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Added sugars drive nutrient and energy deficit in obesity: a new paradigm

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ABSTRACT

Obesity has traditionally been thought of as a state of caloric imbalance, where the intake of calories exceeds the expenditure or 'burning' of calories. However, a more nuanced appreciation for the complex biochemistry and physiology of cellular energy generation suggests that obesity is a state of hormonal imbalance causing increased shunting of food energy into adipose tissue for storage, resulting in decreased satiety and ultimately leading to increased caloric intake. Adding to this hypothesis, we propose that obesity is also a state of nutrient and energy deficit, leading to decreased fatty acid mobilisation and oxidation, the result of which may be a natural disinclination towards physical activity. Added sugars (sucrose, a.k.a. table sugar and high-fructose corn syrup) may provide energy (4 kcal/g) but at current intakes they do not facilitate—and may even hinder—the production of energy. Not only do added sugars displace nutritionally superior foods in the diet, but they may also deplete nutrients from other foods that have been consumed, as well as from body stores, in order to enable their proper oxidation and liberate their calories as energy. Additionally, the consumption of added sugars damages the mitochondria and hence impairs energy generation. Moreover, overconsuming added sugars may result in a kind of 'internal starvation' (via leptin and insulin resistance) leading to further hunger signals in the body. Added sugars promote nutrient and energy deficit and through this novel pathway promote obesity.

INTRODUCTION

Nutrient/energy deficit in obesity

Sugar was first extracted from sugar cane and sugar beets hundreds of years ago, and later 'purified' into a white crystalline form. In modern times, sugar has been isolated and refined to a degree that allows it to be integrated into the food supply in quantities and concentrations that do not occur naturally and are unlikely to have been encountered in human evolutionary history. Pure crystalline sugar, high-fructose corn syrup (HFCS) and other caloric sweeteners consumed in beverages and processed foods provide a supraphysiological glycaemic load,[1] overwhelming the body's processing capacity and leading to detrimental metabolic effects (eg, hyperglycaemia, hyperinsulinaemia and oxidative stress).[1] Because of this refinement, added sugars now behave like drug-like substances.[2 3] Although edible, added sugars cannot be considered a 'food', nor can their consumption be equated to eating foods that contain natural amounts of sugar, but which also provide fibre, vitamins, minerals and other phytonutrients that combat oxidative stress produced by the small amounts of fructose present. As the 'dose makes the poison', the food industry has made it possible for consumers to easily 'overdose' on added sugars, making this an issue of concern for public health worldwide, wherever there is significant consumption of processed, highly refined and sugar-dense foods.

Added sugars are not food

> Sugar is not among the recommended foods. Its recent rationing will not provoke a hardship, for sugar supplies nothing in nutrition but calories, and *the vitamins provided by other foods are sapped by sugar to liberate these calories.*[4] (Emphasis added) (Wilder—*Handbook of Nutrition*)

The definition of food is, 'Material that contains essential nutrients, which are assimilated by an organism to produce energy, stimulate growth and maintain life'.[5] Many types of added sugars do not fit this definition. While caloric sweeteners such as honey, maple syrup, molasses and sorghum syrup (also known as 'free sugars') may provide trace amounts of micronutrients, the sweetening agents most commonly added to processed foods—sucrose and HFCS—do not. In fact, these added sugars not only lack essential nutrients, but they also have detrimental effects on all three important functions of food (eg, produce energy, stimulate growth and maintain life). These two added sugars (sucrose and HFCS) will be the disaccharides of focus in this review.

Added sugars do not produce energy or stimulate growth

Starting with the first necessary function of a food—'produce energy'—added sugars in

fact deplete energy from the body, either by depleting tissue nutrient stores or nutrients obtained from other ingested foods.[4] Added sugars also displace nutritionally superior foods from the diet and at the same time increase nutritional requirements.[4 6] Specifically, vitamins such as thiamine, riboflavin and niacin are necessary for the oxidation of glucose, and phosphates are stripped from ATP in order to metabolise fructose, which leads to cellular ATP depletion.[4 7] The metabolism of fructose also leads to oxidative stress, inflammation and damage to the mitochondria, causing a state of ATP depletion.[8] Hence, the liberation of calories from added sugars requires nutrients and increases nutritional demands, but these sugars provide no additional nutrients. Thus, the more added sugars one consumes, the more nutritionally depleted one may become. This may be particularly extreme in individuals whose habitual diet is already insufficient in key micronutrients.

