Food Addiction

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Abbreviations	
ACh	Acetylcholine
BED	Binge Eating Disorders
CeA	Central Nucleus of the Amygdala
CRF	Corticotropin-Releasing Factor
DA	Dopamine
Delta9-THC	Delta-9-tetrahydrocannabinol
fMRI	functional Magnetic Resonance Imaging
EDNOS	Eating Disorder Not Otherwise Specified
mRNA	messenger Ribonucleic Acid

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NAc	Nucleus Accumbens
OFC	Orbitofrontal Cortex
YFAS	Yale Food Addiction Scale

Brief History

Food is a source of energy and nutrients for growth, survival, and reproduction in animal heterotrophs, including modern humans. Without food for a long period of time, people first become physically and mentally depressed before eventually dying. Thus, strictly speaking, people are dependent on food to function normally – a condition that, as explained later, somewhat complicates the definition of food addiction. For most of human prehistory and until the Neolithic revolution about 8000–5000 BC, people were concerned about foraging for food to avoid starvation, not with eating too much. After the invention of agriculture and the first settlements, people continued to be concerned with procuring food, though the focus seemed to have changed from foraging to securing enough food to maintain an ample supply and storage to feed communities and avoid famine. There have been few selective pressures to evolve strong inhibitory mechanisms over food seeking and taking behaviors in safe environments. The biological imperative for individual eaters seems to have always been predominantly opportunistic: eat as much food as possible whenever and wherever possible, particularly if it is tasty and safe, such as sweet-tasting plant and animal products. However, during this ancient period and until the industrial revolution in the early eighteenth century, overindulgence of food, though considered as a major sin in some cultures (e.g., gluttony in medieval Christians), was rare and only concerned few powerful and wealthy people who could afford and had access to highly palatable foods. It is only very recently with the advent of the modern food industry that the mass consumption of easily accessible high-calorie, tasty foods has produced an evolutionarily novel state in which many people eat too much and become too fat. In fact, in the modern food environment, people report consuming food, particularly intensely palatable or hyperpalatable foods high in sugars and/or fats, no longer only to get calories but also to experience rewarding sensations, to cope with stress or fatigue, to enhance cognition, and/or to ameliorate mood (e.g., relief of negative affect). Thus, highly processed foods containing high concentrations of refined macronutrients are no longer viewed solely from the angle of homeostatic energy regulation. Some refined ingredients, such as sugars, are now also viewed as drug-like and potentially addictive, blurring the line between foods and drugs. For instance, the relatively recent introduction of highly concentrated sugar beverages available in conditioned disposable cans or plastic bottles can be compared to the introduction of injectable pure synthetic morphine with hypodermic syringes at the end of the nineteenth century, which, for instance, spurred the first epidemic of opiate addiction in the US. In both the literature and among the general population, there are also anecdotal

accounts in which people claim to be "addicted" to certain foods (e.g., refined sugars), and this addiction manifests as excessive overeating, a feeling of distress when palatable food is not available, and craving for certain foods. Many popular books, websites, and blogs exist that seek to warn people against the potential danger of hyperpalatable foods and food addiction and that attempt to help those who feel addicted to quit.

Although the term "food addiction" has been used quite often colloquially, its existence and definition in the scientific community has been and still is a subject of debate. At the heart of the debate is the relative difficulty of defining food addiction as opposed to other non-disordered forms of food consumption, of identifying and isolating the active addictive macronutrients within food, and, finally, of determining how these hypothetical addictive ingredients could alter the brain to cause addiction. As mentioned above, contrary to drug use, people are strictly dependent on food consumption for growth, survival, and reproduction. In addition, contrary to heroin or cocaine, refined sugar, for instance, is not acutely harmful or toxic. Thus, it seems, at least at first glance, difficult to draw a bright dividing line between normal, nonaddictive food consumption and food addiction. Another controversial issue surrounding the concept of food addiction is that most modern processed foods are complex objects constituted of many refined ingredients. It is difficult to identify and isolate the active principle within hyperpalatable foods that could cause food addiction as it was successfully done in the case of other complex addictive objects, such as, for instance, nicotine in the case of tobacco addiction or more recently delta9-THC in the case of cannabis addiction. Finally, contrary to drugs of abuse whose addictive effects are thought to primarily depend on their ability to hijack or usurp the reward circuits of the brain (i.e., through direct pharmacological action without soliciting normal sensory pathways), food influences this neurocircuitry through natural exteroceptive (e.g., sweet taste transduction) and interoceptive (e.g., postingestive glucose) sensory pathways that are connected to the brain "liking" and "wanting" pathways. The metaphorical notion of hijacking or usurpation of brain circuits does not seem, prima facie, to be relevant to food ingredients, even highly refined ones. As a result, the notion that hyperpalatable foods could cause addiction by altering, in a durable manner, the brain, as drugs can do, was initially met with some skepticism.

Over the past 10 years, however, most of the controversial issues surrounding the concept of food addiction have been successfully resolved (or are in pass of being so) thanks to a flurry of recent research, involving both animal models and clinical research, on the neurobiology of sugar reward and addiction. This mainly explains why the present chapter focuses on sugar addiction as a paradigmatic example for food addiction. The focus on sugar reward and addiction is also all the more important in view of the inexorable "sweetening of the world's diet." Much daily satisfaction or gratification that people now derive from food consumption comes from the sweet taste of highly sugar-sweetened foods and drinks. In addition, there is growing evidence linking increased sugar availability and consumption,

particularly in infants, to the current worldwide obesity epidemic. However, despite the focus on sugar addiction, some of the main conclusions drawn can be generalized to other types of food addiction. First, controlled research on laboratory animals has demonstrated that increased availability and resulting overconsumption of sugar (mainly sucrose) can induce behavioral changes that recapitulate several behavioral features of addiction, including escalation of consumption, increased motivation, affective withdrawal, and continued consumption despite harmful consequences. Second, the problem of discriminating food addiction from normal food consumption was recently resolved by adapting the current diagnosis of drug addiction. Overall, similar to the experience of a person addicted to drugs, those who feel they are addicted to certain foods find it difficult to stop overeating despite the desire to do so and an awareness of the negative consequences on health, well-being, and self-esteem. Importantly, this diagnostic innovation has led to the discovery that the incidence of food addiction is comparable to that of cocaine addiction (i.e., about 10–15% of people or drug users, respectively) but considerably increases in patients with obesity. Finally, as explained in detail below, the taste of sweet is unique in being an innately and intensely rewarding primary sensory modality that is hardwired to the brain reward circuitry. The neural and molecular code of sweet taste and reward has now been almost completely cracked. However, though high-sugar foods do not hijack the reward system of the brain in a drug-like manner, there is evidence that they may act as supernormal reward stimuli. A supernormal stimulus is an artificial stimulus that is more effective than naturally occurring stimuli in releasing behavior and therefore is more difficult to resist and override. In addition, critical to the notion of food addiction, recent research on animals has demonstrated that chronic overconsumption of sugar-sweetened foods can induce long-term changes in brain reward neurochemical circuits that mimic those seen following chronic exposure to cocaine or heroin. Intriguingly, some of the resulting brain changes are similar to those documented in obese people using in vivo brain imaging. This comparability suggests that the latter changes are probably a consequence, at least partly, of food addiction and obesity. However, one cannot exclude the possibility of a vicious cycle where some of these changes also preexist and predispose an individual toward food addiction and obesity, at least in some genetically specific populations.

