Clinical Chemistry 64:1
64–71 (2018)

Mini-Reviews

Food Addiction, High-Glycemic-Index Carbohydrates, and Obesity

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BACKGROUND: Treatment success in obesity remains low, and recently food addiction has been delineated as an underlying etiologic factor with therapeutic relevance. Specifically, current treatment focuses on reduced food intake and increase of physical activity, whereas interventions for addiction encompass behavioral therapy, abstinence, and environmental interventions such as taxation, restrictions on advertising, and regulation of school menus.

CONTENT: Here, we reviewed the pertinent literature on food addiction with a specific focus on the role of high-glycemic-index carbohydrates in triggering addictive symptoms. Three lines of evidence support the concept of food addiction: (*a*) behavioral responses to certain foods are similar to substances of abuse; (*b*) food intake regulation and addiction rely on similar neurobiological circuits; (*c*) individuals suffering from obesity or addiction show similar neurochemical- and brain activation patterns.

High-glycemic-index carbohydrates elicit a rapid shift in blood glucose and insulin levels, akin to the pharmacokinetics of addictive substances. Similar to drugs of abuse, glucose and insulin signal to the mesolimbic system to modify dopamine concentration. Sugar elicits addiction-like craving, and self-reported problem foods are rich in high-glycemic-index carbohydrates. These properties make high-glycemic-index carbohydrates plausible triggers for food addiction.

SUMMARY: We argue that food addiction is a plausible etiological factor contributing to the heterogeneous condition and phenotype of obesity. In at least a subset of vulnerable individuals, high-glycemic-index carbohydrates trigger addiction-like neurochemical and behavioral responses.

Obesity is among the greatest public health challenges of the 21st century. The mainstays of therapy are lifestyle changes such as diet and exercise; however, only about 5% of people with obesity are able to permanently reduce their excess body weight. A large amount of research has been dedicated to the phenomenon of obesity, but conclusive reasons for the poor long-term treatment success remain elusive.

One concept that has received increasing attention over the past 10 years is the notion of food addiction. Historically, the term addiction was reserved for drugs of abuse and encompassed the loss of control over consumption, increased motivation to consume, and persistent consumption despite negative consequences. The term is now used more broadly to also describe behavioral addictions, also known as "routines" or "behaviors" that are habitually undertaken to attain reward again despite apparent negative consequences *(1)*. Individuals who develop food addiction are proposed to display symptoms analogous to those of drug addiction, including cravings for "problem foods," tolerance (needing more food to satisfy cravings), limited control of food intake, unsuccessful attempts to reduce intake, as well as withdrawal symptoms *(2)* (see Table 1). Repetitive addiction-like behaviors resulting in over-consumption could conceptually contribute to obesity and antagonize weight-loss efforts.

The neurobiological basis for food addiction in animals appears robust; however, findings derived from human studies are more heterogeneous *(3–5)*. Controversial topics include: (*a*) the applicability of all DSM-5 criteria for addiction to food (Table 1); (*b*) the validity of food addiction as a model for overeating (e.g., food is required to sustain life, craving and withdrawal are physiologic reactions and should not be interpreted as pathological "addiction"; and a threshold between normal adaptation and pathologic deviation is not defined); (*c*) the association of food addiction with obesity (addictive-like symptoms and behavioral patterns are inconsistently observed); and (*d*) lack of research identifying the addictive agent in food (most studies in humans are based on mixed foods, typically fast foods, or food cues).

Uncovering the role of food addiction for obesity and identifying possible triggers bears major importance for identifying effective therapeutic strategies: Treatment approaches for obesity and addiction are fundamentally different, the latter including behavioral therapy, abstinence, and environmental control including taxation, restrictions on advertising, and regulation of school menus. In other words, while food intake is essential for sustaining life, the number of specific chemical or nutrient-

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Received August 21, 2017; accepted November 7, 2017.
Previously published online at DOI: 10.1373/clinchem.2017.273532

Table 1. Features of drug and food addiction.

