Current Research

Appetite: Measurement and Manipulation Misgivings

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ABSTRACT
Humans appear to have a genotype that permits, or even encourages, an energy intake that is greater than energy expenditure when food is available. This was functional throughout most of human evolution but is less so in the current environment of inexpensive, palatable, and readily available foods. To achieve dietary goals of weight loss or maintenance, attempts have been made to influence appetitive sensations through the manipulation of the physical properties of foods, their composition, or their pattern of consumption. This has led to limited success, in part, because measurement of appetitive sensations is difficult but, more fundamentally, because the association between appetite and food choice or intake is not robust. This article critically reviews the most common methods for assessment of appetite and the effects of selected food constituents on appetitive sensations. Translation of current knowledge to dietetic practice must be made cautiously.


Although there is a strong genetic component to overweight and obesity, the fact that the incidence of these disorders has increased just recently implicates an environmental and behavioral basis. Some workers have emphasized the increase in energy intake (1,2), whereas others attribute increasing weight gain to decreased energy expenditure because of an increasingly sedentary lifestyle (3). The important point is not that one has changed but why the other has not changed in concert to maintain energy balance. One explanation holds that the decrease in energy expenditure has been too subtle to evoke a change in dietary intake while the increase in energy intake, which has resulted from shifts in the food supply, has elicited little behavioral compensation. The mechanisms linking energy intake and expenditure are unclear, but it seems reasonable to believe that appetite, sensations that promote food ingestion or rejection, is central to the maintenance of energy balance.

Appetite has been viewed as a bridge between energy intake and expenditure that should aid in coupling the two. Could a disruption in the relationship account for the positive energy balance the majority of Americans are now experiencing? Different views have emerged. One explanation argues that the energy imbalance stems from a failure to monitor and appropriately react to internal appetitive cues. Thus, the system is functional but overridden by other factors promoting intake. Another view is that the appetitive system is dysfunctional in the present environment and requires modulation by various dietary or pharmacologic means. Alternatively, it may be hypothesized that the function of appetite is not directly to modulate energy balance to maintain a particular body weight. Rather, it provides motivation to consume food to sustain life processes when energy is limiting and curbs intake to avoid acute physiologic stress. To evaluate these three perspectives, it is important to understand the nature of appetitive sensations, the methods for their measurement, and the degree to which they may be modulated by dietary components and influence food choice.

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NATURE OF APPETITIVE SENSATIONS
Appetite is often divided into three components: hunger, satiation, and satiety. Hunger describes the sensations that promote food consumption and is a multidimensional attribute with metabolic, sensory, and cognitive facets (4,5). Following the initiation of a meal and as eating proceeds, hunger subsides while satiation, the sensations that govern meal size and duration, becomes increasingly dominant (6). Eventually, feelings of satiation will contribute to the cessation of eating and begin a period of abstinence from eating. The sensations that determine the intermeal period of fasting are termed satiety. The mechanisms that regulate hunger, satiation, and satiety, and consequently food intake, have a physiologic basis but may be strongly influenced by environmental factors (eg, availability of food, sensory stimulation) or cognitive issues (eg, health beliefs, habitual meal times) (7,8). Although hunger may be on the opposite end of a scale of appetitive sensation from satiation or satiety, one is not merely the absence of another. The sensations that promote and inhibit eating are governed by overlapping but also distinct mechanisms. Moreover, satiation and hun-
Food Intake as an Index of Appetite

It is frequently assumed that appetite and food intake are so inextricably linked that one can serve as a proxy for the other. However, often, this is not the case because numerous factors disrupt the relationship. For instance, the lack of availability of food or social constraints may prevent or cause one to refrain from eating when hungry. Alternatively, eating in the absence of hunger because of boredom, availability of palatable food, or emotional stress is common (12-14). Inasmuch that eating when satiated and refraining when hungry is a representation of abnormal eating, abnormal eating occurs more commonly than normal eating. This renders the link between food intake and appetite tenuous. In addition, there are substantial difficulties with the measurement of food intake outside of the laboratory setting that may reduce the ability to observe any relationship between appetite and food intake that does exist (15). Furthermore, the association between appetite and food intake is circular. One is said to be hungry if one eats under a given set of conditions and the fact that one eats is regarded as evidence that one is hungry.

