

# Obesity and the Neurocognitive Basis of Food Reward and the Control of Intake<sup>1,2</sup>

Hisham Ziauddeen,<sup>3-5\*</sup> Miguel Alonso-Alonso,<sup>6</sup> James O Hill,<sup>7</sup> Michael Kelley,<sup>8</sup> and Naiman A Khan<sup>9</sup>

<sup>3</sup>Department of Psychiatry, University of Cambridge, Cambridge, United Kingdom; <sup>4</sup>Wellcome Trust-MRC, Institute of Metabolic Science, Cambridge, United Kingdom; <sup>5</sup>Cambridgeshire and Peterborough Foundation Trust, Cambridge, United Kingdom; <sup>6</sup>Laboratory of Bariatric and Nutritional Neuroscience, Center for the Study of Nutrition Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; <sup>7</sup>Anschutz Health and Wellness Center, University of Colorado, Anschutz Medical Campus, Aurora, CO; <sup>8</sup>Scientific and Regulatory Affairs, Wm. Wrigley Jr. Company, Chicago, IL; and <sup>9</sup>Department of Kinesiology and Community Health, University of Illinois, Urbana-Champaign, IL

## ABSTRACT

With the rising prevalence of obesity, hedonic eating has become an important theme in obesity research. Hedonic eating is thought to be that driven by the reward of food consumption and not metabolic need, and this has focused attention on the brain reward system and how its dysregulation may cause overeating and obesity. Here, we begin by examining the brain reward system and the evidence for its dysregulation in human obesity. We then consider the issue of how individuals are able to control their hedonic eating in the present obesogenic environment and compare 2 contrasting perspectives on the control of hedonic eating, specifically, enhanced control of intake via higher cognitive control and loss of control over intake as captured by the food addiction model. We conclude by considering what these perspectives offer in terms of directions for future research and for potential interventions to improve control over food intake at the population and the individual levels. *Adv Nutr* 2015;6:474–86.

**Keywords:** eating behavior, food intake and appetite regulation, obesity, food addiction, neuroimaging, cognitive control

## Introduction

Obesity is a serious global public health concern (1) with 1.46 billion adults and 170 million children categorized as obese (2). In the United States 1 in 3 adults and 1 in 5 children are estimated to be obese (3). Obesity prevention and treatment are important public health priorities in many industrialized nations. Unfortunately, thus far the results from controlled clinical trials in this area are disappointing, and macroenvironmental approaches (e.g., taxing or subsidizing certain foods, modifying access to foods) for improving dietary choices or weight status remain contentious (4).

Important changes in the food environment in recent decades have played a major role in this rising prevalence of obesity (1). A key one is the easy availability of relatively inexpensive, highly palatable, energy-dense foods with little anticipated risk of food scarcity (although not for all individuals). Further, these environments are rich in cues targeted at promoting food intake, for example, advertisements (5). Such cues can induce overeating during periods of hunger by amplifying the salience of food rewards (6), and they retain this motivational power even in the absence of hunger (7). In such environments in which maintaining the homeostatic goals of energy and nutrient balance do not present a challenge, overconsumption is thought to be driven by a more hedonic form of eating (8).

The term hedonic eating refers to intake driven not by metabolic need but by the reward experienced by consuming the food, particularly relevant for highly palatable energy-dense foods (9). We use the term here as a useful shorthand to describe this kind of food intake but acknowledge three caveats. First, food is a primary reward, and there are hedonic aspects to food intake in general. Second, hedonics is only one aspect of reward (see next section) and is important to consider the motivational and learning aspects of reward, which

<sup>1</sup> This article is a review from the symposium "Neurocognition: The Food-Brain Connection" held 28 April 2014 at the ASN Scientific Sessions and Annual Meeting at Experimental Biology 2014 in San Diego, CA. The symposium was sponsored by the American Society for Nutrition (ASN) and by educational grants from ILSI North America, the Dairy Research Institute, Kellogg Company, and PepsiCo.