A Primer on Sweet Taste Perception

Taste in mammals begins on the tongue (Fig. 97.1). The anatomical units of taste detection are the taste receptor cells found in the mouth. Those taste receptor cells are assembled into taste buds, ovoid structures typically composed of 50–100 heterogeneous cells. Three different types of taste buds are topographically distributed across different papillae of the tongue: (1) fungiform papillae at the anterior surface of the tongue, (2) circumvallate papillae at the back of the tongue, and (3) foliate papillae at the posterior lateral edge of the tongue. Many isolated taste buds are also located on the soft palate.

Taste Receptors

Taste receptor cells within a taste bud are arranged in a concentric columnar fashion and project microvillae to the apical surface of the taste bud, where they form the taste pore, the site of interaction between tastants (Fig. 97.1). It is generally accepted that there are five primary taste modalities: sweet, bitter, salty, sour (acidic), and umami (a Japanese word meaning savory, the taste of glutamate or amino acids). Receptor cells for each of those taste modalities are segregated into nonoverlapping populations expressing distinct receptors. Specialized taste cells appear in the human fetus at 7–8 weeks of gestation and are morphologically mature receptors at 13–15 weeks of gestation.

Receptors for Sweet and Umami

The attractive taste modalities, sweet and umami, are mediated by G-protein-coupled receptors that are expressed at the apical surface of the taste receptor cell. This first family of taste receptors (T1R) identified belongs to the class C type and functions as heterodimers. There are three T1R receptors: T1R1, T1R2, and T1R3. The umami receptor is the T1R1/T1R3 heterodimer. The sweet receptor is the T1R2/T1R3 heterodimer. There is also some evidence for a second T1R3/T1R3 homodimer sweet receptor which responds only to very high concentration of sugars (>300 mM). Interestingly, sweet taste cells appear very early in the human fetus at 7–8 weeks.

Receptors for Bitter

The second family of taste receptors is the G-protein-coupled receptors encoding the T2R. The T2R is a bitter receptor, with different T2Rs selectively recognizing different bitter compounds. T2R has a highly variable structure, and the number of bitter receptor genes is variable across species, a sequence diversity that reflects the need to recognize a disparate chemical universe. However, because each bitter-sensing cell co-expresses the majority of the T2R genes, they detect a wide range of bitter compounds but do not distinguish between them and thus all evoke a similar "bitter" sensation.

Receptors for Salty and Sour

Salty and sour tastants modulate taste-cell function through specialized ion channels on the apical surface of the taste receptor cell. Salty taste detection occurs by direct entry of sodium through amiloride-sensitive sodium channels. Sour-sensing taste cells are characterized by the expression of PKD2L1, a transient receptor potential expressed in a population of taste receptor cells distinct from those mediating sweet, umami, and bitter tastes.

Signal Transduction Pathway of T1Rs and T2Rs

Although the receptors for sweet, umami, and bitter are all located in separate subsets of cells, all signals, as in other sensory systems, pass through a common

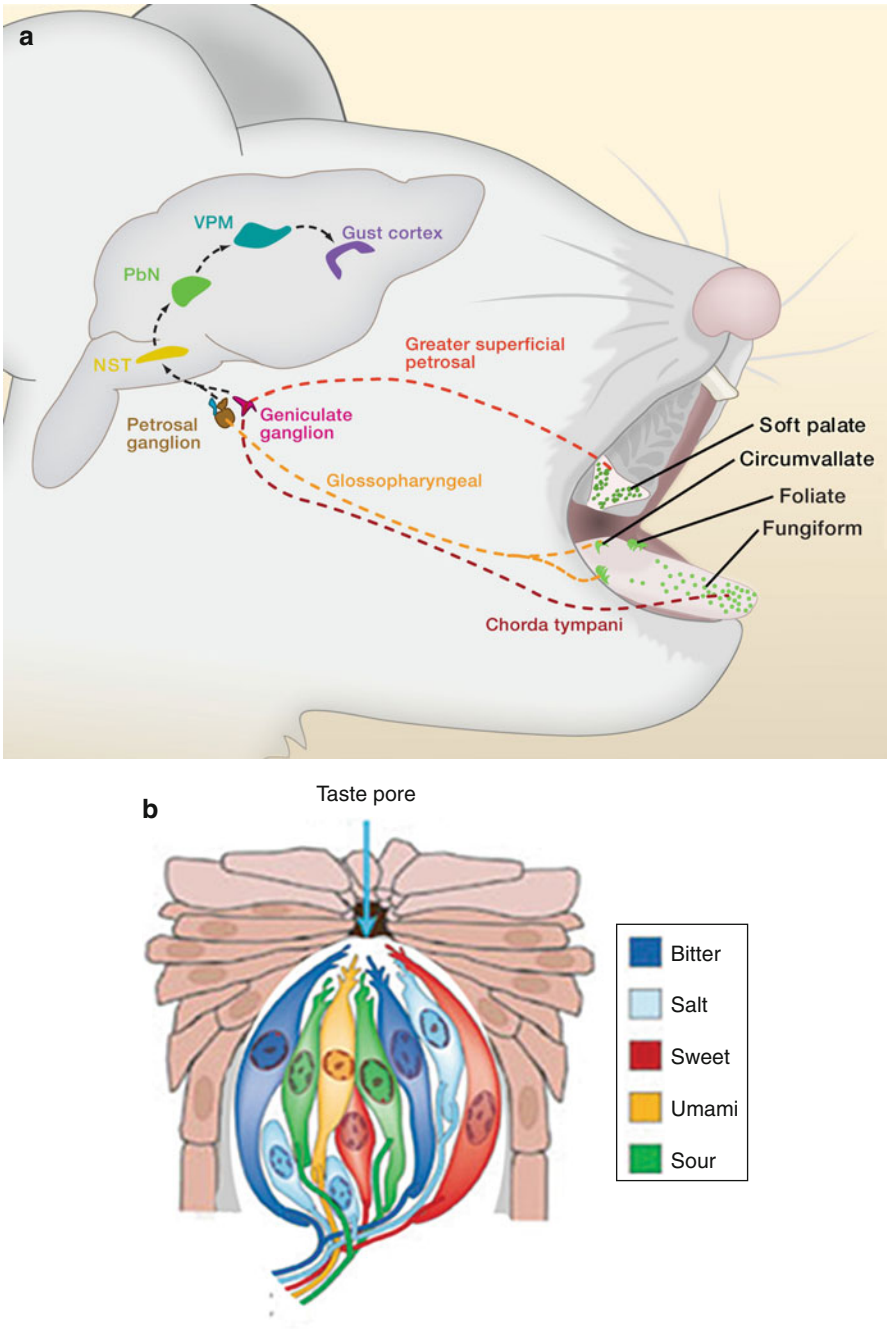

Fig. 97.1 (continued)

pathway to transducer tastant recognition into cell activation. Stimulation of the T1Rs and T2Rs activates G-protein-coupled receptors α-gustducin and PLCβ2 which degrades phosphatidylinositol-4,5-bisphosphate to produce diacylglycerol and inositol-1,4,5- trisphosphate (IP3). IP3 causes the release of calcium from the endoplasmic reticulum, which induces neurotransmitter release from the synaptic vesicles and thus activation and transmission of the information of the nerve fiber.

Encoding Taste Quality

Distinct and strictly segregated populations of taste cells encode each of the taste modality. There is no cell that co-expresses different taste receptor and, thus, no cell that detects different tastants. However, taste receptors for a particular taste are not restricted to a specific part of the tongue but are instead expressed in multiple and different papillae and palate. For example, the T1R2 receptor that detects sweet-sensing cells is expressed in the foliate, circumvallate, and palate. The differential expression of different taste receptors argues that there is a topographic map of taste sensitivity on the tongue. However, the tongue is clearly not segregated into different regions that exclusively recognize different tastes.