Characteristic	Presentation in food addiction	Animal data	Human data
Tolerance	Larger amounts of food needed to achieve same effect (satiation, pleasure)	Increasing sugar intake over time when intermittent access is granted Decrease of dopamine released in response to regular chow	Lower nucleus accumbens activation with repeated food stimuli
Craving	Intense desire to consume a specific food ("selective hunger")	Increased lever-pushing for sugar Heightened anticipatory activation of striatum	Specific cravings for energy-dense or processed foods with high GI +/− fat content
Limited control	Inability to regulate behavior in face of temptations and impulses	Decreased control over food-seeking despite adverse stimulus	Unsuccessful diet attempts Compulsive intake of specific foods
Withdrawal	Distress or dysphoria during dieting	Sucrose abstinence or opioid antagonist causes withdrawal symptoms	No convincing evidence
Unsuccessful attempts at behavioral control	Inability to stop or reduce intake of trigger food or larger amounts of food consumed then intended	NA	Diet failure Compulsive food intake (e.g., bingeing)
Spending a lot of time to obtain, use, or recover	Spending a lot of time eating or obtaining food	Increased food-seeking behaviors or locomotion	Less applicable as food is ubiquitously available
Not meeting other responsibilities–social, occupational	Missing responsibilities due to preoccupation with eating	NA	Less applicable as food intake is socially acceptable
Continued despite negative consequences–health, relationship, general safety	Negative health consequences of obesity	NA	Less applicable (except health) as food consumption is generally well accepted
Addiction transfer	Replacement of one addictive substance for another, e.g., food for cocaine	Animal models of drug addiction use food stimuli for conditioning or training Sucrose may replace drug, or even be preferred	Carbohydrate craving in post bariatric surgery, alcoholics, smokers, and rehabbers crave carbs
Trait			Low dopamine receptor density in obese. Comorbidity of obesity and addiction

The first 8 characteristics are paraphrased or summarized from the 11 diagnostic DSM-V criteria for drug addiction. Addiction transfer and trait are not part of the diagnostic criteria but are commonly cited as evidence of the overlap of obesity and addiction.

based triggers of food addition might be limited and accordingly could be restricted or even avoided altogether.

Here, we performed a targeted review of the literature (*a*) to outline the neurobiological and behavioral basis of food addiction, (*b*) to explore its possible connection with obesity, and (*c*) to highlight the possible role of high-glycemic-index (GI)[3] carbohydrates in triggering addictive symptoms.

[3] Nonstandard abbreviations: GI, glycemic index; VTA, ventral tegmental area; SN, substantia nigra; NAcc, nucleus accumbens; YFAS, Yale Food Addiction Scale; BMI, body mass index.

A Neurobiological Basis for Food Addiction

THE MESOLIMBIC REWARD SYSTEM

When considering the neurobiology of addiction, it is noteworthy that drugs of abuse take effect by "hijacking" brain pathways for natural reward and aversion reactions. Specifically, the mesolimbic reward system (Fig. 1) is ontogenetically evolved to steer organisms toward seeking favorable, potentially life- or kindred-sustaining stimuli; for example, high caloric foods in times of sparse food supply, sweet foods (representing nontoxic energy supplies), and other natural rewards like water and sex.