Questionnaires

Humans can provide unique insights into eating behavior because of their capacity for introspection. To take advantage of this capability, various questionnaires have been developed to assess appetitive sensations. These questionnaires generally fall into two categories: visual analogue scales (VAS) or category scales. A recent advance in appetite measurement, which is more technologic than theoretic, has been the introduction of handheld electronic appetite rating systems based on the Apple Newton (Apple Computer, Inc., Cupertino, CA) or Palm Pilot systems (PalmOne, Milpitas, CA) (16).

VAS, which evolved from scales used to assess pain, are the most common response format to assess subjective ratings of appetite. These scales require the participant to respond to a question by placing a mark on a line, usually of 100 mm or 150 mm in length, that is anchored at each end with opposing statements such as “not at all hungry” and “as hungry as I have ever felt.” Initial questionnaires asked little more than “how hungry are you right now” and ignored the fact that appetite is multidimensional (17). For instance, hunger may vary independently from fullness. Furthermore, a question regarding sensations of hunger may elicit a different response than a question about one’s desire to eat. However, to an untrained individual, these may seem like different means to address a common sensation. This weakness was recognized and, consequently, a set of seven questions was proposed that encompass various facets of appetitive sensations (18). They include the following: How hungry are you right now? How strong is your desire to eat right now? How much could you eat right now? How full are you right now? How strong is your desire to consume something sweet right now? How strong is your desire to consume something savory right now? How thirsty are you right now? These questions have been widely accepted, and they are frequently used in appetitive research. The degree to which people understand the subtle differences between these questions is uncertain. Furthermore, their association with food intake is unreliable. Even in a tightly controlled laboratory study using standard questions, the correlation between prelunch ratings of appetite and subsequent food intake was only weak to moderate (19).

A better correlate of subsequent food intake was obtained with the mean of appetite measurements taken over a 4.5-hour period. Even so, there was only a moderate correlation between each of the questions and actual food intake. Indeed, prelunch appetite ratings only accounted for 8% to 12% of the variability in subsequent food intake. Using the mean ratings over 4.5 hours could only explain 23% of the variability in subsequent intake. Even this modest relationship could dissipate when experimental or lifestyle constraints are relaxed (eg, during the weekend) (20). These observations dictate that the results of studies using questionnaires as a solitary index of appetite should be interpreted with some caution. There is sufficient variability in the relationship between subjective appetite and food intake to dispute that a mere reduction in subjective appetite will ultimately result in a reduction of food intake.

Category scales have also been used to assess subjective appetite ratings. They are used to capture responses to the same questions as VAS. However, rather than one continuous line that is anchored with opposing statements, a category scale will commonly be divided into a number of distinct categories. It should not be assumed that these categories are equally spaced perceptually (eg, the difference between a three and a four is not the same as the difference between eight and nine). Additionally, a hunger rating of eight should not be taken to mean that it is twice as intense as a hunger rating of four. The

Methodology for Measurement of Hunger, Satiation, and Satiety

Appetite is a subjective construct and, as such, is not open to direct measurement. This has necessitated the reliance on several indirect measurements. Three assessment methods are commonly used: eating patterns/food intake, questionnaires, and biomarkers. Other methods, such as the microstructure of eating (number of chews, rate of eating) or salivation have been used to measure appetite, but they have not been widely accepted as valid indices of appetite (9-11).

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labeled magnitude scale, which has a quasilogarithmic response format, has been advocated to reflect more faithfully the intensity sensations (21). This scale purportedly normalizes responses thereby facilitating group comparisons. However, this scale suffers from many of the psychometric limitations of category scales.

Electronic systems are a useful and reliable tool for measuring subjective appetite scores. Because of differences in the actual size of the line and because individuals seem to be more reluctant to use the end of the scales on the electronic systems, this method should not be used interchangeably with pen and paper methods (16). Electronic appetite rating systems (EARS) have a number of distinct advantages over traditional pen and paper methods. Entries on the EARS are marked with a time and date, which allows the integrity of the collected data to be confirmed. The tabulation of data from pen and paper methods is time consuming and prone to error. These problems are avoided with the EARS. Although better protecting data integrity and study compliance, the limitations in data interpretation noted above apply equally to data collected by these devices.