The conversion of food calories into energy in the form of ATP does not occur by chance, with no requirements for input into the biochemical pathways involved. Via glycolysis and the citric acid cycle, carbohydrates—including refined sugars—are converted into energy. The reactions these processes comprise are dependent on required cofactors in the form of vitamins and minerals; however, isolated and refined sugars have been stripped of their micronutrient content, which may impair their conversion into energy and/or result in a net nutrient deficit if such nutrients must be siphoned from body stores in order to keep these processes running efficiently. Contrast this with foods consumed in their whole, unrefined forms, which typically contain at least some of the nutrients required to liberate their energy.

The popularity of low-carbohydrate diets for fat loss, as well as their efficacy for improving a broad range of health conditions,[9–12] has led to an unfortunate across-the-board demonisation of carbohydrates among some nutrition and healthcare professionals. While individuals who are insulin resistant or have type 2 diabetes, pre-diabetes or the metabolic syndrome (which, according to the American Diabetes Association, is well over 100 million people in the USA alone, including as many as 26% of individuals aged 65 or older[13]) may manage their blood glucose and insulin levels best on reduced carbohydrate diets,[10 11 14] it is not carbohydrate-dense foods, per se, that contribute to impaired energy production. Rather, it is carbohydrate foods that have been stripped of their natural complement of nutrients and fibre and extracted from their whole-food matrices that may be placing the largest metabolic burden on the body, particularly when they contain additional carbohydrates in the form of added sugars, such as may be found in soft drinks and cookies, crackers, bread, breakfast cereal, granola bars, etc, made from refined grains with additional sugars and sweeteners added as preservatives and for enhanced palatability.

Glycolysis—the conversion of glucose to pyruvate with a net yield of 2 ATP—requires magnesium as an enzyme cofactor in at least six individual reactions. The pyruvate dehydrogenase complex, which converts pyruvate to acetyl-coenzyme A and is the link between glycolysis and the citric acid cycle, requires thiamine, riboflavin, niacin and pantothenic acid for proper enzymatic function. B-vitamins are required again for effective functioning of the citric acid cycle, which will produce an additional 36 ATP, and is the process by which the majority of energy is generated in all cells except those lacking mitochondria. Unlike isolated refined sugars, carbohydrate-rich whole foods—such as sweet potatoes, white potatoes, beets, parsnips and winter squashes, as well as whole grains, such as hard red winter wheat and millet—provide critical minerals and B-vitamins required for the proper use of these foods in the body. Added sugars provide fuel in the form of carbohydrate but lack the accessory nutrients needed to convert that fuel into energy. We are not suggesting that each food consumed must, in isolation, contain the full complement of nutrients required for its metabolism and oxidation; a varied omnivorous diet would be expected to meet these basic nutritional needs. However, consumption of large amounts of added sugars may displace nutritionally superior foods in the diet, ultimately resulting in a net deficit of vitamin and mineral enzyme cofactors required for not only the oxidation of the glucose, itself, but for that of whole foods.

Additionally, fructose consumed at current levels found in much of the industrialised world has been found to deplete cellular ATP levels in vascular endothelial cells,[15] with as little as 50 g of fructose (found in approximately one 24 oz soft drink) being able to deplete hepatic ATP levels in humans.[16 17] This results in appetite stimulation and increased hunger signals, prompting increased caloric intake, which may ultimately lead to weight gain and obesity.[8] As the average American consumes 83.1 g of fructose per day,[18] with up to 20% of the population exceeding 100 g/day,[15] current levels of fructose consumption may lead to chronic energy depletion causing increased hunger and lack of energy to exercise. Thus, increased caloric intake and reduced physical activity are logical consequences of overconsuming added sugars. However, while the end result may be obesity in susceptible individuals who are simply following the biological cues prompted by these hijacked metabolic processes, increased caloric intake and a reduction in physical activity (ie, eating more and moving less) are merely the proximal causes of body fat gain; consumption of large amounts of refined sugars is the ultimate underlying cause, triggering the cascade as a whole.[19] As many soft drinks are produced with HFCS that contain up to 65% fructose, this is particularly concerning.[20–22] The overconsumption of added sugars does not produce energy despite providing energy, which is somewhat of a paradox. In order for a substance to be classified as ‘food’, it must produce or at

least facilitate the production of energy, not just provide energy.