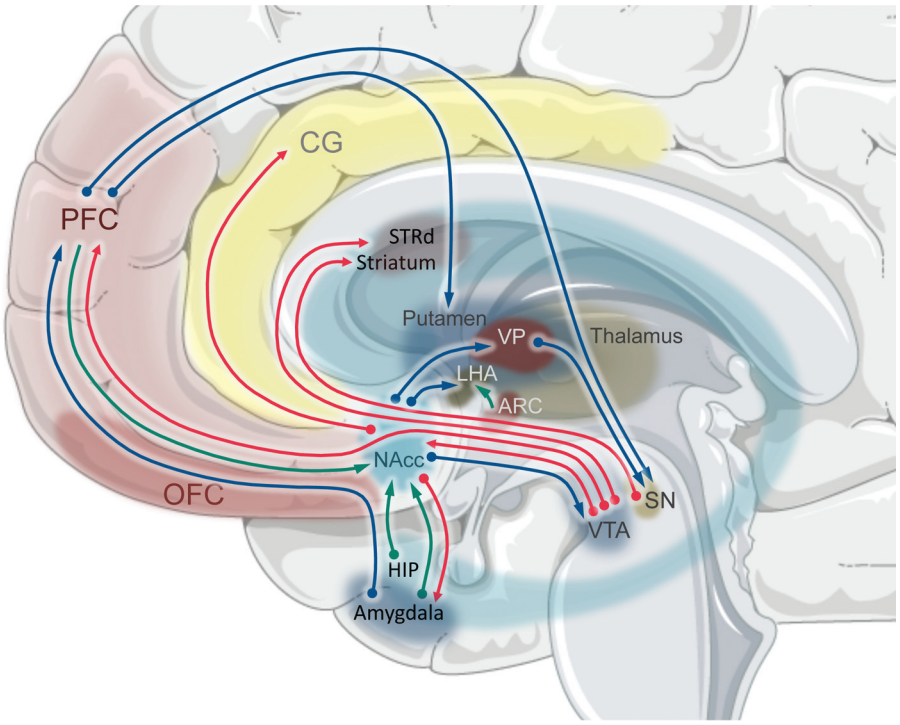

Fig. 1. Brain areas and transmitters of the mesolimbic reward system.

The main mesolimbic input is derived from the ventral tegmental area (VTA) and substantia nigra (SN) to the nucleus accumbens (NAcc). The NAcc plays a central role in processing reward and salience. The amygdala and hippocampus (Hip) are involved in forming memories of stimulus–reward relationships. The orbitofrontal cortex (OFC) regulates decision-making and reward or punishment anticipation. The prefrontal cortex (PFC) and anterior cingulate gyrus (CG) provide inhibitory control and emotional regulation. Projections exist between the different areas and are depicted by arrows: dopamine – red, GABA – blue, glutamate – green. In addition, direct connections to the hypothalamic nuclei regulate homeostatic food intake: lateral hypothalamic area (LHA) arcuate nucleus (ARC); and the ventral pallidum (VP).

Dopaminergic projections extend from the ventral tegmental area (VTA) and substantia nigra (SN) to a network of interconnected brain areas with specific functions in reward processing. The nucleus accumbens (NAcc) plays a central role and processes reward and salience. The amygdala and hippocampus are involved in forming memories of stimulus–reward relationships. The orbitofrontal cortex regulates decision-making and anticipation of reward or punishment. The prefrontal cortex and anterior cingulate gyrus provide inhibitory control and emotional regulation. As a whole, the mesolimbic reward system plays a pivotal role in food intake regulation (Fig. 1).

Transgenic mice that lack dopamine signaling demonstrate a complete loss of food-seeking behavior and die of starvation. Restoring dopamine production in the dorsal striatum reinstates feeding on regular chow, whereas restoration of dopamine production in the NAcc reinstates motivational behavior. Replacement of dopamine to either region restores preference for sucrose or a palatable diet *(6)*. While dopamine is a critical neurotransmitter in the mesolimbic system, numerous other neurotransmitter families are involved and modify dopamine concentration. For example, local infusion of opioid agonists increases food motivation and ad libitum food intake, *(7)* and hormones like insulin, leptin, ghrelin, and GLP-1 modify natural- and drug reward *(8)*. In addition to hedonic input through VTA and SN, the mesolimbic system receives direct projections from hypothalamic nuclei that regulate energy homeostasis.

NEUROBIOLOGY OF SUBSTANCE ADDICTION

Hijacking the above-outlined mesolimbic systems, drugs of abuse signal through a variety of different pathways that ultimately converge to increase dopamine concentration in the NAcc. The supraphysiologic dopamine concentrations initially increase salience and therefore motivation toward drug-related cues to reinforce drug taking. However, repeated drug use results in blunted dopamine release in the NAcc over time *(9)*. Instead, drug-related cues (e.g., images, situations) produce an

anticipatory dopamine release in the dorsal striatum (caudate and putamen) and basolateral amygdala *(10)*. The resulting shift is critical: as cue-based activation increases, drug seeking and craving rapidly increase due to the heightened anticipatory reward. At the same time, the blunted activation in response to actual consumption is associated with the need for increased intake to achieve the same level of reward. As this behavior becomes progressively elicited by drug-related cues, it is ultimately consolidated as a habit *(9)*. Over time, habitual drug consumption leads to functional impairments in the prefrontal, dorsolateral, and inferior cortices, leading to increased compulsivity and reduced executive control of drug intake *(11)*. Morphologically, drug addiction has been associated with low density of dopamine receptors in animal and human studies. The low density of dopamine receptors can be the result of a combination of preexisting low dopamine receptor availability in vulnerable individuals (e.g., genetic polymorphisms) *(12)* and down regulation of dopamine receptors *(13)* in drug tolerance, in which drug consumption no longer elicits a positive effect but rather mitigates a negative state to avoid dysphoria and withdrawal *(14)*.

