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WOODS, SC; STRUBBE, JH; Woods, Stephen C.

Published in:
Psychonomic Bulletin & Review

DOI:
10.3758/BF03200770

Publication date:
1994

Psychonomic Bulletin & Review
1994, 1 (2), 141-155

The psychobiology of meals

STEPHEN C. WOODS
University of Washington, Seattle, Washington

and

JAN H. STRUBBE
University of Groningen, Groningen, The Netherlands

Meals are considered as bouts of behavior that, although necessary for supplying nutrients to the body, result in undesirable perturbations of homeostatically controlled parameters. If the environment dictates that an animal mainly eat very large meals, these meal-associated perturbations become potentially dangerous. When the opportunity to eat a very large meal is regular and predictable, animals adopt strategies that maximize the efficiency of the process while minimizing the threatening homeostatic disturbances. Hence, prior to the onset of meals, animals elevate their body temperatures, presumably to facilitate critical processes involved in ingestion and/or digestion. Temperature continues to rise during the meal, and as it approaches potentially dangerous levels, the meal is terminated and temperature falls to "safer" levels. Animals also undergo a slow decline of blood glucose prior to the initiation of meals, thus minimizing the postprandial elevation of blood glucose caused by the absorption of ingested carbohydrates. Analogously, prior to meals, animals undergo a decrease of metabolic rate, thus precluding the necessity for postprandial increases of metabolic rate to reach even higher absolute levels. These premeal changes of regulated parameters have been interpreted by others as indicating depletion of one or more energy supplies so that the animal is compelled to eat. Contrary to this, we interpret the changes as ones that enable the animal to prepare adequately to consume a large meal when the environment is predictable.

Humans and animals engage in bouts of energy intake (i.e., feeding) called meals. Meals occur intermittently and vary in size from very small to quite large within any given individual. The size of meals estimated under experimental conditions is obviously dependent upon the criteria used to define them. This is especially true for distinguishing individual eating bouts in freely feeding subjects (see Kissileff, 1970; le Magnen & Tallon, 1966). Most definitions of meals state the requirements that some minimum amount of food be ingested in a short window of time for the meal to be said to be initiated, and that no eating occur within a subsequent window of time for the meal to be said to have terminated. Using such a definition, parameters such as meal size, intermeal interval, and pre- and postmeal intervals can be determined. There is general agreement that in the oft-studied free-feeding laboratory rat there are from 10 to 16 meals per day (e.g., Baker, 1953), and that they range in size from 2 to 20 kCal; the actual size varies with the characteristics of the individual (gender, size, age, strain), the time of day, and the hedonic quality of the food. The size of individual meals is the focus of intense research, as scientists investigate compounds (known as satiety factors) that regulate the termination of meals and hence require animals to consume smaller or larger meals. One rationale behind these studies is that compounds that alter meal size might have long-term therapeutic benefit in terms of modifying caloric intake and body weight. Many reviews of such satiety factors exist, and they make a strong case for relatively strict physiological controls over the termination of meals (Gibbs & G. P. Smith, 1991; Morley, Bartness, Gosnell, & Levine, 1985; G. P. Smith & Gibbs, 1992; Woods & Gibbs, 1989). The aim of the present paper is to make the case that the initiation of meals, rather than resulting from deficits of one or more energy stores in the body, is a well-anticipated and orchestrated behavior intended to maximize the passage of energy into the body while minimizing the homeostatic disruption to the body.

Collier and his colleagues have found meal size to be flexible and a slave of sorts to the economics of the overall feeding situation (e.g., Collier, 1986; Collier & Johnson, 1990; Collier, Johnson, Hill, & Kaufman, 1986). When food has essentially no cost, so that at any time an animal can freely initiate eating and consume any desired amount, individuals of many species tend to consume relatively small individual meals. They maintain body weight and adiposity by initiating many individual meals each day. Hence, given a choice, animals opt for numerous small (i.e., low-calorie) meals, and are called nibblers. However, if costs are placed upon initiating meals (such

This project was supported in part by NIH Grant DK 17844 to S.C.W. and by the Netherlands Organization of Science (NWO). Although many colleagues contributed to the discussion, we would particularly like to thank L. Arthur Campfield, Francoise J. Smith, Ilene L. Bernstein, Robert C. Bolles, Anthony Sclafani, Anton J. W. Scheurink, Jan de Vries, James C. Smith, Daniel Porte, and Douglas S. Ramsay. Address correspondence to S. C. Woods, Department of Psychology, NI-25, University of Washington, Seattle, WA 98195.

as imposing physical demands to obtain access to a food bin), animals adapt by eating fewer individual meals each day while proportionately incrementing meal size. The point is that meal size appears to be malleable as other variables (costs) change. What remains relatively constant (and what, therefore, appears to have perhaps more fundamental importance to the animal) is total daily caloric intake, which of course serves to maintain body adiposity. There are many reviews describing the role of food intake in the regulation of body adiposity (e.g., Bray, 1976; Stallone & Stunkard, 1991; Woods, Decke, & Vasselli, 1974; Woods, Lattemann, Schwartz, & Porte, 1990).

When animals are forced to exert either more or less physical activity (i.e., to exercise either more or less) than normal each day, they compensate for the altered expenditure of energy by adjusting their daily caloric intake to match energy expenditure and hence circumvent major challenges to the level of adiposity. Therefore, if the extremes of exercise are not too severe, animals under these conditions maintain a relatively constant body weight. Likewise, if metabolic energy expenditure is varied (e.g., by housing animals in different ambient temperatures or during pregnancy or lactation), animals adjust daily caloric intake and maintain body weight. One strategy employed by rats in a cold or warm ambient temperature is to change average meal size. Rats maintained in warmer ambient temperatures eat less food per day and have smaller meals; rats in a cold environment increase average meal size and, consequently, total daily caloric intake (e.g., Bolles & Duncan, 1969; de Vries, Strubbe, Wildering, Gorter, & Prins, 1993). Again, the message is that, within limits, rats are quite flexible and will adopt a strategy that will maintain body weight. The precise strategy that is chosen undoubtedly depends upon prevailing conditions and restraints, and there may well be priorities of strategies available under some conditions. The principles involved presumably reflect the homeostatic defense of critical parameters coupled with the costs of individual responses.

As an example, lactating rats, like rats with other enhanced demands for energy, initially increase their meal size (see Figure 1). When energy demand increases further, they next increase the number of dark-phase meals they eat each day. Finally, when energy loss via lactation is at its maximum, they also eat more meals during the light phase of the day. It seems as if there is a hierarchy of sorts in that average meal size is the first to change, but it can only be increased by a certain amount. The next parameter to be sacrificed is meal number during the dark, then meal number during the light (Strubbe & Gorissen, 1980). This experiment, like many others (see Woods, 1991), suggests that there is a maximum meal size that animals will tolerate. If conditions dictate that more food be consumed each day than can be accommodated with a small number of large meals, more meals will be eaten each day.

