9-20-2019

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A Sweet State of Mind
The Effects of High Fructose Corn Syrup on the Brain

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Honors 101 (Introduction to Research and Creative Work at Mānoa)
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As both a palatable treat and necessary nutrient in moderation, sugar is a highly prized substance present in the majority of foods and drinks. However, consumed in excess, sugar is known to have adverse health effects which can infringe on an individual’s quality of life. This article aims to address and analyze the effect of sugar, specifically high fructose corn syrup, on the brain. Through the gut-brain-axis, nutrients from digested food can directly reach the brain. In other words, an individual’s diet may impact his or her mental health. This concept of brain function and health in relation to what is consumed prompts many to wonder about the short and long-term effects sugar consumption has on the brain. Thus, studies have found evidence to support a correlation between excess sugar consumption and an increased risk for the development of neurodegenerative, psychological, and metabolic disorders including Alzheimer’s and Type 2 diabetes.

Introduction

Imagine a bottle of Coke, a can of Campbell’s Tomato Soup, and a loaf of bread. What do these have in common besides sodium? If you guessed sugar, you would be partially correct. These three typical supermarket items all contain high fructose corn syrup, a specific type of processed sweetener. If this is surprising, then take a look down the aisles of your local Target or Walmart and count how many foods and drinks contain this additive.

Since its humble introduction in the 1950’s, high fructose corn syrup, or HFCS, has gained the favor of food and drink manufacturers around the globe. From TV dinners to salad dressings to cold cuts, HFCS has become an essential part of the daily American diet. However, this begs the question of how consuming this additive in food affects one’s behavior and overall health. Moreover, sugar consumption and metabolism in the gut has been linked to a variety of psychological and neuro-degenerative diseases as well as metabolic syndrome disorders [1]. This, in turn, prompts investigation on how high sugar consumption affects the neurological pathways in the brain.

Sugars are simple carbohydrates that include monosaccharides and disaccharides. Monosaccharides are the building blocks of disaccharides and polysaccharides, which are complex sugar molecules. In supermarkets, the most common...
monosaccharides are glucose and fructose; both of which constitute the disaccharide known as sucrose, or table sugar. Derived from corn starch, HFCS is a manufactured sweetener with the monomers of glucose and fructose. While corn syrup processed from corn starch contains a high concentration of glucose, manufacturers of HFCS use an enzyme called glucose isomerase to convert a portion of the glucose into fructose, which is a much sweeter sugar.

The prevalence of HFCS in the modern diet points to the possibility of health risks in later life. Thus far, research has linked sugar consumption with various diseases such as diabetes, dementia, and even addiction. Moreover, scientists have also found that different sugars affect the brain differently. This article aims to identify how sugar affects the brain, behavior, and the risk for disease through the interactions between the gut, brain, and body.

Sugar, the GI tract, and the body

Any sweet-tasting, soluble carbohydrate is considered a sugar by definition. Sugar, or more specifically glucose, is the body’s main source of energy. The process of glycolysis breaks down glucose molecules into adenosine triphosphate, which is an energy molecule, and pyruvic acid. Glycolysis is the first of four processes of cellular respiration which in turn generate the energy to fuel the necessary biological activities needed to sustain life.

While plants can generate their own glucose by means of photosynthesis, animals rely on food to supply glucose to the cells. Depending on the type of food consumed, the amount of expendable glucose for cellular use varies. An effect of eating foods with high glucose turnover is elevated blood glucose levels which, mean there is an above average amount of glucose in the bloodstream. For example, consuming carbohydrates yields one hundred percent glucose for the body to use. Therefore, blood sugar levels become elevated shortly after ingestion. On the other hand, meats and fats provide significantly less amounts of glucose, which cause little to no increase in blood sugar levels [2].

The human body is programmed to receive and process glucose, which is a monomer of sugar disaccharides like sucrose and lactose. Therefore, once the food is ingested, the job of the gut-microbiota is to break it down into molecules the body can use [3]. The gut-microbiota can be seen as the millions of bacteria that reside in the gastrointestinal tract (GI tract). These bacteria help support and maintain gut homeostasis which has direct effects on immune and epithelial function in the lining of the GI tract [4]. Studies have proven that the composition of the microbiota is affected by environmental factors rather than an inherent set of bacteria present from birth [3]. Thus, depending on the food one consumes, the types of bacteria that make up his or her gut-microbiota will vary. This suggests that diet plays a crucial role in the makeup of the host gut microbiota [3]. Therefore, since the gut microbiota aids in energy metabolism and digestion of nutrients, the materials consumed by the host will be processed to the ability of the specific bacteria that compose the microbiota.