Open-ended questions regarding appetitive sensations are less frequently used. The reasons are multiple. First, they generally generate a wide array of responses rendering aggregation difficult. Second, there is a lack of agreement as to what sensations are being reported. Open questions will commonly yield reports of sensations in different regions of the body with limited quantitation of intensity. This is especially problematic in populations with limited or dissimilar language skills. Third, responses require greater effort than is needed for VAS or category scales, so motivation becomes a larger issue and one that is difficult to quantify.

Temporal Indices

Eating patterns have also been used as a means to assess appetite. The assumption is that there is a direct relationship between the intermeal interval and hunger. However, the longest period of time most people fast is overnight, and few report peak daily hunger ratings early in the morning. There are data supporting an association between the size of a meal and the postmeal interval, but intake at a meal is not strongly associated with the time since the last meal (22). This is, in part, because of social influences on portion sizes (23).

Biomarkers of Appetite

Many physiologic changes, such as gut peptide concentrations, are related to appetitive ratings or food intake and can be used as biomarkers of appetite. Some work suggests that this relationship is causal, although the measured variable is often experimentally raised or depleted to nonphysiologic levels, leaving open questions regarding the practical importance of the effects. Interest in the use of biomarkers as indices of appetite or an inclination to eat is based on their presumed lower susceptibility to modification by cognition and environmental factors. However, this cannot be assumed because it is well-known that these factors do modify physiologic processes related to food digestion as well as nutrient absorption and utilization. Well-documented examples include cognitive and sensory influences on salivation, salivary composition, gastric acid secretion, gastric motility, gastrointestinal peptide release, pancreatic exocrine and endocrine secretions, renal function, hemodynamic shifts, and thermogenesis (24-28). For a biomarker to be useful, it must meet a number of criteria. Perhaps most importantly, the measurement of the biomarker must be feasible and measurable without incurring undue stress or require overly invasive procedures. The biomarker must clearly relate to appetite physiology and be sensitive to changes in appetite. Furthermore, measurement of the biomarker must be reproducible under similar conditions (29). A review of selected candidates follows.

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Glucose has formed the central tenet of many short-term appetite regulation theories since the proposal of the glucostatic theory of eating in the 1950s (30). Proponents of this theory point to laboratory studies demonstrating that a spontaneous meal request is frequently preceded by a transient decline in blood glucose utilization (31,32). Thus, it has been proposed as an appetitive biomarker candidate. However, this may not be the case because glucose is not a robust measure of meal initiation. Meal requests occur in the absence of transient declines in blood glucose. Furthermore, the association between transient glucose declines and meal requests disappears when subjects are in negative energy balance such as during an energy-restricted diet (33).

A more recently identified potential biomarker of meal initiation is the gut peptide ghrelin. A clear preprandial rise in ghrelin concentration is followed by a rapid postprandial decline (34). Moreover, the rise and fall in ghrelin levels strongly mirror subjective ratings of hunger (35), although this, in itself, does not prove a causal relationship. Furthermore, data have shown ghrelin to be a potent stimulator of food intake. Energy intake has been observed to increase by 28% following intravenous ghrelin infusion (36). Ghrelin may not only be influential in short-term appetite regulation. Its concentration was noted to rise by 24% in an obese group who had lost weight (37). This suggests that ghrelin may also operate in the longer term to correct an energy-deficient state. A dietary intervention that reduces concentrations of ghrelin may be expected to reduce hunger and consequently food intake.

Cholecystokinin has been the most extensively studied gut peptide associated with satiation. It is released in response to the presence of fat or protein in the duodenum. Its appetite-suppressing effect is augmented by stomach distention (38). It is associated with feelings of satiation and meal termination in a dose response manner (39). However, the association is not reliable, and
there are sensitivity and specificity difficulties with its measurement (40).

Stomach distention is strongly associated with satiation and meal termination (41). It may be an adequate stimulus for satiation, but it is not necessary. Some data demonstrate that meal volume is a more important determinant of meal size than energy or macronutrient content (42). However, other work reveals no association between gastric emptying and self-reported appetite (43). Artificial distention of the stomach by inflatable balloons decreases hunger (41), but tolerance to this manipulation develops quickly.

