The Neurobiological Underpinnings of Obesity and Binge Eating: A Rationale for Adopting the Food Addiction Model

Dana G. Smith and Trevor W. Robbins

The food addiction model of overeating has been proposed to help explain the widespread advancement of obesity over the last 30 years. Parallels in neural substrates and neurochemistry, as well as corresponding motivational and behavioral traits, are increasingly coming to light; however, there are still key differences between the two disorders that must be acknowledged. We critically examine these common and divergent characteristics using the theoretical framework of prominent drug addiction models, investigating the neurobiological underpinnings of both behaviors in an attempt to justify whether classification of obesity and binge eating as an addictive disorder is merited.

Key Words: Addiction, binge eating, dopamine, drug abuse, obesity, opioid

There has been a surge in waistlines and weight gain around the world over the last 30 years, with up to two thirds of the population of some western nations classified as overweight or obese. Obesity-related maladies, such as type II diabetes, hypertension, and liver disease, have replaced smoking as the leading cause of preventable death in adults, reducing life expectancy by an estimated 6 to 7 years (1,2). The health and science communities have responded to this epidemic by working to discover the physiological and psychological underpinnings of obesity and excessive food consumption, in the hopes of understanding the multitude of factors that have contributed to our present state.

One plausible motivational approach is that overeating reflects an addiction analogous to drug abuse, with individuals becoming physically and psychologically dependent on foods high in fat and sugar. The case for classifying overeating as an addictive disorder is particularly strong in instances of binge eating, defined as "recurring episodes of eating, in a discrete period of time, an amount of food that is definitely larger than most people would eat during a similar period of time [with a]…lack of control during the episodes" (3). These criteria closely match those used to describe drug dependence (Table 1), and binge eating is currently being considered for classification as an addiction spectrum disorder in the upcoming DSM-V (www.dsm5.org/ProposedRevisions/Pages/proposedrevision.aspx?rid=372#). Specifically, addicted individuals experience a lack of control in the face of food or drugs of abuse; have a continuation of overuse despite severe health, social, legal, and financial problems; and are unsuccessful at attempts to cut back or reduce their consumption. These behaviors are typically accompanied by feelings of guilt, remorse, and distress.

In addition to analogous behavioral traits, there are also similarities in the brain structure and neurochemical profile of substance-dependent and obese individuals. These include abnormalities in the dopamine and opioid neurotransmitter systems, changes in fronto-striatal circuitry, and associated dysfunctional impulsive and compulsive behaviors. Individuals at risk for developing drug or food dependency show a decrease in striatal dopamine D2 receptor availability, potentially making them more vulnerable to the rewarding properties of pleasurable stimuli (4). Highly palatable food and drugs of abuse directly affect the mesolimbic dopamine and opioid pathways, with consumption of each type of substance increasing neurotransmitter levels (5–7). Additionally, cue-induced anticipation of these substances can elevate activity in the fronto-limbic circuitry, thought to correspond with striatal dopamine release (5,8–10). The reward deficiency hypothesis has been advanced to explain how a baseline hypofunctioning dopamine system might lead to compulsive consumption of drugs of abuse, as individuals attempt to self-medicate via direct manipulation of neurotransmitter levels (11). This theory has also been proposed for obese individuals, similarly self-medicating flattened baseline dopamine functioning by overconsumption of high-fat/high-sugar foods (11,12).

This review will investigate the neurobiological underpinnings of obesity and binge eating, taking direction from drug addiction literature, as a rationale for adopting a food addiction model. While this idea has been proposed previously, this review will synthesize the work from several labs in the fields of drug addiction and obesity in an attempt to provide a new perspective on the issue. We will incorporate in one comprehensive survey data from both preclinical and human research and will use the theoretical framework of prominent drug addiction hypotheses over the last 40 years to structure and direct the argument. We will discuss common and divergent neural substrates, neurochemistry, and behavioral characteristics existing between the two conditions in an attempt to justify classification as an addictive disorder.

Opponent-Process Theory: A Binge-Eating Model of Food Addiction

Withdrawal is one of the primary instigators of relapse in drug-dependent individuals, particularly opiate users, negatively reinforcing drug administration in an opponent-process model (13,14). Positive reinforcers that produce affective or hedonic experiences are followed by disparate processes producing contrasting negative effects in a simple dynamic control system (13). These withdrawal symptoms typically manifest as opposing physiological and psychological reactions to those experienced

From the Behavioural and Clinical Neuroscience Institute and Department of Psychology, University of Cambridge, Cambridge, United Kingdom.
Address correspondence to Dana G. Smith, B.A., University of Cambridge Behavioural and Clinical Neuroscience Institute, Department of Psychology, Downing Street, Cambridge CB2 3EB, United Kingdom; E-mail: ds555@cam.ac.uk.

Received Jul 1, 2012; revised and accepted Aug 31, 2012.