NEUROBIOLOGY OF FOOD ADDICTION

The food addiction model asserts that excessive consumption of problem foods may have similar phenotypic characteristics and implies the same neurobiological framework to link food- and drug addiction. Conceptually, the neurobiology of consuming a problem food would increase dopamine concentration in the mesolimbic system and consequently increase salience and food motivation. Over time, dopamine signaling would shift from the NAcc to the dorsal striatum and perpetuate craving and food seeking. Consumption would become habitual and compulsive as prefrontal control is altered. Once dopamine receptors are down-regulated, food intake would become driven by the need to avoid withdrawal symptoms rather than by pleasure and homeostatic needs. In line with research of chronic drug use, dopamine receptor levels may represent a vulnerability marker and the central dopamine- and receptor concentrations are modified by excessive intake over time.

Indeed, NAcc dopamine neurons are activated by novel food rewards; with repeated exposure, the associated activation decreases over time, and predictive cues of the food begin to induce more pronounced striatal activation *(15)*. The resulting cue-based signaling along with a decreased consummatory response has been proposed to drive craving and habitual food intake *(16)*. Furthermore, Gearhardt et al. have shown that humans with high self-reported symptoms of food addiction had increased activation in the mesolimbic reward system in response to food cues, and reduced activation in inhibitory regions in response to food intake *(17)*. Importantly, these responses are similar to those observed in drug-dependent individuals when viewing drug cues *(17)*.

Simply put, from a neurobiological perspective the intended function of the mesolimbic systems is to ensure food intake toward favorable energy sources. These life-sustaining responses can be exaggerated to the point of addictive-like patterns. Assuming a continuous biological spectrum of activation patterns and associated behaviors to triggering food sources, the controversy regarding food addiction becomes a matter of defining a threshold of normal adaptation vs. pathological addiction.

Linking Food Addiction to Obesity

EPIDEMIOLOGIC OVERLAP OF FOOD ADDICTION

As a behavioral phenomenon, symptom capture requires self-reported psychometric tools, and The Yale Food Addiction Scale (YFAS) has been established as a reliable tool to identify those individuals who exhibit addictive symptoms with the consumption of foods *(18)*. As assessed by YFAS, individuals with obesity have higher rates of food addiction than nonobese control populations. Specifically, in a metaanalysis, Pursey at al. demonstrate that food addiction prevalence increased with body mass index (BMI) from 10% in normal weight to about 25% in people with obesity (higher with increasing BMI) *(19)*. Furthermore, people with obesity who have higher YFAS scores show decreased weight-loss responses to treatment *(20)*. Nonetheless, obesity is a heterogeneous phenotype, and the overlap with food addiction is incomplete: according to Pursey et al., most obese individuals do not show a distinct addiction phenotype, and conversely a minority of lean individuals report addictive symptoms. In addition to heterogeneity in objectively studying behavior in obese patients ("obesity ethology"), the imperfect association of food addiction and obesity may be increased by methodological issues relating to sensitivity and specificity of the YFAS, and a lack of reliable definitions of food addiction.

NEUROBIOLOGICAL OVERLAP OF ADDICTION AND OBESITY

In a metaanalysis of 87 functional neuroimaging studies, Garcia et al. reported similar brain activation patterns in response to reward in participants with obesity, substance addiction, and nonsubstance addiction *(21)*. Wang et al. *(22)* and other groups demonstrated a negative correlation of striatal dopamine transporters with BMI. Assuming obesity as a proxy of habitual overeating, this may parallel dopamine receptor paucity (trait) or downregulation in response to habitual intake (tolerance) described in drug addiction. The resulting dopamine signal deficiency has been postulated to promote compensatory pathological eating to activate reward circuits *(23)*. Thus, functional neuroimaging studies demonstrate a shared neurobiological framework of obesity and addiction.