Moreover, compelling evidence from studies in genetically modified mice has shown that activation of the different taste receptor cell types is sufficient to generate specific behavior programs (i.e., labeled-line organization). For example, mice expressing a spiradoline receptor, a nontaste receptor, in sweet cells become attracted to solutions containing this normally tasteless compound. Conversely, after expression of the same receptor in bitter cells, mice exhibit a strong repulsion for spiradoline. Finally, expression of a bitter receptor in sweet-sensing cells attracts mice to the bitter taste. Together, these results demonstrate that dedicated taste pathways mediate attractive and aversive behaviors and that taste receptor cells are hardwired to behavioral outputs. That is, behavioral responses to taste stimuli are determined by the identity of the stimulated cell type and its associated nerve fibers but not by the properties of the taste receptor molecule or even the tastant itself.

Fig. 97.1 (**a**) Anatomy of taste. Taste buds on the tongue are innerved by three afferents nerves that carry taste information to the nucleus of the solitary tract (*NST*). Tatse responses are then transmitted through the parabrachial nucleus (*PbN*) and the ventral posterodorsal thalamus (*VPM*) to the gustatory cortex. (**b**) Taste receptor cells and bud. Schematic representation of a taste bud composed of multiple taste receptor cells. Taste receptor cells project microvillae to the apical surface of the bud where they form the taste pore for the interaction with the tastant. Taste receptor cells for each of the five taste modalities are present within the same taste bud (Reproduced and modified from Yarmolinsky et al. (2009))

Sweet Taste Sensitivity and Consumption

Genetic Variations

Taste is an important determinant of food consumption, and genetic variations in the sweet subunit T1R2 have been shown to contribute to variations in sugar sensitivity and consumption. The sequences of these T1Rs are poorly conserved (only 70% identical), a genetic variation that could underlie the difference in sweet taste perception between species. For example, although humans taste as sweet both natural and artificial sweeteners, the rat and mouse taste natural sugars but only a few artificial ones (e.g., they are indifferent to aspartame). Notably, these differences in sweet taste sensitivity and selectivity are a direct reflection of T1R-sequence variation between species. Indeed, introduction of the human T1R2 gene into mice completely humanizes mouse taste to aspartame. Similarly, domestic and wildcats, which lack a functional T1R2 receptor due to a mutation in the T1R2 early in their evolution, lost all sweet taste and do not eat sweet food.

Structural Variations

As mentioned above, sweet taste occurs almost exclusively via a T1R2/T1R3 receptor that has the capacity to recognize both simple sugars and a wide range of artificial sweeteners. Recent structure-function studies have identified several distinct binding sites on the T1R2/T1R3 heterodimer, each of them representing a potential site for the integration of the sweet signal: (1) a large extracellular N-terminal domain, the Venus flytrap domain; (2) the transmembrane C-terminal domain; and (3) a shorter cysteine-rich domain. The existence of multiple binding sites in each sweet receptor may explain their ability to respond to a broad range of tastants. Sucrose and noncaloric sweeteners such as aspartame and neotame interact within the Venus flytrap domain of T1R2, other noncaloric sweeteners interact within the transmembrane C-terminal domain of T1R3, and sweet-tasting proteins interact with the cysteine-rich domain of T1R3.

In addition, a few substances have been shown to alter the way sweet taste is perceived. One class of these inhibits the perception of sweet tastes, whether from sugars or from highly potent sweeteners. For example, lactisole in humans inhibits the activation of the human T1R2/T1R through interactions with the transmembrane domain of T1R3. Moreover, whereas at low concentrations they bind to a high-affinity binding site leading to perception of sweetness, at high concentrations, they bind to a second low-affinity inhibitory site that causes the receptor to shift from an activated to an inhibitory state, therefore inhibiting the cellular responses to other sweeteners. The other class enhances the sweet perception. These molecules have no taste of their own but potentiate the sweet taste of sugars. As mentioned above, sweetness binds to the hinge region and induces the closure of the Venus flytrap domain of T1R2. The enhancer binds to the opening to further stabilize the closed, active, conformation of the receptor. Taste inhibitors and enhancers differentially influence the chorda tympani nerve response to sweet-tasting compounds and produce different neural response profiles in brainstem gustatory nuclei.

The Ascending Neural Pathways of Food Reward

Sweet Taste Ascends from the Brainstem

Taste receptor cells are not neurons and do not send axonal projections to the brain. Instead, they are innerved by three afferent cranial nerve endings that transmit information to the taste centers of the cortex through synapses in the brainstem and the thalamus (Fig. 97.1). As taste ascends through the brain, reward properties are added at several stages. The first stop for taste sensation in the brain is deep in the brainstem medulla oblongata, in the nucleus of the solitary tract. Taste signals are delivered from the tongue to the nucleus of the solitary tract by the facial (seventh cranial) nerve and glossopharyngeal (ninth cranial) nerve. From the nucleus of the solitary tract, taste travels up through the pons (pausing in most animal brains in the parabrachial nucleus, but possibly not stopping in humans). These brainstem systems can discriminate sweet from bitter even by themselves and control basic positive or negative facial reactions to taste. The brainstem site near the parabrachial nucleus in the pons can even enhance positive reactions when neurochemically stimulated, beginning to amplify basic food reward properties of a sweet taste. By itself, the brainstem mediates positive reactions simply as a reflex. But in normal brains, when the forebrain and brainstem are interconnected and the forebrain is in control of brainstem activity, all the levels of the brain operate in coordination with each other to control food reward.

Forebrain Structures for Food Reward

Most food reward processing occurs in the forebrain (Fig. 97.2). As taste signals rise to the forebrain, they split into two paths. The low path (sometimes called the limbic taste path) travels from the brainstem to subcortical reward structures: the nucleus accumbens (NAc), ventral pallidum, amygdala, and hypothalamus. These limbic structures can be activated in human brains by seeing, smelling, or tasting a palatable food.

An upper path (sometimes called the sensory taste path) travels first to the thalamus and then ascends to the taste sensory cortex, which is on the ventral lateral surface of the prefrontal lobe that is covered in humans by the temporal lobe. Taste signals in the cortex then are relayed forward to pleasure-coding sites in the orbitofrontal cortex (OFC) and insula regions of the prefrontal cortex. The OFC is a primary site for hedonic coding, with a mid-anterior site where functional magnetic resonance imaging (fMRI) activation specifically tracks the pleasantness of a particular food. For example, people who are satiated on chocolate milk reported a drop in the pleasure of its taste, which was tracked by reduced activation in the mid-anterior OFC. If the same people then tasted tomato juice, which they still liked and had not yet drunk, the OFC activated highly. Conversely, if they drank lots of juice instead of milk, then OFC activation and reported pleasure declined to the tomato taste while the chocolate milk taste remained liked and able to activate the OFC.