The same general conclusion about the flexibility of meal size can be reached with more physiological interventions. If an animal is automatically given an injection

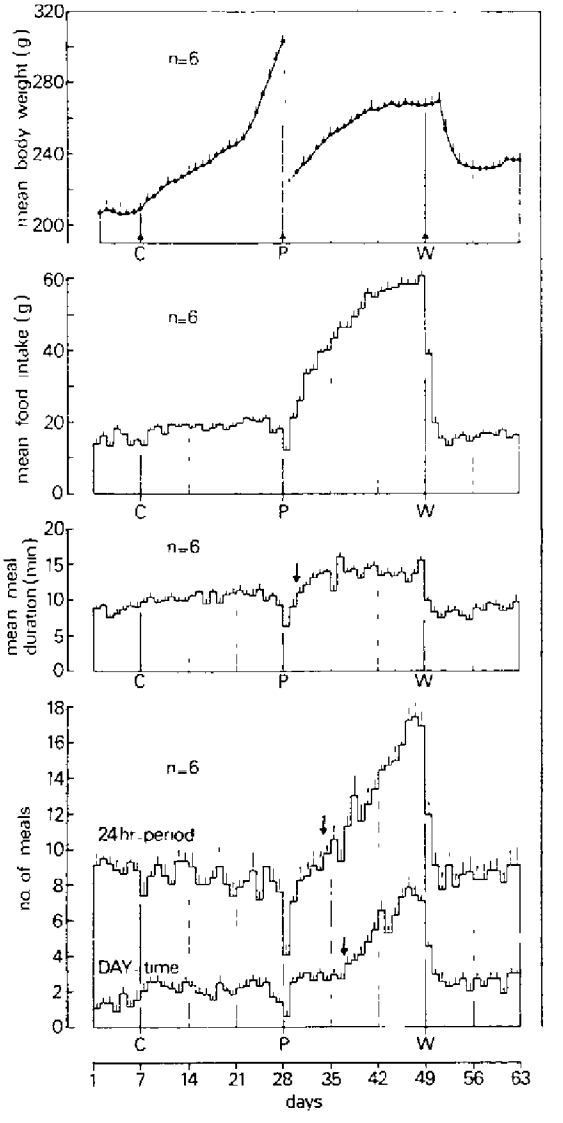

Figure 1. Mean body weight, food intake, meal duration, and meal frequency of a group of female rats during 1 control week (Days 1–7), 3 postconception weeks (Days 8–28), 3 postpartum weeks (Days 29–49), and 2 postweaning weeks (Days 50–63). Arrows indicate points at which changes in the strategy for taking in food were initiated. C = conception; P = parturition; and W = weaning. From "Meal Patterning in the Lactating Rat," by J. H. Strubbe and J. Gorissen, 1980, *Physiology & Behavior*, 25, p. 776. Copyright 1980 by Pergamon Press. Reprinted by permission.

of a satiety agent every time it initiates a meal (thus precluding eating a large meal), it compensates perfectly by adjusting its meal number. Hence, West and colleagues forced rats to eat meals approximately half the size of their preferred (control) meal size by having a computer-controlled pump infuse the satiety hormone cholecystokinin (CCK) every time they began eating (West, Fey, & Woods, 1984). Although every meal was reduced in size,

the rats doubled the number of meals they initiated each day. The result was that daily caloric intake and body weight remained essentially unchanged over a period of several days. Likewise, when rats are given only a small amount of food each time they start eating, they readily initiate more individual meals each day and maintain a constant daily caloric intake (Levitsky, 1970; Skinner, 1938). Sclafani (1972, 1978) observed the same phenomenon in rats with hypothalamic hyperphagia. The point is that the animal's preferred meal size and/or number appears to be readily adaptable to ensure the maintenance of a constant body weight.

If meal size is limited because of digestive constraints (e.g., following subdiaphragmatic vagotomy, which slows the rate that ingested foodstuff leaves the stomach—Snowden & Epstein, 1970; or by increasing intragastric pressure, thus simulating a partially filled stomach—Deutsch, Young, & Kalogeris, 1978), animals adopt a lifestyle of consuming an increased number of smaller meals each day in defense of their weight. In fact, one popular explanation for CCK's ability to reduce meal size is that it slows gastric emptying and thereby causes animals to stop eating sooner (Moran & McHugh, 1982). It must be recalled, however, that even when every meal is limited in size by CCK, rats adapt by eating proportionately more meals each day.

It must be stressed that the discussion above assumes that an animal is at or near its "ideal" weight. In fact, several factors, including genetics, relative weight (i.e., relative to some "ideal"), and environmental conditions, continually interact with the control of meals. These factors determine the background upon which the factors that influence meal size must work and provide the long-term influence that is necessary for the animal to meet its various needs. When the weight of rats has been displaced either up or down by means of forced overfeeding or dieting, it reverts toward its preintervention level when the intervention is stopped (e.g., Bernstein, Lotter, Kulkosky, Porte, & Woods, 1975; Bray, 1976; Stallone & Stunkard, 1991; Woods et al., 1974). The overweight rat eats very small meals until weight is reduced, whereas the underweight rat eats larger meals. If the weight restriction has been severe, the rat may increase its meal frequency for 1 or 2 days, but its principal strategy for regaining lost weight seems to be to increase meal size (Levitsky, Faust, & Glassman, 1976).

Therefore, the persistence of small individual meals whenever conditions allow, and the ubiquity of small meals across individuals and species, suggest that these behaviors hold some fundamental value to an animal. When this preferred strategy cannot be met, animals have an armamentarium of alternative strategies to enable them to adapt their behavior to whatever conditions are imposed. However, the success of these alternatives depends in large measure upon the predictability of the environment.

Meals and Drug Taking

Woods (1991) has postulated that there is a (often quite subtle) cost to individual meals, particularly very large ones. In his schema, meals can be considered to be like drugs, in that as food is taken into the body, its processing and very presence disrupt numerous precisely controlled homeostatic processes. The body responds to meals as it does to drugs; it does what it can to minimize the homeostatic perturbation in both magnitude and duration. One way it does this is to anticipate meals and initiate homeostatic preserving responses as early in the food-taking process as possible. Hence, in a perfectly predictable environment, animals initiate changes of critical parameters sufficiently far in advance of a meal to keep meal-related disruptive excursions of homeostatically maintained variables to a minimum. This meal-anticipatory process can also be used whenever the environment dictates that an animal eat relatively large meals in order to get adequate nutrition. In all of the situations cited above (i.e., placing costs on individual meals, limiting meal size, physiological changes), the animals do not change their meal pattern simultaneously with the change in the environment. Rather, the changes in meal size occur over several days as the animals learn what to expect and what the consequences of a particular meal size are. One apparent exception occurs when animals are offered novel, highly palatable foods. In this situation, rats tend to consume a larger meal the first time the novel flavor is added, but it could be argued that the palatable flavor initiates an intensified anticipatory response (see below), which in turn enables a larger meal. With increased experience with the novel flavor and the consequences of consuming it, animals adjust their meal size appropriately.

It should be noted that experience with large meals leads to unlearned as well as learned adaptive changes. For example, the capacity of the stomach evidently enlarges with repeated consumption of large meals, and it reduces again when average meal size is small (e.g., Geliebter et al., 1992; Holeckova & Fabry, 1959). This anatomical adaptation presumably facilitates the habitual intake of large (or small) meals and is not due to learning.

