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Biocontrol Systems in Food Intake*

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1. INTRODUCTION

Energy balance is maintained by a multiple-sensor, closed feedback system, with a regulated input as well as output. Food intake is one of the major effector elements for regulating input in this system. In this chapter I would like to discuss the system controlling feeding behavior as a problem in psychobiology, or more specifically, in behavioral physiology (Jacobs, 1965). I shall first outline the currently accepted view of feeding regulation, note its limits, outline an alternative view consistent with current trends in the literature, and report some behavioral and physiological evidence in agreement with it.

The data to be presented comes from three sources: (1) behavioral evidence, measuring intake of various diluted diets selected to evaluate taste and calories as potential signals for ingestion; (2) electrophysiological evidence, to get at the problem of information transfer in the sensing elements of the system; and (3) general physiological evidence, to get at the metabolic changes in the system.

2. SCHEMATIC: TWO POTENTIAL DETECTOR SYSTEMS

Figure 1 outlines the potential feedback loops involved in food intake. Ingestion of any foodstuff provides two classes of stimuli, which, on activating receptors in the afferent loop of system, are carried to the brain (CNS), where efferent decisions are made, stopping intake by activating a satiety mechanism, or increasing it by potentiating appetite. The two categories of signals have been labeled metabolic and sensory. The metabolic class has been of major concern to biochemists and nutritionists interested in the metabolic consequences of ingestion, and to regulatory physiologists, who have implicated them as factors in the control of food intake. For example, the ingestion of glucose provides sweetness, a sensory signal, plus three potential metabolic signals, glucose (a specific carbohydrate), its caloric value, and the additional heat produced by its specific dynamic action (SDA). The sensory class has been of major concern to sensory physi-

*Empirical correlations between food and water intake suggest that they are both controlled by a unitary system for water-energy homeostasis. However attractive, this assumption can occasionally be misleading, and detailed analyses of its implications are lacking (Jacobs, 1964). Thus, in this chapter food intake will be discussed as if it were independent of the factors controlling water intake.

ologists and psychologists, who have been concerned with the operation of sensory systems (Hayashi, 1967) and with the relation between the perception of combinations of these sensory signals and the affective or hedonic qualities of food (Pfaffmann, 1961).

For our purposes, we can ignore the complexities of the two systems in Fig. 1 and substitute the term calories for the metabolic class and taste for the sensory class, as shown in Fig. 2. Although I shall use the terms taste and calories in this discussion, what I call calories may be heat, blood glucose shifts, etc., and what I call taste may be taste or olfactory stimuli, and so on.

3. CLASSIC VIEW: PRIMACY OF METABOLIC DETECTORS

For the most part, the analysis of the role of taste and calories in food intake has been carried out by two independent groups of investigators.

One group has been interested in taste and has emphasized either the problem of information transfer in peripheral receptor systems (Hayashi, 1967), or that of analyzing the role of sensory qualities in the acceptability of foodstuffs and relating it to the psychological problems of motivation, emotion, pleasure, acceptance, etc. (Young, 1966). In terms of the outline in Figs. 1 and 2, this approach would focus on the taste (sensory) properties of food, and would emphasize the nervous pathway between the peripherally located receptors and the central nervous system. With a few important exceptions, based upon new approaches to be discussed in the next section, these investigators limit their study to taste and olfaction, the classical chemoreceptor systems whose receptors are located in the oral-pharyngeal cavity. For the most part, the sensory physiologist and psy-

