Is Fast Food Addictive?

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Abstract: Studies of food addiction have focused on highly palatable foods. While fast food falls squarely into that category, it has several other attributes that may increase its salience. This review examines whether the nutrients present in fast food, the characteristics of fast food consumers or the presentation and packaging of fast food may encourage substance dependence, as defined by the American Psychiatric Association. The majority of fast food meals are accompanied by a soda, which increases the sugar content 10-fold. Sugar addiction, including tolerance and withdrawal, has been demonstrated in rodents but not humans. Caffeine is a "model" substance of dependence; coffee drinks are driving the recent increase in fast food sales. Limited evidence suggests that the high fat and salt content of fast food may increase addictive potential. Fast food restaurants cluster in poorer neighborhoods and obese adults eat more fast food than those who are normal weight. Obesity is characterized by resistance to insulin, leptin and other hormonal signals that would normally control appetite and limit reward. Neuroimaging studies in obese subjects provide evidence of altered reward and tolerance. Once obese, many individuals meet criteria for psychological dependence. Stress and dieting may sensitize an individual to reward. Finally, fast food advertisements, restaurants and menus all provide environmental cues that may trigger addictive overeating. While the concept of fast food addiction remains to be proven, these findings support the role of fast food as a potentially addictive substance that is most likely to create dependence in vulnerable populations.

Keywords: Adolescence, dieting behavior, eating disorders, fast food, food addiction, menu labeling, obesity.

INTRODUCTION

Fast food is part of the American way of life. On any given day, one-third of adults in the U.S. will eat fast food [1]. About 7% of Americans report eating fast food every day [1]. Certain groups are more likely to be more frequent users. Youth are the biggest consumers: adolescents and young adults get 20% and 31.5% of their total daily calories from fast food, respectively [2]. Lower socioeconomic status (SES) is also associated with higher fast food intake [3-5]. Fast food restaurants are overrepresented in poorer neighborhoods, where healthy alternatives are more difficult to find [6, 7]. Numerous studies have established a clear link between fast food intake and obesity in all age groups [8-16]. In longitudinal studies, fast food intake predicts weight gain [8, 9, 11, 12] and increased risk for diabetes [12]. The link to poor health outcomes is often attributed to increased calorie intake [13, 17], but fast food intake is also associated with generally poorer diet quality. Fast food eaters have overall higher intakes of fat, soft drinks and sodium, and lower intakes of fruits and vegetables [5, 18-20].

Despite the collective damage to our personal and public health, America's dependence on fast food is growing. In 1953, when hamburger stands were beginning to spring up by the roadside, fast food accounted for only 4% of food purchased outside the home; by 1997 it accounted for 34% [21]. Today, fast food represents about one-third of a restaurant industry that reported $580 billion in sales in 2010 [22]. In fact, fast food was the only segment of the restaurant industry that boasted increasing sales despite the recent economic downturn [22]. The parallel phenomenon of increasing fast food intake in the face of increasing obesity and chronic disease begs the question of whether America is addicted to fast food. This topic has been touted in the popular press for years and is not confined to the U.S. According to the British Broadcasting Corporation, a 2008 market research survey put Great Britain ahead of the U.S. in so-called "fast food addiction". Forty-five percent of Britons agreed that they "like the taste of fast food too much to give it up", compared to 44 % percent of Americans and 37 % of Canadians [23].

The current scientific evidence is insufficient to definitively answer the question of whether fast food is indeed addictive. To begin with, there are problems with the actual concept of food addiction [24-26]. Food is required for daily living and a line must be drawn between normal consumption and overconsumption, which can be highly subjective. Drug dependence, on the other hand, is more easily defined since psychoactive substances are not necessary for survival and any amount could be considered overuse. Second, experiments demonstrating physiological dependence are currently limited to animal models [27-31] and have yet to be reproduced in humans. A third key problem is the routine comparison of food addiction with known eating disorders despite fundamental differences in psychopathology and presentation [32]. For instance, food addiction is most often compared to Binge Eating Disorder (BED), which now became a clinical diagnosis in the 5th edition of the American Psychiatric Association (APA) Diagnostic and Statistical Manual (DSM-V). Finally, as pointed out by Pelchat [26], the pattern in which the food is

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consumed or made available may be more important than the nutrient content of the food itself.

In addition to the problems with the concept of food addiction, fast food intake has not been well studied despite our enormous consumption. Studies of food addiction have not used brand-name fast food, instead they have used single nutrients, like sucrose, or generic highly palatable foods, such as nachos and pizza. Studies using single nutrients have been crucial to establish the physiology of food addiction but do not address the potential synergy of the multiple nutrients present in high amounts in fast food. This issue is addressed by studies using highly palatable foods, but generic versions do not test the potential effects of the associated environmental cues like packaging. Thus, the topic of fast food addiction is relatively unchartered. In fact, a PubMed search using the key words "fast food" and "addiction" revealed only 16 papers. Therefore, we did not intend to perform a systematic review of the evidence. Instead, the purpose of this paper is to critically analyze features of fast food that may enhance its addictive potential. Specifically, we examined three aspects of fast food: 1) Nutritional Components; 2) Individual Factors; and 3) Environmental Cues. All levels of evidence were included, however, for clarity, studies were roughly separated based on design. In the *Nutritional Components* section, animal models of nutrient addiction are presented separately from human studies. Under *Individual Factors*, epidemiological data are separated from experimental studies examining potential mechanisms.

OVERVIEW OF SIMILARITIES BETWEEN DRUG AND FOOD ADDICTION

While drug use is modulated solely through the hedonic (reward) pathway, food is necessary for survival, and its consumption should be tightly regulated. The homeostatic pathway controls appetite to maintain energy balance and normal body weight [33, 34]. Hunger, satiety, and metabolic signals that guide the motivation to eat for survival are orchestrated in the hypothalamus. The ventromedial hypothalamus (VMH), including the arcuate nucleus, contains first-order neurons with hormone receptors that receive peripheral signals related to adiposity (leptin), metabolism (insulin), hunger (ghrelin), and satiety (peptide $YY_{3–36}$) [34]. These hormones transmit signals to the paraventricular nucleus and lateral hypothalamic area within the hypothalamus [34]. The second order neurons in these areas integrate either anorexigenic (e.g. α-melanocyte stimulating hormone, cocaine-amphetamine-regulated transcript) or orexigenic (e.g. neuropeptide Y [NPY], agouti-related protein) signals *via* their melanocortin-4 receptors to alter caloric intake and energy expenditure [34]. The VMH is connected to other regions of the limbic brain that guide other behaviors that are necessary for survival and reproduction [35].

The hedonic pathway for palatable food and addictive drugs travels from the Ventral Tegmental Area (VTA) to the nucleus accumbens (NAc), which is also called the "pleasure center" of the brain. These reward mechanisms are thought to have evolved to reinforce behaviors that are essential for perpetuation of the species, such as sex and feeding [33, 36]. Studies of food addiction have focused on the overlapping neural systems that may reinforce the intake of both drugs and food.

Mesolimbic dopamine signaling between the VTA and NAc is believed to be the central feature of the hedonic pathway for both reward eating and drug abusing. The effects of dopamine are dependent on the site of action. In the hypothalamus, dopamine signaling inhibits feeding through its action on NPY and POMC in the VMH [37]. Of the five subtypes of dopamine receptors, stimulation of D_2 receptors slows the rate of eating, while D_1 receptor stimulation reduces the duration (and therefore size) of the meal [37]. In addition to inhibiting feeding short-term, dopamine assists in long-term energy and body weight regulation through its response to insulin and leptin [37]. Dopamine stimulation in the NAc reinforces feeding [37] and intake of drugs [38] and alcohol [39]. A reinforcer is a stimulus that increases the probability that an animal or human will respond to the addictive substance; reward is a form of positive reinforcement [40]. The reinforcing effect of dopamine is attributed to D_2 receptor stimulation. Blocking or knocking out D_2 receptors in rats decreases the reinforcing effects of alcohol, morphine and cocaine. Opioids also play an important role in the reinforcement of both drug and food intake [27]. Stimulation of δ- and μ-opioid receptors releases dopamine in the NAc. As discussed later, opioid antagonists can precipitate signs of withdrawal in models of addiction [28]. Thus, dopamine signaling is believed to plays a dual role in control of feeding; inhibition of normal eating through its action in the hypothalamus, and reinforcement of pleasure eating through its action in the NaC. Highly palatable foods encourage addictive overeating and contribute to obesity by overriding hunger and satiety signals, and fostering reward [37].