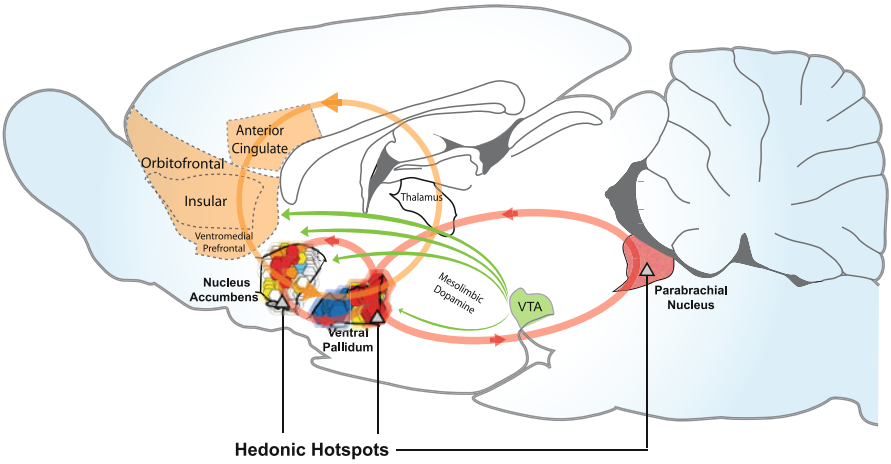

Fig. 97.2 Food reward circuits in the brain. Hedonic hotspots that amplify "liking" for sweetness are in *red* and *yellow*. Mesolimbic dopamine systems of "wanting" food rewards are in green. VTA, ventral tegmental area

Similarly, the insular cortex may code changes in taste pleasure due to satiety. For example, a decline in fMRI activation simultaneous with a decline in pleasure has been produced for the taste of chocolate candy after satiation. Reward coding was shown by having people eat several bars of chocolate until they did not want to eat anymore. At that time, the taste no longer activated the insular cortex.

After the prefrontal lobe, the upper forebrain path for food reward then converges again with the lower path. The prefrontal cortex of the upper path sends reward projections down to the NAc of the lower path. Conversely, the lower path from the NAc projects to the ventral pallidum and hypothalamus, and then up to the thalamus and to the prefrontal cortex again (including orbitofrontal and insula regions). Thus, the two forebrain paths eventually form a loop, in which food reward signals may circulate around the forebrain.

Generating "Liking" for Food Reward

Taste pleasure is created in the brain, via an active transformation of the sweet or creamy or other sensation to magnify hedonic impact. The pleasure of taste is amplified by particular neurochemicals released to act within several subcortical hedonic hotspots, which are brain sites specialized for enhancing liking of a pleasant sensation. The NAc contains one hedonic hotspot, in a rostrodorsal site located in its subdivision known as the medial shell. In that hotspot, opioid neurotransmitters (natural brain heroin-like chemicals; especially enkephalin and beta-endorphin that activate the mu subtype of opioid receptors) and

endocannabinoid neurotransmitters (natural brain marijuana-like chemicals such as anandamide) cause increases in "liking" reactions to sweetness. Another hedonic hotspot is found in the posterior section of the ventral pallidum, which is a chief target structure of outputs from NAc. Each hotspot is about a cubic millimeter in volume in the brain of a rat and might be about a cubic centimeter on each side of a human brain. The hotspots are rather specialized and tiny, constituting only one-tenth to one-third of the brain structure that contains it.

Together, hotspots form a distributed brain network for hedonic amplification (Fig. 97.2). The whole network functions as an integrated hierarchical circuit. At the relatively high level of the forebrain, the enhancement of taste "liking" by hotspots in the NAc and ventral pallidum act together as a single cooperative network, needing unanimous "votes" by both hotspots. For example, hedonic amplification by opioid stimulation of one hotspot automatically recruits neurons in the other hotspot into action. Conversely, pleasure enhancement by network activation can be disrupted by defection of any hotspot. For example, blocking the opioid receptors in one hotspot will prevent any enhancement of taste "liking" from being caused by activating opioid receptors of another hotspot. This may make intense pleasure enhancements rather fragile, rare, and vulnerable to disruption.

Generating "Wanting" for Food Reward

Research has indicated that "liking" and "wanting" rewards are dissociable both psychologically and neurobiologically. "Wanting" here means incentive salience, a type of incentive motivation that promotes approach toward and consumption of rewards and which has distinct psychological and neurobiological features. Psychologically, pulses of "wanting" can be triggered by cues related to food rewards, especially when hungry or stressed. Neurobiologically, brain substrates for "wanting" are more widely distributed and more easily activated than substrates for "liking."

Mesolimbic DA systems especially, and DA interactions with corticolimbic glutamate and other neurochemical systems, are important for generating "wanting" for food reward. Pharmacological manipulations of some of those systems can readily alter "wanting" without changing "liking." For example, amplification of "wanting" without "liking" has been produced by temporary activation of DA systems by drugs and by the near-permanent neural sensitization of those DA systems by repeated administration of high doses of addictive drugs.

In susceptible individuals, drugs of abuse may produce incentive sensitization: excessive levels of incentive salience that generate compulsive "wanting" to take more drugs, whether or not the same drugs are correspondingly "liked." Similarly for food, compulsive levels of "wanting" to eat might conceivably be produced. This idea is compatible with suggestions that sensitization-like changes in brain mesolimbic systems are produced by exposure to dieting and food bingeing cycles, discussed below.

Brain Reward Circuits Interact with Hypothalamic Regulatory Circuits of Hunger and Satiety

Food rewards fluctuate in reward value depending on whether an individual is hungry or full. As an explanation, recent studies have shown that hunger states and satiety states, which are processed by hypothalamic circuits of homeostatic regulation in the brain, cause neural and chemical signals to be sent to brain reward circuits that modulate "liking" and "wanting" for tasty foods. Conversely, brain reward circuits send signals to the hypothalamus that may allow cues for tasty food to activate hunger circuits.

For example, during hunger, neuropeptide Y and orexin are released in the hypothalamus, both of which contribute to appetite. Orexin has been suggested to activate brain hedonic hotspots that amplify "liking" and to activate mesolimbic DA systems that generate "wanting" for food rewards. Such connections may make foods more liked and wanted during states of hunger. Conversely, satiety states elevate neurochemicals such as leptin, which suppress mesolimbic reward circuits and reduce motivation to eat.

Evidence for Food Addiction: The Case for Sugar Addiction

The first scientific evidence for food addiction was originally obtained in rats following daily extended access to a high-sugar diet. Rats are, by far, the most frequently used animal model in experimental research on addiction. Like humans, rats have a sweet tooth, and they self-administer most drugs of abuse (e.g., cocaine, heroin). Most breakthrough advances in the neurobiology of drugs of abuse have been originally obtained through research using rats. This seminal research on sugar addiction has now been confirmed and extended to other types of food, including commercially available high-fat high-sugar products (e.g., chocolate cookies, cheesecake). Most importantly, it has also encouraged a serious reconsideration of the relevance and validity of the concept of food addiction to better understand obesity.

Evidence for Food Addiction from Animal Models

When given daily prolonged (e.g., 6–12 h), but not restricted (e.g., 1 h), access to some drugs of abuse, such as heroin or cocaine, rats can develop behavioral changes that recapitulate most of the clinical signs of addiction. These behaviors can include escalation of drug intake, episodic overconsumption (bingeing), increased drug motivation, affective withdrawal, and craving for more drugs during abstinence. The paradigms used to assess behavioral signs of addiction to drugs of abuse can be adapted so that these behaviors can be measured in rats that are potentially dependent on sugar. Thus, an animal model was developed to study addiction to sugar in laboratory rats. The model has been described in detail previously, and findings using this model are discussed in previous reviews and in Table 97.1. In

Table 97.1 Overlaps between substance dependence criteria and data derived from an animal model of sugar (or fat/sugar) dependence

Substance dependence (DSM-IV-TR)	Sugar addiction-like behavior in animals
Tolerance, escalation of drug intake	Escalation of sugar intake
Drug withdrawal	Somatic and affective withdrawal
Consuming more than intended	Deprivation effect
Continued use despite negative consequences	Resistance to punishment

brief, in this model of sugar addiction, rats are offered voluntary daily 12-h access to a 10% sucrose solution (or 25% glucose in some studies) and rodent chow, followed by 12 h of food deprivation, for approximately 1 month, referred to as a binge schedule of intake. Control groups are fed either sugar and chow ad libitum, fed chow only ad libitum, given 12-h access to chow only, or exposed to sugar on only a few occasions (two or three 12-h periods of access).