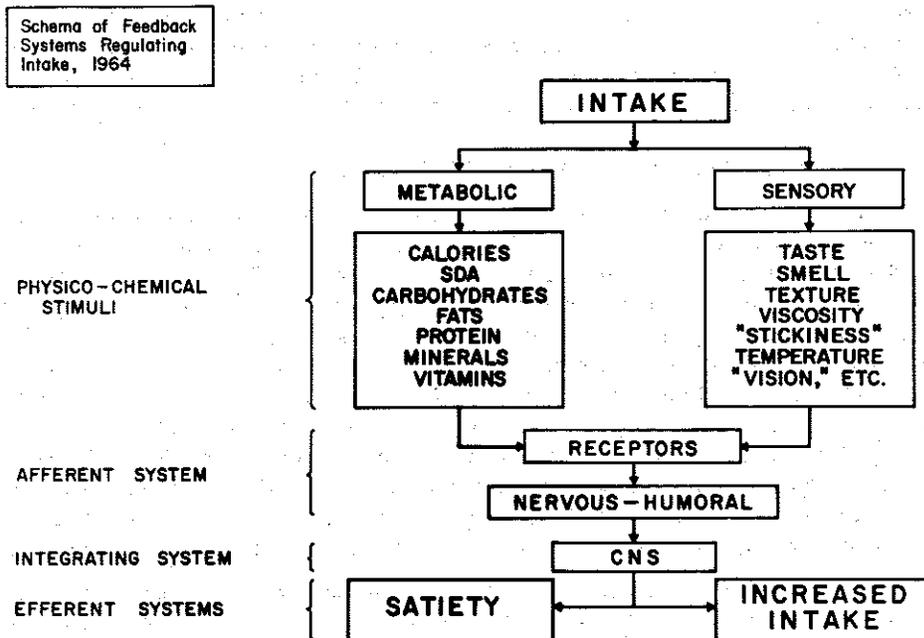


Fig. 1. Generalized schema of multiple feedback loops in the control of food intake (Jacobs, 1968).

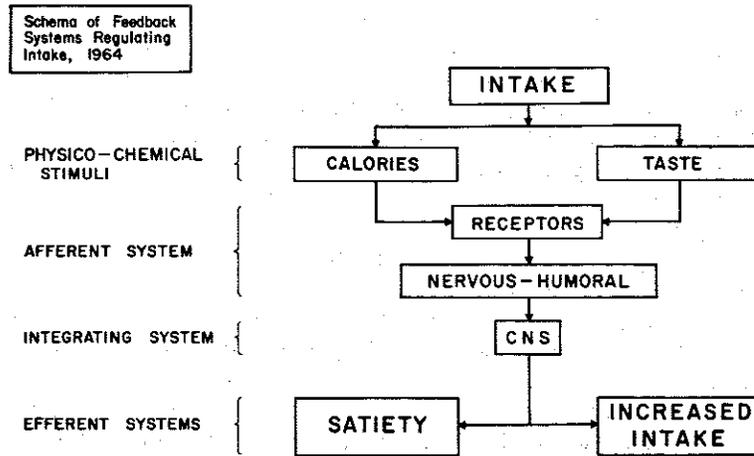


Fig. 2. Simplified schema of taste and calories as cues in the control of food intake (Jacobs, 1968).

chologist has had little direct interest in the regulation of body weight and food intake.

Thus, the classic view of the control system in food intake has been developed by a second group of investigators who have focused on the caloric (metabolic) properties of foodstuffs (Hollander, 1955). Following Fig. 2, we can outline this view quite simply. The metabolic products of ingested food (calories) are assumed to reach the brain via the blood (the humoral path in Figs. 1 and 2), there to be monitored by a hypothalamic detector system containing specialized receptors (e.g., glucoreceptors). This detector system then activates the efferent loop, which controls further intake. This view asserts that both detection and control occur in the central nervous system and pays little attention to the peripheral nervous system as part of the physiological system regulating food intake (Stellar, 1967).

In behavioral terms, this view would assert that the organism eats for calories. Behavioral evidence for this hypothesis has accumulated rapidly for over three decades (e.g., Cowgill, 1928; Adolph, 1947; Teitelbaum and Epstein, 1963). For the most part, this evidence comes from diet-dilution experiments. If the caloric density of a diet is changed by the addition of nonnutritive bulk, by fat, or by flavor additives, volume intake is adjusted to maintain constancy of caloric intake. Figure 3 shows the results of such an experiment in our own laboratory. Rats ingesting 22 grams of stock diet per day on ad libitum feeding increase intake of a 40% cellulose diet (2.4 kcal/g), return to normal on the stock diet (4.0 kcal/g), and decrease intake on a 25% corn oil diet (5.10 kcal/g). These adjustments of intake to caloric density are typical of the kind of behavioral evidence in agreement with the current view that caloric signals activate a central detector and control system for food intake.

4. EVALUATION OF CLASSIC VIEW: CURRENT DATA

Peripheral Detection of Metabolites. Sporadic bits of evidence have been accumulating over the past several years which suggest that peripheral chemorecep-

tor systems may extend well beyond the classic taste and olfaction modalities in the oral-pharyngeal cavity into the intestinal tract and intraperitoneal cavity. First, a study by Sharma and Nasset (1962) showed that intestinal perfusion with glucose and amino acids changed electrical activity recorded from the mesenteric nerves. More recently, Nijima (1968) suggested the existence of a glucoreceptor system in the liver. Figure 4 shows the results of one of Nijima's experiments recording electrical activity from the hepatic branch of the vagus nerve of an excised guinea pig liver in which various substances could be perfused into the portal vein. Inspection of Fig. 4 shows that perfusion with Ringer solution resulted in a relatively stable baseline activity (A), which was not changed with the introduction of mannose (B). However, perfusion with glucose sharply inhibited the electrical activity (C), which resumed when Ringer solution was again introduced (D). Results of this type led both investigators to postulate the existence of two chemoreceptor systems, a glucoreceptor and possibly an amino acid receptor system in the intestine (Sharma and Nasset, 1962), and a glucoreceptor system in the liver (Nijima, 1968) which possibly sends information about metabolites in the intestine, or in the portal vein, to the central nervous system. A similar study by Sudakov (1962) suggested that a similar system may be located in the gastric cavity. This investigator measured the electrical activity of the gastric vagus in food-deprived, anesthetized cats following intragastric loading of foodstuffs. Figure 5 shows the results of an experiment in which the application of intragastric loads of milk sharply inhibited the electrical activity of the gastric vagus.

