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Eating for Life: Designing Foods for Appetite Control

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Abstract

We are all well aware that rising levels of obesity in developed countries is having a significant impact on the health of the population. This is despite the availability of a wide range of low-calorie foods and an awareness of how important it is to adopt a healthy lifestyle. A new and emerging approach is to design foods that enhance the physiological regulatory mechanisms controlling appetite and energy intake. This is achieved through either promoting gastric distension or slowing intestinal transit in order to promote satiety-enhancing neuroendocrine feedback responses. This commentary explores the background and mechanisms involved in developing these strategies.

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The obesity "epidemic," as many see it, is originally thought to stem from our changing diet and lifestyle, which began approximately 10,000 years ago.[1] We have evolved to maximize the extraction efficiency of energy from food and store surplus energy as fat during times of plenty to improve our chances of surviving times of famine. Thus we have developed a survival strategy of encouraging a manageable positive energy balance and inhibiting a negative one.[2] Early developments in agricultural technology and animal husbandry, combined with more recent industrialization of food production and the use of highly refined food ingredients over the past 150 years, has resulted in wide-scale availability of energy-dense foods throughout the year in developed countries. In addition, our increasing sedentary lifestyle following automation and mechanization means that our energy requirements are generally lower. A consequence of these changes is that our genome has not been able to adapt quickly enough to these relatively rapid changes in our diet and lifestyle. Therefore the regulatory mechanisms that we have evolved to control energy intake based on our ancient diet are now unable to cope with a modern, westernized diet and lifestyle. Hence significant cognitive processes are required to consciously control our energy balance. These conscious approaches are actively reducing our energy intake through a reduced-calorie diet and increasing our energy expenditure through exercise. However, this requires active participation and restraint against the incredibly strong desires to consume energy-dense foods when hungry, so this is not a viable option for some individuals.

An increasingly adopted approach is to exploit the regulatory mechanisms that control our feeding habits, such as hunger, satiation, and satiety. In certain cases, medical intervention is required, and various antiobesity drugs can be used to modulate appetite or accentuate satiety,[3] although some natural appetite suppressants, such as *Hoodia*, are beginning to be developed as food additives.[4] Metabolically active compounds such as

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Abbreviations: (CCK) cholecystokinin, (GI) glycemic index, (GLP-1) glucagon-like peptide 1, (PYY) peptide YY

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conjugated linoleic acid, ephedrine, and caffeine can be used to treat obesity[5] through a variety of mechanisms. However, this commentary focuses on how foods themselves can be designed to reduce appetite and promote satiety. As knowledge of our gastrointestinal regulatory mechanisms becomes more widely known, preventative measures are being developed for incorporation into common foods. Hence there are a number of food products being developed that claim to stem hunger or promote satiety.[6] In this article I briefly explore the different approaches taken and their purported mechanisms of action.

Appetite, hunger, and satiety are largely influenced through neuronal and humoral signaling to the central nervous system, usually via the hypothalamus and brain stem. There are three main ways by which these signals are generated:

1. Digestion of food: Neuronal and humoral signals are generated in response to the physicochemical properties of food and their presence in certain sections of the gastrointestinal tract.

2. Nutrient status: Hormones such as ghrelin initiate hunger sensations in response to blood nutrient levels and elevate during periods of fasting.

3. Physiological status: Hormones such as leptin are secreted by adipose tissue to reduce energy intake.

For more extensive reviews of the neuroendocrine control of energy intake, please refer to Smith and Ferguson,[2] Chaudri and colleagues,[7] Karhunen and colleagues,[8] and Maljaars and colleagues.[9] In order to control appetite following food consumption, the regulatory response to food itself is an obvious target. The presence of food in the gastrointestinal tract can stimulate a range of responses designed to reduce appetite and regulate energy metabolism. I will look at how strategies are being developed to maximize the response.

There are two principle processes that directly result in appetite reduction: satiation and satiety.