After just a few days on the sugar-binge access schedule described above, the rats begin to escalate their daily intake and binge on the sugar, as indicated by an increase in their intake of the sugar solution during the first hour of access. In addition to a binge at the onset of access, the daily feeding pattern changes in these animals, as evidenced by these rats consuming larger meals of sugar throughout the access period compared to control animals fed the sugar ad libitum. When administered the opioid-receptor antagonist naloxone, somatic signs of withdrawal, such as teeth chattering, forepaw tremor, and head shakes, occur in rats that have been binge eating sugar. Sugar-bingeing rats also exhibit anxiety-like behaviors, as measured by the reduced amount of time spent on the exposed arm of the elevated plus maze. Signs of opiate-like withdrawal also emerge without naloxone, when all food is removed for 24–36 h. Sugar-bingeing rats also show signs of increased motivation to obtain sucrose; they will lever press for more sugar in a test after 2 weeks of abstinence than they did before. Conversely, a control group with prior 0.5-h daily access to sugar followed by 2 weeks of abstinence did not show the effect. This suggests a change in the motivational impact of sugar that persists throughout a prolonged period of abstinence, leading to enhanced intake. The results further suggest that relatively brief bouts of sugar intake are not sufficient to result in enhanced intake following abstinence, but rather, prolonged daily binge-type eating is needed to produce the effect.

Additionally, other studies suggest that sugar-bingeing rats are sensitized to the stimulant effects of some drugs of abuse. Psychomotor sensitization is a well-documented behavioral change associated with persistent alterations in brain glutamate and DA synapses and is generally associated with an increased incentive or motivational value of the drug. Rats with a history of overeating sugar are hyperactive in response to a low dose of amphetamine that has little or no effect on drug-naïve animals. This cross-sensitization between sugar and amphetamine could result from the activating effects of sugar consumption on striatal DA signaling (see below). Further, when rats are bingeing on sugar and then forced to abstain, they subsequently show greater intake of 9% alcohol. This suggests that intermittent excessive sugar intake may foster alcohol consumption. Finally, there is also

evidence that rats with a long history of sugar consumption become tolerant to the analgesic effects of opiates, such as morphine. This cross-tolerance between sugar and morphine could result from the activating effects of sugar intake on opioid signaling within brain pain pathways. Together with the neurochemical findings described below, the results from this model suggest that bingeing on a sugar solution produces multiple indications of addiction-like behaviors.

A strength of this model is that it is the first animal model in which a comprehensive set of criteria associated with addiction has been described when rats overconsume a palatable food. Another strength of this model is that, since the bingeing rats do not become overweight, the behavioral variable of overeating of the sugar can be isolated. This is important, as it is known that the effects of obesity can impart changes in the brain that influence reward. Thus, by isolating the variable of binge-type overeating from the consequence of increased body weight, the effects of palatable food bingeing on the brain and behavior can be determined.

Other laboratories have reported complementary findings that suggest signs of addiction can emerge when using other intermittent sucrose access schedules. Intermittent sucrose access cross-sensitizes with cocaine and promotes sensitization to the DA agonist quinpirole. Interestingly, however, there is no cross-sensitization between cocaine and saccharin, suggesting the possible involvement of postingestive neurochemical processes. In this context, it is interesting to note that sucrose consumption can increase striatal DA signaling independently of sweet taste transduction in genetically engineered sweet-blind mice (i.e., carrying a targeted deletion of the gene coding for sweet taste receptors), presumably through postingestive glucose. Also, anxiety-like behavior has been reported in rats with a daily binge-like access to a high-sucrose diet. Other physiological and behavioral changes that suggest a negative state have been noted in rats that intermittently consume sugar. For instance, the removal of sugar has been reported to decrease body temperature and instigate signs of aggressive behavior. In addition, others have shown that different palatable foods, such as those rich in sugars and fats, can produce signs of addiction, including anxiety and compulsive-like consumption. For instance, in an elegant series of experiments, rats given daily extended access to cheesecake, chocolate, and bacon were shown to become obese and tolerant to suppression of food intake by punishment. Tolerance to punishment is currently considered in drug addiction research to be one of the best operational measures of compulsive-like behavior, though it could also represent another independent measure of increased motivation for food.

Evidence for Food Addiction from Clinical Research

Empirical support for the occurrence of food addiction in humans has also been steadily growing. Initially, much of the evidence for food addiction came from the presence of behavioral indicators of addiction in eating-related problems (see Table 97.2). For example, individuals struggling to lose weight continue to consume food excessively despite negative health consequences, and they are often

Table 97.2 Diagnostic criteria for substance dependence as stated by the DSM-IV-TR

Behavioral criteria	Definition
Tolerance	(i) The need for markedly increased amounts of the substance to achieve intoxication or desired effect
	(ii) Markedly diminished effect with continued use of the same amount of the substance
Withdrawal	(i) The characteristic withdrawal syndrome for the substance
	(ii) The same (or closely related) substance is taken to relieve or avoid withdrawal symptoms
Impaired control	Taking the substance often in larger amounts or over a longer period than was intended[a]
Difficulty to abstain	There is a persistent desire or unsuccessful effort to cut down or control substance use[a, b]
Increased time spent	Spending a great deal of time in activities necessary to obtain or use the substance or to recover from its effects
Neglect of alternative activities	Giving up social, occupational, or recreational activities because of substance use
Continued used despite negative consequences	Continuing the substance use with the knowledge that it is causing or exacerbating a persistent or recurrent physical or psychological problem[a, b]

[a]Associated with binge eating disorder
[b]Associated with obesity

incapable of successfully cutting down on high-calorie foods. Binge eating disorder (BED) is also associated with both of these factors, as well as another core feature of substance dependence – diminished control over consumption. These behavioral similarities strengthened the hypothesis that an addictive process may be playing a role in some types of excessive food consumption.

To further explore this concept, the Yale Food Addiction Scale (YFAS) was developed to examine whether the diagnostic criteria for substance dependence were present in eating problems. Specifically, the YFAS translates the substance dependence diagnostic criteria as defined by the Diagnostic and Statistical Manual of Mental Disorders IV (Text Revision) to relate to the consumption of high-fat and high-sugar foods (e.g., ice cream, chocolate, French fries). To meet the threshold for food addiction, three or more food addiction "symptoms" must be present in the past 12 months, as well as clinically significant impairment or distress. In the preliminary validation of the measure in a nonclinical student sample, 11.7% of the participants met the food addiction "diagnosis." Additionally, the YFAS accounted for a unique variance in the severity of binge eating symptoms above and beyond measures of emotional eating and disordered eating attitudes. In an examination of food addiction and BED, 57% of obese patients with BED met the food addiction threshold. The YFAS was also associated with more frequent binge eating episodes in this sample above and beyond indicators of disordered eating and negative affect. Thus, there appears to be significant behavioral evidence that an addictive process may play a role in eating-related problems.