These studies are not yet definitive in clearly defining the specificity of these chemoreceptor systems, and have not attacked the important problem of the relation between the peripheral receptor system and areas of the CNS involved in food intake. However, they do demonstrate that fast-acting peripheral sensory sys-

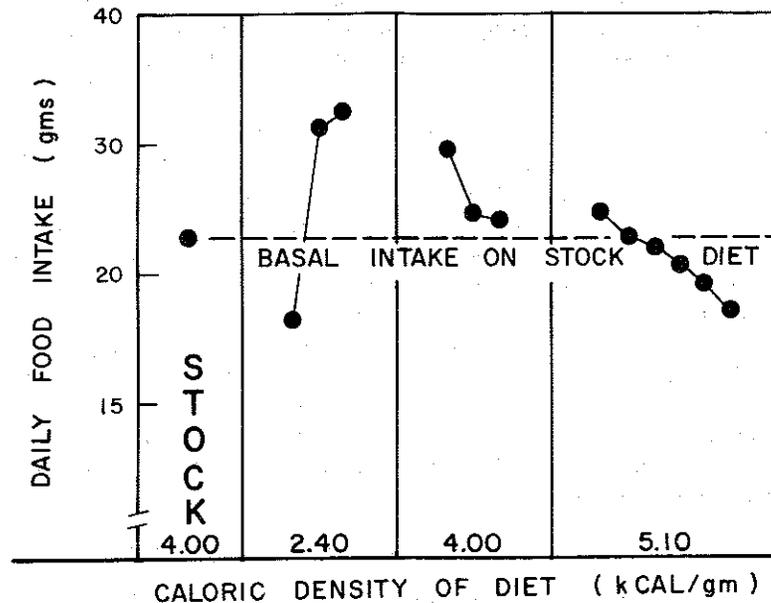


Fig. 3. Eating for calories in ad libitum fed rats (N = 12) (Jacobs, 1968).

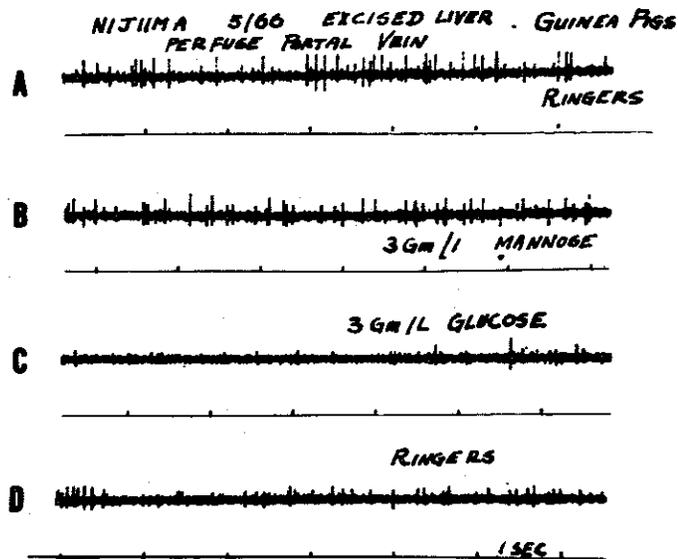


Fig. 4. Effect of perfusion of liver on electrical activity of the hepatic branch of the vagal nerve in the guinea pig (after Nijima, 1968).

tems can detect ingested metabolites. The existence of this previously unsuspected pathway for information from ingested metabolites to reach the brain raises some doubts about the description of the classic system in Section 3, in which it was assumed that both detection and control were limited to the central nervous system, and that metabolic products of ingestion arrived at the brain only via the systemic circulation, only after intestinal absorption, and only after processing by the liver.