Satiation

Satiation is the feeling of fullness achieved during food consumption, which promotes the termination of eating during a meal. Gastric stretch receptors detect the distension of the stomach wall in the presence of food, which directly stimulates neuronal pathways to the brain to trigger satiation and appetite reduction.[9] The response is dependent on distension volume, and not nutritional composition, so the effect can be achieved with saline,[9] low-energy foods,[10] aerated foods,[11] and under experimental conditions, for example, inflated balloons.[12] However, the sensation is short lasting, and as soon as the stimulus is released, the effect disappears.[9] Therefore it is an effective way to reduce food intake during a meal, but it is not effective at reducing subsequent energy intake following the meal. Oesch and colleagues[12] showed with inflatable balloons that gastric distension above a certain volume reduced feeding, but when removed, did not reduce appetite.

Foods and food supplements have therefore been developed to promote this satiation effect to reduce energy intake. The aim is to maintain the feeling of fullness for as long as possible. The most popular approach is to use foods that gel in the acid conditions of the stomach and increase viscosity so they remain in the stomach longer and promote the feeling of satiation. Satiation has been correlated with the viscosity of the gel.[10] However, this viscosity is quite high and would be difficult to consume and therefore would not constitute an acceptable food product. This is an important point, as the foods have to be edible in terms of flavor, aroma, and sensory perception. Researchers have looked at calcium-dependent gel formation, but here consumers had to consume the gel and the calcium solution separately to allow gelation in the stomach and not in the mouth.[13] Another approach is to use an acid-setting gel, so the viscosity is low during consumption but quickly forms a thick gel in the stomach and is slowly digested.[10] Aeration of foods can increase the volume but not the energy content and has been shown to reduce appetite in preloaded meals.[14] Meal replacements, usually in the form of milkshake-style drinks, are a popular weight-control strategy. However, to be effective, these products have to impart the satiation/satiety attributes of a higher-energy meal in order to satisfy the consumer until their next meal.[10]

Satiation, however, does not affect the longer-term satiety signals directly, and in the next section, I will look at how satiety is controlled and how it can be modulated.

Satiety

Satiety is the lack of appetite or hunger for a period following a meal. It is largely controlled by a combination of humoral signals in response to food in the gastrointestinal tract and nutritional or physiological

status. Strategies are being developed to design foods that accentuate the gastrointestinal signaling in response to the presence of food in the gastrointestinal tract. One of the important mechanisms is considered to be the ileal brake, where satiety-promoting events are generated in response to food or nutrients in the distal ileum.[9] The following peptides are secreted by the gastrointestinal tract and are thought to be important for control of satiety.

Cholecystokinin (CCK) is secreted mainly by I cells in the duodenal and jejunal mucosa, reducing appetite and slowing gastric emptying. Cholecystokinin is thought to enhance the nervous response to gastric distension, and CCK exerts only a short-term effect (approximately 30 min) and thus regulates food intake during consumption.[8]

Glucagon-like peptide 1 (GLP-1) is an incretin hormone released by L cells in the distal small intestine and colon in response to food intake. Nutrient composition is important for the magnitude of the response, with small sugars playing a key role. Glucagon-like peptide 1 accentuates insulin release, is thought to be involved in the ileal brake mechanism for promoting satiety, and is sensitive to the presence of proteins and carbohydrates. Fats also stimulate a GLP-1 response, but the stimulation is delayed.

Peptide YY (PYY) is secreted by endocrine L cells from the distal parts of the gastrointestinal tract, especially ileum, colon, and rectum. Peptide YY mediates ileal and colonic brakes that slow gastric emptying and promote digestive activities to increase nutrient absorption. Dietary fat and proteins stimulate a strong response, which is sensitive to fatty acid chain length and structure. Dietary fiber can induce a more sustained PYY expression.