> The consumption of sugar and of other relatively pure carbohydrates has become so great during recent years that it presents a serious obstacle to the improved nutrition of the general public.[4] (The Council on Foods and Nutrition, 1942)

Written over 70 years ago, this observation may be even more relevant today. Indeed, many of the concerns about the detrimental effects of sugar stem from its current excessive consumption worldwide. Recent estimates indicate that the average annual per capita consumption of sugar ranges from 77 to 152 pounds,[23 24] which is ~20-fold to 40-fold greater than estimates of consumption just a few hundred years ago.[25] This level of consumption equates to around 400–800 calories per person per day from added sugars. On a diet of 2000 calories per day, 800 calories from added sugars represents a dilution of 40%, or a 40% displacement of foods with higher nutrient density by foods that not only provide fewer nutrients, but which may, in fact, require increased nutrient intake simply to be metabolised. It is easy to understand how consuming added sugars leads to nutritional deficit.[4 6]

Soft drink consumption is associated with lower intakes of calcium and other nutrients,[26] which may lead to malnutrition, especially in children.[2] Additionally, the overconsumption of added sugars is linked to the development of insulin resistance in humans and animals,[27–30] which decreases the body's ability to use glucose as energy. Moreover, the ensuing rise in insulin levels decreases the body's ability to use its other key fuel source, fats. (Via inhibition of hormone-sensitive lipase, chronically elevated insulin keeps fatty acids sequestered in adipose tissue, reducing their availability for β-oxidation and the generation of ATP.[31 32]) In essence, cells are starved for energy because energy generation from fatty acids is inhibited when insulin levels are high, resulting in what has been referred to as 'internal starvation' or 'hidden cellular semistarvation'.[33] More colloquially, it can be thought of as 'starvation in the land of plenty'. Not only that, but elevated insulin levels increase energy requirements,[31] further leading to a net energy loss with the consumption of added sugars. Owing to the lack of access to fuel substrates, individuals with obesity and hyperinsulinaemia/insulin resistance may fit the description of 'overfed but undernourished'. While they are carrying thousands of calories of stored fuel in the form of adipose tissue, the hormonal pattern that they are locked into due to the overconsumption of refined sugars suggests that, at the cellular level, they are starving.

Sugar also has the ability to derail an appetite for nutrient-dense foods, causing further nutrient depletion.[2] This is likely caused by the elevation in insulin levels prompted by refined carbohydrates, which may lead to cravings for yet more carbohydrate due to insulin's effect on fuel partitioning and its inhibition of energy generation from fatty acids.[31] Animal studies also show that feeding sugar to rats hinders growth and shortens lifespan.[18 34] Several other experiments in a variety of animal species show that the addition of sugar to otherwise adequate diets causes these animals to malnourish themselves to death.[35] And numerous studies in animals indicate that replacing starch with sugar shortens their lifespan, so again, it is not carbohydrate, per se, that has a detrimental effect, but rather, refined and nutritionally void sugars.[36–38] The aforementioned data do not support the definition of food.

Finally, fructose and glucose favour the growth of bacteria and yeast,[2 39–41] particularly in those who already have elevated levels of yeast.[42] Glucose has been found to increase the proliferation and virulence of *Candida albicans*.[40 43] As *C. albicans* competes with host cells for nutrients[44] and requires a high influx of glucose (yielding just two molecules of ATP for each molecule of glucose metabolised via fermentation),[45] this may be of particular concern with added sugars feeding increasing populations of intestinal yeast that then siphon nutrients and energy from the rest of the body. Sugar has also been shown to irritate the linings of the stomach and intestine,[2 25] which may compromise digestive function and the absorption of nutrients. Finally, the hyperosmolar effect of fructose can induce diarrhoea,[46] which may lead to a further loss of nutrients.[2] Box 1 provides an overview of the mechanisms relating the consumption of added sugars with overall nutrient and energy depletion, making added sugars unfit to be considered food.

Box 1 How added sugars promote obesity through energy/nutrient depletion

- Displaces nutritionally superior foods.[2]
- Decreases appetite for more nutritious food.[2]
- Depletes nutrients within the body (in order to liberate the calories from sugar, as well as from an increase in bacterial and yeast overgrowth).[2]
- Provides zero nutrition.[2]
- The consumption of added sugars has been shown to cause insulin resistance.[27–30] This will result in decreased use of glucose for energy (decreased uptake into cells),[47] as well as impaired oxidation of fatty acids for energy.[31 32] Energy requirements are also increased due to elevated insulin levels.[33] Thus, because the consumption of added sugars can lead to insulin resistance, they can induce a state of 'internal starvation', also referred to as 'hidden cellular semistarvation'.[33]
- Decreases nutrient absorption due to intestinal irritation/damage.[2 25]
- Increases nutrient excretion caused by fructose malabsorption leading to diarrhoea.[46]
- Damages the mitochondria and depletes ATP.[8]
- Produces unnatural drug-like cravings leading to a vicious cycle of continued consumption and further nutrient depletion.