The Effect of Hunger. Review of the behavioral evidence for the hypothesis that animals eat for calories shows that most of the studies showing this type of regulation were carried out on ad libitum fed animals (Jacobs and Sharma, 1968). However, when hungry animals are used taste seems to become more important. Figure 6 shows the result of such an experiment by Bacon and co-workers (1962) using saccharine, in which the caloric signal is absent. Rats were given a 30-min drinking test for various concentrations of sodium saccharine while under ad libitum feeding conditions, or when hungry. The bottom curve in Fig. 6 shows that ad libitum rats show maximum preference for a .45% solution. In the upper curve, food deprivation shifts the preferred concentration from the mildly sweet solutions to an extremely sweet, 3% solution. Thus, hunger seems to potentiate the role of sweetness as a sensory signal for ingestion of solutions.

Since the classic evidence for adjustment to caloric signals was obtained with dry diets rather than solutions, it became necessary to use the former as well as to check the relative importance of taste vs. calories as a function of hunger.

Figure 7 shows the results of a cellulose dilution experiment comparing ad libitum fed with hungry animals. As expected (see Fig. 3), the ad libitum animals eat for calories, increasing intake when the diet is diluted with 40% cellulose (A). The hungry animals (B) decreased intake with cellulose dilution, ignoring the

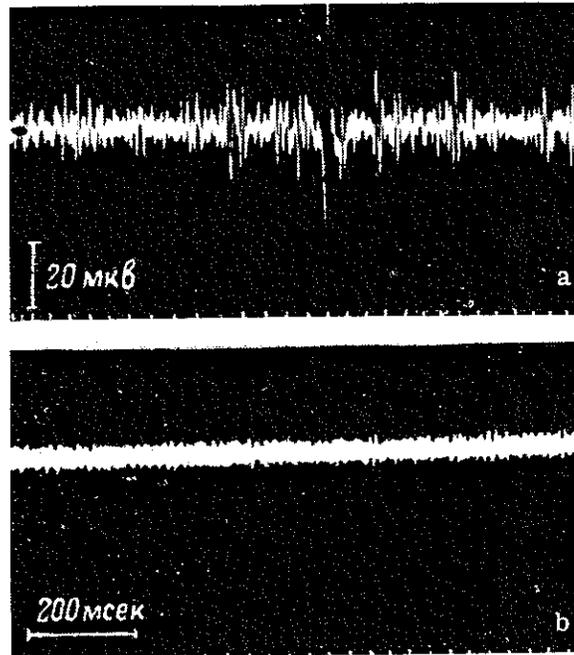


Fig. 5. Changes in the electrical activity of the gastric branch of the vagal nerve of the cat after intragastric loading of 50 ml of warm milk. a) With the stomach empty; b) 3 min after milk loading. MvB) microvolts; Msec) milliseconds (Sudakov, 1962).

change in caloric density. Perhaps this was because the hungry animals found the cellulose additive unpalatable. If this were true, it should be possible to increase the intake of the cellulose-dry-diet mixture by changing its taste. The addition of a palatable mixture of corn-oil and water (C), previously shown to be ignored by ad libitum fed animals, increased intake.

A more direct test of the hypothesis that cellulose is unpalatable to hungry animals but could be made palatable by appropriate additives is shown in Fig. 8. Hungry rats completely avoid a dry diet consisting of pure cellulose. However, the addition of water, Tween-80 (a standard commercial emulsifier), and saccharine all increased intake. All of these changes in intake took place in the complete absence of caloric signals.

Our interpretation of the results presented in Figs. 7 and 8 is that the hungry animals ignored the change in caloric density with cellulose dilution and adjusted intake on the basis of taste.

5. NEW MODEL: A DUAL DETECTOR SYSTEM

These and other studies suggested that the relative importance of taste and calories is related to the state of energy balance (Jacobs and Sharma, 1968). This view is formalized in Fig. 9, a simple extension of the schematics in Figs. 1 and 2.

The model in Fig. 9 shows that physicochemical information from the diet

feeds into two detector systems which can respond to signals from taste (left) or calories (right). Whether the central nervous system makes use of either set of signals in monitoring intake is a function of the state of energy balance. The energy pool acts as a biasing system, assigning priority to taste when the animal is in deficit, and to calories when it is in balance, or in surfeit.

It should be pointed out that this model does not assume a digital system in which either detector system can be completely shut off. The animal is always capable of responding to either taste or calories; energy balance merely changes the relative importance of each in monitoring intake. The key difference between this model and the classic view of intake described in Section 3 is that in Fig. 9 taste (sensory qualities) is actively involved in the physiological mechanisms controlling intake, and that peripheral detection and control assume equal status with central detection and control.

Summarizing the data outlined thus far, we have suggested that peripheral receptor systems can detect caloric information just as quickly as the classic taste system responds to flavor cues, and we have shown that taste can control intake in hungry animals (Section 4). To complete the contrast with the classic view, we can now ask whether taste (sensory qualities) can control output and metabolic events as well as input. The answer, although preliminary, is in the affirmative.