DEFINING FOOD ADDICTION

Although several food addiction hypotheses have been published in the scientific literature [27, 32, 33, 37, 41-44], there is currently no standardized definition. Mechanistic studies in animals focus on physiologic addiction using the classic features of the addictive cycle [45] as defined below:

1) ***Bingeing*** in animals is defined as an escalation of intake. This can be measured by a significant increase in lever presses to self-administer a substance [46], or eating after satiation [29]. In humans, this definition is highly subjective, since what is a large amount to some may not be perceived as unusual by others. The definition of bingeing in the APA's Diagnostic and Statistical Manual 4th Edition Text Revision [DSM-IV-TR], for the purposes of diagnosing bulimia nervosa, is "eating in a discrete period of time an amount of food that is definitely larger than most individuals would eat under similar circumstances." [47] The time period is also subjective and is usually restricted to less than 2 hours. The definition of bingeing for BED is similar, but includes additional descriptions of a binge, such as eating until uncomfortable, eating when not hungry, eating alone due to shame, feeling disgusted, depressed, or guilty after overeating, and marked distress over the bingeing.

2) ***Withdrawal*** is based on signs and symptoms of opioid deficiency and characterized by physical signs (such as tremors) [28], anxiety, and depression [27]. In animals, anxiety and depression are indicated by unwillingness to spend time in an open-arm maze [27]. Studies of food addiction in humans have instead focused on negative affect or dysphoria by self-report [48, 49]. ***Tolerance*** is also often included as a criterion for dependence and is defined as need for more substance to get the same effect, or the same amount of substance produces less effect with continued use [27]. This has been attributed to dopamine D_2 receptor down-regulation in the NAc [50].

3) ***Craving* or *seeking*** in the dependence literature is described as an intense drive to self-administer drugs [27]. In food addiction research, craving is illustrated by the motivation to seek food. Serotonin and opioids are thought to play key roles in this process; serotonin receptor agonists [51], and opioid and cannabinoid antagonists [52] significantly diminish motivation to eat. Drug craving and seeking have been experimentally described as a form of learning, where dopamine signaling facilitates the consolidation of memory such that past experiences are used to inform future decisions [53]. In other words, rats 'press the lever' for drugs because they have learned that it is rewarding [54]. Of note, fast food is included in the validated Food Craving Inventory developed by White *et al*. [55].

4) ***Sensitization*** is defined as a progressive increase in locomotor response observed with repeated administration of a substance [27, 56]. It is attributed to engrained changes in mesolimbic dopamine signaling [56], possibly mediated through up-regulation of the dopamine D_3 receptor [57]. In animals, sensitization is usually measured as increased locomotion in response to the substance [27]. Once sensitized, animals or subjects may demonstrate hyper-responsiveness to a new substance. This is referred to as ***cross-sensitization*** [27].

In humans, food addiction is often examined by comparison with established criteria for substance dependence [32, 41, 43, 44, 58]. One problem with this approach is that it shifts focus away from the potentially addictive properties of the food and onto the individual 'afflicted' with addiction. An alternative approach would be to focus on the addictive potential of the food itself by placing it in the scope of other identified addictive substances. Under U.S. federal law, the Comprehensive Drug Abuse Prevention and Control Act of 1970 created five classifications of substances based on potential to create dependency and safety for use as medications. Starting with schedule 1, the addictive potential decreases with descending classification. For example, schedule 1 includes heroin, while schedule 5 includes cough suppressants. However, alcohol and tobacco are entirely missing from this classification system. Alcohol is likely the most analogous substance to fast food for several reasons. First, many people can use it in large amounts or recurrently for long periods of time without difficulty, while others using it in the same fashion become addicted. Second, both fast food and alcohol have nutritive value. Third, intake of both alcohol and fast food are socially acceptable, even *encouraged*, in many facets of modern American culture (see *Environmental Cues*). Therefore, the U.S. drug schedules are not suitable to evaluate the addictive potential of fast food in their current form. Recently, a British group published an alternative classification system using nine categories that places alcohol and tobacco in the mid-range, as potentially more addictive than marijuana, LSD and ecstasy [59].

Human substance dependence is currently defined by the APA as "a maladaptive pattern of substance use leading to clinically significant impairment or distress" [47]. There are seven criteria for substance dependence according to the DSM-IV-TR, and five of them are psychological. Dependence is defined as meeting 3 of the 7 criteria, provided below in summary form. If criteria 1 or 2 are met, it is considered physiological dependence; criteria 3-7 are considered psychological dependence. Despite the potential problems with defining food addiction as substance dependence discussed above, we will use the APA criteria here to examine the potentially addictive properties of fast food because they are sufficiently broad to examine both physiological and psychological aspects of addiction and have been used in other examinations of food addiction [32, 41, 43, 44, 58].

1) ***Tolerance*** (progressive use over time)

2) ***Withdrawal*** (symptoms, or substance use to relieve symptoms)

3) ***Greater amount or longer duration of use than intended***

4) ***Desire or attempts to cut down or quit***

5) ***Seeking*** (significant time spent obtaining, using or recovering from use)

6) ***Interference with life*** (important work, social or other life activities are compromised)

7) ***Use despite negative consequences*** (continued use despite knowledge that use is making problems worse)

DEFINING FAST FOOD

Fast food is often described in nutritional terms as "high fat", "high sugar", "highly palatable" or as a "refined food". Ifland *et al*. used the above DSM-IV criteria to propose the "refined food addiction" model [41]. The hypothesis is that processed foods are addictive substances and bingeing is an addictive behavior. Their definition of refined food includes flour, sweeteners, HFCS, sugar-sweetened beverages, frozen potatoes and cereal. Fast food embodies the simultaneous presentation of these refined foods, namely flour, sweeteners, HFCS, sugar-sweetened beverages, and frozen potatoes. However, fast food cannot be adequately described by its nutrients alone since combinations of nutrients and methods of packaging and presentation may make fast food even more attractive. Fast food is not just processed food, it is a multi-billion dollar enterprise. As the "quick-service" segment of the restaurant industry, it provides food cheaply,

quickly and without table service in ubiquitous and convenient restaurants (mostly chains) around the world. As discussed below, strategies such as packaging and restaurant environment increase the salience of fast food and may foster psychological dependence.

In addition to shared neural circuits, there are similarities between the "delivery system" for addictive drugs and fast food. To begin with, the starting substances are not usually addictive in their natural form. For example, tobacco leaves are dried, processed and packaged into cigarettes for mass consumption. This process increases the potency of the primary addictive component, nicotine [60]. Similarly, fast food starts with a handful of commodities, namely soy, corn, potatoes, wheat, beef and dairy, and processes them into a wide range of menu items. These items deliver much higher amounts of macronutrients in various combinations and in a smaller package than what could be achieved in nature. For example, as the food group that is highest in naturally-occurring sugar, fruit is virtually devoid of fat. The few fruits commonly eaten in the U.S. that do contain significant amounts of fat, coconut, avocado and olives, are the lowest in sugar [61].

A second similarity in the industrialization of addictive drugs and fast food is the addition of other compounds to increase saliency. Many drugs are mixed or cut with other compounds. Going back to the tobacco example, menthol is frequently added to cigarettes [62]. The Tobacco Products Scientific Advisory Committee of the Food and Drug Administration (FDA) concluded in 2011 that the scientific evidence showed that "menthol has cooling and anesthetic effects that reduce that harshness of cigarette smoke," and this effect "could facilitate initiation or early persistence of smoking by youth." Furthermore, while mentholated brands make up about 30 percent of the cigarette market, they are favored by 80% of African-American smokers, who suffer from disproportionate rates of cardiovascular disease [63] and lung cancer [64]. Similarly, food processing uses additives to enhance flavor, color, texture, shelf-life and other attributes of palatability that are not represented in the base ingredient. For example, the presence of High Fructose Corn Syrup (HFCS) in fast food hamburger buns increases the sweet flavor, but also promotes browning and extends shelf-life [65]. Similarly, trans-fats are superior for deep frying (such as doughnuts and French fries) because they oxidize less readily than vegetable oils in their non-hydrogenated (polyunsaturated) state [66]. Indeed, in a study examining how fast food restaurants plan their menus, senior executives identified shelf-life and spoilage as major obstacles to offering healthier items [67]. In the end, food processing results in a product that delivers combinations and concentrations of nutrients that are not present in nature.