When rats are allowed to eat only one or a few meals per day, they are said to be on a meal-fed schedule. They adapt over 1-2 weeks by eating increasingly large meals (Ghent, 1951; Lawrence & Mason, 1955), but even then they may not be able to eat meals that are sufficiently large to maintain weight (Cohn, Joseph, Bell, & Allweiss, 1965; Leveille & O'Hea, 1967). Although the studies demonstrating that rats gradually come to eat larger meals are confounded with increased motivation due to weight loss, Moll (1964) observed the same incrementing of meal size in rats whose weights had been reduced prior to being placed on the fixed feeding schedule. Rats placed on a meal-fed schedule initially respond by eliminating small meals, and therefore eat only very large meals when given the opportunity. However, even a few very large meals may not be sufficient for weight maintenance. This inability to maintain normal weight can be circumvented somewhat by placing rats on a meal-fed schedule when very young, in part because they learn to eat at a faster rate. When this is done, subsequent episodes of restricted feeding as adults are marked with an exaggerated tendency

to eat large meals (Levine, 1957; Mandler, 1958; Marx, 1952).

The point is that when rats must eat all of their daily food in a short window of time, there is a maximum meal size possible, and if more food per meal must be eaten to maintain weight, the rat sacrifices weight instead of consuming that much food at one time. Thus, the disruption of other, related systems, caused by increasing the size of a meal, may elicit other corrective responses (in this case, the premature cessation of meals when additional food remains, or early satiety) to protect other perturbed systems. The animal that is forced to survive by consuming only very large meals faces a dilemma. The metabolic costs of the individual meals may become pitted against the cost and desirability of maintaining a certain level of adiposity. Compromises are presumably met in such instances. The implication from all this is that meal size may be quite adaptable in the maintenance of body weight, but only so long as it remains sufficiently small so as not to compromise the metabolic milieu to too great an extent. A certain flexibility is built into the system so that when large meals must be consumed for survival, and when the environment is perfectly predictable, anticipatory responses enable a further incrementing of meal size. It should be clarified that in this paper we use the word *anticipation* to indicate a rat's response to either (1) the predictable presentation of food or the predictable opportunity to eat in situations in which food is not continuously available; or (2) internal timing mechanisms, anchored to the day/night cycle, that enable the rat to synchronize various physiological parameters in situations in which food is continuously available but consumed in distinct bouts or meals.

Anticipatory Responses

One of the most important aspects of this regulatory schema is that the anticipatory response on the part of the animal expecting to initiate eating begins well before the meal itself. Pavlov (1927) was among the first to demonstrate that a number of digestive-related secretions begin occurring whenever a dog is able to predict that receiving food is imminent. The adjective *cephalic* has aptly been applied to such anticipatory responses because they are initiated by cues in the animal's environment that reliably predict meals, and the brain triggers these responses on the basis of conditioned stimuli as opposed to interoceptive signals generated by ingested nutrients. Further evidence that these cephalic responses are unique is the observation that the effects of exteroceptive conditioned stimuli can be dissociated from those more directly related to postingestional events by selected brain lesions (Roozendaal, Oldenburger, Strubbe, Koolhaas, & Bohus, 1990). The secretion of most exocrine and endocrine digestive compounds has been shown to have a cephalic phase in addition to a postingestive phase (e.g., Powley, 1977).

Premeal insulin secretion is an often-studied cephalic response (Steffens, 1976; Strubbe & Steffens, 1975; Teff, Mattes, & Engelman, 1991; Woods & Kulkosky, 1976). This is an increase of insulin secretion that can be elicited by any stimulus that reliably predicts the onset of a meal. The investigation of cephalic insulin responses has generally occurred when subjects are well adapted to the eating/testing situation. When this criterion is met, robust responses have been measured. Failure to comply fully with this requirement may account for the relative unreliability of assessing cephalic insulin responses in humans, since rarely are such responses measured in the individual's normal eating situation or environment. Weingarten (1992) has argued that measurable cephalic insulin is often reduced to a small and unreliable response because of factors outside the control of the experimenter. It is noteworthy that when cephalic insulin is prevented by any of several means, animals typically eat smaller meals (Inoue, Bray, & Mullen, 1978). One reason seems to be that a normal-sized meal, in the absence of cephalic insulin, results in exaggerated levels of postprandial blood glucose (Berthoud, Bereiter, Trimble, Siegel, & Jeanrenaud, 1981; Fritschy et al., 1991; Louis-Sylvestre, 1978; Strubbe & van Wachem, 1981). Hence, the cephalic insulin enables the animals to consume a larger meal without experiencing such large excursions of blood glucose.

Of particular interest for the present discussion are the premeal changes that occur in free-feeding animals when there are no experimentally identifiable cues to herald the onset of food availability. In this instance, the only reliable external cues are those related to the day/night cycle (i.e., time of day), and perhaps others related to the times that the experimenter routinely changes the food or otherwise disturbs the animal. The ability of experimental subjects to predict regular light/dark changes is well known and often studied, and it is noteworthy that the largest meals of the day occur at these very predictable times. Other meals are scattered throughout the day/night cycle in a more or less ordered fashion, but meal size tends to be greatest at the time of greatest predictability. When food intake is precisely tracked around the clock, the largest average meal occurs in close proximity to the time of light offset, and the second largest meal occurs in close proximity to the time of light onset (e.g., Armstrong, 1980; le Magnen, 1981; Strubbe, Dijkstra, Keyser, & Prins, 1986). Because the overall activity pattern of rats is also closely linked to light onset and offset, the large meals at those times can be considered examples of the animals' following an innate program. For example, rats can anticipate the period of daytime quiescence by taking in sufficient food at the time of light onset (Kersten, Strubbe, & Spiteri, 1980; Strubbe et al., 1986).

Meals occurring at light offset and light onset are distinguished both by their size and by the low variance of timing of meal initiation. When rats can predict precisely when something will happen in real time, they can anticipate the event and initiate and synchronize sufficient cephalic responses to permit taking in more calories. In this schema, rats eat larger meals when the lights change because they have prepared their bodies to cope with a greater caloric load at that time—not because of some fun-

damental aspect of diurnal cycles per se. If food is routinely presented to rats at times remote from the changing of the lighting, their food-intake patterns (as well as their activity patterns in general) readily shift to the new cues (Boulos, Rosenwasser, & Terman, 1980; Coleman, Harper, Clarke, & Armstrong, 1982; Stephan, 1984, 1992; Terman, Gibbon, Fairhurst, & Waring, 1984). Hence, the largest meals are eaten at the time that food is routinely presented, even if food is continuously available throughout the 24-h period (Bolles, 1961; Calvin & Behan, 1954). Activity cycles (and related hormonal patterns) are in turn able to become imprinted upon both regular meals and the day/night cycle (e.g., Aschoff, 1987; Krieger, Hauser, & Krey, 1977; Strubbe, Prins, Bruggink, & Steffens, 1987). We previously found that any stimulus that reliably predicts food availability, including time of day as well as arbitrary stimuli, can acquire the ability to elicit meal anticipatory responses (Strubbe, 1992; Woods, 1976; Woods & Kulkosky, 1976; Woods et al., 1977).