A large portion of the sugar consumed in the daily diet comes from fructose, sugar found naturally in fruits and honey. With modern technology, scientists developed a way to manufacture high-fructose sweeteners from cash crops such as corn. A popular example of this sweetener is HFCS.

To make HFCS, an enzyme is added to regular corn syrup. This enzyme is known as glucose isomerase, and it converts a portion of the glucose into fructose. According to the Food and Drug Administration (FDA), the most commonly used commercial forms of HFCS contain 42 or 55 percent fructose [5]. When compared to the amount of fructose content in a single peach, which is about one percent of its entire weight, the fructose content in HFCS accounts for half of the compound’s total weight [6]. While consumption of fructose through fruits is supplemented by other nutrients such as fiber and vitamins, additive sugars like HFCS reside in foods which are less nutritionally beneficial. For example, sodas and condiments are high in natural and additive sugars, but they have little nutritional gains to balance it out. (Fig.1) [7]. Comparison of the sugar content among various food and drink items sold at Target in Salt Lake, Oahu are listed in Table 1. These items—which all contain HFCS as an ingredient—are also commonly sold on school campuses and in other supermarkets around the island.

The gut-microbiota does not process all sugars the same way. This means there are various ways sugar can be processed in the body. Although fructose is similar in chemical structure to sucrose, studies show that the different sugars take different metabolic pathways, meaning fructose is metabolized differently from glucose [7]. The primary metabolic pathway for glucose involves cellular respiration, which produces adenosine

![Figure 1](image-url)
triphosphate (ATP) to drive other metabolic processes. However, the bulk of fructose metabolism occurs in the liver and kidneys. These pathways require fructose-specific transport proteins such as ketohexokinase (KHK) and aldolase. Certain regions in the brain express the same genes present in kidneys to metabolize fructose. Researchers also found that KHK and aldolase were 5-10 times more active in the brain, rather than in the liver. This suggests the possibility that fructose can reach the brain in order to be used for energy production [1].

**The gut-brain-axis**

The gut-brain-axis is a bidirectional communication system that links the central nervous system (CNS) and the gastrointestinal tract which houses the gut-microbiota. The gut, brain, and body interact through this system. Therefore, anything entering the gut has the potential to influence our cognitive activity and brain responses.

Considering the interrelatedness between the gut and the brain, certain neurological disorders and diseases have been associated with an unhealthy diet, primarily those that contain high amounts of sugar [4]. These disorders include but are not limited to anxiety, depression, Alzheimer’s disease, and diabetes [8,4]. Furthermore, when an individual experiences dietary variation, the human microbiome will adjust to those alterations.

Because changes in the gut-microbiota directly affect the integrity of the GI tract, studies have found an association between intestinal permeability and certain diseases such as celiac disease and multiple organ dysfunction syndrome [8,9,10]. Though a controversial topic in the medical world, increased permeability of the intestinal tract, referred to as “leaky gut syndrome,” allows bacterial metabolites and byproducts to leak into systemic circulation [11]. This causes the host to be vulnerable to diseases like inflammatory bowel disease (IBD) and diabetes as well as a number of psychiatric disorders [8,11]. While most medical professionals do not consider leaky gut to be a condition, there have been numerous studies citing a relationship between intestinal permeability and susceptibility to disease. A study conducted on rats aimed to establish a link between host susceptibility to chemically-induced colitis, a specific type of IBD which affects the large intestine, and high sugar diets. The scientists concluded high-sugar diets increase host susceptibility to colitis in rats [12]. A second study investigated the effect of high fructose diets on intestinal permeability and the development of nonalcoholic fatty liver disease (NAFLD). The study found that high fructose consumption may lead to bacterial overgrowth in the intestine, causing increased intestinal permeability and risk for development of NAFLD [13]. Therefore, although these studies have been limited to rodent subjects, they emphasize the idea that the effects of high-sugar diets may extend beyond the associated neurological disorders.
Sugar “Addiction”

The neurons in the brain, which are cells that relay signals throughout the body, require an enormous amount of energy to function properly. Therefore, these cells rely on a continuous flow of energy which, in turn, makes the brain consume about twenty percent of all glucose-derived energy [16]. While there is extensive research on the direct effect of glucose on the brain, little is known about the effects of fructose.