For the purposes of this review, we analyzed the nutrient content of a typical fast food meal. A market share analysis of McDonald's, the largest hamburger chain in the world, shows that the Big Mac and French fries are the top two most popular menu items [68]. In "What People Buy from Fast Food Restaurants", Dumanovsky *et al*. showed that over 70% of purchases at McDonald's, Wendy's, and Burger King were combination or value meals [69]. In that study, the most popular combination at McDonald's was a Big Mac, medium French Fries and medium regular soda, providing 1130 calories for $5.99. In another study, one-third of 7318 customers at fast-food restaurants ordered 1,000 calories or more at lunch [70]. Since we were interested in addictive overeating, we analyzed the nutritional content of a *large* portion of this "combo" meal. Fig. (**1**) shows the nutrient breakdown of this meal, a Big Mac, large French fries, and large Coke (32 oz.), in the format of a food label. The entire meal would provide 1360 kcals, 58 grams of fat, and 95 grams of sugar. For a person on a 2000 calorie diet, this meal would provide 68% of the total calories, 89% of the total fat, and 57% of the sodium recommended daily. These percentages are shown in Fig. (**1**) as % Daily Value (%DV). No %DV is listed for sugar because there is currently no recommended daily intake. However, recognizing that added sugar is contributing excessive calories to the American diet and is a primary risk factor for cardiovascular disease, a scientific statement released by the American Heart Association in 2009 (**co-authored by R.H.L.**) recommends a limit of 21 g for women on an 1800 calorie diet and 38 g for men on a 2200 calorie diet [71]. Using this recommendation, the extra value meal would provide 450% of the recommended limit for added sugar for a woman and 250% for a man.

Nutrition Facts

Serving Size 1 Big Mac, 1 large French fries, 1 Large Coke (1,269g)

Amount Per Serving

Calories 1,360	Calories from Fat 520
	% Daily Value*
Total Fat 58g	**89%**
Saturated Fat 12g	**58%**
Trans Fat 1.5g	
Cholesterol 80mg	**26%**
Sodium 1,380mg	**57%**
Total Carbohydrate 190g	**63%**
Dietary Fiber 10g	**40%**
Sugars 95g	
Protein 32g	

Vitamin A 8% • Vitamin C 20%

Calcium 30% • Iron 30%

* Percent Daily Values are based on a 2,000 calorie diet. Your Daily Values may be higher or lower depending on your calorie needs:

	Calories:	2,000	2,500
Total Fat	Less than	65g	80g
Sat Fat	Less than	20g	25g
Cholesterol	Less than	300mg	300mg
Sodium	Less than	2,400mg	2,400mg
Total Carb		300g	375g
Dietary Fiber		25g	30g

Fig. (1). Nutrition information for McDonald's extra value meal [Big Mac, large French fries, and large soda] presented as a Nutrition Facts Label [72].

NUTRITIONAL COMPONENTS OF FAST FOOD THAT MAY BE ADDICTIVE

As described above, fast food is high in calories, sugar, fat, and sodium. In addition, it is highly processed, palatable, and energy dense. The majority of the fiber and a portion of the vitamins and minerals present in original food are extracted in processing. Sugar, salt, and other additives are used to boost flavor. The end product is packaged and sold conveniently to deliver the contents, along with a drink that provides high levels of sugar and caffeine. Which of these components could be addictive?

Sugar

Adding a soda to the fast food meal above increases the sugar content ten-fold. At McDonald's, 71% of beverages purchased are sugar-sweetened soft drinks [73]. While soda intake is independently related to obesity [74], fast food eaters clearly drink more soda. In one study, adolescents who ate fast food four or more times per week drank an average of 12.88 cans of soda (12 oz.) per week, as compared to less than 1 can per week in those who ate fast food once per week or less [19].

Animal Studies: All four features of sugar addiction have been demonstrated in rodent models [28, 31, 46, 54, 75-77]. Rats exposed to intermittent sugar access [following restriction] will binge [28, 31, 46]. Second, these animals show signs of withdrawal (teeth chattering, tremors, shakes and anxiety) when the sugar is withdrawn or opioids are blocked with the μ-opioid antagonist naloxone [28]. Third, seeking and craving have been demonstrated along with a deprivation effect where animals consume more sugar after imposed abstinence [46]. Elevated dopamine levels [54] perpetuate the binge and overconsumption increases with time, consistent with tolerance. Finally, cross-sensitization has been demonstrated in sugar-addicted rats who readily switch to alcohol [75] or amphetamine use [76, 77] with increased locomotion and blood pressure. A major caveat to the extrapolation of these data to human food addiction is that these rats do not develop obesity. In fact, they compensate for the excessive calories ingested during a binge by restricting their intake at other times such that body weight remains relatively stable [31, 76].

Human Studies: There is also some evidence that sugar may be addictive in humans. Ifland *et al*. provide anecdotal reports from self-identified food addicts who describe withdrawal as feeling "irritable", "shaky", "anxious" and "depressed" [41]. Experimental studies show that subjects will use sugar to treat psychological symptoms. Overweight women who were self-reported carbohydrate-cravers reported greater relief from dysphoria in response to a carbohydrate-containing beverage as compared to a protein drink [48, 49]. While the authors interpret the dysphoria as a psychological manifestation of dependence criterion 2, withdrawal [41], the directionality of this relationship is unclear. It is not known whether the negative effect is purely a symptom of withdrawal, or, more likely, that these subjects had some degree of dysphoria that preceded the dependence on sugar to medicate it. Other areas that warrant study of potential sugar addiction in humans are craving and tolerance. Benton points out that sugar craving can vary widely by age, menstrual cycle and time of day [25]. In addition, preference for sweet is more prominent in children and diminishes with age, contrary to what would be expected for tolerance [25].

Future directions: Another caveat to the extrapolation of current animal models of sugar addiction to humans is that these models have used either glucose [28, 31, 46] or sucrose [54, 75-77], when by far the greatest source of dietary sugar in American fast food is HFCS [78]. For example, more than 90% of the sugar in the meal shown in Fig. (**1**) comes from the soda in the form of HFCS. HFCS is thought to be similar to sucrose in that they are both half fructose [55%], although this percentage has recently come into question when an analysis of store-bought sodas in Los Angeles revealed a fructose content of 65% using High Performance Liquid Chromatography [79]. This difference is relevant, as Lustig has synthesized evidence to suggest that fructose may be more addictive than glucose [80]. In the glycogen-replete [e.g. sated] state, fructose promotes hepatic and muscle insulin resistance [81]. The resultant hyperinsulinemia blocks leptin's ability to extinguish mesolimbic dopamine signaling, promoting tolerance and withdrawal. Through this pathway, fructose may foster overconsumption, obesity and metabolic syndrome. This hypothesis [80] has been challenged [82] on the basis that human feeding studies using "normal" consumption of less than 50 g/day fructose [83] do not demonstrate signs of insulin resistance and the accompanying metabolic changes (such as dyslipidemia) [84, 85]. However, customers would meet or exceed this 50 g limit by consuming the single sample meal shown above (which would provide 47-53 g fructose, depending upon how much of the sugar added to the food is sucrose *vs* HFCS). This is consistent with more recent intake data in adults from the National Health and Nutrition Examination Survey (NHANES) 2003-2006, showing a median fructose intake of 74 g/d [86]. In addition, Hudgins *et al*. recently showed that some individuals may be more sensitive to the effects dietary sugar in a subset of study subjects [87]. In this study, a single dose of fructose and glucose was sufficient to increase *de novo* lipogenesis and result in dyslipidemia in a subset of study subjects [87]. Studies are needed to establish a safe threshold for dietary fructose, and to examine its addictive potential.

Fat

The high fat content of fast food is vital to its rewarding properties. Our nutrient analysis (Fig. **1**) showed that the sample fast food meal contains 89% of the daily fat intake for an individual on a 2000 calorie diet as suggested by the dietary guidelines for Americans [88]. In feeding studies, excess calories from fat are more efficiently stored than excess calories from carbohydrate (90-95% *vs* 75-85%) [89]. Therefore, fat intake has traditionally been assumed to be the major determinant of weight gain.