<sup>2</sup> Author disclosures: H Ziauddeen and N Khan, no conflicts of interest. M Alonso-Alonso receives research support from Ajinomoto and the Rippe Lifestyle Institute and has been a scientific advisor for Wrigley and ILSI North America. JO Hill has received research support from the American Beverage Association, Coca Cola Company, and McCormick Science Institute and serves on advisory boards for General Mills, McDonalds, Walt Disney Company, Calorie Control Council, and Novo Nordisk. M Kelley is employed by the Wm. Wrigley Jr. Company, Chicago, IL

\* To whom correspondence should be addressed. E-mail: hz238@cam.ac.uk.

are more relevant to environmental cues. Third, when we consider intake in excess of homeostatic need (more precisely intake beyond the limits of the homeostatic system's ability to maintain balance over time without storing excess energy), the term hedonic eating seems to capture both this excess and its putative drivers, namely the rewarding aspects of food consumption.

However, despite an overall rightward shift, a normal variability remains in body weight to suggest that individuals vary in their susceptibility to overconsumption. Although this is likely mediated by multiple genetic and environmental factors (10), including the degree of and susceptibility to exposure to these environments, these factors ultimately affect the extent to which the individual is able to control his or her food intake. Over the past 2 decades interest has increased in how alterations in food reward processing in the brain relate to overeating and obesity (6). In this review we focus on the brain reward system and its role in the control of food intake. We begin with an overview of the system, which have been elegantly characterized through animal studies, and then examine the human functional neuroimaging studies of these systems in the context of obesity. After this we consider 2 different perspectives on the control of food intake: the first examines cognitive control of food intake and the second, loss of control over intake in a specific model of dysregulated eating, namely food addiction (FOA)<sup>10</sup>. Finally, we consider what research directions these perspectives suggest for the field and for the development of potential treatment interventions.

## Brain Systems Controlling Food Intake and Eating Behavior

The brain's reward and homeostatic systems are often considered separately when examining their roles in food intake and eating behavior. However, these systems are not structurally or functionally separate, so they are described together here.

The homeostatic system responsible for regulation of energy balance is centered in the hypothalamus which integrates neural and nutrient signals with hormonal signals that originate in the small intestine, pancreas, liver, adipose tissue, and brainstem (11). Two neuronal populations are critical in the arcuate nucleus of the hypothalamus: the orexigenic agouti related peptide (AGRP)/neuropeptide Y neurons and the anorexigenic pro-opiomelanocortin neurons. The organization of the circuit safeguards consumption as the preferred behavior, and destruction of the AGRP neurons in adult animals results in cessation of eating and death (11–13). Note however that animals can survive early life ablation of these neurons, and even adult animals if kept alive for a period can recover from such lesions (14). In close proximity to the hypothalamus are critical nodes of the

reward circuitry centered on the ventral striatum (VS): the nucleus accumbens (NAcc), ventral pallidum (VP), and the ventral tegmental area (VTA). Both the hypothalamus and VS receive inputs from the prefrontal (PFC) and orbitofrontal cortex (OFC) (15), the amygdala, and the hippocampus. The VS also receives inputs from the anterior cingulate cortex and a large dopaminergic projection from the midbrain (16).

Berridge and Kringelbach (17) describe three components of reward, liking, wanting, and learning, that are linked but yet dissociable in terms of their neural substrates. Liking and wanting, respectively, refer to the hedonic impact of and the motivation for a reward, and we focus on these 2 components here. Learning comprises the associations with and predictions about rewards. The animal literature implicates opioid and cannabinoid systems in hedonic experience and dopamine in the wanting and learning components (18). Distinct hedonic hotspots have been identified in the reward circuitry, sites where stimulation causes the amplification of hedonic liking reactions (19). In the rodent brain, such hotspots were identified in the NAcc, the VP, and the parabrachial nucleus of the pons. In the medial shell of the NAcc is an opioid hotspot, and stimulation here with opioid agonists produces vigorous enhancement of liking reactions to a sweet taste (20, 21). Interestingly, in the rest of the medial shell, opioidergic stimulation amplifies wanting without enhancing liking. An endocannabinoid hotspot that overlaps this opioid hotspot was also identified (22). Another opioid hotspot was identified in the posterior VP (23) which forms a bidirectional circuit with the NAcc hotspot to generate liking reactions (24). The VP hotspot appears to be the most crucial because only its destruction leads to the loss of liking reactions and their conversion to disliking reactions (6). For wanting, the mesolimbic dopamine system is the key neural substrate. Dopaminergic or electrical stimulation in this region enhances wanting and motivational responding with increased food consumption but with no enhancement of liking reactions (25, 26). Sensitization of this system (e.g., by drugs of abuse) leads to enhanced wanting that can occur in the absence of liking, even without declarative awareness (27). Indeed, wanting can occur even when the hedonic experience is aversive; electrical stimulation in the lateral hypothalamus causes increased intake alongside disliking reactions to sucrose in rats (28).