SHARED VULNERABILITY FOR ADDICTION AND OBESITY

A shared vulnerability for addiction and obesity is suggested by genetic polymorphisms and observations of addiction transfer. For example, Carpenter found an association of higher BMI with the *Taq*I A1 allele of the dopamine receptor D2 (*DRD2*)[4], a polymorphism associated with cocaine, alcohol, and opioid use *(24)*. Another circumstantial piece of evidence is addiction transfer from drugs to high-GI carbohydrates and vice versa. For example, people with alcoholism display higher sweet preference and cravings, which is further increased by abstinence *(25)*. Subsequent to bariatric surgery, when the imposed anatomical and physiological barriers restrict food intake, patients often manifest new substance addictions *(26)*. Several studies report associations of these new substance disorders with preoperative food addiction symptoms, and an addiction transfer from food addiction has been proposed *(27)*. Fowler et al. *(28)* found that self-reported problems specifically with intake of high-GI or high-carbohydrate, low-fat foods was associated with an increased risk for developing substance addictions postoperatively, suggesting an addiction transfer.

Collectively these findings indicate a significant clinical and neurobiological overlap between addiction and obesity.

What Triggers Food Addiction?

BEHAVIORAL ADDICTION

Considerable debate remains around the triggering mechanism of food addiction. Hebebrand et al. and others have argued that food addiction may be a behavioral addiction, analogous to gambling disorder, which was recently included among addiction disorders in the DSM-5 catalog. Behavioral addictions are thought to be mediated by Pavlovian conditioning and habit formation, *(29)* ultimately also converging on the mesolimbic reward system through the VTA. Akin to chemical addiction, behavioral addictions modulate function and plasticity of the mesolimbic reward system and manifest in symptoms including craving, impaired control over the behavior, tolerance, withdrawal, and high rates of relapse *(30)*. Strictly speaking, no chemical trigger is necessary to elicit addictive symptoms. Indeed, most human food addiction literature has relied on cue-based paradigms such as food pictures or mixed meals and allows no conclusions toward possible chemical triggers.

However, food contains a variety of compounds that may serve as chemical or metabolic triggers. It is noteworthy that all commonly suspected problem foods share nutritive properties, suggesting a chemical or metabolic link rather than a mere behavioral phenomenon.

COMMONLY SUSPECTED TRIGGER FOODS

When Theron Randolph first proposed the concept of food addiction in the 1950s, *(31)* he reported addictive consumption of common foods with high energy density, such as corn, milk, and potatoes. Randolph postulated that the rapid shifts in metabolic fuels that follow consumption of these foods are akin to the pharmacokinetic properties of drugs of abuse and may trigger addictive behaviors. The modern food addiction literature has focused on processed, energy-dense foods with high GI and high fat content (i.e., fast foods and sweets). Schulte et al. *(2)* asked healthy participants how likely they were to experience food addiction–type problems with a list of 35 foods. Highly processed foods containing either mixed macronutrients or pure high-GI carbohydrates ranked highest. Further, the group found that glycemic load (the product of carbohydrate amount and glycemic index), *(32)* fat, and salt content of food items predicted problem rating. While these foods at first glance seem rather distinct from what Randolph proposed in the 1950s, they share an important physiologic property. Processed carbohydrates, corn, and potatoes all have a high GI and cause rapid shifts in blood glucose, insulin, and other metabolic fuels and hormones. These rapid shifts are pharmacokinetically akin to the rapid shifts in neurotransmitters seen after consumption of substances of abuse.

While fat intake per se does not cause rapid metabolic shifts, dietary fat content has been linked to food addiction in several studies and it seems that fat intake does contribute to brain activation and addictive behaviors. In an elegant set of experiments, Hoch et al. *(33)* demonstrated increased food seeking and mesolimbic brain activation in rats in response to a mixed meal dependent on the ratio of carbohydrate to fat: Maximum behaviors were triggered by diets containing approximately 35% fat and approximately 45% carbohydrate, while sugar alone or fat alone triggered minimal responses. Hoch further assessed food seeking and brain activation in response to potato chips (with similar macronutrient composition) and found the largest response, suggesting a role of other ingredients or palatability in triggering behaviors and brain activation. Literature on the role of fat as an isolated macronutrient in food addiction is sparse. Animal literature was recently reviewed by Avena et al., *(34)* and dietary fat has been associated with binge eating and increased body weight in rats, *(35, 36)* likely via effects on the opioid system and/or by enhancing palatability *(35, 37)*. However, bingeing on fat-rich foods does not induce opiate-like withdrawal symptoms after the food is removed, as seen in sugar bingeing *(38)*. To our knowledge, no isolated fat (e.g., butter or oil) has been proposed in association with food addiction in hu-

[4] Human Gene: *DRD2*, dopamine D2 receptor.

mans, and no macronutrient-selective studies using only fat have been performed; high-GI carbohydrates have received considerably more attention.