These phenomena might explain the observation by Leibowitz's group (Shor-Posner et al., 1991; Tempel, Shor-Posner, Dwyer, & Leibowitz, 1989) that when rats have a choice of macronutrients, the relative proportion taken as carbohydrate is greatest near the time that the lights change (and therefore occurs when the largest daily meal is taken). It may be that, to the extent that the animal can reliably predict exactly when the lights will change, it can muster sufficient cephalic insulin to cope with a greater consumption of carbohydrates at that time. (Coping with ingested carbohydrates seems to be particularly troublesome, perhaps because carbohydrates are digested and absorbed sooner than other macronutrients; see Woods, 1991.) At the same time (i.e., when a meal is perfectly predictable and imminent), it is safe for the animal to generate whatever brain transmitters will favor the consumption of excess carbohydrates. Hence, it has been reported that the levels of neuropeptide Y (NPY) in the areas of the brain that are important in the control of food intake are highest in rats around the time of light offset (Jhanwar-Uniyal, Beck, Burlet, & Leibowitz, 1990). When NPY is administered into those same areas, it causes a relatively selective increase of carbohydrate intake (Leibowitz, 1990, 1992), and NPY's ability to stimulate increased consumption is greatest around the time that lights go off (Tempel & Leibowitz, 1990). Hence, both NPY levels and hypothalamic sensitivity to NPY are increased at the time of light offset and, therefore, at the time the largest meal of the day (and the greatest carbohydrate load) is consumed.

The only other time that NPY is reliably elevated is when an animal is greatly undernourished, either by the withholding of food or by creating diabetes mellitus (for reviews, see Schwartz, Figlewicz, Baskin, Woods, & Porte, 1992; Schwartz, Figlewicz, Woods, Porte, & Baskin, 1993). The point is that when an animal can reliably anticipate an exact moment in time, it has the luxury of being able to prepare for, and consume in relatively large quantities, those foodstuffs that otherwise would cause the greatest homeostatic perturbations. We would interpret the increased levels of hypothalamic NPY, the selective increase of carbohydrate consumption, and the relatively large meal size that all normally occur at the time that lights go out as being caused by the animal's ability to anticipate the event and hence prepare for a large meal. Leibowitz (1988, 1990, 1992), on the other hand, attributes the same phenomena to naturally occurring diurnal fluctuations of NPY and other transmitters involved in the regulation of feeding.

Premeal Responses

It is instructive to look at metabolic/physiological changes that precede "spontaneous" meals. Such changes have often been used to support the hypothesis that these metabolic changes are causal to meals—that is, as one or more energy store becomes depleted, the fuel depot itself is monitored; the animal must switch to some alternative source of fuel and the changeover is monitored, or different fuels will appear and be detected in the circulation (e.g., see Friedman, 1991; Friedman, Tordoff, & Ramirez, 1986). The presumption is that the animal is able to sense the metabolic change, and it must seek food (or some particular macronutrient) in order to replenish the dwindling commodity. It is important to note that these depletion hypotheses can be based upon the assumption that there are sensors located in any of several possible important metabolic centers, such as the liver or in the brain itself. The important point of the hypothesis is that the animal detects and then responds to some change in its own fuel source, metabolism, or other relevant internal parameter. The consumption of a meal is then seen as a response to a signal that indicates real or impending nutritional deficit.

It is equally plausible that the changes that antecede meals are themselves the manifestation of a previously initiated complex anticipatory response that prepares the animal to eat an upcoming meal. Hence, rather than indicating the apparent waning of critical nutrients or bodily energy stores, such changes may simply reflect the animal's anticipation of an impending opportunity to consume a meal. It would certainly be difficult to support the argument that the "depleted" and hence "hungry" animal must eat and replenish its vital fuel stores in order to survive. Unless an animal is on the brink of survival in a nutritional sense, it has more than ample reserves to last well beyond the time of the next meal. A free-feeding animal in the laboratory is never in a true emergency situation for lack of available energy. This is not to say that there are not emergency response systems that do drive an animal to eat when some parameter of the system is sufficiently depleted to warrant immediate action. Perhaps the best examples are the impressive eating initiated by creating hypoglycemia via the administration of insulin (e.g., Grossman, 1986; Lotter & Woods, 1977; MacKay, Callaway, & Barnes, 1940), by blocking glucose metabolism in cells by the use of 2-deoxyglucose (G. P. Smith

& Epstein, 1969), or by the administration of lipid metabolism blockers (e.g., Langhans & Scharrer, 1987; Ritter & Taylor, 1989). The food intake in such situations is real, but the spectrum of metabolic features that accompany it may be relatively rare, except in real emergencies, and may never exist prior to normal or spontaneous meals.

In the discussion that follows, we review several physiological parameters that have been experimentally monitored before and during meals, and that have been used to support one or more depletion models of food intake. In every case, we feel that the very data used to support depletion models of eating can also be used to support a model of eating that posits that, when animals know they are going to eat, they can prepare their bodies to accommodate the food. As will be seen, correlative data that have been used to imply causality may in fact support a quite different interpretation of meals.

Body Temperature

Homeotherms are so named because they are able to recruit several physiological as well as behavioral responses in order to maintain a relatively constant internal temperature. However, body temperature varies considerably in homeotherms such as humans and rats, with diurnal fluctuations being predominant. It has also long been recognized that body temperature increases during and after meals due to an increase in metabolism. Hence, the act of eating food (and hence providing more fuel for metabolic processes) can be considered a means of warming the body. On the basis of this observation, and the fact that animals that are maintained in warmer environments eat less food and those in colder environments eat more food, Brobeck originally postulated the thermostatic theory of eating (Brobeck, 1948; Strominger & Brobeck, 1953). Simply stated, the thermostatic theory posits that temperature in some critical sensor in the body is a major determinant of meals. When temperature is low, animals eat; when it is high, animals stop eating. Details supporting this view are found elsewhere (Davies, 1977; de Vries et al., 1993; Gordon, 1990).

With the use of temperature-sensitive devices small enough to be implanted in animals, the temperature of essentially any region of the body can now be continuously monitored in freely moving and behaving animals. When this is done, two major patterns of temperature variation become apparent. The first is related to the light/dark cycle, with nocturnal animals such as the rat having higher average temperatures in the dark. The second is related to meals. When rats have free access to food, enabling them to eat meals spontaneously, their temperature follows a very stereotyped pattern. During the meal itself, temperature rises rapidly and starts to decline soon after the termination of eating. In fact, de Vries et al. (1993) have observed that during the dark phase of the day/night cycle, virtually all spontaneous meals end when the temperature inside the liver reaches the same (high) level (39.3° C, in their experiments). It is as if the animal will not tolerate its hepatic temperature's getting any higher (see Figure 2). In that same experiment, temperature was also monitored continuously from under the skin, but hepatic temperature was the more reliable correlate of meal cessation. It has been pointed out by de Vries et al. that the hepatic temperature at which virtually all meals stop is near the threshold for causing trauma or damage to the tissue (e.g., Brauer et al., 1963; Brauer, Leong, & Rosenwasser, 1954; Skibba & Collins, 1978). The implication is that if the meal were any larger, and temperature rose any higher, serious consequences would result. There is therefore a potential thermal penalty associated with the necessity for eating particularly large meals, as discussed in detail in Woods (1991).