6. SENSORY CONTROL OF METABOLIC EVENTS

The respiratory quotient (RQ) and blood glucose are two classic indicators of

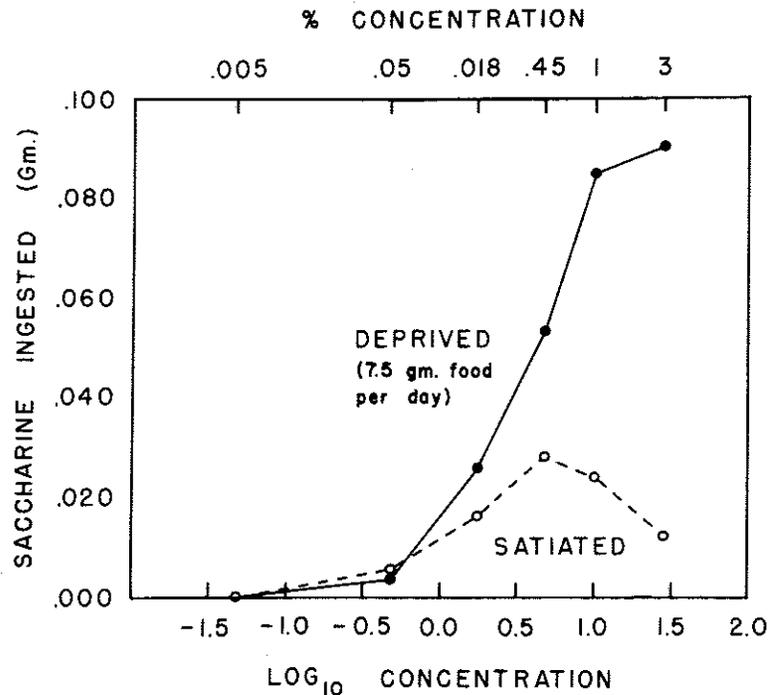


Fig. 6. The relative preference for sodium saccharine in food-deprived (N = 18) and satiated (N = 18) rats (after Bacon et al., 1962).

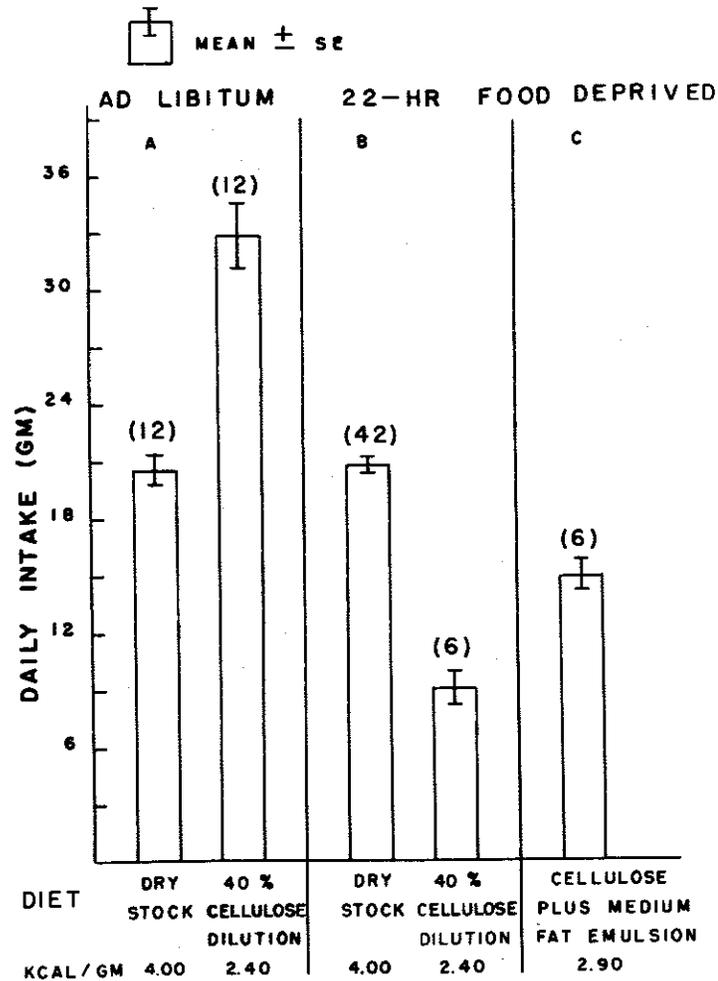


Fig. 7. Effect of food deprivation on eating for calories as caloric density is changed by dilution with cellulose and corn oil. Parentheses enclose number of observations in each treatment (Jacobs, 1968).

postabsorptive metabolic changes following food ingestion. For example, ingestion of a high-carbohydrate diet would produce an increase in blood sugar level on a short-term basis and increase RQ on a long-term basis. The former results from glucose entering the systemic circulation via the intestine or liver, and the latter reflects the type of molecule catabolized by cells, approximating 0.7 when metabolizing lipids, and rising to 1.0 when metabolizing carbohydrates.