Glucagon-like peptide 1 (GLP-1) is released predominantly in the ileum as a response to the appearance of nutrients. GLP-1 release influences gastrointestinal motility and, through this mechanism, may moderate appetite (44). Its ability to reduce appetite has been demonstrated by studies that observed a 12% decrease in food intake following the infusion of this hormone (45). Continuous infusion of GLP-1 over a 6-week period results in decreased sensations of appetite and, more importantly, a reduced body weight (44). GLP-1 may prove to be a suitable biomarker for quantifying changes in appetitive ratings.

Leptin is synthesized primarily by the adipose tissue and provides information to the hypothalamus regarding the body's fat stores (46). Plasma leptin levels correlate strongly with total body fat stores. Leptin seems to have a role in long-term energy balance, especially when energy balance is disturbed through under- or overfeeding (47,48). In such times, leptin correlations become very strongly correlated with hunger ratings (49). The effect of leptin on short-term eating behavior is less clear. Leptin concentrations do not change reliably in response to a meal (50), although subjective ratings of hunger clearly do. Consequently, leptin is a poor biomarker for short-term appetite studies.

DIETARY MODULATION OF APPETITE

Knowledge of appetitive sensations may serve multiple purposes. It can be a tool to understand basic metabolism as well as behavior. From a dietetics perspective, the primary interest lies in the assumed associations between appetitive indices and the interest in eating, food choices, energy balance, and body weight. Presumably, foods with high satiation or satiety value should aid in controlling energy intake, whereas items with low values should provide a weaker barrier to consumption. The former may be beneficial among individuals attempting to moderate energy intake (eg, overweight/obese patients), whereas the latter may hold value for those requiring increased intake (eg, certain patients with cancer, human immunodeficiency virus infection, or elderly adults). Accumulating knowledge provides insights on food and meal components that may be manipulated to achieve these dietary goals.

MACRONUTRIENT COMPOSITION

Fat

Fat has traditionally been regarded as the macronutrient with the strongest satiety property. This stems from the historical focus on the stomach as a primary source of hunger/satiation cues and knowledge that fat clears from the stomach more slowly than the other macronutrients. Thus, it prolongs gastric distention. However, this view suffers from a failure to recognize that gastric cues are only one of multiple determinants of appetitive sensations. Indeed, gastrectomized patients have normal appetitive sensations (51).

More recent literature provides compelling evidence that fat is actually the least satiating of the macronutrients (6). This is most clearly demonstrated in preload-type studies in which individuals report to a laboratory after a fast of some length, commonly overnight, and are provided a fixed portion of a food with a particular concentration of a macronutrient. Hunger is then tracked over a period of time, commonly 2 hours. This may be followed by presentation of a preweighed meal, and the quantity consumed is covertly monitored. Alternate designs may involve the use of different foods in which the predominant source of energy is from a particular macronutrient. This paradigm typically reveals that fat is least effective at suppressing self-reported hunger and food intake. This, of course, is consistent with the common experience that it is not difficult to ingest a large amount of energy from high-fat meals. If fat had a high satiety property, this would not be expected. Thus, fat, preferably unsaturated, may be added to the diet to promote energy intake or reduced (preferably saturated) to moderate intake.

A recent discussion concerns potential differential effects of fatty acids varying in saturation on appetite (52). Studies in rats indicate that unsaturated fatty acids hold stronger satiety value than saturated fatty acids (53). It was hypothesized that this was attributable to the fact that saturated fatty acids are absorbed less efficiently and are oxidized less readily than unsaturated fats. Consequently, if availability of an oxidizable substrate provides a satiety signal, it would be less effective. This concept was examined in several human trials. However, neither infusion of fatty acid emulsions nor consumption of foods containing polyunsaturated fatty acids, monounsaturated fatty acids, or saturated fatty acids supported a differential effect on appetitive sensations. One trial did find a small transient lesser effect of monounsaturated fatty acids on prospective consumption (54), but this was not replicated in a subsequent study by the same group. Caution must be used when extrapolating data on a food constituent to all foods containing that component. Because fat holds weak satiety value does not mean that all high-fat foods have weak satiety properties. Nuts are high-fat foods that possess strong satiety value (55). They evoke a robust compensatory dietary response (ie, reduced subsequent energy intake) that offsets approximately two thirds of the energy contributed by the nuts. (55-59). This explains, in part, epidemiologic evidence that frequency of nut consumption is inversely associated with body mass index (BMI) and intervention trials reveal little or no weight gain during feeding trials with nuts.