Animal studies: Animals will binge on pure fat when given intermittent access [90-92]. This has also been demonstrated with shortening free of trans-fat, suggesting that it is the fat *content* and not the type of fat present in fast food that encourages overeating [91]. However, these rodent models are notably different in that they do not demonstrate other features of addiction, such as withdrawal [93].

Human studies: Blundell *et al*. have identified a "high-fat phenotype" among human subjects, characterized by a preference for high fat foods and weak satiety in response to them, which may act as a risk factor for obesity [94]. However, so-called "high-fat foods" are almost always also high in carbohydrates (e.g. pizza or cookies) in experimental design and in the real world. In fact, Drewnowski *et al*. showed that adding sugar significantly enhanced preference for high fat foods among normal weight human subjects [95]. And while some foods could be too sweet (decreased preference), there was no limit for preference with increasing fat content. Thus, the synergy of high fat along with high sugar is likely to be more effective at stimulating addictive overeating than fat alone.

Future directions: When water content is subtracted, the fat content of a food is the primary determinant of energy density [96]. The concept of energy density is a high amount of calories in a small volume; in practice high energy density is high-fat. For example, a large serving of McDonald's French fries weighs 154 g, which is nearly equal to a standard serving size for baked potato of 148 g [61]. However, to equal the calories and fat in the French fries, one would have to eat 3.5 baked potatoes and more than 6 pats of butter [60]. The energy density of our sample meal without the beverage is 79.5 kcal/oz. This is consistent with Prentice &Jebb's calculations of three major fast food chains, showing an average energy density of 75 kcal/oz, more than twice the density of a traditional African diet (31 kcal per oz) [97]. Energy density has been recognized as potentially more important predictor of overeating and weight gain than dietary fat intake [96-98]. In a cross-sectional analysis of NHANES data from 1999-2002, energy density was significantly associated with obesity, elevated fasting insulin levels, and metabolic syndrome in adults [98]. Future studies of food addiction in humans could utilize energy density to capture the important effect of fat while still recognizing the potential synergy of other nutrients that are both present (such as sugar) and missing (such as fiber).

Caffeine

As described above, soda is an integral part of the fast food meal. If the soda accompanying the sample meal shown in Fig. (**1**) were a cola, the caffeine content would be approximately 58 mg [61]. Soft drink manufacturers identify caffeine as a flavoring agent in their beverages, but only 8% of frequent soda drinkers can detect the difference in a blinded comparison of a caffeine-containing and caffeine-free cola [99]. Thus, the most likely function of the caffeine in soda is to increase the salience of an already highly rewarding (high sugar) beverage.

Human studies: Dependence on caffeine in children [100], adolescents [101] and adults [102] is well established. We do not review the animal data here because caffeine is established as a "model drug" of dependence in humans [103], meeting the DSM-IV criteria for both physiological and psychological dependence. In fact, up to 30% of people who consume caffeine may meet DSM criteria for dependence [103]. Headache [102, 104] attributed to increased cerebral blood flow velocity [102], fatigue and impaired task performance [100, 102] have been shown during withdrawal, as well as reinforcement leading to tolerance [101, 103].

Future directions: While adolescents and children get their caffeine from soft drinks and chocolate, adults get most of their caffeine from coffee and tea [105]. An 8 oz. cup of brewed coffee contains 95-200 mg caffeine, depending on how it is brewed [61]. However, few customers these days order a regular brewed coffee at chain restaurants. A study of Starbucks customers showed that 2/3 are ordering blended drinks [106]. These drinks average 239 calories and provide high amounts of sugar [106]. In 2009, McDonalds invested $100 million in advertising their new premium coffee line [107]. McCafe was touted as a cheaper alternative to Starbucks, which subsequently lost market share and closed 890 stores [108]. McCafe sales were estimated at $1.15 billion in 2009 [109]. These drinks may be acting as a gateway for caffeine-dependent customers to visit a fast food restaurant and purchase fast food. In fact, Dumanovsky *et al*. showed that once people enter a fast food restaurant, more than 80% will purchase more than one item [69]. This may explain why McDonald's breakfast sales shot up after the introduction of McCafe, accounting for 60% of their growth during the economic downturn [110]. Thus, as a known substance of addiction, the role of caffeine from coffee drinks and soda must be considered in the potentially addictive properties the fast food meal.

Salt

The sample meal shown in Fig. (**1**) contains 1380 mg sodium. The 2005 Dietary Guidelines for Americans provided a Tolerable Upper Intake Level of 2300 mg sodium/day [111], which is why the %DV of the sample meal is 54%. However, the new 2010 Dietary Guidelines [88] set an Adequate Intake level of 1500 mg for people who are black, have hypertension or are over 51 years old. In this case, the sample meal would provide 92% of the daily sodium level recommended for about half of the U.S. adult population. There is no question that fast food is high in sodium by these standards. Indeed, processed foods of many sorts contribute more than 67% of 3400 mg of sodium per day in the average American diet [88], as salt is one method by which the food industry can preserve foods to increase shelf life.

Animal studies: Data to support the potentially addictive properties of salt are currently confined to animal models. Studies in rats show mesolimbic dopamine signaling in response to salt [112, 113] and stimulation of μ-opioid receptors encourages salt intake in animals who are salt replete (bingeing) [114, 115]. Other key features of dependence have been demonstrated in rodent models including cross-sensitization with amphetamines [30] and salt craving, interpreted as a potential sign of opiate withdrawal [116]. Like sugar, these models rely on salt restriction to get an effect.

Human studies: In humans, salt intake has traditionally been conceived as a learned preference [117] rather than an addiction. At low levels, salt intake is well known to be tightly regulated [118]. For example, patients with salt-losing congenital adrenal hyperplasia modulate their salt intake based on their degree of salt loss [119]. In fact, the

notion that human sodium intake is "physiologically fixed" has been used to criticize recent public health efforts to reduce sodium intake so drastically [120]. However, the preference for salty foods is likely learned early in life. Four to six month-old infants establish a salt preference based on the sodium content of breast milk, water used to mix formula, and diet [121]. A study in Korean teens showed a correlation between frequent fast food intake and preference for saltier versions of traditional foods [122]. On the other hand, studies show that people can 'reset' their preference for less salty items. This has been demonstrated in adolescents deprived of salty pizza on their school lunch menu [116] and hypertensive adults who were retrained to a lower sodium diet within 8 to 12 weeks [117]. Because energy dense processed foods and fast foods are high in salt [88], the preference for salty foods is associated with higher calorie intake.

Future directions: Evidence is lacking to suggest that salty foods stimulate reward and encourage addictive overeating in humans. In the "salted food addiction hypothesis", Cocores& Gold examined 27 subjects undergoing opiate (mostly oxycodone) withdrawal and showed significant increases in fast food intake and weight gain over 60 days [116]. The authors interpret this finding may be interpreted as evidence of cross-sensitization between opiates and fast food. This and other addictive features of salt should be investigated separately from the potential effects of sugar and fat. If salt does indeed have addictive properties (as described in animals), it is another potential pathway that could encourage overconsumption of fast food.

INDIVIDUAL FACTORS THAT INCREASE SUSCEPTIBILITY TO FAST FOOD ADDICTION

Although one-third of the U.S. population eats fast food on any given day [1], only a subset of individuals seems to become addicted. Thus, the attractiveness of highly palatable food is not only dependent on the nutritional content but also on the state of the individual consumer. Obesity, stress, and dieting behaviors may render an individual more susceptible to addictive overeating.