Table 97.3 Main neurobiological changes in the nucleus accumbens

Signaling pathways	Direction of change
D1 receptor binding	Increased
D2 receptor binding	Decreased
D3 receptor expression	Increased
Preproenkephalin expression	Decreased
ACh/DA balance	Altered

Neurobiology of Food Addiction

In addition to the behavioral signs of addiction that can emerge in response to drugs of abuse, chronic sugar or fat consumption can impart long-term effects on the brain (Table 97.3). There are concomitant, addiction-like changes in the reward-related brain regions that are seen in conjunction with the behaviors noted above in response to overeating sugar, as revealed by animal models. This section focuses on four neurotransmitter systems that have been studied within the context of sugar addition and are also known to play roles in the rewarding and/or aversive aspects of some drugs of abuse.

Food-Induced Changes in Brain Dopamine Signaling

Drugs of abuse can alter DA receptors and DA release in mesolimbic regions of the brain. Similar changes have been noted when rats are overeating sugar. Specifically, there is an increase in D1 receptor binding in the NAc and a decrease in D2 receptor binding in the NAc and dorsal striatum relative to controls. Rats with intermittent sugar and chow access also have decreased D2 receptor mRNA in the NAc and increased D3 receptor mRNA in the NAc and caudate-putamen compared with controls. These results are supported by findings using other models of sugar overeating in which alterations in accumbens DA turnover and DA transporter have been reported. In addition, others have recently shown that daily extended access to high-fat high-sugar diets which induce obesity in rats also trigger a progressive decrease in brain reward thresholds that is causally associated with a downregulation of striatal DA D2 receptors.

However, one of the strongest neurochemical similarities between sugar bingeing and drugs of abuse is the effect on extracellular levels of DA. The repeated increase in extracellular DA within the NAc shell is a hallmark effect of drugs that are abused, whereas normally during feeding, the DA response fades out after repeated exposure to food as it loses its novelty. When rats are bingeing on sugar, the DA response is more like that of a drug of abuse than a food, with DA being released upon each binge. Control rats fed sugar or chow ad libitum, rats with intermittent access to just chow, or rats that taste sugar only two times develop a blunted DA response that is typical of a food that loses its novelty. Thus, overeating sugar produces a DAergic response that is quite different from

casual sugar consumption, even if total sugar intake is similar in both conditions. These changes in DA receptors and release may explain the sensitivity to drugs of abuse (alcohol or amphetamine) that is seen when rats overeat sugar using this model.

Food-Induced Changes in Brain Opioid Signaling

In addition to the effects on DA, endogenous opioid systems are also affected by sugar overeating in a manner that is consistent with the effects of some drugs of abuse. The fact that sugar-bingeing rats are sensitive to the effects of the opioid antagonist naloxone, which can precipitate signs of withdrawal, suggests that repeated bouts of excessive sugar intake can alter brain opioid systems. Further, findings from brain assays suggest that sugar bingeing decreases enkephalin mRNA in the NAc, and mu-opioid-receptor binding is significantly enhanced in the NAc shell, cingulate, hippocampus, and locus coeruleus, compared with chow-fed controls. These results underscore the role of opioid systems in the development and expression of sugar addiction.

Food-Induced Changes in Brain Acetylcholine Signaling

A rise in extracellular levels of ACh in the NAc has been associated with the onset of satiety, and studies have begun to characterize the role of specific cholinergic receptors in the initiation and cessation of feeding. Normally, extracellular ACh levels in the NAc rise as the meal progresses and peak at the point at which the meal stops. However, when rats are bingeing on sugar, they develop a delay in the rise of extracellular ACh, which may explain, in part, why the size and length of the binge meal increase over time. Accumbens cholinergic neurons also appear to have a role in aversive behaviors. Behavioral signs of drug withdrawal are often accompanied by alterations in DA/ACh balance in the NAc; DA decreases while ACh increases. This imbalance has been shown during withdrawal from several drugs of abuse, including morphine, nicotine, and alcohol. Rats bingeing on sugar also show this neurochemical imbalance in DA/ACh during withdrawal. This result occurs both when rats are given naloxone to precipitate opiate-like withdrawal and after 36 h of food deprivation.

Food-Induced Changes in Brain Stress Pathways

Anxiety behavior seen in sugar-withdrawn rats is associated with an increased expression of the stress-related neuropeptide corticotropin-releasing factor (CRF) in the central nucleus of the amygdala (CeA). Increased CRF signaling in the CeA is also seen during withdrawal from many drugs of abuse, including opiates and cocaine. Pharmacological blockade of brain CRF signaling prevented sugar

withdrawal-associated anxiety and reduced sugar bingeing, suggesting increased CRF in the CeA. Likewise, CRF antagonists have similar effects on excessive consumption of cocaine and opiates and on anxiety-like states during withdrawal from these drugs. Thus, it seems that once induced by excessive sugar consumption, chronic hyperactive CRF signaling in the CeA, together with the shift in the DA/ACh balance described above, contributes to maintain excessive sugar consumption.

In summary, when offered daily prolonged access to a palatable sugar solution (or solid diet), rats voluntarily and readily consume it, and they also come to show behaviors and changes in the brain that are like what would be seen if a rat was dependent on or addicted to a drug of abuse, such as cocaine or heroin.

Neuroadaptive Changes Associated with Obesity in Humans

In line with the animal model research, there is mounting evidence showing that similar neural systems appear to be implicated in drug use and food consumption in humans, especially the opioid and DAergic systems. Further, when a food is rated more positively, the DAergic response to consumption of this food is elevated. Therefore, highly processed foods that are engineered to be extremely rewarding may be the most likely to trigger strong responses in these neural systems, which may translate into greater addictive potential for these foods. Moreover, obese individuals appear to exhibit neurobiological indicators associated with substance dependence. First, obesity and substance dependence are both related to greater DA-related neural activation in response to food cues and drug cues, respectively. For example, obese and substance-dependent individuals exhibit greater activation in the medial OFC, amygdala, insula, striatum, anterior cingulate cortex, and dorsolateral prefrontal cortex during exposure to relevant cues. Second, obesity and substance dependence are both linked with reduced availability of D2-like DA receptors. This effect is associated with less activation in reward-related regions (i.e., medial OFC, dorsal striatum) during food consumption and drug consumption, respectively. Interestingly, recent findings suggest that the DA reduction may be more of a late-term consequence of overeating and weight gain, rather than the original cause of obesity. Instead, the cause of overeating may more likely be high activation of food reward circuits. Subsequent overstimulation of those circuits by eating tasty foods, or the accumulation of extra satiety signals as obesity grows, may gradually suppress the systems, as an exaggerated form of the normal suppression that occurs after a meal. Therefore, a condition connected with excess food consumption (i.e., obesity) may share considerable neurobiological overlap with substance dependence.

Some cases of intense binge eating might also result from inappropriate activation of brain reward circuits. For example, particular individuals who show an intense binge eating disorder, with addictive-like features of loss of control and relapse, have been suggested to carry gene alleles that code overactivation of opioid receptors and DA receptors. This might elevate “liking” and “wanting” for food

rewards to unusually intense levels. Similarly, particular individuals, people born with a monogenic-based deficiency of leptin, become obese early in life and have exaggerated liking ratings for foods and their brains show high NAc activation by food stimuli measured by fMRI, even if they have recently eaten a full meal.