Preload studies generally indicate that carbohydrate has a satiety effect that is intermediate to fat and protein (60,61). An exception occurs when high-fat and high-carbohydrate foods are matched on energy density (kilo-
calories per gram of food) (62). In this instance, their satiety values are comparable, indicating that the low satiety value of dietary fat is likely because of its high energy density rather than another chemical property.

**Carbohydrate**

The role of carbohydrate in regulation of appetite and energy balance has recently attracted attention (63). Although the type and amount of carbohydrate consumed influences many ingestive processes, one mechanism of particular current interest concerns the concept of glycemic index. Glycemic index is defined as the positive area under the glucose response curve after consumption of 50 g of available carbohydrate from a test food. Glycemic index values are expressed relative to the glucose response observed after the ingestion, by the same person, of the same amount of a reference food, typically glucose or white bread. Theoretically, high-glycemic-index foods prompt an early and sharp increase in blood glucose, which elicits a strong insulin response. This, in turn, promotes the clearance of glucose from the blood and a rebound relative hypoglycemia. It is believed that this stimulates appetite, with consequent increased energy intake, positive energy balance, and weight gain.

However, another view is that selected low-glycemic-index foods may also be problematic. There has been considerable interest in the association between soda ingestion and body weight. A recently proposed mechanistic hypothesis holds that the high-fructose corn syrup used as the primary sweetener in these beverages has low-glycemic-index properties (64). This results in a small insulin response to their ingestion. This then has little stimulatory effect on release of the satiety hormone leptin. As a result, hunger is not suppressed and food intake increases, resulting in positive energy balance and weight gain (65). Thus, hypotheses based on the glycemic index value of carbohydrate-containing foods suggest that both low and high insulin responses to foods promote hunger and energy intake. One mechanism assumes that blood glucose is a primary determinant of hunger. However, euglycemic clamp studies reveal that independent manipulation of either glucose or insulin do not elicit commensurate shifts in hunger (66). The other view is predicated on leptin as a key postprandial regulator of appetite. However, because of its strong correlation to body fat, there is considerable question regarding leptin’s role in meal-to-meal control of appetite. Thus, the importance of carbohydrate in appetite control warrants further study.

**Protein**

There are compelling data indicating that protein has the highest satiety value of the macronutrients (66,67). This has been documented in preload studies based on appetite ratings as well as by measuring food intake. Still, this work has raised issues that require such a view be made with qualifications. First, the type of the food used as a protein source can modify its response. Solid foods with high protein content reliably hold strong satiety value as measured by appetite ratings and food intake. However, the preponderance of evidence based on protein manipulations in fluids fails to support these effects (68). Second, there is increasing interest in effects from different protein sources. Although isolated studies revealed particularly strong influences of selected proteins such as chicken or whey, these require further substantiation. The high satiety value of proteins has been credited with helping to curb hunger during adherence to high-protein diets, but this has not been established through objective testing. Alternative explanations such as monotony and ketosis may also contribute.

**Fiber**

Several recent studies indicate that ethanol enhances hunger (69). Whether this is due to learned associations, a psychoactive property of the ethanol, an effect on food palatability, or metabolic phenomenon is not known. Strikingly consistent evidence indicates that ethanol ingestion elicits little dietary compensation, so energy intake increases by an amount roughly equal to the energy provided by the ethanol (70-74). Although this would be expected to promote weight gain with regular use, the epidemiologic and clinical literatures are mixed on the effects of moderate ethanol ingestion on body weight (75). Many studies fail to document an increment of body weight with ethanol use, thus raising questions about whether the weak satiety value of ethanol poses a threat to weight gain. Resolution of this paradox awaits further study.

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trient absorption, resulting in a metabolic profile that enhances satiety.

Preload studies have been the most common approach to demonstrate the appetitive effects of dietary fibers (34). Fairly consistent dose response relationships have been observed. The absolute magnitude of efficacy is less well characterized. Commonly, doses of 20 to 35 g of fiber are provided in a preload meal, and appetitive sensations are monitored. In a population that typically consumes only approximately one third to one half this amount daily, questions should be asked about the relevance of the findings.