Obesity

Epidemiological and population data: Perhaps the most persuasive reason to believe that fast food is addictive is that Americans continue to eat it despite the known link to obesity [8-16] and poor health outcomes [8, 9, 11, 12]. Examining population trends over the last 25 years, obesity rates in the United States have more than doubled, with nearly two-thirds of Americans (63%) now considered either overweight (37%) or obese (26%) [78]. Obesity is estimated to account for 50,000-170,000 deaths per year in the U.S. [123] and up to $215 billion in economic costs ranging from direct medical expenditures to transportation costs (such as jet fuel) [124]. The indirect costs due to missed workdays and impaired job performance associated with obesity are significant [125] and felt in every sector, including the U.S. military [126]. The social stigma of obesity should not be underestimated. Of note, some view the investigation of food addiction as a potential source of *increased* stigma since it could serve to medicalize the problem. Nevertheless, obese adults currently face interpersonal difficulties at work and in social situations, and report lower self-acceptance and diminished psychological wellbeing [127]. Obese children rate their quality of life on par with children undergoing cancer chemotherapy [128]. Despite these negative consequences, fast food sales have continued to rise [22]. In fact, overweight adults eat significantly more fast food than their normal weight counterparts [4, 13].

Proposed mechanisms: Once obese, some fast food eaters may meet the criteria for psychological dependence. For example, those who suffer the detrimental effects on career and relationships mentioned above may meet criterion 6, 'missing important work, family, social, recreational activities, withdrawal from usual life or inability to engage in normal activities' [47]. Those who continue to consume fast food despite these and other negative consequences may meet criterion 7, 'use despite negative consequences' [47]. Ifland *et al*. described this poignantly in food addicts, one of whom reported: ''I eat in spite of horrible knee and leg pain. I'm so uncomfortable after a binge that I can't lay down without regurgitation coming up into my esophagus. I'm miserable. I have embarrassment and fear about being in social situations but I overeat anyway." [41].

These respondents are clearly able to connect their eating behavior with the consequent obesity and other negative outcomes, however there are no such reports from fast food eaters. While studies show that adolescents [3, 5, 129] and adults [4] are aware that fast food can negatively impact weight and health, they cite other more compelling reasons for their intake, including convenience and location [130, 131]. Accessibility must be recognized in the discussion of food addiction since, unlike substances of abuse, food is necessary for survival and not sought for pleasure alone. Nevertheless, frequent fast food eaters do cite psychological reasons, such as to "treat" themselves [129]. In one study, overweight adolescents ate more fast food than normal weight teens in part because they perceived higher barriers to controlling their weight, including feeling deprived [132]. These findings indicate that some individuals may depend on fast food for psychological reasons and, once obese, may meet criteria for substance dependence. Failure to associate their intake with negative consequences may be due in part to the overriding positive reinforcement associated with fast food. This is analogous to tobacco use in the 1950s, when the social acceptability of smoking in nearly all settings provided little social incentive to quit [133].

In addition to psychological dependence, physiological disruption of hunger and satiety signals may contribute to addictive overeating in obesity. Erlanson-Albertson reviewed the animal experiments showing that high-fat/high-sugar feeding upregulates NPY and downregulates other satiety signals such as cholecystokinin [134]. Once obese, both leptin and insulin levels are increased. Under normal conditions, these hormones should indicate adequate adipose stores to the hypothalamus, which responds to this message with satiety signals and energy expenditure sufficient to maintain body weight. These signals should also modulate food reward. However, as chronic hyperinsulinemia blocks hypothalamic leptin signaling promoting leptin resistance, the obese individual is left in a perpetual state of energy

storage, hunger, and need for reward [42]. One criticism of this hypothesis centers on the paradoxical role of insulin and leptin. Insulin acts as powerful anorexigen when administered centrally in the insulin sensitive state [135, 136]. However, insulin and leptin signaling are defective in obesity, diabetes, and related metabolic disorders [136]. Indeed, chronic hyperinsulinemia promotes leptin resistance [137]. Clearly, longitudinal studies beginning in childhood (or earlier) are needed to follow the development of insulin resistance, obesity and these endocrinological changes.

Another explanation for continued food intake in the face of obesity is altered reward. Stoeckel *et al.* used functional Magnetic Resonance Imaging (fMRI) to provide neuroanatomic evidence that obese women exposed to pictures of cheesecake and nachos had increased stimulation in the region of the NAc, as compared to normal weight controls [138]. Further, Stice *et al.* showed greater activation in reward and sensory-related brain regions among obese adolescent girls anticipating a milkshake, yet lesser activation in response to ingestion of the milkshake, as compared to normal weight girls [139]. Volkow *et al.* reviewed the evidence to explain this paradox of greater reward expectancy with decreased sensitivity in addiction, concluding that repeated exposure to an addictive substance "resets reward thresholds" [140]. The proposed mechanism to explain decreased sensitivity to reward is centered on downregulation of D_2 receptors in the NAc. This has been shown using PET scanning in subjects who are addicted to alcohol, cocaine, heroin, or amphetamines [141]. Wang *et al.* has shown this in obese subjects, with receptor availability decreasing in proportion to BMI [142].

Initially, these neurochemical were thought to pre-exist the development of obesity [143, 144]. Stice *et al.* showed decreased expression of the Taq1A A1 allele of the D_2 receptor, which reduces D_2 receptor expression by 30-40%, in relation to increased weight gain over time [143]. These findings are consistent with the reward deficiency hypothesis, which asserts that a pre-existing hypo-responsiveness to reward in these individuals requires more food to get the same pleasurable effect, thereby contributing to overconsumption, with resultant obesity. The major problem with reward deficiency hypothesis is that it assumes a pathway to obesity that is predicated upon eating foods that are not rewarding (or less so) [144].

Newer evidence indicates that D_2 receptor downregulation may be the *result* of chronic overstimulation due to perpetual consumption, as has been shown with addictive drugs. First, Stice *et al.* demonstrated a prospective decrease in striatal response to intake of palatable foods using fMRI in women who gained weight over 6 months [145]. Second, Steele *et al.* demonstrated that the reward-dampening effect may be reversible: improved D_2 receptor binding relative to the amount of weight lost was shown using PET scan in women post-bariatric surgery [146]. These findings do not rule out the possibility that a pre-exisiting resistance to rewarding foods increases risk for obesity. Rather, they have been interpreted to indicate that obesity may exacerbate blunted reward by further downregulating D_2 receptors [146]. Brain changes that could *result* from obesity and exposure to highly palatable foods would illustrate the phenomenon of tolerance (whereby continued use requires use of more of the substance to get the same effect), criterion 1 for physiological substance dependence according the DSM-IV-TR. Tolerance as a result of long-term exposure to highly palatable food has been linked to compulsive food seeking in rats [147] and remains to be shown in humans.

Stress and Dieting

Epidemiological data: The mechanism to explain overeating in response to stress this is likely evolutionarily derived, since food shortage was a common threat to survival and eating when food is made available would potentiate survival. In fact, high-calorie, energy-dense foods would be good options when eating for survival. Clearly, this type of stress eating is detrimental in developed countries today, where people face chronic psychosocial stress while food is plentiful. In fact, economic analyses show that energy dense/nutrient poor "junk food" is even cheaper than healthier options [148]. Several large prospective studies have shown a relationship between stress and weight gain. In a nine-year prospective study, psychosocial stress was significantly related to weight gain among adults in the U.S. [149]. In the Whitehall II study, Brunner *et al.* showed a dose-dependent effect of stress on obesity over 19 years, in relation to lower fiber, fruit and vegetable intake [150]. A survey of nearly 1800 European University students in three countries found that young women, but not men, reported increasing fast food consumption when stressed [151].

While there is no direct evidence for fast food addiction due to stress, the industry has certainly positioned itself to serve a high stress clientele. As discussed in the *Environmental Cues* section below, fast food restaurants cluster in low SES areas [7]. In fact, poverty is recognized as one of the most salient chronic stressors [152]. Not only are fast food restaurants overrepresented in poorer neighborhoods, value meals and other pricing strategies promise to stretch your dollar to provide more food (calories) for less. The convenience of fast food is also a big draw for people with stressful and hectic lives. Both adults [4] and adolescents [5, 132] who are frequent fast food eaters identify convenience as a major reason to indulge, and, conversely, time constraints as a major barrier to eating healthfully.