Nicolaidis, working in LeMagen's laboratory at the College de France (Nicolaidis, 1968) has initiated a program of work to investigate the role of sensory processes in these phenomena.

Figure 10 shows the effect of food ingestion on RQ. Hungry rats are allowed to eat to satiety, the meal lasting from 15 to 25 min. Within 1 min of starting to

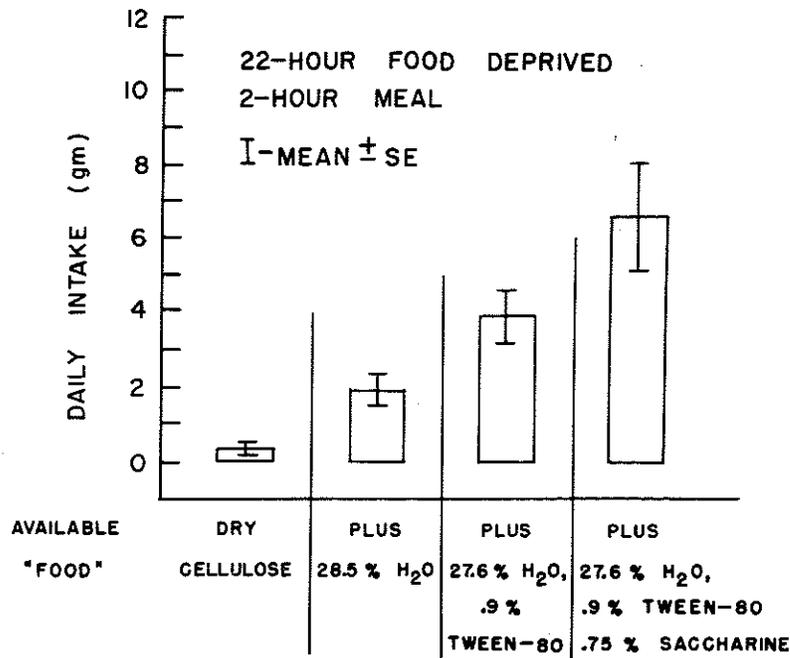


Fig. 8. Effect of palatable, nonnutrient additives on the ingestion of pure cellulose in food-deprived rats (N = 6) (Jacobs, 1968).

eat, RQ significantly increased, reached asymptote in 15 to 20 min, and remained elevated throughout the 40-min period of measurement. These changes were too rapid to be a function of nutritional processes. Nicolaidis hypothesizes that they are produced by anticipatory reflexes mediated through the taste system. Thus, the taste of food increases RQ immediately, anticipating the metabolically produced increase in RQ to occur later.

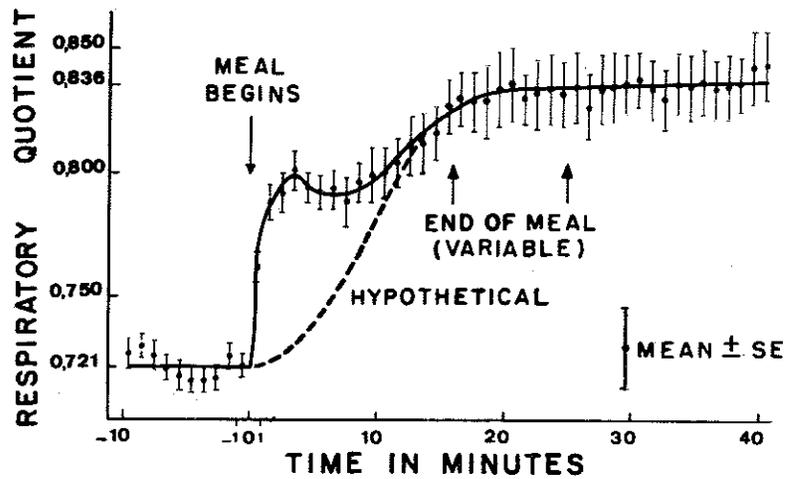


Fig. 9. Model of the role of energy deficit in the control of food intake (Jacobs, 1968).