Gastrointestinal distress is a common adverse effect of excessive fiber ingestion and would be expected to elicit responses reflecting a low interest in eating (81). In one carefully conducted trial, foods with graded levels of fiber were tested along with an egg meal (82). The latter is high in protein but void of fiber. Only the highest fiber load prompted stronger satiety than the fiber-free egg. Thus, fiber does offer a means to enhance the satiation and satiety value of the diet, but use within the range that is tolerable in the US population will likely have only modest efficacy. Questions about its long-term efficacy are also open. One review of the literature reported that 20% of trials using fiber supplementation through foods failed to demonstrate beneficial effects on appetite (76). High-fiber diets led to a 10% reduction in energy intake, but the extent to which this was due to enhanced satiety is not known. High-fiber diets also tend to be lower in fat and energy density.

Because of a hypothesized influence of fiber on the gut and interest in its application to management of obesity, potential differences in gut size and function in the lean and obese are central to understanding the potential for this intervention. Contrary to popular views, gastric volume is not directly related to hunger or BMI (83). Thus, whereas obese individuals require larger food volumes to reach a comparable level of satiation with a lean individual, this is not necessarily attributable to their having larger gastric volumes. They also have higher energy needs. In one recent study, overweight/obese individuals required and additional 225±57 kcal to reach maximal satiation compared with lean participants (80). The extent to which volume displacement of this caloric difference can be met by fiber on a chronic basis is not known. Large resting gastric volume is also associated with low satiation. A 50-mL increment in gastric volume was associated with the need for an increment of 114±32 kcal to reach maximal satiation. The significance of this is not known.

**FOOD VOLUME OR WEIGHT**

For over a decade, fat was considered a prime contributor to positive energy balance. This was attributed to its palatability, low satiation value, efficient metabolism, and high energy density. The latter was viewed as problematic because of evidence that humans tend to eat a constant weight or volume of food daily (84). This was first demonstrated in feeding trials in which participants were allowed ad libitum access to foods of varying macronutrient composition. Under these conditions, the gram weight of intake was relatively constant across interventions, resulting in higher energy intake with increasing fat content or energy density. This was termed *passive overweight*. To combat this threat to energy balance, diets composed of foods with low energy density, ie, items with high fiber and water content, were promoted. Preliminary experience with this approach has yielded a complex picture. Adherence to such a diet does help to control hunger, is regarded as palatable, and does promote weight loss (85). However, the higher cost and inconvenience of the diet, which relies heavily on fresh fruits and vegetables, resulted in poor long-term compliance. Apparently, controlling hunger is necessary but not sufficient for successful dieting.

More recently, concern has been focused on increasing portion size as a contributor to positive energy balance (86). This is an issue because studies in children and adults indicate that energy intake is directly related to the portion of food provided (87). However, these findings pose a quandary at several levels. First, for this to be a factor, it must be posited that the controls on appetite failed as of about 25 years ago when body weight began to rise. There is no basis to support such a degradation of function. Alternatively, it may be that, with the increased availability of low-cost, palatable foods, people simply choose to override appetitive cues. Only anecdotal evidence supports this hypothesis at the present time.

The second problem with attributing positive energy balance to increasing portions is the fact that the very concept that intake is proportional to portion size conflicts with the well-supported view, outlined above, that humans eat a constant weight of food. Can both mechanisms be operational? One hypothesis that accommodates both mechanisms holds that there is no physiologic monitor of ingested food volume or weight but, rather, that the constancy of intake reflects social dictates of appropriate portion sizes (eg, two slices of bread make a sandwich meal). However, over the past quarter century, social norms have shift toward larger portions. Resolution of this question awaits systematic testing.

Thus, there are strong data supporting a low satiation value to foods with high energy density. Low–energy-dense foods may be proposed to address the problem of positive energy balance, but additional research is needed to identify ways to make such foods fit consumers’ lifestyle. The recent trend for larger portion sizes appears to defy historical appetitive controls on feeding. It may be that hunger, with its many facets (eg, cognitive, sensory, metabolic), is more powerful than satiation/satiety mechanisms. This is consistent with the asymmetry in regulatory control mechanisms between weight loss (stronger) vs gain (weaker). Evolutionarily, an energy surplus was less life threatening than an energy deficit. If true, this calls into question weight management approaches based on refocusing awareness of and sensitivity to appetitive signals. Greater cognitive control may be required to moderate portion sizes. Whether a reversal is possible and sustainable and how long it will take to achieve are questions worthy of further investigation.