Added sugars do not maintain life

Mankind has survived without isolated, refined sugar for almost 2.6 million years.[48] The body—in particular, the brain—has been thought to require upwards of 200 g of glucose per day, leading to the often cited dogma that glucose is 'essential for life'.[1] While it is true that glucose is essential for sustaining life, there is no requirement for dietary glucose, as fatty acids can be turned into brain-fuelling ketone bodies, and amino acids and glycerol are gluconeogenic substrates.[49] Indeed, in the relative absence of dietary glucose, ketone bodies may supply upwards of 75% of the brain's required energy, with the remainder supplied by gluconeogenesis provided by amino acids (from dietary protein or catabolism of body proteins) and from glycerol (provided by the breakdown of triglycerides in adipose tissue).[33] Thus, exogenous glucose (eg, from added sugars) is not essential for sustaining life in humans, and in most people, restricting dietary carbohydrates seems to produce no ill effects.[49] In fact, according to the Food and Nutrition Board of the Institute of Medicine of the US National Academies of Sciences, 'The lower limit of dietary carbohydrate compatible with life apparently is zero, provided that adequate amounts of protein and fat are consumed'.[50]

Administration of fructose or sucrose in humans has been shown to cause each of the abnormalities that define the metabolic syndrome (eg, elevated triglycerides, low high-density lipoprotein, insulin resistance, glucose intolerance, elevated blood glucose, elevated blood pressure and weight gain (specifically around the abdomen)),[30 51–55] as well as features found in patients with coronary heart disease (eg, increased platelet adhesiveness and hyperinsulinaemia),[56 57] all of which can be reversed entirely upon reverting to a diet low in sugar.[47 52 56 58–60] Consumption of added sugars at current levels of intake is proposed as a contributing factor in a multitude of other diseases associated with early mortality, such as cardiometabolic disease,[61–64] obesity,[30 61 65–68] β-cell dysfunction and type 2 diabetes,[6 20 69–71] hypertension,[51 64 72] non-alcoholic fatty liver[7] and atherosclerosis.[6 73 74] Because of this, added sugars cannot be considered food.

Moving forward

As ~75% of all packaged foods and beverages in the USA contain added sugars,[75] efforts should focus on their reduction in order to combat numerous chronic disease states and improve the general nutritional status of the population as a whole. We are not here advocating for the total elimination of added sugars from the food supply. Such an approach is not only unnecessary, but is also economically unrealistic and culturally insensitive, as there are special events and celebrations that may call for traditional foods that contain large amounts of added sugars. Rather than complete removal of added sugars from one's diet, these metabolically taxing elements should be limited to occasional consumption and not be considered daily dietary staples.

There are myriad ways to accomplish a population-wide reduction in added sugars, including but not limited to: widespread public education campaigns; revision of food labels to call attention to added sugar; increased nutrition education in medical schools and for other primary healthcare providers; the taxing of edible goods high in added sugar;[76–80] prohibition of government subsidies for foods high in added sugars;[81] restricting the sale of beverages and edible goods high in added sugars (such as sports drinks, energy drinks and sodas) in schools and hospitals; and adding warning labels to sugar-sweetened beverages and other high-sugar products, similar to those applied to alcohol and tobacco.[81] Such changes could contribute substantially to reducing population-wide intake of added sugars to a reasonable 5–10% of total caloric intake, which would likely lead to substantial improvement in public health.[82]

CONCLUSION

We propose that obesity is a state of nutrient and energy deficit brought about, in part, by the overconsumption of added sugars (specifically high-fructose corn syrup and sucrose). Added sugars provide energy (calories), but in the context of consumption at current intake levels, they hinder the production of energy, and through the direct influence on a wide array of cardiometabolic disease processes, they lead to reduced quality of life and decreased lifespan, and thus cannot be considered food. As added sugars devoid of micronutrients displace more nutrient-dense foods in the diet, dilute nutrients from the body's stores and promote a host of disease states that impair nutrient absorption and energy homeostasis, efforts should be made to reduce their ubiquity and current levels of consumption.

Competing interests AB has written a book about nutrition and health.

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