As mentioned before, these systems are not separate. The lateral hypothalamic area (LHA) is thought to integrate homeostatic and reward-related information (29) and through its projections, to modulate the VTA and brainstem nuclei such as the nucleus tractus solitarius, critical in the modulation of gut signals and satiety signaling (11). Another important link is the endocannabinoid system. CB1 receptors in the hypothalamus mediate the activity of the arcuate nucleus of the hypothalamus and LHA neurons that project to the nucleus accumbens (30, 31). Both systems are also modulated by hormonal signals from the circulation. Leptin and insulin modulate the activity of the AGRP and pro-opiomelanocortin neurons, serving as adiposity-negative feedback signals. Low

<sup>10</sup> Abbreviations used: AGRP, agouti-related peptide; BED, binge eating disorder; dlPFC, dorsolateral prefrontal cortex; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; D2, dopamine-D2 receptor; FOA, food addiction; LHA, lateral hypothalamic area; NAcc, nucleus accumbens; OFC, orbitofrontal cortex; PET, positron emission tomography; PFC, prefrontal cortex; VP, ventral pallidum; VS, ventral striatum; VTA, ventral tegmental area; YFAS, Yale Food Addiction Scale.

concentrations signal lower peripheral energy stores and promote food consumption, with leptin having a much larger effect (11). The gastric peptide ghrelin serves as a hunger signal at the hypothalamus and brainstem (32, 33), whereas gut peptides such as cholecystokinin, glucagon-like peptide-1, and peptide YY, serve as satiation signals (34, 35). These signals also act on the reward circuitry, either directly or via projections from the hypothalamus and brainstem nuclei such as the nucleus tractus solitarius. Leptin LepRb neurons from the LHA project to the VTA and NAcc (36). These projections seem to inhibit VTA neurons and increase levels of tyrosine hydroxylase and dopamine in the NAcc (37), allowing leptin to modulate the incentive salience of food. Leptin-deficient individuals show intense drives for food, with strong striatal activation (using fMRI) that is unaffected by food consumption. Leptin replacement restores the normal pattern of activation and normalizes eating behavior (38). Glucagon-like peptide-1 concentrations were shown to correlate with increased blood flow in the dorsolateral PFC (dlPFC), suggesting an enhancement of inhibitory control with satiation (39). Experimentally replicating physiologic concentrations of PYY<sub>3-36</sub> produces activation in the left caudolateral OFC, and this predicts subsequent food consumption (40). Ghrelin was shown to directly potentiate the VTA in animal models (41), and in humans supraphysiologic concentrations of ghrelin increase the neural response to food pictures compared with nonfood pictures in the amygdala, OFC, insula, and striatum (42). Finally, corticotropin-releasing factor and glucocorticoids play important roles in both systems, in their development (43) and in mediating stress-related responses (6), but also by affecting peripheral endocannabinoid signaling (44).

The aim here was to emphasize the connectedness of the homeostatic and hedonic circuitry. Perhaps the most elegant demonstration of this comes from the animal studies of salt depletion-induced salt appetite. In this state, both the palatability (45) and the neural coding of a normally aversive salty taste in the VP (46) change to resemble the normal response to an appetitive sweet taste. In addition, a cue that previously signaled the aversive salty taste acquires motivational salience and is able to elicit the anticipatory behavior previously elicited by the cue for the sweet taste (47), despite having never been experienced in the salt-depleted state. Alterations in homeostatic state change reward processing and behavior. A final point to emphasize is that the homeostatic system safeguards food intake but is sensitive to satiation. However, liking and wanting are go systems and, although the go signaling may attenuate with satiation, it does not switch to a stop state (6); that is, satiation may decrease liking for the food but does not make it aversive (48, 49)