**DIETARY OR SENSORY VARIETY**

Whether sensory variety is inherently pleasing and promotes overconsumption can be debated. Restriction of variety is an effective short-term weight management approach because monotony results in a spontaneous re-
duction of intake (88). However, the desire for variety is so strong that, almost invariably, adherence to such a diet fails and weight is rapidly recovered. Dietary variety was not promoted in the previous dietary guidelines because of concern that the message would be interpreted as a recommendation to increase food intake. This was based, in part, on evidence that, under carefully controlled laboratory conditions, sensory variety within a single eating occasion or meal leads to increased intake relative to the condition in which only a single food of fixed sensory properties is served repeatedly (89). Although this observation did provide useful insights on meal-related ingestive behavior, the phenomenon was not demonstrated to hold across meals (69). Thus, it ignores the possibility for compensation and leaves open questions about its nutritional relevance. Other data, based on a small sample not representative of the US population, revealed an inverse association between variety and energy intake for a number of food categories (90). However, an inverse association was also observed between variety and vegetable intake. This calls into question the role of variety vs diet composition in the promotion of positive energy balance. Indeed, in a study with rats provided monotonous or varied diets, weight gain was only observed when variety was accompanied by a high-energy diet (91). Thus, at present, there is limited evidence that variety overrides satiation/satiety cues and what risk there is of this should be weighed against the demonstrated benefits of variety on nutritional quality.

**RHEOLOGY**

Consumption of energy-yielding beverages has increased in concert with body weight over the past 2 decades, prompting concern that it is causally related. There are strong data indicating that the energy from beverages adds to the diet rather than replacing other energy sources (92). That is, energy-yielding beverages do not evoke dietary compensation (93). Beverages now contribute approximately 25% of the energy in the US diet (94). Although carbonated soft drinks contribute the largest proportional share, understanding and addressing the issue are obscured by focusing on this one source. There are data demonstrating weak compensatory responses to beverages of varying types (eg, milk, coffee, juice) and energy sources (eg, carbohydrate, fat, ethanol) (93,95). Thus, the failure of beverages to elicit satiation or satiety signals is likely due to their fluid nature. Surveys increasingly document associations between beverage consumption and body weight or BMI (86,96), and intervention trials support the epidemiologic findings (92,97).

The mechanisms by which fluids escape appetitive controls is not known, but may include cognitive, sensory, osmotic, gastrointestinal transit, endocrine, and other processes. Noncaloric beverages do not promote increased energy intake in humans. Thus, caloric fluids appear to be a major, and largely unregulated, source of energy in the diet. The solution to this problem is not to restrict fluid intake. Maintenance of normal hydration is essential. However, consumers may choose to either switch to lower calorie beverages or to monitor cognitively their intake and make appropriate dietary modifications to maintain energy balance. Appetitive cues alone do not appear to be effective.

**DIETARY PERIODICITY**

Meal frequency and timing have also been implicated in the overweight/obesity problem, the common beliefs being that fewer meals and eating in the evening promote positive energy balance. Interest in meal frequency stems from observations of an inverse association between self-reported eating frequency and indices of girth or body fat. However, a critical review of this work reveals alternative explanations (98). First, reverse causality is a likely explanation of the association. That is, heavier individuals reduce eating frequency in an attempt to reduce body weight. Second, while underreporting of energy intake is widespread, it is more pronounced among the overweight and obese. This occurs, in part, by a failure to acknowledge eating occasions. The degree of underreporting is greatest among those reporting the fewest eating occasions.

Based on existing literature, there are clear benefits to an eating pattern that entails more frequent, smaller volume eating occasions (eg, improved lipid profiles and glucose tolerance) (99), but maintenance of energy balance is not well supported. Indeed, there are data suggesting a positive association between eating frequency and weight gain because of the failure of meal size to be appropriately decreased (100,101). The notion that eating late in the evening is more prone to result in energy storage does not fit with common experience or the epidemiology literature (102). If this were the case, cultures in which late dining is the custom, such as Western Europe, would be expected to have the highest prevalence of overweight, and this is not observed. Furthermore, reviews of national data (eg, National Health and Nutrition Examination Survey) reveal no association between the time of eating and BMI (102).