Proposed mechanisms: The hallmark of the stress response is elevated circulating glucocorticoids in response to activation of the Hypothalamic-Pituitary-Adrenal (HPA) axis and release of Corticotropin-Releasing Factor (CRF). Endogenous opioids are released in response to HPA axis stimulation and feedback negatively to shut off the stress response. These opioids serve to ameliorate the stress response. Recalling that palatable foods also stimulate opioid release, it has been postulated that people may choose these foods to medicate their stress [153]. Consistent with the substance dependence literature, Adam & Epel have proposed a model of stress-induced food addiction, where they postulate that cortisol and endogenous opioids released in response to stress drive overeating of palatable food [153]. High levels of glucocorticoids (cortisol in humans, corticosterone in rats) are also linked to overeating and obesity through upregulation of NPY and resistance to insulin and leptin [153]. Cortisol is believed to increase the

drive for and salience of food, while insulin promotes the seeking of highly palatable food. For example, adrenalectomized rats repleted with corticosterone increase their intake of chow in proportion to circulating corticosterone concentrations and lard in proportion to insulin levels [154].

Response to stress may to help to explain why most Americans eat fast food yet only some appear to become addicted. The role of the stress response in transitioning from substance use to dependence has been reviewed by Koob [155]. Initial drug administration is associated with the classical stress response, which contributes to the reward associated with drug administration and the motivation to seek more. However, repeated HPA axis stimulation results in high circulating levels of glucocorticoids, which simultaneously feedback negatively to shut off the HPA axis and sensitize other areas of the brain to release CRF. This effect has been shown with chronic use of cocaine, opioids, nicotine, and alcohol. Hyperactivity of these extra-hypothalamic stress systems (particularly the amygdala) is believed to be a key contributor to the negative affect experienced during withdrawal [155]. Thus, while the stress response is associated with the intoxication phase of early use, it is also contributes to the compulsive drug-seeking behavior that marks the transition from use to addiction. In addition to withdrawal, other features of substance dependence have been demonstrated in experimental models of stress. For example, stress-induced sensitization to ethanol has been demonstrated in rodents [56]. Stress is therefore viewed as a behavioral sensitizer that may increase the likelihood of addiction.

Studies investigating the role of stress in human eating behavior have been plagued by the paradox that some subjects eat more under stress, while others eat less. This is partly due to the perception of the stressor, whether as a threat (e.g. social rejection) or challenge (e.g. achievement) [156]. Threat stress where coping skills are perceived as inadequate and social standing is challenged is highly effective at activating the HPA axis. Another and perhaps more important determinant of eating behavior under stress is individual stress reactivity. Epel *et al*. examined this variable in slightly overweight women exposed to psychosocial stressors including public speaking [157]. High stress-reactors (those with the highest cortisol levels in response to the stressors) ate more calories, particularly high fat choices, following the stressor. Similar to the D_2 receptor changes seen in obesity discussed above, it is not known whether high stress reactivity is a pre-existing individual difference or an effect of repeated exposure. In this study, there was no difference in BMI or dietary fat intake between the high and low reactors [157]. This suggests no major overall differences in long-term intake between high and low reactors, and may indicate that high reactors compensate for stress eating by restricting intake on other days. These findings provide insight into individual differences that may contribute to overeating in response to stress.

Dietary restriction and stress may work in combination to put addictive overeating into overdrive. Boggiano *et al*. have shown this in rats, who binge eat under the combined condition of stress and food restriction [158, 159]. In humans, dieting appears to mediate the relationship between stress and overeating [160]. That is, dieters eat more in response to an acute stressor [160]. This may explain the gender effect of stress-eating, whereby women tend to eat more and men eat less in response to stress, since women are more likely to be on a diet and eat for emotional reasons [161]. The tendency for women who are dieters to eat more when under stress has also been measured outside of the laboratory in subjects with significant work-related stress [162]. In fact, under stress, women tend to eat the foods that are normally forbidden when they are on a diet [160]. In the U.S., where highly palatable foods are ubiquitous, dieters may also be conditioned to associate the foods they are not supposed to have with feeling restricted or deprived [132]. This perceived deprivation may increase the risk of overeating. Young children have been shown to overindulge foods that they feel are "forbidden" [163]. The potential relationship between fast food intake and psychological dependence was discussed above, where people who feel deprived may turn to fast food to "treat" themselves [129].

Animal models of sugar addiction are predicated on the effect of intermittent access to perpetuate the addictive cycle of bingeing [28, 31, 46, 54, 75-77, 159]. This has led some to conclude that it is not the foods themselves that are addictive but, rather, the manner in which they are presented or obtained [26, 32]. In contrast to drugs, the dopamine response diminishes over time with continuous access to highly palatable foods [164]. Intermittent access, on the other hand, appears to be an effective way to maintain sensitivity in rodent models. In humans, dieting may create the same effect. Fedoroff *et al*. showed that women who were restrained eaters (dieters) were more susceptible to food cues, and rated higher cravings for pizza and cookies after exposed to the smell of those foods [165]. This may be interpreted to mean that dietary restraint, like stress, sensitizes the individual to reward. On the other hand, these women may have become dieters as a means to control their heightened reward sensitivity and tendency to gain weight. If dieting does perpetuate reward-eating, this would fit substance dependence criterion 4, 'desire or attempts to cut down or quit'. It would also help to explain the recidivism of obesity and the finding from longitudinal studies that dieting acts as a risk factor for weight *gain* [166].

ENVIRONMENTAL CUES THAT MAY STIMULATE ADDICTIVE OVEREATING

Studies indicate that environmental cues are not only important, but *required* to create addictive patterns. Environmental cues act as powerful external stimuli that trigger reward in both animals [29] and humans [167-169]. For example, rats exposed to wallpaper and other cues in a "cookie cage" containing Oreos will overeat in the presence of those cues even if the food being offered at the time is not as palatable as the cookies [29]. This vulnerability to environmental cues may explain the difficulty people have sticking to a diet when living in an obesogenic environment such as ours and is similar to drug-associated cues that trigger relapse, like the sight of an ashtray to a smoker [170]. The brain regions responsible for sensitivity to environmental cues have been identified by Passamonti *et al*. using fMRI in normal weight subjects exposed to pictures of palatable food as compared to bland foods [167].

Environmental cues are particularly effective at stimulating cravings. Robinson and Berridge have described a dual system of food reward that distinguishes between the pleasurable effects of a substance ("liking") *vs* the salience of the substance ("wanting"). They describe craving as the pathological form of "wanting" [144]. For example, addicts will report continuing to want a drug even though they no longer like (enjoy) using it. The "wanting" component is proposed to be dopamine dependent and mediated by the food environment. That is, sensitization to a stimulus (food or drug) is not just created by repeated exposure, it is learned in connection with the environment in which the use occurred.

Advertisements: The differences in levels of exposure and sensitivity to food cues are wide in our society. Fast food restaurants are more prevalent in poorer communities, with a geographic density of 2.5 restaurants per square mile in poor neighborhoods *vs* 1.5 per square mile in affluent ones [7]. Residents in poor areas are more likely to pass by a fast food restaurant when out in the neighborhood. Children in neighborhoods disproportionately affected by crime spend more time indoors watching television [171], where they will be exposed to more advertising for fast food. Tiggeman & Kemps showed that food cues induced cravings in college students, and that visual images were most effective as compared to taste or smell cues [172]. Consistent with this finding, the fast food industry invests most of their advertising dollars in television. Television viewers are bombarded with food advertisements; food and snacks are consumed or referred to an estimated 3-5 times per 30 min of prime time TV [173]. Studies in multiple populations show that kids eat what they see on TV [174, 175]; those who watch more television eat more fast food [5, 15]. Wiecha *et al*. showed a prospective increase in fast food intake related to television viewing: each additional hour of television was associated with an increase of 167 kcal/d [175].

In addition to differences in exposure, studies indicate that there are differences in sensitivity to food cues that may make some individuals more susceptible to overeating after watching a commercial. Cue-reactivity has been studied extensively in the addiction literature in relation to cravings and potential for relapse [170]. As discussed earlier, functional imaging studies have shown heightened sensitivity to food cues in obese subjects [138-140]. Behavioral studies have investigated reward sensitivity as one of two major components of impulse control. Poor impulse control has been associated with obesity in children [176] and adult women [177], as well as failure of obesity treatment in children [178]. Guerrieri *et al*. found that children who were more reward-sensitive ate significantly more in calories than other children from tempting foods (varied in color, shape and texture) but not monotonous foods [179]. However, the children in this study were all normal in weight; longitudinal studies are needed to determine if impulsivity contributes to weight gain. In additional, the effect of various cues (e.g. television *vs* billboards) should be examined to inform policy efforts to limit advertising to children. Collectively, however, these studies support a pathway to overeating and food seeking through learned environmental cues, particularly visual images, which may trigger cravings in those who are susceptible.