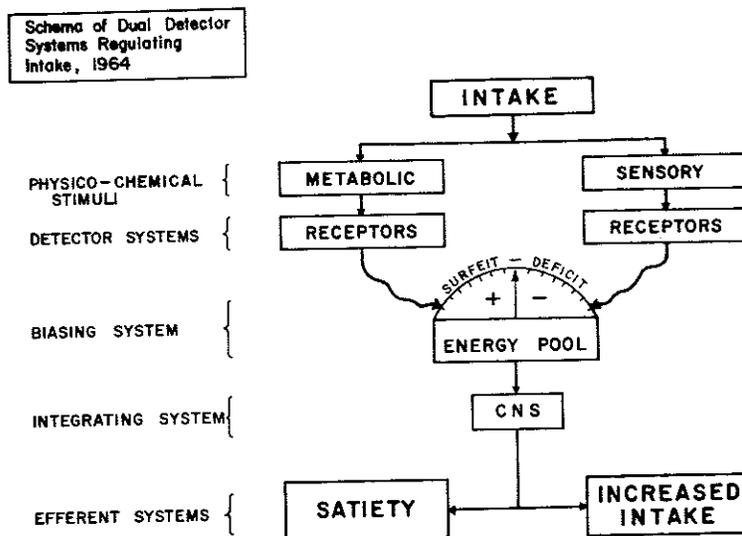


Fig. 10. Effect of food intake on short-latency changes in RQ. Results from 17 experiments on rats. The hypothetical dashed line corrects for possible effects of activity and hyperventilation associated with the beginning of eating (after Nicolaidis, 1968).

Figure 11 shows the effect of taste on blood sugar level. The ingestion of either sucrose or saccharine solutions significantly increased blood glucose level in less than 5 min in hungry animals but not in those fed ad libitum. The short latency of the response and the fact that saccharine produces it argues against a metabolic interpretation.

In both cases, Nicolaidis interprets these results as indicating that sensory signals can control metabolic events. In terms of the model in Fig. 9, we would say that the receptor systems for taste signals not only become more important in controlling intake, but feed back into the efferent system controlling the energy pool (not shown in the model), producing some of the metabolic changes ordinarily controlled biochemically at the cellular level. In common sense terms, it could be hypothesized that the hungry animal eats for taste, and that the taste cues accompanying ingestion directly initiate some of the satiety signals (e.g., hyperglycemia) which classically follow the normal processes of digestion. Thus, satiety cues are produced in two phases, first as an anticipatory reflex initiated by the taste of food, and secondly, by the postabsorptive metabolic events.

7. SUMMARY

In summary, I have reviewed the classic view of food intake which emphasizes the role of the central nervous system in controlling intake, in which detector systems in the hypothalamus responds to metabolic signals. In this view animals eat for calories and taste is important for sensory pleasure, operating independently of the biological system controlling intake.

I have also reviewed electrophysiological, behavioral, and metabolic evidence suggesting the inadequacy of the classic view and outlining a model in agreement

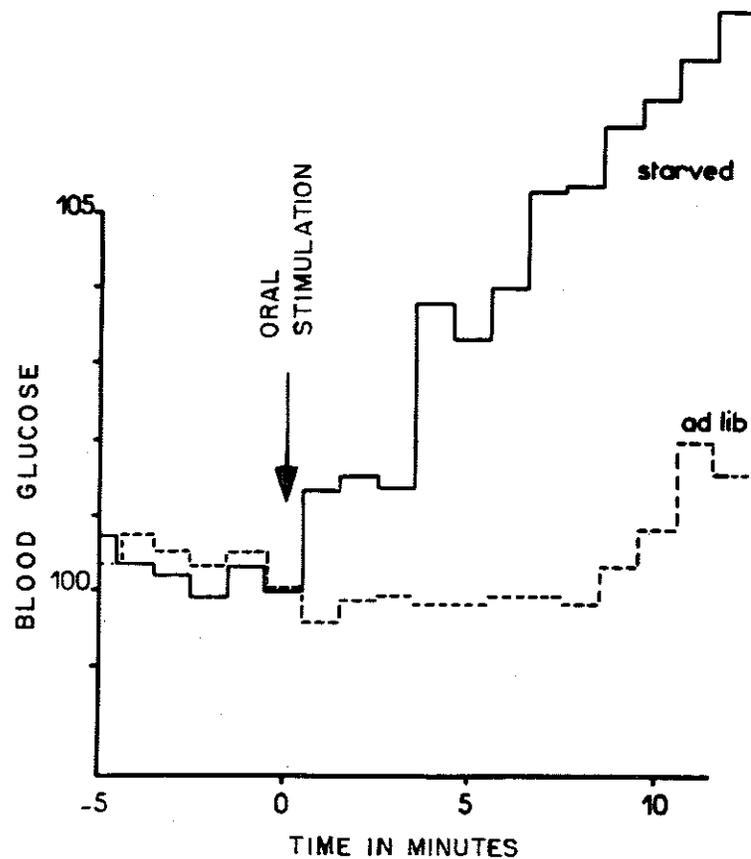


Fig. 11. Effect of oral stimulation with sweet solutions (either 30% sucrose or 0.01 saccharine) on blood glucose levels of rats ($N = 22$). Results expressed as mean percent change from baseline, which is taken as 100% (after Nicolaidis, 1968).