Sugar, Artificial Sweeteners, and High-GI Carbohydrates

Sugar elicits addiction-like craving, compulsive food seeking, and withdrawal in rats and has therefore been used in substance abuse models for some time. Several reviews have summarized the addictive properties of sugar *(39–41)* and high-GI foods *(42)*. In addition, nonnutritive sweeteners have been proposed as a possible trigger for food addiction because their intake is associated with increased preference and cravings for sweet foods, and weight gain *(43)*.

SUGAR AND FOOD ADDICTION

Extensive evidence in animal models suggests that sugar may be an addictive agent in highly palatable foods. Rats given intermittent access to sugar show behavioral signs of addiction, such as binge consumption, tolerance, and cross-sensitization to other drugs of abuse *(44)*. Bingeing on sucrose produces a repeated increase of dopamine akin to drugs of abuse, rather than the gradual decline over time that is typical for natural rewards *(45)*. Mu-opioid receptor binding *(46)* is increased in a similar manner to drugs of abuse. When the sugar is removed from the diet or when an opiate antagonist is administered, rats experience signs of opiate-like withdrawal *(44)*, such as anxiety, teeth chattering, and aggression. Two properties of sugar participate in mediating these manifestations: hedonic sweetness and homeostatic, rapid metabolic shifts following its ingestion. Studies relying on intragastric administration, the use of artificial sweeteners, and high-GI carbohydrates without sweet taste can help untangle these factors.

NONNUTRITIVE SWEETENERS AND FOOD ADDICTION

Nonnutritive sweeteners elicit an intense sweet taste, but do not evoke a rise in blood glucose. In other words, the sweet perception is dissociated from nutritive satisfaction. In rats, intense sweetness from both nutritive and nonnutritive sweeteners surpasses cocaine and nicotine reward and elicits strong food-seeking behaviors *(47, 48)*. These data suggest that sweet taste alone can mediate reward and craving. In addition, dissociating sweet taste from nutritive satisfaction may elicit compensatory sweet cravings to restore the anticipated effect and ultimately condition alterations in homeostatic control. Indeed, rats exposed to nonnutritive sweeteners display increased compensatory intake of sugar-sweetened foods (not chow) and excess weight gain if allowed access to such foods *(43)*. To distinguish the effects of palatable vs nutritive signaling, Tellez et al. *(49)* used a paradigm of licking sucralose during intragastric glucose or sucralose administration in rats. Sucralose taste increased dopamine concentration in the ventral striatum (NAcc) regardless of the intragastric infusion, whereas dorsal striatum dopamine release occurred only with the nutritive infusion of glucose.

In human imaging studies, decreases in stress-related cortisol levels and hippocampus activation have been observed in response to sucrose, but not saccharose, *(50)* and habitual intake of artificially sweetened beverages decreases amygdala activation *(51)*. Both can be interpreted as correlates of stimulus–reward disconnect. Epidemiologic studies show an association between artificial sweetener intake and increased BMI, but the possibility of confounding and reverse causation cannot be excluded *(52)*. Raben et al. did not find increased caloric or sugar consumption after intake of artificial sweeteners in a 10-week interventional study in 20 overweight participants *(53)*.

In summary, artificial sweeteners have been shown to alter food reward and food cravings in some but not all studies. Behavioral data on binge consumption, tolerance, cross-sensitization, and withdrawal are not available for artificial sweeteners. Thus, artificial sweeteners cannot be excluded as etiologic factors of food addiction.