For a more comprehensive review of satiety regulating peptides, please refer to Chaudri and colleagues,[7] Karhunen and colleagues,[8] and Maljaars and colleagues.[9]

In order for food-induced satiety to be an effective strategy to reduce energy intake, the satiety signals need to be prolonged in order for energy intake to be modulated during subsequent meals. Therefore the transit time of the foods that illicit the satiety response has to be increased. One of the most effective satiety-inducing signals receiving much attention emanates from the ileal brake response.[9] Here nutrients that reach the distal ileum promote the further release of PYY and GLP-1 and are capable of promoting satiety for extended periods and inducing weight loss. In addition, the ileal brake does not appear to be susceptible to adaptation,[9] therefore providing a potentially sustainable approach to reducing energy intake in the long term.

Attenuated digestion of proteins, fats, and carbohydrates have all been reported to induce feelings of satiety and reduce energy intake.[8] The key is to supply the nutrients in a form that slows digestive breakdown and hydrolysis. Low glycemic index (GI) carbohydrate-based foods are, by definition, those in which digestion and uptake is modulated and are therefore capable of prolonging satiety,[15] probably through stimulated GLP-1 release.[16] High GI foods, however, are digested more quickly and can induce very short-term satiety in response to plasma glucose levels.

Fat uptake is normally very efficient, so by modulating lipolysis, delayed digestion of fats can induce satiety through the ileal brake. Diepvens and colleagues[17] showed that a formulation containing a novel fat surrounded by a layer of digestion-resistant lipids could promote satiety in young, normal-weight individuals but were less effective in older, overweight subjects. Modulating lipid digestion could be an effective strategy, but inhibiting lipid digestion entirely can promote fatty diarrhea due to the presence of excess fat in the colon.[3] It has also been shown that oils rich in pinolenic acid (C18:3) can elevate levels of CCK and GLP-1 and reduce energy intake,[18] but the mechanism is not clear.

Proteins are known to promote satiety, and the benefits of high-protein diets seem, in part, to be due to the satiety-enhancing effects of a protein-rich diet.[19] Having a high protein load in a meal is likely to slow the protein digestion and hence prolong transit and promote satiety. The specific effect on gastrointestinal hormones seems to vary between different proteins,[20] suggesting that certain proteins may be more effective than others. However, the long-term benefits of a high-protein diet warrant further investigation.[19,20]

A key to the success of this strategy of using satiety-promoting foods to reduce energy intake is to improve our understanding of the digestion of foods and food structures in order to develop foods, or preparation techniques, that can prolong digestion and reduce appetite. For example, lipid structures (such as chloroplasts) in green leaves and cereals are rich in galactolipids, which are thought to reduce lipid digestion,[17] but it is not known if they are available following conventional cooking or processing. To maximize their effect in everyday foods,

they may have to be processed or prepared in a way that improves their efficacy as a satiety-promoting agent. Another important aspect is that the foods need to be appealing, desirable, affordable, and able to fulfill other dietary targets (e.g., vitamin and mineral content) in order for consumers to actively use these products. It should also be stressed that such products are likely to have a modest impact on dietary energy intake when used in isolation, but used as part of an active approach to improving health, they could help individuals maintain an effective and sustainable weight-control strategy.

It is becoming apparent that certain individuals are genetically predisposed to weight gain. These could be due to problems with energy metabolism and storage pathways and/or hormonal or hypothalamic dysfunctions. Similarly, satiety control has been shown to be more effective depending on psychological attitudes to food intake.[13] Therefore control of appetite may not be an appropriate strategy for all individuals. However, for the majority of subjects with normal metabolism, our strong, innate impulse to feed requires some modulation in controlling appetite. Therefore food-induced satiety regulation could make a significant contribution toward controlling obesity levels in the future. In particular, the ileal brake seems to be the mechanism that could be targeted by everyday food products specifically designed to be slowly digested. However, the health claims made by such foods will have to be carefully considered. Current developments in international food regulations will require that health claims made by food products are substantiated by clinical or scientific evidence[21] through, for example, controlled dietary intervention studies similar to those currently used in nutrition research projects. Finally, the other side of the energy balance equation should never be ignored (i.e., energy expenditure). Exercise is not only beneficial in reducing risk factors for a whole range of lifestyle-related disorders, but it has also been shown to help reduce appetite.[22]

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