments and Communications

"Funginert"—A Designation for Inherently Fungus-resistant Material

During and following World War II there has been increasing recognition of the importance of biological factors in the deterioration of engineering materials. Fungi and other microorganisms, already known to be destructive to products such as lumber and cotton textiles, were found to exert a malign effect also on electrical equipment, with resultant degradation and operational failure. In many cases damage was indirect, as when operational failure resulted from corrosion of a metal surface, caused in turn by metabolic products from fungi supported by an adjoining nutrient surface.

In attempts to prevent such damage, military and other specifications are now increasingly being phrased to require that materials used in equipment have resistance to fungus growth. For the kind of resistance that depends on fungistatic or fungicidal chemicals, the terminology and test methods for the chemicals and for the treated engineering materials may follow somewhat along the lines of the older parallel usages in medicine and agriculture. In other cases, however, materials are desired which have innately the property of not supporting fungus growth because of absence of nutrients rather than because of presence of fungistatic chemicals. Such materials have been designated as "nutriently inert" or "not supporting fungus growth" in certain publications (Bureau of Ordnance Specification 52T15 (Ord). *Treatment, moisture- and fungus-proofing, of elements, components, and assemblies, electrical and electronic: general specifications.* 22 pp. Proposed draft, Feb. 14, 1947), which have also provided special test procedures by which this property of "nutrient inertness" might be demonstrated. With these inconveniently long terms it was still necessary to add modifying words to make the meaning precise.

As the concept discussed is applied more and more broadly (for example, to plastics, tape, transformers, and electrical insulated wires), it becomes desirable to designate it by a distinct and concise name. To fill this need, the coined words "funginert" for the adjective and "funginertness" for the characteristic are proposed. Definitions are:

Funginert. Not supporting fungus growth because the material, part, or component in question does not furnish the necessary nutrients for such growth. To be distinguished from both "fungistatic," which indicates presence of a chemical or physical agency that actively prevents growth of fungi, and "fungicidal," which indicates presence of an agency (usually chemical) that can kill