A second observation is also noteworthy. Temperature declines very rapidly following the peak attained near the end of each meal. This is somewhat surprising, since the very act of digesting and otherwise processing the food is thought to generate even more heat. It is as if an active and highly important process is elicited, which lowers temperature at a time when it would otherwise be increasing even further. Importantly, close analysis of both hepatic and skin temperature during and after meals reveals that the peak occurs later in time in the skin than

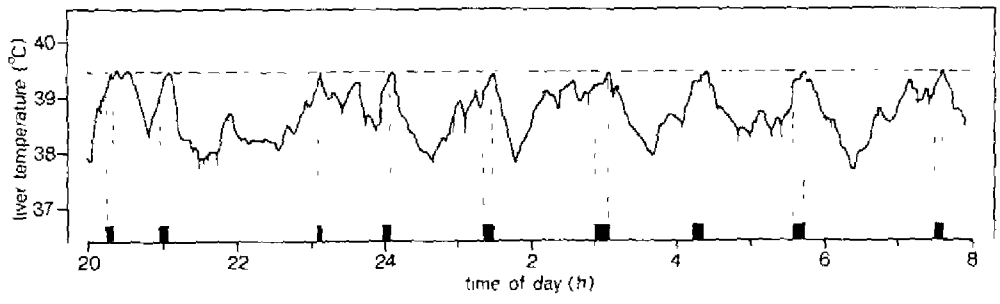

Figure 2. Hepatic temperature over a 12-h interval during the dark phase in 1 representative rat with food continuously available. Food was consumed during the intervals indicated by the black bars. From "Patterns of Body Temperature During Feeding in Rats Under Varying Ambient Temperatures," by J. de Vries, J. H. Strubbe, W. C. Wildering, J. A. Gorter, and A. J. A. Prins, 1993, *Physiology & Behavior*, 53, p. 232. Copyright 1993 by Pergamon Press. Reprinted by permission.

in the liver (see Figure 3). This suggests that the heat generated by the core of the body during the meal is rapidly dissipated as the meal ends. The level of temperature achieved by the immediate postmeal decline is the same level that is normally maintained by the animal at that phase of its light/dark cycle and with a particular ambient temperature. If the interval until the next meal is relatively long, temperature remains relatively stable at this low level. However, approximately 30 min before the next meal is initiated, temperature slowly starts increasing. It increases relatively steadily until the meal begins, then it increases even further until the meal ceases and it again rapidly drops to its "baseline" or basal value. This is depicted in Figure 3 for meals of different size and duration. Although the function of the slow, premeal rise of temperature is not clear, it may well be related to the animal's preparing the body to be able to eat. As pointed out below, numerous other parameters are also altered prior to meals, and this entire preparatory phase may either require more heat to be efficient, or may itself generate heat as it is carried out. It is noteworthy that rats maintain a lower basal body temperature during the light portion of the day when they tend to eat fewer meals, and that the premeal increase of temperature must reach the same absolute value as that during the dark phase prior to initiation of a meal.

Although not predicted by the thermostatic theory of eating, the slow, premeal increase of temperature would be predicted if animals, in anticipation of eating, must ready the body for the meal-taking process. Further, the fact that the anticipatory change of temperature prior to a meal (i.e., an increase) is in the same direction as the change that occurs during the meal (i.e., a further increase) demonstrates that the direction of anticipatory responses, relative to changes of bodily parameters caused by natural events such as meals, cannot always be easily predicted. This phenomenon is therefore at odds with hypotheses suggesting the predictability of the direction of anticipatory responses (e.g., Eikelboom & Stewart, 1982). It is, however, in agreement with the view that the animal, anticipating a meal, adjusts relevant controlled parameters (body temperature, in this example) to levels that optimize accomplishing the behavior. Hence, the animal that anticipates a meal must elevate its temperature in order to be able to eat, and as soon as the act of eating is completed, the animal actively reduces its temperature in a direction away from potentially dangerous levels.

The rather rapid decline of temperature soon after the meal ends is curious. It seems to decrease to the defended level appropriate for the current phase of the light/dark cycle—that is, the level to which temperature decreases after a meal is higher during the dark than during the light.

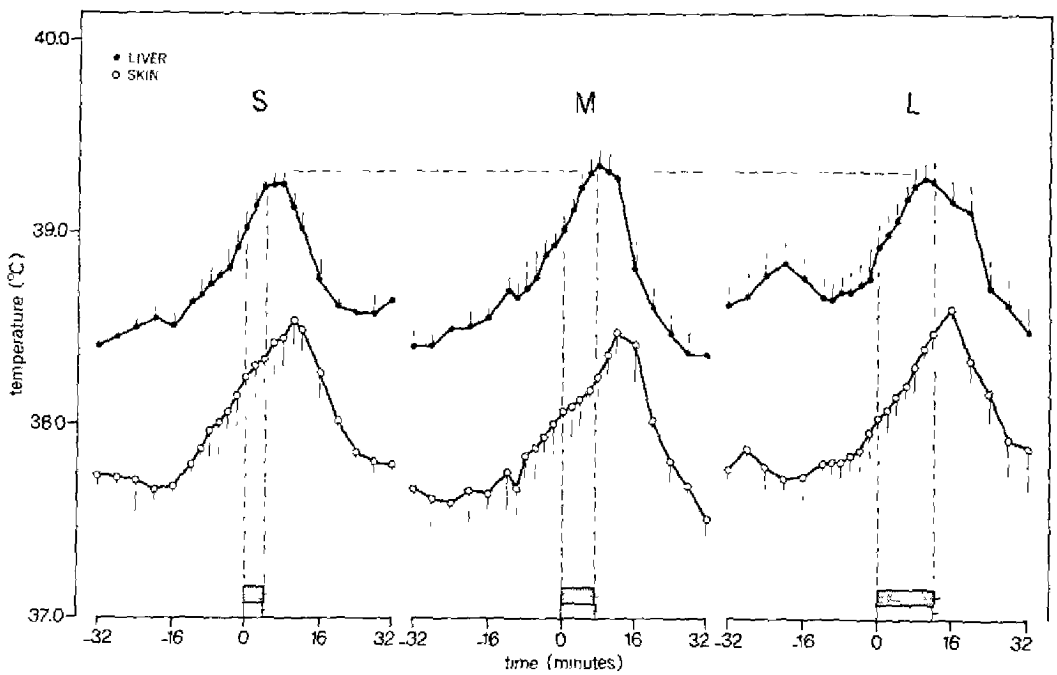

Figure 3. Mean (+1 *SEM*) hepatic and skin temperatures for separate groups of rats consuming relatively small (S), medium (M), or large (L) meals during the dark phase of the day/night cycle. The dashed horizontal bars (+1 *SEM*) indicate the mean durations of the meals associated with the depicted hepatic temperatures; the open horizontal bars (+1 *SEM*) indicate the mean durations of the meals associated with the depicted skin temperatures. From "Patterns of Body Temperature During Feeding in Rats Under Varying Ambient Temperatures," by J. de Vries, J. H. Strubbe, W. C. Wildering, J. A. Gorter, and A. J. A. Prins, 1993, *Physiology & Behavior*, 53, p. 233. Copyright 1993 by Pergamon Press. Reprinted by permission.

This probably reflects the fact that the animals are far more active during the dark and that vital systems may well require and/or generate more heat at that time. The pattern of temperature that occurs between meals suggests that the animal typically keeps its temperature as low as possible and that, far in advance of an anticipated meal, it begins preparing for the meal by slowly raising its temperature. Hence, during the dark cycle when animals are more active, they keep their basal body temperature higher, perhaps so that activity can be more efficient. However, it is still maintained at a relatively low level, since activity per se raises temperature and moves the body nearer to the maximum tolerable level. During the dark phase, the active animal, which is also taking in more and larger meals, is particularly prone to overly elevated temperatures. Keeping temperature as low as possible between meals may be a survival strategy that prevents the perturbations caused by (unanticipated) instances of arousal (such as that occurring in response to a predator) from becoming overly severe.