HIGH-GI CARBOHYDRATES AND FOOD ADDICTION

High-GI carbohydrates elicit the most pronounced metabolic response of all macronutrients. In analogy to the pharmacology of addictive drugs, blood glucose and insulin levels rise and fall quickly, with associated shifts in other metabolic fuels and hormones. The blood glucose excursion is tightly associated with changes in insulin levels *(54)*. Glucose and insulin both signal directly and indirectly to the mesolimbic system. Insulin increases dopamine reuptake in the presynaptic membrane and suppresses food-motivated behavior *(55)*. In addition, insulin receptors are found on neurons projecting from the hypothalamus to the VTA *(56)*. Glucose modulates SN dopamine neuronal activity by the actions of ATP-sensitive potassium channels *(57)*. In addition, the mesolimbic system receives direct projections from other glucose-sensing brain areas: Domingos et al. *(58)* showed that melanin-concentrating hormone-producing neurons in the lateral hypothalamus respond to extracellular glucose levels and project to dopaminergic neurons in the striatum and midbrain regions. While mice show a preference for sucrose over the nonnutritive sweetener sucralose, transgenic mice lacking melanin-concentrating hormone neurons do not show this preference.

There are at least 5 studies indicating unique central activation patterns in response to high-GI carbohydrates: (*i*) Spring and colleagues showed a preference for carbohydrate beverage over a taste-matched mixed carbohydrate and protein beverage in 61 overweight women with "carbohydrate-craving" *(59)*. Insulin and glucose levels have been associated with altered brain activity in regions

associated with reward processing. (*ii*) Page et al. found that mild hypoglycemia preferentially activated limbic-striatal brain regions in response to food cues and produced a greater desire for high-calorie foods *(60)*. In another study, (*iii*) Page demonstrated increased connectivity between the hypothalamus and striatum in response to glucose but not fructose ingestion. These alterations were associated with higher excursions in blood glucose and insulin levels *(61)* (*iv*) Anthony et al. found than insulin infusion increased metabolism in ventral striatum and prefrontal cortex, and decreased metabolism in right amygdala/hippocampus and cerebellar vermis *(62)*. Insulin's effect was attenuated in ventral striatum and prefrontal cortex in the insulin-resistant study participants. The authors concluded that brain insulin resistance exists in regions mediating appetite and reward, diminishing the link between intake control and energy balance. (*v*) Lennerz et al. showed NAcc activation in response to nutrient-matched milk shakes with high vs low GI *(63)*.

Together, these data indicate a role of nutrient signaling in addiction that is independent of hedonic taste signals. Nonnutritive sweeteners mimic some of the properties of nutritive carbohydrate and seem to increase the propensity for developing addictive behaviors toward carbohydrates. This notion bears similarity to the gateway drug theory, in which use of a less deleterious drug can increase the risk for using more potent substances *(64)*. However, the data on nonnutritive sweeteners are heterogeneous and more studies are needed.

Diagnostic and Management Implications

As outlined above, there is a need to translate our partial (mechanistic) and neurobiological understanding of how nutrients contribute to food addiction and obesity. Even if not all DSM-5 criteria are applicable, this does not discredit the phenomenon. It merely underlines the importance of more targeted diagnostic criteria and the development of thresholds for defining healthy adaptation vs pathological addiction. The concept of food addiction may open new avenues for obesity prevention, treatment, and public health policy *(65)*. Current obesity therapy focuses on moderation of food intake and increase of physical activity, whereas therapeutic approaches for addiction encompass behavioral therapy and abstinence. One cannot abstain from food; however, at least in a subset of vulnerable individuals, high-GI carbohydrates can be considered a specific trigger that can be reduced or avoided. Other successful strategies to fight addiction are environmental interventions such as restrictions on advertising and/or taxation that have all been proven successful in reducing, for example, smoking prevalence *(66)*. It is therefore no surprise that taxation of sugar-sweetened beverages has been proposed *(67)*; clarification of the specific role of food addiction will be paramount to make informed public health decisions.

Summary

In summary, food addiction is—at least in some individuals—a plausible causal factor contributing to obesity. The concept of food addiction may reveal new avenues for intervention on an individual and public health levels, especially if specific triggers can be identified and mechanisms clarified. High-GI carbohydrates are a possible trigger that mediates neurochemical responses similar to addiction. As a neuro-psycho-biological entity, food addiction requires an evidence-based, multidisciplinary classification system to ultimately improve assessment and management.

Author Contributions: *All authors confirmed they have contributed to the intellectual content of this paper and have met the following 3 requirements: (a) significant contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (b) drafting or revising the article for intellectual content; and (c) final approval of the published article.*

Authors' Disclosures or Potential Conflicts of Interest: *No authors declared any potential conflicts of interest.*

Acknowledgment: The authors thank Dr. David Ludwig for stimulating discussions and critical revision of the manuscript.

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