Restaurants: Fast food restaurants capitalize on reward-eating by creating a fun and familiar environment that is welcoming to families and enticing to young children. Multiple studies have demonstrated that children eat more in positive emotional environments [180]. This evidence is normally cited as a mechanism for structuring family meals to foster healthy eating in young children. However, it has also been a successful strategy for creating customers at very young ages. Toys (including characters and cross-promotions) are perhaps the best example of the effect of incentive-based learning on food intake in children. In their report to Congress, the Federal Trade Commission noted that Fast food restaurants sold more than 1.2 billion meals with toys to children in 2006 [181]. This cost the industry $360 million; their second highest child-directed expenditure next to TV advertising [181]. While this is not evidence of addiction, it is an example of an effective pairing of a positive stimulus (the toy) with a food that sensitizes children to reward at an early age. Additionally, children motivated by toys incentivize their parents by pestering. Another way that fast food restaurants create a rewarding environment is by association with positive social activities, such as play structures and birthday parties. This association also serves to increase the food reward. Birch *et al*. showed that children's liking for a neutral food (that they initially neither liked nor disliked) can be increased by using that food as a reward over 6 weeks [182]. Thus, in addition to its inherently rewarding properties (reviewed under *Nutritional Components*), children may learn to like fast food simply by going there every time their team wins the baseball game.

Menus: A third way in which the fast food environment may cue addictive eating patterns is paradoxical: the offering of both novel and familiar menu items. Novel items appear to be a straightforward way to keep the business exciting and customers happy. From an addiction standpoint, it could be viewed as a way to overcome tolerance to the usual offerings. As discussed earlier, the dopamine burst in response to a novel food is attenuated with repeated exposure [164]. This is recognized as a key difference between chronic drug use and chronic overeating of palatable foods, and requires the constant introduction of novel foods or intermittent restriction to perpetuate the addictive cycle (see *Stress and Dieting*). On the other side of this paradox are familiar foods, which can also be rewarding [183]. In children, food neophobia is thought to be evolutionarily protective in that it might prevent eating items that are not food, poisonous or spoiled [184]. The median number of refusals of a new food is 11 times per meal in 1-year olds (up to 89 times) [185]. Repeated exposure is an experimentally established method to get children to like and eat more of a specific food [186, 187]. Thus, fast food restaurants may be appealing to our innate desire for comfort and familiarity by offering staple menu items. Indeed, French fries have been on the menu at McDonald's since 1955 and continue to be the #1 most ordered item [68]. Studies suggest that familiar foods can become craved even if they are not highly palatable. Pelchat *et al*. showed that subjects on a monotonous 5-day liquid diet that they did not particularly like craved other foods as expected [183]. Surprisingly, subjects reported craving the liquid once they returned to eating normal foods.

Portions: Portion size is an important external cue to assist in the regulation of satiety. Large portions shift the perception of normal consumption upward and cause people to overeat. For example, study subjects ate 73% more soup from a "bottomless bowl" that was continuously refilled by a hidden tube [188]. In restaurant settings, subjects who are served a larger portion eat 30% [189] to 43% more [190]. This is also true for children as young as 5 years old, who ate 23% more when portions were doubled [191]. Portion distortion is substantial in the fast food industry. Since the 1970s, sodas have increased by 49 calories, French fries by 68 calories and hamburgers by 97 calories [192, 193]. People do not appear to compensate for the extra calories associated with large portions by eating less during the rest of the day [194]. This may explain in part why frequent fast food eaters consume more calories per day [195] on average than non- or infrequent-eaters [13]. There is evidence to show that obese individuals might be more vulnerable to overeating in the face of large portions because they rely more on external cues (such as portion size) *vs* internal cues (such as feelings of satiety) to regulate their intake [196]. On the other hand, portion size is a stronger influence on overall calorie intake than body size [189, 196]. Consistent with this, Wansink *et al*. concluded that "portion size [is] no respecter of person" [197]. That is, large portions cause people of all ages, sizes, educational and income levels to overeat. Ebbeling *et al*. found that overweight adolescents overate to the same degree even when a fast food meal was served in smaller portions or at timed intervals [198]. Thus, while large portion sizes do seem to encourage overeating, there is experimental evidence to suggest that the nutritional content of fast food may be more compelling. Once eating fast food, it is difficult to stop.

Packages: In addition to the large amount of food, the manner in which fast food is priced and packaged encourages larger purchases and leads customers to believe that the larger overall portion is normal [199]. The vast majority of meals ordered at hamburger chains are combination or value meals [69]. Combination meals averaged 1100 calories across Wendy's, McDonald's and Burger King, as compared to 326 calories on average among customers who purchased a single item only. Menu items that carry health claims are also misleading since customers tend to underestimate the calories and overestimate the healthfulness of these items [200]. For example, salads and apple dippers are also on the McDonald's top 10 list, along with the Big Mac and French fries [68]. However, while a McDonald's Southwest Chicken Salad with dressing provides more vegetables, fiber and less saturated fat, it also contains more calories than a Quarter Pounder (420 *vs* 410 calories). In addition to not being able to accurately assess the true benefit of these "healthy" options, several studies have shown that customers make up for any calories saved by ordering other high calorie items [200, 201]. Downs *et al*. showed this so-called "halo effect" [200] among customers ordering at a fast food sandwich shop; those who ordered a healthier entrée were more likely to add French fries or sugared drinks [201].

While fast food customers are overeating on average [97], they don't seem to be aware of it. In the bottomless soup bowl experiment, subjects were not aware that they ate more, nor did they report feeling more full than subjects who normal portions from regular bowls [188]. Although it is true that people are generally not good at estimating calories [202], this seems to be worse when it comes to fast food. In a study of McDonald's, Burger King, Wendy's and Kentucky Fried Chicken, 63% of adolescents underestimated the calories in their meal by an average of 466 calories (more than the calories in a double cheeseburger) [131]. If the underestimated number represents what customers *intended* to eat, the discrepancy between what was intended and what was actually eaten may illustrate substance dependence criteria 3, 'Use of more substance than intended.' While this is due in part to large portion sizes, as discussed above, it is also influenced by the enduring perception that large portions are a good deal. For example, subjects served a large portion of highly palatable low fiber food (macaroni and cheese) attempted to finish the meal even when they rated the initial serving as too large [189]. Having eaten more than they wanted, customers still see these large meals as a great value, compared to a smaller portion [190].

CONCLUSIONS

We have reviewed selected evidence to support the role of fast food as an addictive substance according to current the APA criteria for substance dependence [47]. Despite our enormous and growing intake [1], relatively few studies have examined fast food intake. The vast majority of studies investigating food addiction have used generic highly palatable foods (such as pizza) or single nutrients (such as sucrose). Fast food, and the people who eat most of it, have characteristics that may increase the likelihood of transitioning from use to dependence. Further, the packaging and presentation of fast food may make it more salient than generic versions of highly palatable food. We propose that fast food exerts its effects on reward eating through three routes: 1) nutritional composition; 2) individual factors that increase susceptibility; and/or 3) environmental cues. First, fast food contains several nutrients that have been investigated for addictive properties. However, as a high-sugar, high-fat, high-salt food that often includes a caffeinated beverage, fast food is unlikely to exert its effects through any single nutrient alone. In fact, there may be synergistic properties of combinations of these nutrients, such as fat and sugar. Second, once a person becomes obese (a health outcome that has been established in longitudinal studies of fast food intake [8, 9, 11, 12]) they may meet selected criteria for substance dependence. Dieting behavior and stress may further sensitize an individual to reward and contribute to addictive overeating. Third, several cues in the environment from the neighborhood level (e.g. number of restaurants per square mile), to the restaurant level (e.g. collectible toys included with meals), to the level of the menu item (e.g. combination meals) may facilitate addictive overeating. These collective features are unique to fast food, an industry that has been wildly successful at garnering and maintaining a diverse and growing customer base.