Therefore, temperature (both generally within the body and specifically within the liver) rises when animals anticipate the onset of meals. This may be a means of preparing the body to eat and cope with the anticipated nutrient load, since many digestive-related enzymes are also cued by the time of feeding (Stevenson & Fierstein, 1976), and since such enzymes function best at very specific temperatures. It is noteworthy that changes of temperature (as well as of digestive-related enzymes) easily entrain upon the time of feeding, suggesting that the responses are truly anticipatory and do not reflect some time-dependent process instigated by a previous meal (Saito, Kato, & Suda, 1980; Saito, Murakami, & Suda, 1976; Stevenson & Fierstein, 1976). The observation that many different anticipatory responses occur prior to a meal is important (and the case is made even stronger in the discussion that follows). The synchronization of so many interrelated events presumably provides a narrow window of opportunity for consuming a meal. If an animal delays initiating a meal for too long once the anticipatory process is under way, it may not begin at all and might in fact have to wait for a considerable amount of time to "reset" the appropriate parameters anew.

Blood Glucose

With the use of chronic indwelling intravenous catheters, it is now possible to monitor continuously the level of blood glucose in an awake, behaving animal. This is accomplished by withdrawing blood at a slow constant rate and passing it through a nearby glucose analyzer. The data can be displayed visually and stored for future analysis. Although there is a slight lag between the time when a sample actually leaves the vasculature and when its value of blood glucose is displayed (typically 2 min), the lag is constant, so precise temporal relationships among events can be determined.

This procedure was initially used in the lab of Jacques le Magnen in Paris (Louis-Sylvestre & le Magnen, 1980) to track blood glucose levels before and during meals, and it has been systematically investigated by Campfield and F. J. Smith and their colleagues (see reviews in Campfield & F. J. Smith, 1990a, 1990b). In a typical experiment, rats are individually housed and have free access to food and water. In these experiments, baseline blood glucose rarely varies by more than 1% or 2% over long intervals. Prior to a spontaneous meal, blood glucose levels begin to drop, and the decrease continues for an average of 12–20 min (see Figure 4). While blood glucose is changing in this systematic way, the rat may be active, it may be lying quietly, or it may in fact appear to be asleep. Its overt behavior appears to be independent of these glucose changes.

Once a nadir is reached, typically around 12% below baseline, blood glucose starts to increase, and within a very few minutes the rat reliably initiates a spontaneous meal (see Figure 4). According to Campfield and F. J. Smith (1990a), this pattern of glucose change is invariably followed by a meal, and virtually all meals are preceded by such a change. Hence, the premeal decline of blood glucose is highly predictive of an impending meal, and since glucose is a major fuel source for much of the body and is an obligatory fuel source for the brain, it has been concluded from such experiments that the stereotyped pattern of glucose changes (and hence, presumably, fuel availability) reflects some fundamental change of ongoing metabolism. As a consequence, the rat eats. These data are obviously quite supportive of Mayer's (1953, 1955) glucostatic hypothesis, which posits that a decrease of glucose utilization, when detected by critical sensors in the brain, is sufficient to cause an animal to seek and ingest food. Also consistent with the glucostatic hypothesis is the fact that as the rat eats and the food is absorbed, blood glucose rises to above its initial baseline.

Through the use of selective drugs and their judicious administration, F. J Smith and Campfield (1993) have

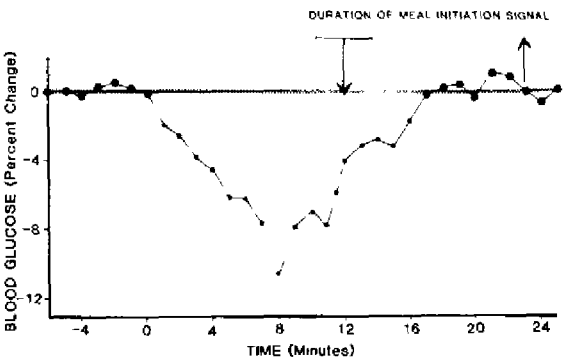

Figure 4. Composite time course of the functional coupling between transient declines of blood glucose and meal initiation. Points represent meal percentage changes of blood glucose from several experiments, normalized to the time of onset of the decline (0 min). Mean time of meal onset is indicated by the downward arrow, and mean time of meal offset is indicated by the upward arrow. From "Functional Coupling Between Transient Declines in Blood Glucose and Feeding Behavior: Temporal Relationships," by L. A. Campfield and F. J. Smith, 1986, *Brain Research Bulletin*, 17, p. 431. Copyright 1986 by Pergamon Press. Reprinted by permission.

been able to duplicate this naturally occurring pattern of blood glucose changes. When the artificially induced decrease of blood glucose precisely mimics the pattern of a normal premeal decline, the rat eats. Such data appear to support the hypothesis that the pattern of change of glucose dynamics that occurs before spontaneous meals "causes" the meals to begin. Hence, advocates of the glucostatic hypothesis can point to the reliable decrease of blood glucose (and glucose availability) that precedes meals, and to the reliable increase of blood glucose (and presumably glucose availability) that occurs during eating, to support their point of view.

An alternative interpretation of the same data is also possible. Given that a meal (particularly that of a mixed diet, such as the one available to Campfield and F. J. Smith's rats) reliably causes blood glucose to increase, and that elevated blood glucose appears to be undesirable on the part of animals (see Woods, 1991), an animal ought to do whatever it can to minimize the increment. If the animal can anticipate when it will eat, it can mobilize centrally controlled reflexes to circumvent the magnitude of the changes caused by the meal itself. Hence, in order to neutralize the inevitable rise of postprandial glucose, the wise animal can secrete insulin sufficiently far in advance of a meal to lower its blood glucose slightly, and then begin eating. Hence, the premeal decline of glucose documented by Campfield and F. J. Smith, rather than indicating a change of metabolism or waning of some internal fuel supply or even some sort of timing signal related to the previous meal, may simply be a reflection of the animal's anticipatory response. It is noteworthy that Campfield and F. J. Smith have observed that the premeal decline of blood glucose is itself preceded by a small increment of plasma insulin (1986a, 1990a). Hence, the rat that knows the consequences of the particular diet it has been eating and the exact time of day it will consume its next meal can prepare itself to consume a meal of particular size without allowing too great an increase of prandial glucose. The anticipatory response, coupled with the early increment of even more insulin as the food interacts with the gut, combine to keep postprandial glucose levels as low as possible (Strubbe & Bouman, 1978). Further, the increment of cephalic insulin coming when it does circumvents the need for a much greater postprandial insulin response. Hence, cephalic insulin contributes to a more stable plasma glucose, and its activation is a parasympathetic event (e.g., Strubbe & Steffens, 1993; Woods & Porte, 1974). As animals age, they develop parasympathetic dysfunction, and the consequent reduced cephalic insulin output may cause exaggerated postprandial insulin secretion and contribute to the pancreatic islet dysfunction in old age by exhausting the islets (e.g., see Buwalda, Strubbe, Hoes, & Bohus, 1991).