Finally, a new study found similar patterns of neural activation for substance dependence and addictive-like eating behaviors. A sample of young women ranging from lean to obese was shown a milkshake cue and a neutral cue during an fMRI paradigm to examine neural differences in food-cue responses. During the paradigm, participants also consumed a milkshake and a tasteless solution to explore neural differences in consummatory response. Individuals who endorsed a higher number of food addiction symptom scores based on the YFAS exhibited greater activation in the amygdala, anterior cingulate cortex, caudate, dorsolateral prefrontal cortex, and medial OFC during exposure to a palatable-food cue (i.e., picture of milkshake) relative to a neutral cue (i.e., picture of a glass of water). This pattern of neural activation has also been found in substance dependence and has been implicated in elevated levels of craving and incentive salience for substance-related cues. In relation to consummatory differences, food addiction was associated with less activation in the lateral OFC during milkshake consumption relative to the tasteless solution, which has been implicated in disinhibition for substance-dependent individuals. The results of this study suggest that food addiction and other addictive behaviors appear to share similar neurobiological underpinnings. Thus, in humans, similar behavioral and biological factors are implicated in substance dependence and problematic patterns of eating.

Assessment of the Relative Addictive Potential of Sugar

There exist clear behavioral, psychological, and neurobiological commonalities between palatable foods and drugs of abuse in both animals and humans. Little is known, however, about the relative rewarding and addictive potential of the former compared to the latter. For instance, are hyperpalatable foods, such as those high in sugars, as addictive as cocaine which is currently the prototypical drug of abuse? This information will be useful in updating the hierarchy of addictive substances and activities and in helping to prioritize public health action. In the recent past, the direct comparison of the behavioral and neurobiological effects of nicotine – which was initially thought to be nonaddictive – with those of cocaine or heroin contributed substantially to changing public awareness about the addictive potential of some tobacco products. In light of the difficulties inherent in conducting direct comparisons between hyperpalatable foods and drugs of abuse in humans, this question was again first explored in controlled laboratory experiments using rats.

To assess the relative rewarding and addictive value of sugar, cocaine self-administering rats were allowed to choose between drinking water sweetened with sucrose (or saccharin) or taking an intravenous bolus of cocaine (Fig. 97.3). Cocaine, especially when it is delivered rapidly to the brain following smoking or intravenous injection, induces intense rewarding sensations that are thought to

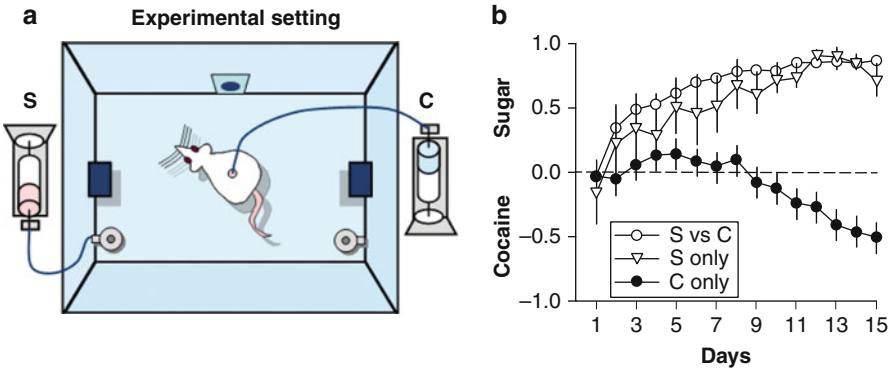

Fig. 97.3 (**a**) Experimental setting. The diagram represents the top view of a rat facing a choice between two actions: pressing the right lever to receive an intravenous dose of cocaine (*C*) or the left lever to have access to a drinking cup containing sweet water (*S*). (**b**) Main outcomes. This panel shows that when facing a choice (*S* vs. *C*), rats prefer sweet water over cocaine. As expected, when only one option is available (*S* or *C* only), rats orient their choice toward it

contribute to its addictive liability. At the neurobiological level, cocaine boosts DA signaling in the ventral striatum by inhibiting the DA transporter. In addition to these acute effects, extended use of cocaine also induces long-lasting structural and functional synaptic changes in several brain regions that may explain some of the behavioral symptoms of addiction, including escalation of cocaine use, increased motivation, and tolerance to punishment.

To make their choice, rats had to press on one of two levers, one associated with sweet water, the other with cocaine (Fig. 97.3). Each daily choice session consisted of several discrete, spaced trials. During each trial, the cocaine- and sweet-associated levers were presented simultaneously, and rats were free to respond on either lever to obtain the corresponding reward. When one reward was selected, the two levers retracted simultaneously until the next trial. As a result, selecting one reward excluded the alternative reward, thereby allowing rats to express their preference. As it turns out, rats developed a rapid and marked preference for sweet water and almost completely ignored cocaine, a finding that is consistent with previous research in rats with concurrent access to cocaine and saccharin. Importantly, the large majority of cocaine self-administering rats refrains from cocaine use not because the available dose of cocaine is too low. Gradually increasing the dose of cocaine up to the subconvulsive dose of about 3 mg/kg has no or little effect on cocaine choice, even after a history of extended access to cocaine. This lack of dose-dependent effect on cocaine choice shows that for most cocaine self-administering rats, the value of cocaine is bounded with a maximum lower than the value of sweet water. In support of this interpretation, cocaine choice was shown to increase when the concentration of sweet water is decreased or when the relative cost of sweet water is increased. However, for most rats, it takes a large

decrease in magnitude or a large increase in cost to shift preference to cocaine, showing that the reward value of sweet water is largely higher than that of cocaine.

As mentioned above, following extended access to cocaine self-administration, rats are more likely to escalate their consumption of cocaine and work harder for and take more risk to obtain the drug, suggesting an increased drug value. Thus, a key issue is whether preference for sweet water can be overridden by this increase in cocaine value. To answer this question, rats were first allowed to have daily extended access to cocaine self-administration during several weeks before choice testing (i.e., 6 h per day, 6 days a week). As expected, following extended access to cocaine self-administration, most rats escalated their consumption of cocaine. Surprisingly, however, when offered a choice between cocaine and sweet water, most rats rapidly acquired a strong preference for the latter regardless of the cocaine dose available. Thus, although the value of cocaine increases during extended drug self-administration, this increase is not sufficient to override sweet preference, at least in the majority of individuals.

Using a different approach based on food demand elasticity, it was recently estimated that the reward value of food, including sucrose, is much greater than that of intravenous cocaine in hungry rats from different strains. This difference in value persisted even following chronic cocaine self-administration and evidence for escalation of cocaine self-administration. These observations are also consistent with older, though often overlooked, experiments showing that under some circumstances, palatable foods can compete with direct electrical stimulation of brain reward circuits. Finally, a recent study using optogenetic methods showed that when offered a choice, mice prefer sucrose over direct stimulation of midbrain DA neurons. Altogether these different findings suggest that palatable diets, in general, and sweet diets, in particular, can clearly be more rewarding – and thus potentially more addictive – than intravenous cocaine in laboratory rats. Though one cannot, of course, directly extrapolate these findings to humans, they should nevertheless contribute to prompt a serious reconsideration of the hierarchy of potentially addictive substances and activities, with certain palatable foods and drinks, particularly those rich in sugars and fats, possibly taking precedence over major drugs of abuse.

More speculatively, these findings suggest that hyperpalatable foods may act as supernormal taste stimuli. A supernormal stimulus is an artificially engineered sensory stimulus that is more effective than naturally occurring stimuli in releasing behavior and therefore is difficult to resist and override. For instance, as shown originally by the Nobel Prize–winning ethologist Nikko Tinbergen, by exaggerating some egg features (e.g., size, color, patterns), some brooding birds can be made to choose the fake eggs over their own eggs. Similarly, since the concentrations of sugars found in many modern commercially available foods and drinks are exaggerated compared to those that can be found in nature, one can consider these products as supernormal taste stimuli to which it is difficult not to respond. Thus, in a certain sense, these supernormal stimuli could be considered as producing a hijacking-like process of the brain circuits that normally elicit eating but to the detriment of natural foods (e.g., fruits).