Due to the paucity of studies on brand-name fast food and addiction, we did not perform a systematic review. Instead, this is a critical analysis of the evidence to show that nutrients present in fast food, the characteristics of fast food consumers or the associated environmental cues may contribute to the addictive potential of fast food. Consistent

Table 1. Summary of Selected Scientific Publications (by Reference Number) Linking the Nutrients Present in Fast Food or the Characteristics of Fast Food Consumers to APA Criteria for Substance Dependence [47]

	Animal Studies	Human Studies
1). Tolerance (progressive use over time)	28, 31, 46, 54, 75-77 (sugar)	101, 103 (caffeine) 142-146 (obesity)
2). Withdrawal (symptoms or substance use to relieve symptoms)	28, 31, 46, 54, 75-77 (sugar)	48, 49 (sugar) 100, 102-104 (caffeine)
3). Greater amount or longer duration of use than intended	28, 31, 46, 54, 75-77 (sugar) 90-92 (fat)	198 (fast food)
4). Desire or attempts to cut down or quit	---	160-163
5). Seeking (significant time spent obtaining using or recovering from use)	51, 54 (sugar) 52 (lab chow)	---
6). Interference with life (important work social or other life activities are compromised)	---	124-128
7). Use despite negative consequences (continued use despite knowledge that use is making problems worse)	---	3-5, 129

with the literature on food addiction, we defined food addiction using the to the current APA criteria for substance dependence. The criteria with some available evidence in either animal or human studies (regardless of strength of study design) are shown in Table **1**. We recognized the limitations to the concept of food addiction in the introduction. In addition, we did not review the evidence on other potentially important determinants of an individual's potential to become addicted to food, including genetic and epigenetic factors, which are outside the scope of this paper and have been reviewed elsewhere [25, 44]. Another crucial area that warrants further examination is the role of poverty, food security and maternal stress [203]. Despite these limitations, we found evidence from human studies to support every criterion of substance dependence except for seeking. Seeking behavior would be difficult to establish in population studies within the U.S., where fast food is so ubiquitous that seeking behaviors may be obfuscated. Therefore, in their refined food addiction hypothesis, Ifland *et al*. [41] suggested focusing on the recovery aspect of this criterion, such as excessive sleeping after a binge. Nevertheless, experimental studies to examine food seeking behavior and food addiction are needed.

Currently, the most complete data to support physiological food addiction is limited to animal models using either glucose [28, 31, 46] or sucrose [54, 75-77]. These models demonstrate all of the features of addiction, including tolerance, withdrawal, craving and cross-sensitization, and have been reliably reproduced. In humans, there is some support for withdrawal in self-identified "carbohydrate cravers" [48, 49] and neuroimaging studies in obese subjects show patterns that could be interpreted as signs of tolerance to highly palatable foods [142-146]. There is currently no direct evidence for sugar addiction in humans.

Despite rodent models of bingeing on pure fat [90-92], the high fat content of fast food is likely to work in synergy with other nutrients. Virtually all high-fat foods that people are reported to crave or binge on are carbohydrate-containing [41, 94, 138, 139]. Studies investigating reward pathways in response to high fat foods have mostly used high fat foods that contain significant carbohydrate, such as cookies in rats [31, 158] and nachos in humans [138, 139]. A salted food addiction hypothesis has been put forward based on animal data showing that salt acts as an opiate agonist [116], however the effect of salt alone has not been tested. Finally, caffeine is considered a "model" substance of dependence [103] that is an increasingly common component of the fast food meal [109].

Certain individuals are more susceptible to transitioning from fast food use to dependence. Several lines of evidence now suggest that individuals who are obese, dieting, and/or under stress, are more likely to eat for reward. These individuals are more likely to meet the criteria for substance dependence. For example, dieting behavior fits criterion 4 and has emerged as an important contributor to addictive overeating as a mediator of stress-eating. That is, human subjects with high dietary restraint eat more under stress [160-162]. Dieting and stress may sensitize a person to reward, as food restriction appears to do in animals [158, 169]. Indeed, the stress response has been shown to play a key role in the transition from drug use to addiction [155]. In addition, dietary restraint is a cognitive state that may be impossible to maintain under stress or when surrounded by forbidden foods. Once obese, people may meet criteria 6 and 7 if their obesity interferes with their life or they experience negative health-related or psychosocial outcomes.

Fast food is more than the sum of its sugary, fatty, salty, and caffeinated parts; it is packaged and presented in a way that greatly increases the incentive value. Vivid visual advertisements may sensitize a wide audience beginning at a very young age [5, 16, 174]. Children are drawn to fast food restaurants by non-food incentives, including toys and play structures, and they pester their parents to bring them. Once there, the familiar, fun and positive restaurant atmosphere fosters an association between fast food and reward [180, 182]. Menus provide staple items, which engender acceptance in young children [186, 187] and appeal to the need for familiarity later on [183]. Simultaneously, novel items serve to overcome potential tolerance in established customers [164]. Huge portions and value packaging appeal to lower income customers and students and families on a budget; they also encourage overeating by shifting our consumption norms [197]. The degree to which people are unaware that they are overeating fast food may illustrate

criterion 3, "Use of more substance than intended". Collectively, these food cues in the environment may encourage overeating and facilitate the transition from use to dependence on fast food. It is not known at what point this may occur, however childhood and adolescence are the most likely critical windows of exposure.

We recognize that fast food addiction as a verifiable phenomenon remains to be proven; however, evidence is emerging from several fields to provide collective support for the concept. Studies are needed to investigate several aspects of this putative relationship. First, there are several instances where cross-sectional studies demonstrate findings consistent with an addiction criterion in humans. For example, D_2 receptor downregulation has been shown in obese subjects, consistent with tolerance [142-146]. However, it is unclear whether this finding may *cause* susceptibility to food addiction or *result* from obesity and/or long-term exposure to highly palatable food. Evidence is currently leaning toward the latter. Nevertheless, long-term studies are needed to examine the development of addictive eating patterns and obesity in relation to fast food intake and other potential risk factors such as stress. Second, more information is needed about the trajectory of fast food use in at-risk populations. Several studies have described fast food intake among adolescents [3, 5, 8, 18, 129, 131], which is a high-use group. However, longitudinal studies are needed to determine if sensitization to fast food, like drugs of abuse, increases the likelihood of future overconsumption.

If exposure at an early age sets expectations for a lifetime of reward-seeking, this would strengthen policy efforts such as restricting fast food marketing to children or establishing nutrition standards for meals that include toys. Finally, current policy efforts warrant more careful assessment. Studies of menu labeling legislation, requiring fast food restaurants to post calories on menu boards, have thus far has shown little to no effect [70, 106, 131, 201]. However, these studies were not designed to examine individual and societal factors that impact food choice and eating behaviors. These factors, including obesity, dieting behavior, stress and SES, are crucial to understanding eating behavior and must be considered in the effort to ease our national dependence on fast food.

Future Research Questions:

- Fast food intake and fast food eaters have not been well-characterized. Large cross-sectional studies are needed to describe use and examine features of dependence, particularly among frequent fast food eaters.
- Fast food addiction has not been demonstrated or tested in humans. Interventions are needed to examine whether human subjects exposed to fast food who then abstain exhibit features of dependence, including withdrawal.
- Recent studies suggest that the neurochemical differences associated with obesity may result from long-term exposure to highly palatable food. Long-term prospective studies are required to determine whether there are critical windows of exposure to fast food, such as during childhood and adolescence, which increase the risk of dependence.

Key Learning Objectives:

- The concept of food addiction is highly controversial. Sugar dependence has been demonstrated and reproduced in animal models, with some evidence to show bingeing on fat. Caffeine is considered a "model" substance of dependence, as demonstrated in both animals and humans. While salt addiction has been suggested, the current evidence supports the concept of salt preference. Nevertheless, fast food contains high levels of all of these nutrients and therefore represents the ideal combination to elicit reward eating.
- Just as some individuals can drink alcohol and never become addicted, one-third of Americans will eat fast food on any given day without becoming dependent. Yet 7% of the population eats fast food every day. What characteristics may make certain individuals more vulnerable to developing dependence on fast food? Studies suggest that obesity, stress and dieting may alter food reward and increase susceptibility.
- Environmental cues act as powerful external stimuli that trigger reward and are likely required to create addictive patterns. Fast food restaurants present multiple, repeated stimuli that encourage addictive overeating, including ubiquitous advertising, a fun and familiar restaurant environment, carefully crafted menus, large portions, and attractive packaging.

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