The data that argue most persuasively for a causal role for the premeal decline of glucose in the initiation of meals are those in which a comparable change of glucose is simulated via the use of drugs, and the animal begins eating (F. J. Smith & Campfield, 1993). Although the explanation for this important observation may well lie in other effects of the infused drugs (i.e., effects that might facilitate food intake), it is certainly also the case that, in a perfectly predictable environment such as that in which the laboratory rat exists, some sort of association might normally develop between the premeal pattern of change of glucose and eating. Hence, to the extent that the animal can detect the pattern of glucose elicited in these experiments (Campfield & F. J. Smith, 1990a, 1990b, explicitly state that it is the pattern of glucose changes rather than the absolute level that is detected and that initiates meals), it might respond to the pattern by initiating a meal because of an historic association. The animal would essentially be responding to the pattern of glucose as if it were a conditioned stimulus. Over innumerable "conditioning" trials, every time this premeal pattern of glucose occurred, eating a meal was presumably better tolerated, and the resultant association that developed may have bestowed upon the glucose pattern the status of a signal that indicates that the body is "ready" and a meal can commence. Hence, the rat eats. An analogous situation might exist with regard to stomach contractions and other premeal events. Given that they reliably precede meals and can be detected, any premeal event, including the premeal pattern of glucose decline, might contribute to the initiation of meals through an associative process.

Body Metabolism

Metabolic rate is the sum of all of the bodily activities occurring at any moment. It is based upon energy expenditure caused by muscle activity (exercise), by breathing, and by keeping all of the activities of the various organ systems intact and functional. When an animal is resting quietly or sleeping, metabolic rate and energy expenditure are very low. Importantly, during and after meals, metabolic rate increases greatly as energy is burned at a greatly increased rate. This phenomenon has been known for many years, and its function is still uncertain. However, it is reasonable to hypothesize that the increased metabolic rate and energy expenditure associated with meals create a challenge to ongoing homeostatic processes. Hence, the animal that can anticipate the meal can also anticipate the obligatory increased metabolic rate. If an animal has the capacity to control its metabolic rate, it therefore ought to be able to reduce its metabolic rate in anticipation of a meal.

Nicolaidis and Even (1984; see also Even & Nicolaidis, 1985) have developed a sophisticated apparatus for determining ongoing oxygen consumption, carbon dioxide production, energy expenditure, and metabolic rate in unrestrained rats with ad-lib access to food. Their apparatus is also sensitive to any movement on the part of the animal so that they can eliminate the effects of motor behavior from their estimates of metabolic rate. They have reported that before a rat initiates a spontaneous meal, its metabolic rate begins to decline. This decline begins 10–15 min before the meal, and after it reaches a nadir, a meal is initiated. Once the meal is started, metabolic

rate rises to a level above the original baseline. Nicolaidis and Even have interpreted the premeal decline of metabolic rate as resulting from a vital change of energy substrate at a sensor in the brain. The subsequent meal is therefore viewed as occurring because of this energy-related signal.

Metabolic rate, like blood glucose, changes prior to the onset of a meal in a direction opposite to that caused by the meal itself. The taking of food is obviously a necessary behavior in order to provide energy for survival. However, even though energy is expended continuously, it is obviously necessary for the animal to replenish energy stores intermittently. When the environment dictates that energy intake be in the form of large, infrequent meals, the potential perturbance caused by the meal can be quite great. When the animal finds itself in such an environment and can predict when these large bouts of eating will occur, it can prepare itself (at least to some extent) to cope with the homeostatic disruptions of the food-taking process. One strategy it uses is to adjust the value of impacted parameters to more appropriate, and perhaps safer, premeal starting levels. In support of this, if rapidly digestible liquid food is infused into the stomachs of rats, thus presumably simulating many changes that would normally be caused by ingesting food, the start of the next meal is delayed until the perturbations decline. The animal thereafter initiates meals of normal size (Strubbe et al., 1986).

There may well be many other parameters that would be expected to change in anticipation of a meal. One strategy to ascertain potential candidates would be to look at the "drug effect" of meals—that is, the changes to homeostatically controlled parameters caused by ingesting and absorbing food. Premeal changes of the same parameter, but in the opposite direction, might be expected to occur in an animal that is anticipating a meal. Hence, the observations that blood glucose and body metabolic rate increase during and after meals imply that these parameters might decrease before a meal, and they do. However, this strategy can also be misleading. Body temperature increases to very high levels during meals, and this might be interpreted as implying that a premeal decline of temperature should be predicted. There is in fact a decline of temperature between meals, but it occurs in closer proximity to the prior meal than to the upcoming one. Further, temperature actually increases just prior to meals, presumably reflecting processes that, although necessary for efficient meal taking, actually parallel meal-related increments of temperature.

A Test of the Anticipatory Hypothesis

If the changes that reliably precede spontaneous meals are actually manifestations of the animal's preparation to eat, as opposed to reflecting waning fuel supplies that, as they reach some threshold, actually compel the animal to eat, there are certain implications. For example, suppose that the premeal pattern of blood glucose is causal to meals. If a rat is disallowed access to food when a "premeal" decline begins, what would the two positions dictate? The view that the rat is compelled to seek and eat based upon a depletion model would suggest that a second decline of blood glucose should occur, and with a relatively short latency. It seems clear that if an animal were about to eat, that the intent of the meal was to replenish some storage depot in the body, and that no (or an insufficient) accumulation of new energy actually occurred, the animal should initiate a second meal sooner than it would otherwise. On the other hand, the hypothesis that the premeal decline of glucose, rather than being causal, is but part of a coordinated sequence of several anticipatory events, would make a different prediction. For example, the prevention of the anticipated meal might require the animal to reset all of the various metabolic control systems that had been synchronized in anticipation of the meal. If so, an entire coordinated sequence of many regulated parameters would have to be reinitiated.

Although there are few studies that have addressed this point, the data that do exist support the position that the premeal decline of glucose is part of an anticipatory response. Campfield and F. J. Smith (1986b) allowed rats to undergo a normal premeal decline of glucose, and then prevented them from eating by covering the food hopper for a few minutes at the time they were anticipated to eat. Instead of initiating a second premeal decline of glucose (and a consequent meal) in less time than would normally occur at that time of the day, the rats did not in fact initiate a second decline of glucose until after an additional, normal-length intermeal interval starting after the disruption had occurred. Although incompatible with the view that depletion of various stores (and hence perhaps hunger as well) increases as a function of time since the previous meal, these findings are predicted by the view that the premeal change of glucose is part of a coordinated anticipatory response. As an example, since temperature would have reached relatively high levels at the time the rat was about to eat (see Figure 3) and food was withheld, temperature would have to be relowered and the entire sequence begun anew. Likewise, blood glucose and metabolic rate, as well as numerous other parameters, would all have to be reset.

Consistent with this, rats that are habitually given food only at a particular time of day eat less than they do at the habitual time if food is presented after a delay of several hours or more, even though they are more deprived (Bousfield & Elliott, 1934); they also eat more slowly (Bousfield, 1935). Others have observed similar phenomena when testing rats with both shorter and longer deprivation times (Baker, 1955; Lawrence & Mason, 1955). As pointed out above, there may be a relatively narrow window of opportunity to initiate a "spontaneous" meal. The resetting and coordinating of so many parameters undoubtedly requires some minimal amount of time. Alternatively, the timing of the next meal could reflect some internal timing mechanism that allows meals to be initiated only during specific, regularly spaced windows of time.

What Signals the Opportunity to Eat?