Thus far, there have been studies conducted on rodents that indicate there are detrimental side effects of high-sugar diets, specifically those composed of high-fructose [12,15]. Since the gut-brain-axis allows digested nutrient monomers to interact with the brain and nervous system, high sugar diets have the potential to play a direct role in the onset of neurodegenerative, psychological, and metabolic diseases. In 2018, a study conducted on rats linked the consumption of HFCS to neuronal hyperexcitability, a behavior normally associated with bipolar disorder [15]. Furthermore, a study conducted on patients with Type 2 Diabetes (T2D), a form of the metabolic disorder known as diabetes that is associated with insulin resistance, concluded impairment of insulin signaling increases the person’s risk of developing dementia [4]. However, although there is substantial evidence of a correlation between increased sugar consumption and a higher risk of disease development, Americans continue to consume it in excess on a daily basis.

The answer to America’s insatiable sugar cravings may lie in the science behind addiction, which is broadly characterized by dependence on a substance or habit. While sugar is unlike typical addictive substances such as nicotine or heroin, studies show that rats demonstrate addiction-like behaviors on sugar diets [16]. One study in particular found that when rodents predisposed to sugar addiction went on a sugar diet, they began exhibiting signs of addiction to the substance at around three to four weeks [17]. In these studies, sugar consumption leads to opioid and dopamine (DA) release in the brain. These findings produce the idea of a shared neurobiology between actual drugs and sugar [16]. However, because these studies have been limited to rodent subjects, researchers are limited to inferences in order to examine how sugar addiction displays itself in humans. Therefore, the idea of whether or not sugar is an addictive substance, rather than one that produces only similar habits when consumed, is a controversial topic. More research needs to be conducted on the correlation between sugar content and addictive potential as well as the effect of prolonged sugar consumption in animals.

Discussion/Conclusion

Considering the prevalence of HFCS in the American diet, consumers need to be aware of the neurological and psychological effects of ingesting this form of sugar. While the FDA makes no claims against the consumption of HFCS, the organization recommends consuming the additive sweetener in moderation [5]. Although this claim is substantiated by evidence that HFCS is not a toxic substance, the World Health Organization (WHO) reduced their recommended daily added sugar intake to less than 5% of all caloric intake [18]. This puts a tough limit on the amount of added sugar consumed since a large amount of foods and drinks contain excessive amounts of HFCS and other artificial sweeteners. One study catalogued the HFCS content in popular sodas and juices consumed by the public. The scientists found that the most popular sodas such as Coke, Pepsi, Sprite, and Mountain Dew have a 60:40 fructose to glucose ratio. Moreover, they discovered that not only do fruit juices contain similar ratios, but some contain even higher fructose levels than the total fructose content in sodas [19]. Currently, the American Heart Association recommends consuming less than 100 calories of sugar per day for women and less than 150 calories per day for men [20]. Since one gram of sugar is equivalent to four calories, this means about 25 grams and 37.5 grams respectively. To put this in context, a 12-ounce bottle of Coke exceeds an individual’s entire daily recommended sugar intake by about 14 grams for women and 1.5 grams for men. In conclusion, these drinks alone, which are widely consumed by kids and adults alike, make a substantial contribution to the daily added sugar intake.

A common misconception about increased sugar consumption is that it only leads to obesity. However, because of the gut-brain-axis, the effects of sugar on overall health extend further than that. Although Alzheimer’s and diabetes may be consequences of long-term excessive sugar consumption, the short-term consequences begin with cognitive impairment accompanied by a stifled learning capability [21]. Although a majority of studies have been limited to rodent observations and tests, the findings should raise awareness of the potential consequences of a high-sugar diet if consumption is not limited.

People need to be more aware of what they put into their bodies. Sugar, both the natural and additive types, is found in everything regardless of whether it can be tasted or not. Moreover, the United States is the world’s leading per-capita consumer of HFCS [13,22]. This is further accompanied by rising rates of obesity. Therefore, reducing sugar intake by opting for ‘unsweetened’ or ‘low sugar’ alternatives would be an effective preventative step towards reducing risks for diabetes, Alzheimer’s, obesity, and other disorders. While the phenotypic effects of these diseases usually present themselves after prolonged accumulation of various substances including sugar, this information about the interrelatedness between food, the brain, and the body allows individuals to make better decisions when it comes to their sugar consumption.
Works cited