with the new evidence. The classic view asserts that both central and peripheral detector systems are involved in the regulation of intake. Taste or sensory factors, including receptor systems in the gastrointestinal tract and liver that can provide short-latency detection of the metabolic properties of ingested food, are more broadly defined in this view. Taste is also given emphasis in that it supplants calories as the critical signal modulating intake when the organism is in energy deficit. In this view, taste signals can also initiate metabolic events before the occurrence of the nutritional changes usually producing them.

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The ideas and some of the data were discussed with and contributed to by Dr. Stelios Nicolaidis, College de France, Paris, an independent collaborator of parallel thought. Dr. Nicolaidis has been concerned with the problem of the role of peripheral reflex systems in biological regulation in general and used electrophysiological and metabolic measurements (Nicolaidis, 1968), while the author has emphasized the regulation of food and water intake and used behavioral and

general physiological measures (Jacobs and Sharma, 1968).

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REFERENCES

- Adolph, E. F., "Urges to eat and drink in rats," *Am. J. Physiol.*, 151: 110-125 (1947).
- Bacon, W. E., Snyder, H. L., and Hulse, S. H., "Saccharine preference in satiated and deprived rats," *J. Comp. Physiol. Psychol.*, 55: 112-114 (1962).
- Cowgill, G., "The energy factor in relation to food intake: experiments on the dog," *Am. J. Physiol.*, 85: 45-64 (1928).
- Hayashi, T. (ed.), *Olfaction and Taste*, Vol. II, Pergamon Press, New York, 1967.
- Hollander, F. (ed.), "The regulation of hunger and appetite," *Ann. N. Y. Acad. Sci.*, 63: 1-144 (1955).
- Jacobs, H. L., "The interaction of hunger and thirst: experimental separation of osmotic and oral-gastric factors in the regulation of caloric intake," in: *Thirst Symposium*, Wayner, M. (ed.), Pergamon, Oxford, 1964, pp. 117-137.
- Jacobs, H. L., *Behavior Physiology: A review of basic readings in neuropsychology*, Isaacson, R. L. (ed.), New York, Harper and Row, in: *Contemp. Psychol.*, 10: 91-92 (1965).
- Jacobs, H. L. and Sharma, K. N., "Taste vs. calories: sensory and metabolic signals in the control of food intake," in: *Neural Regulation of Food and Water Intake*, Morgane, P. J. (ed.), *Ann. N. Y. Acad. Sci.* 157, Art. 2: Jacobs, 1084-1125 (1969).
- Nicolaidis, S., "Early systemic responses to oro-gastric stimulation and their electrophysiological basis in the regulation of food and water balance: Function and electrophysiological data," in: *Neural Regulation of Food and Water Intake*, Morgane, P. J. (ed.), *Ann. N. Y. Acad. Sci.* 157, Art. 2: Nicolaidis, 1176-1203 (1969).
- Niiijima, A., "Afferent impulse discharges from glucoreceptors in the liver of the guinea pig," in: *Neural Regulation of Food and Water Intake*, Morgane, P. J. (ed.), *Ann. N. Y. Acad. Sci.* 157, Art. 2: Niiijima, 690-700 (1969).
- Pfaffmann, C., "The sensory and motivating properties of the sense of taste," in: *Nebraska Symposium on Motivation*, Jones, M. R. (ed.), University of Nebraska Press, 1961, pp. 71-110.
- Sharma, K. N. and Nassett, E., "Electrical activity in mesenteric nerves after perfusion of gut lumen," *Am. J. Physiol.*, 202: 725-730 (1962).
- Stellar, E., "Hunger in man: comparative and physiological studies," *Am. Psychol.*, 22: 105-117 (1967).
- Sudakov, K. V., "The afferent and efferent activity of the gastric fibers of the vagus nerve during fasting and after taking food," *Fiziologicheskii Zhurnal SSSR imeni I. M. Sechenova*, 48: 728 (1962). In: *Fed. Proc.*, 22: T197 (1963) (translation supplement).
- Teitelbaum, P. and Epstein, A. N., "The role of taste and smell in the regulation

of food and water intake," Symposium on Olfaction and Taste, Zotterman (ed.), Pergamon, London, 1963.

Young, P. T., "Hedonic organization and regulation of behavior," Psychol. Rev., 73: 59-86 (1966).