All of this speculation of course begs the question of what is the cue that triggers the spectrum of meal anticipa-

tory responses that includes a reduction of blood glucose. There is no easily identifiable culprit, but it may well be the time of day (e.g., Amstrong, 1980; Terman et al., 1984; Zucker, 1971). Many of Campfield and F. J. Smith's data are collected near the time of day that the lights normally go out (personal communication, April 1993). The rationale for this is obvious: The time that the lights go out is the time of the most probable onset of a meal, and also of the largest meal by rats. It is also therefore an ideal time to observe a premeal decline of glucose. One of us (J.H.S., unpublished data) has also observed premeal declines of blood glucose, including those for the second meal of the dark period. In this instance, the decrease of glucose is decreased relative to that preceding the initial meal of the dark cycle, and it starts slightly sooner. It may be that when an animal is anticipating a larger meal (i.e., the first meal of the dark cycle), it undergoes a greater premeal decline of glucose.

In a study related to this, Strubbe and D. Kalsbeek (unpublished data) placed rats on a schedule for several weeks, in which they had access to food for six 10-min intervals each day. All six meals occurred during the dark portion of the day/night cycle, and the rats ate about the same amount of food in each. With frequent sampling of blood for assessment of blood glucose (Figure 5), the rats developed a pattern wherein they reduced their blood glucose before each of the meals. Further, when the intermeal intervals were predictably long, blood glucose remained relatively constant until just prior to the next meal, when a premeal decline occurred. Again, the rat appears to be able to adapt to whatever feeding schedule is imposed, as long as it is predictable.

A corollary of what is presented in this paper is that most "spontaneous" meals, rather than being caused by some physiological need, are in fact initiated by stimuli that have been associated with meal taking in the past. While in disagreement with most contemporary theories of fuel depletion, such a position agrees with the work of others, who have found that animals become conditioned to expect certain foods and know how to deal with them (Booth, 1990; Sclafani, 1991; Weingarten, 1992). In the present paper we take this position one step further and suggest that the timing of the meal is also critical, in that if the animal knows precisely when it will eat, it can prepare for the consequences.

Final Remarks

In summary, we suggest that premeal changes of physiological factors prepare an animal to cope with the effects of consuming a meal. Hence, a decrease of glucose is elicited to minimize the impact of the inevitable rise of postprandial glucose. Metabolic rate decreases in anticipation of a meal to minimize the impact of the large increase of metabolism elicited by processing the meal. Body temperature is elevated to enable efficient consumption and processing of the food. The amount of food that can be safely consumed and tolerated is, at least in part, dictated by the starting point of critical metabolic variables—that is, if the animal's homeostatic system will disallow some parameters to surpass certain levels during and after a meal, moving the parameter in a direction away from that level will be helpful. When the parameter is necessarily moved in the same direction prior to the meal as that during the meal, and when extreme values of that parameter cannot be tolerated (as with hepatic temperature), a threshold seems to exist beyond which no more eating occurs. And temperature is rapidly displaced below this threshold once it is attained.

It has been found (de Vries et al., 1993) that when rats initiate meals at a lower body (or hepatic) temperature, they eat larger meals; when they initiate meals at a higher body (or hepatic) temperature, the meals are smaller (see Figure 3). In both instances, the animal terminates the meal when the same hepatic temperature is attained. Related to this, Gordon (1993) allowed rats to choose their own ambient temperature by housing them in a tubular environment with a temperature gradient extending from one end to the other. The distance along the tube where the animal tended to spend most of its time presumably reflected its preferred ambient temperature. Gordon monitored the temperature that the rats chose as a function of the time of day. During the light phase, when rats eat very

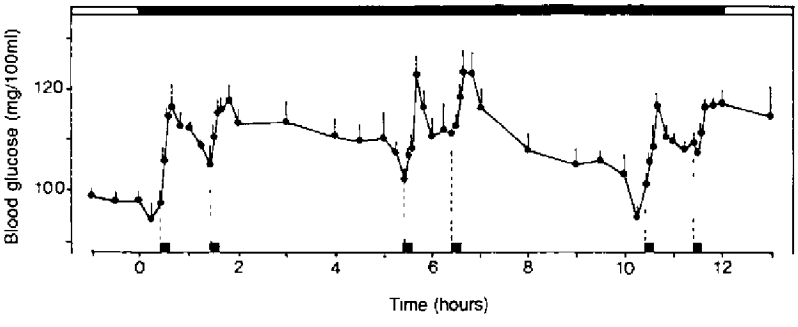

Figure 5. Mean (+1 *SEM*) blood glucose levels for a group of rats maintained on a schedule of receiving all of their daily food in six meals during the dark phase. The timing of the availability of food is indicated by the bottom black bars, and the time that the lights were out is indicated by the black horizontal bar at the top of the figure (Strubbe & Kalsbeek, unpublished data).

little, are less active, and hence are less likely to experience severe postprandial hyperthermia, the rats opted for a relatively warm temperature. During the dark phase, when rats are active, eat many meals, and experience multiple bouts of meal-related hyperthermia, they chose a much cooler ambient temperature.

Close analysis of the data of de Vries et al. (1993) suggests that, as a rat initiates a spontaneous meal, subsequent meal size can be predicted by the temperature that exists at the moment of the first bite. In every instance, the rats stopped the meal when the liver reached its thermal threshold, and the rate of temperature increase from first bite to threshold was essentially constant in any given ambient temperature. It is tempting to speculate that a rat, knowing how much it intends to eat, begins eating sooner or later during the slow premeal rise of temperature in order to be able to accommodate a particular meal size—but this cannot be ascertained with the current data.

The previously mentioned analogy between meals and drug taking is now more apparent. There is compelling evidence that when drug-tolerant animals anticipate receiving the drug, they initiate bodily changes that ultimately minimize the homeostatic impact caused by the drug itself (Poulos & Cappell, 1991; Woods, 1991). Hence, an animal that anticipates a hypothermia-inducing injection of ethanol elevates its temperature (Le, Poulos, & Cappell, 1979; Mansfield & Cunningham, 1980), and an animal that anticipates an analgesic amount of morphine increases its pain sensitivity (Siegel, 1975). The animal changes its internal milieu to better accommodate the impending presence of the drug effect. As a result, it is able to tolerate a quantity of drug that otherwise would create too great a homeostatic disturbance.

Similarly, the animal anticipating that it will soon eat a large meal adjusts its temperature to enable the behavior to occur and prepares itself for the postprandial rise of glucose and for the meal-generated increases of metabolic activity. When its environment is predictable, the animal is best able to prepare for the effects of any given meal. It undoubtedly makes many other (as yet unknown) anticipatory responses that will enable it to better tolerate the impending intake of nutrients. As discussed elsewhere (Woods, 1991), the tendency of most species to drink water prandially may be an example of these homeostatic meal-related responses.

When the meal is commenced and the food is actually ingested, digested fuels enter the blood. The body copes with the rapidly increasing tide of glucose, fats, and amino acids by getting them out of the blood and facilitating their uptake into tissues. Fuels are also expended during the immediate postprandial period, and this in turn is associated with an increase of metabolic rate. Even though body temperature would normally increase with the rise of metabolic rate, it tends to decrease soon after the meal, presumably enabling the animal to be cool enough to exert sudden motor behavior if necessary, and to be ready for a subsequent meal. The animal does all of this safely and efficiently if it has the luxury of knowing when the meal will occur and the ability to prepare itself for the process. We suggest that the production of premeal anticipatory responses enables animals to tolerate large meals in a predictable environment. Analogously, as soon as a meal ends, the animal makes other anticipatory responses (e.g., rapidly lowering its body temperature) to prepare for activities that occur in the intermeal interval (sleep, exercise, safety from predation).

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(Manuscript received August 25, 1993;
revision accepted for publication February 28, 1994.)