0006-3223/$36.00
http://dx.doi.org/10.1016/j.biopsych.2012.08.026

Table 1. DSM-IV-TR Definitions of Substance Dependence and Binge Eating Disorder

Comorbid Symptom	Substance Dependence	Binge Eating Disorder
Escalation of Use	The substance is taken in larger amounts or over a longer period than intended.	Eating large amounts of food when not feeling physically hungry.
Loss of Control	There is a persistent desire or unsuccessful effort to cut down or control substance use.	A sense of lack of control during the episodes, e.g., a feeling that one can't stop eating or control what or how much one is eating.
Social Consequences	Important social, occupational, or recreational activities are given up or reduced because of use.	Eating alone because of being embarrassed by how much one is eating.
Personal Distress	The substance use is continued despite knowledge of having a persistent physical or psychological problem that is likely to have been caused or exacerbated by the substance.	Feeling disgusted with oneself, depressed, or feeling very guilty after overeating; marked distress regarding binge eating; eating until feeling uncomfortably full.

A categorical comparison of the DSM-IV-TR definitions of substance dependence and binge eating criteria for both bulimia nervosa and binge eating disorder (3).

during the initial high, motivating drug users to take more of the drug to alleviate the unpleasant symptoms. Withdrawal can be initiated through drug deprivation or administration of opioid receptor antagonists, systemically or into the striatum (15). Both manipulations result in a depletion of dopamine and an upregulation of acetylcholine in the nucleus accumbens, resulting in shivering, sweating, vomiting, anhedonia, and negative affect (16). In rodents, withdrawal symptoms present as anxiety, behavioral depression, and somatic responses such as tremor, teeth chattering, and head shaking.

Similar to opiate dependence, rats raised on a binge model of sucrose consumption show withdrawal-like symptoms when sucrose access is removed or after administration of an opioid antagonist (17–20). Following a 12-hour intermittent food deprivation availability cycle, Avena, Hoebel, and colleagues (18) were able to initiate binge-like tendencies for a high-sucrose solution in rats. Self-administration of food or drugs in a binge manner is consistent with the behavior of dependent users, who take copious amounts when the drug is first available and sporadically increase their dosage as tolerance builds. When highly palatable food is intermittently made available, particularly following a fast, animals display similar tendencies, consuming up to 58% of their daily calories within the first hour of access (18,21). These behaviors are in contrast to animals to which sucrose and food chow have been made readily available, suggesting it is the intermittent access and fast-feast model that prompts the binges. After several weeks of these consummatory patterns, bingeing rats display evidence of withdrawal, suggesting physical dependence has developed via changes in neurotransmitter systems, similar to drugs of abuse. While physical withdrawal symptoms from highly palatable foods have not been reported in humans, dysphoria has been anecdotally described after removing sugar from the diet, potentially indicating psychological withdrawal (22). The overlap of psychological symptoms in humans is notable, suggesting a common pathway involving affect and motivation in food and drugs of abuse. However, physical withdrawal presents only with opiate use, indicating an additional effect from the more potent direct manipulation of the opioid system, likely acting on autonomic pathways (23). Elucidating the distinction between physiological and psychological withdrawal could be a target for future research, parsing out possible underlying differences in these affective and autonomic opioid pathways and the unique effects that food and drugs of abuse have on them.

Craving for drugs is another common contributor to relapse, causing individuals to seek drugs despite a goal to remain abstinent. In animal models, drug seeking is demonstrated via compulsive lever pressing to obtain the substance, despite attempts at extinction and devaluation of the behavior through aversive consequences (24,25). Analogous tendencies have been demonstrated in response to sugar removal in rats, with enhanced motivation to obtain a sucrose solution after a period of abstinence (26). Similar experiences of craving, particularly for carbohydrates, are reported in human dieting literature (22). Former opiate-dependent individuals also often report cravings and binges on sweets, as well as food-hoarding behaviors (27,28).

This cross-substitutability of preference is also seen between highly palatable foods and stimulant drugs (18). Known as consummatory cross-sensitization, or the gateway effect, prolonged intake and sensitization with one substance can lead to increased consumption of another. For example, animals that preferred the taste of sucrose exhibited greater self-administration of cocaine (29). This could be due to an overall greater preference for hedonic substances or could stem from a hypothetical sensitizing or priming effect on shared receptors.

Opioid System Involvement in Drug and Food Addiction

Opioid pathways are crucially implicated in the hedonic properties of pleasurable stimuli (30), and both endogenous analgesics and synthetic opiate-based drugs have a long history of abuse due to their euphoria-inducing properties. The rewarding effects of opioids are thought to stem both from their direct activation of the opioid system in the striatum, as well as an indirect excitation of the mesolimbic dopamine pathway via gamma-aminobutyric acid receptor inhibition (30,31). The dopamine and opioid systems can therefore work in tandem to reinforce the pleasurable and rewarding properties of a stimulus.

Opioids are also implicated in eating, particularly of palatable foods (see [30,32] for review), and injection of opioid agonists into the striatum increases preferential intake of high-fat/high-sugar items, even in previously sated animals (33,34). Opioid agonists increase pleasurable taste reactivity (32,35), as well as willingness to work for a food reward, increasing the breakpoint in a progressive ratio schedule (30,36). Conversely, opioid receptor antagonists will selectively reduce ingestion of high-fat/high-sugar items (20,37,38) and self-report pleasantness ratings (37,39). As such, opioid receptor antagonists, currently used to treat opiate and alcohol dependency, can decrease food