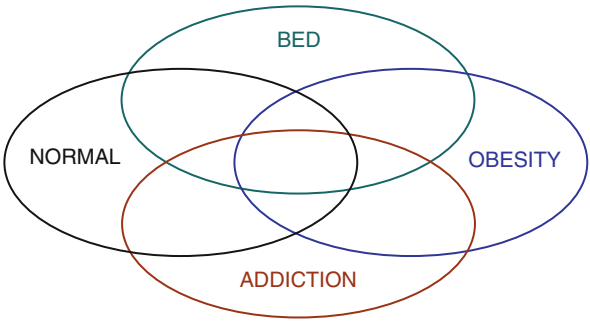

Fig. 97.4 Proposed relationship between food addiction, binge eating disorder (*BED*), obesity, and normal body weight

Implications for the Current Obesity Epidemic

An important direction in understanding the implications of food addiction is the role it may play in the elevated consumption of high-calorie foods and obesity. Although a specific quantity of excessive consumption is not explicitly stated in the current diagnostic criteria for substance dependence, it is implicit in many of the criterion (e.g., more of the substance is consumed than intended). Therefore, if certain people are addicted to food, it would follow that they would excessively consume certain foods. This pattern of eating may lead to the development of obesity and other diet-related diseases, such as diabetes (see Fig. 97.4).

Yet, it is important to consider the differences between obesity and addiction. Obesity is defined by a body mass index (BMI) equal to or greater than 30 with no explicit definition of how one got to that point. Moreover, obesity is a multifaceted disorder than can arise from factors other than excess food consumption, such as physiological dysfunction (e.g., thyroid disorder) and a lack of physical exercise. Thus, equating obesity with food addiction would likely lead to overidentification of addictive eating behaviors for individuals who are not consuming food in a problematic way. Further, even if obesity was caused by overconsumption of food, this would not definitely prove the existence of food addiction. In other words, one can excessively consume an addictive substance without meeting the criteria for substance dependence. For example, large numbers of college students drink alcohol in large quantities (e.g., binge drink), but a significantly smaller portion of college students are alcohol dependent. Therefore, someone may be obese due to the consumption of potentially addictive foods, but they may not become addicted to these foods. Finally, the impact of overconsumption of foods on BMI can be masked through the use of compensatory mechanisms, like compulsive exercise or periods of fasting. Thus, assuming that obesity is synonymous with food addiction would also likely lead to underidentification of food addiction for normal-weight participants. As substance dependence is designated by a number of behavioral criteria, using these same criteria to understand addictive-like eating behaviors will likely lead to the most precise identification of food addiction.

Currently, there is limited empirical evidence that explores the relationship between obesity and food addiction. Up to this point, food addiction as measured by the YFAS has typically been explored in samples with a limited range of body weights. For example, the preliminary validation of YFAS was conducted in a sample of participants that were mostly normal weight and the examination of YFAS in BED included all obese participants. In both of these studies, the association between food addiction and BMI was not significant. The study that explored the neural correlates of food addiction did include young women that ranged from normal weight to obese, yet there was also no significant association between food addiction and BMI. In other words, participants with elevated food addiction scores appear to be normal weight, as well as obese.

To more effectively understand the association between food addiction with dietary problems and obesity, further studies will need to be conducted. Specifically, the examination of food addiction in studies of dietary intake (e.g., food diaries, food-frequency recall) and compensatory behaviors will lead to a greater understanding of food consumption and weight-management practices in addictive-like eating. Further, given the restricted weight ranges in previous studies, the exploration of food addiction in samples that are sufficiently powered and have participants with a wide range of BMIs will likely result in a greater understanding of the role of addictive eating in obesity. To more fully understand the time course, it will also be essential to conduct longitudinal studies on the relationship between food addiction and obesity. For example, it is possible that symptoms of addictive eating could cause overconsumption of high-calorie foods, which could result in obesity. In contrast, obesity could precede the development of addictive eating, which could then lead to further weight gain or difficulty in losing weight. Finally, individuals who are normal weight, but are exhibiting symptoms of food addiction, may be at greater risk for the future development of obesity and may be an important target for prevention.

Another relevant consideration is the relationship between BED, food addiction, and obesity. Previous studies have identified a strong association with BED and obesity. As BED and food addiction share many characteristics (e.g., diminished control, continued use despite negative consequences), it is possible that addictive eating may only increase the risk of obesity when it co-occurs with BED. Similarly, it is possible that BED might mediate the relationship between food addiction and obesity. In other words, the development of addictive-like eating behaviors may increase the likelihood of BED, which would then result in obesity. It is also possible that food addiction increases the likelihood of obesity even when BED is not present. For example, even when accounting for a diagnosis of BED, eating disorder not otherwise specified (EDNOS) is the most prevalent type of eating disorder diagnosis. It is possible that some of these unspecified cases of disordered eating may be accounted for by food addiction and may result in an increased risk of obesity.

Finally, if certain foods are capable of triggering an addictive process, subclinical issues with addictive foods may be widespread and may be the cause of weight gain. Take the example of alcohol consumption. Only 5–10% of individuals meet

the diagnostic criteria for alcohol dependence during their lifetime, but 90% of people consume alcohol. Further, alcohol-related problems are prevalent, such as health problems caused by binge drinking or injuries sustained while intoxicated. Alcohol is currently the third leading cause of preventable death in the United States, which is driven in part by individuals exhibiting subclinical problems with alcohol. If food can be addictive, it is likely that a similar pattern may be taking place. In other words, only a subset of individuals may be experiencing a clinical level of food addiction, but many people may be experiencing a subclinical degree of addictive-like eating which may be sufficient to increase consumption of high-calorie foods and elevate the risk for obesity.

Outlook

There is now compelling evidence for food addiction thanks to a flurry of recent research, involving both animal models and clinical research, on the neurobiology of sugar reward and addiction. First, controlled research on laboratory animals has demonstrated that increased availability and resulting overconsumption of sugar (mainly sucrose) can induce behavioral changes that recapitulate several behavioral features of addiction, including escalation of consumption, increased motivation, affective withdrawal, and continued consumption despite harmful consequences. Second, the diagnosis of drug addiction has been adapted to and validated for food consumption. Overall, similar to the experience of a person addicted to drugs, those who feel they are addicted to certain foods find it difficult to stop overeating despite the desire to do so and an awareness of the negative consequences on health, well-being, and self-esteem. Importantly, this diagnostic innovation has led to the discovery that the incidence of food addiction is comparable to that of cocaine addiction (i.e., about 10–15% of people or drug users, respectively) but considerably increases in patients with obesity. Finally, the taste of sweet is unique in being an innately and intensely rewarding primary sensory modality that is hardwired to the brain reward circuitry. The neural and molecular code of sweet taste and reward has now been almost completely cracked. However, though high-sugar foods do not hijack the reward system of the brain in a drug-like manner, there is evidence that they may act as supernormal reward stimuli. In addition, critical to the notion of food addiction, recent research on animals has demonstrated that chronic overconsumption of sugar-sweetened foods can induce long-term changes in brain reward neurochemical circuits that mimic those seen following chronic exposure to cocaine or heroin. Some of the resulting brain changes are similar to those documented in obese people using in vivo brain imaging. This comparability suggests that the latter changes are probably a consequence, at least partly, of food addiction and obesity. However, one cannot exclude from available evidence the possibility of a vicious cycle where some of these changes also preexist and predispose an individual toward food addiction and obesity, at least in some genetically specific populations.

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