**SUMMARY**

Despite a long history of research, the mechanisms and functions of appetitive sensations remain poorly characterized. This is, in part, because of difficulties in identifying the key metrics and methods to quantify them. Work on the topic has increased recently because of a belief that the current overweight/obesity epidemic results from a failure to respond to appetitive cues that attempt to balance energy intake and energy expenditure. However, the underlying premise of this view is questionable because there is no clear adaptive advantage for an organism to consume just enough food to maintain energy balance. Such a system would fail to protect against future gaps in food availability. A strong hunger drive would act to encourage overconsumption and promote energy storage for use during intermittent food shortages. The tendency of modern humans to overeat and efficiently store the excess energy is testament to the strong selective pressure for this genotype. Unfortunately, this genotype is maladaptive in modern societies in which food is inexpensive, palatable, and readily available. Thus, recommendations to become more sensitized to internal appetitive cues that guide food choice may not have the intended effect on energy balance and body weight.

Attempts to modulated appetite for therapeutic purposes through manipulation of food properties have
yielded limited success. This is likely because of the compensatory inputs from other elements of the redundant system that ensure energy needs are met or exceeded. Work in this area should be pursued but with recognition that there are additional factors (e.g., cognitive, social) guiding food choice. Appetite and food intake are not synonymous. Thus, the ultimate goal must be moderation of energy intake rather than appetite.

FUTURE DIRECTIONS

Future efforts to elucidate the mechanisms and functions of appetite will be most productive if they emanate from the recognition that appetite is multidimensional. It has a biologic basis composed of a wide array of redundant (e.g., multiple endocrine signals that promote and reduce appetitive sensations) and interacting (e.g., gastric stretch with incretin release) components that may be viewed as an integrated system to balance energy needs with supply. However, there are also sensory and cognitive components that may modulate the biologic systems and do not necessarily have an inherent inhibitory counterweight. It is likely that these components are considerably less uniform and predictable within and among individuals than the biologic cues and, as a result, promote highly idiosyncratic appetitive responses. This raises questions regarding the ultimate function of appetite in the present context (as opposed to its historical role). Resolution of this question may require new approaches to old problems.

There is, first and foremost, a fundamental need to develop methodologies to better characterize and quantify appetitive sensations. Without an ability to identify and measure appetite adequately, efforts to modify or exploit it for any intended purpose will likely be futile. Although the goal is to understand free-living behavior, the field may be advanced by establishing a quantitative lexicon for appetitive sensations in a manner similar to that developed by sensory scientists in the flavor and fragrance industries. Trained judges should provide more standardized responses and help to elucidate treatment effects. Advances in imaging techniques should provide new opportunities to explore the bases of sensations and a possible a means to quantify them as well. Additional research is also needed on the nature of the sensations. Is there one set of sensations that are generated to varying degrees under different conditions or are their qualitative differences in sensation linked to an individual’s condition (e.g., do caloric restriction and increased energy expenditure lead to the same appetite sensation)? What are the nature and magnitude of individual differences in appetitive sensations under a common set of conditions?

Response formats must also undergo further consideration. Both subjective and objective measures must be pursued. The most popular assessment approach relies on self-reports to questions using visual analog scales. Although convenient, its veracity, reliability, association with purported mechanisms, and predictive power for behaviors of interest (e.g., food choice, energy intake) are not sufficiently established to permit unequivocal interpretation of the data it yields. It is not clear that continued use of this approach without evidence of its value would be productive.

To date, research has focused primarily on individual appetitive mechanisms in isolation (e.g., the effect of a single peptide concentration on appetite). However, to understand the role of appetite in free-living individuals, it will be necessary to quantify the individual and combined environmental, psychologic, and physiologic conditions that generate, modulate, and terminate appetitive sensations in healthy and diseased individuals. The findings will help to guide discovery of the dominant components of the appetite system so that the most effective intervention strategies can be developed. This work will be most productive if conducted as collaborations between researchers and clinicians from multiple disciplines.

Finally, because appetite is in constant flux and is strongly influenced by individual eating occasions, it is commonly viewed as a modulator of acute motivation and behavior. However, its impact on health will depend largely on persistent effects. Compensatory dietary behaviors can offset effects of acute natural or manipulated appetitive sensations. Longer-term studies are needed to illuminate further the role of appetite in health and disease.

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