### Studying Reward Systems in Human Obesity

Over the past 2 decades functional neuroimaging has enabled the study of the reward circuit in humans and how perturbations in these systems may occur in or lead to obesity. The techniques used have been fMRI and, to a much lesser extent, positron emission tomography (PET). PET imaging uses radioactive tracers that include ligands for

specific receptors to examine regional blood flow and receptor densities in the brain. fMRI relies on the changes in magnetic field that accompany blood flow changes in the brain by using the blood oxygen level dependent response. By using cognitive or sensory tasks (e.g., tasting liquid rewards in the scanner) targeted at specific processes, it is possible to delineate the functional neuroanatomy of the circuits involved in implementing those processes. This has mainly been with fMRI which is noninvasive and has relatively high spatiotemporal resolution but not of a level that allows examination of specific hypothalamic nuclei or neuronal subpopulations within a structure, which is an important limitation in this area (50). The design principles and assumptions of these fMRI experiments are shown in **Table 1**. The points made are not meant to detract from the findings of neuroimaging experiments but to advocate caution in their interpretation. Functional neuroimaging is an extremely useful tool that has great value in examining the brain mechanisms and in evaluating different models of brain function. What is measured in the scanner may not necessarily reflect what happens in the normal free-living state, for example, patterns of brain activation during peeling an apple were different when subjects did this inside the MRI scanner compared with when they did it outside the scanner (51). However, a more appropriate evaluation of the ecologic validity of fMRI findings is to establish their relations with other measures or with outcomes in the real world, that is, as explanatory or predictive variables.

Two broad approaches have been used in this field. The first has sought to identify a perturbation(s) in reward response that occurs in obese individuals but not in control participants, suggesting that the perturbed process may be relevant to obesity (as a cause, consequence, or correlation). The second approach has sought to characterize the activity of a particular part of the circuit and to examine its predictive value in terms of determining future food intake or weight gain. A third approach that may well become more prominent in the coming years is from neuroeconomics and food-related decision-making field (see next section). Relatively little work has been done in obese populations in this area, but this will no doubt happen shortly.

Presentation of food rewards as pictures (52), tastes (53), or smells (54) produces increased brain activation in the VS, caudate, putamen, and OFC. Not unexpectedly other rewards such as drugs (55), sex (56, 57), music (58), and money (59) produce similar responses. Studies have shown differential activation to food pictures in obese individuals compared with lean control participants in the VS and dorsal striatum, midbrain, OFC, and medial and lateral PFC (52, 60–64). The issue is not with the individual findings but with the lack of consistency among the different studies. With similar (although not identical) experimental paradigms, these studies have shown activations in different regions and in different directions. The same is true for the studies of anticipatory and consummatory food reward, whereby the prediction (from the drug addiction literature) was that of an enhanced anticipatory reward in obesity with

**TABLE 1** Design aspects of functional neuroimaging studies of reward processing in obesity<sup>1</sup>

Aspect	Details	Considerations
Design	Case-control obese cases (BMI > 30) vs. healthy weight controls. Some studies have also included bulimia and BED.	Obese cases are likely to represent heterogeneous phenotypes rather than a homogeneous case phenotype. This is particularly relevant in studies with typical sample sizes of 10–30. Cross-sectional designs cannot distinguish between causation, correlation, or consequence.
Reward processes of interest and experimental paradigm	Anticipatory and consummatory reward to cues predicting, and the actual receipt of liquid reward delivery compared with neutral liquid delivery. Brain responses to pictures of rewarding foods compared with pictures of less rewarding foods or neutral images.	There are 2 assumptions here: 1. A brain process that is specifically targeted by the experimental task is clearly defined. 2. The control condition (e.g. neutral liquid) adequately captures any other processes activated by the task, allowing attribution of any differences to the variable of interest. This is not always clear (e.g., differential responses to a picture of a burger compared with picture of a whole raw cabbage) can be due to a high- vs. low-calorie, appetizing vs. bland, or edible vs. not readily edible distinction or likely a combination of the above.
Outcome measure	Differential brain response to the test condition compared with the control condition, and how this differs between the control and obese groups	The outcome measure depends on the above factors and assumptions.

<sup>1</sup> BED, binge eating disorder.

a blunted consummatory response (53, 65–68). Although studies have shown alterations in anticipatory or consummatory reward (not always in the predicted direction), there is little consistent evidence for this specific pattern [see (69) for a review]. Further, for most of these findings, given the cross-sectional nature of studies, it is not possible to determine whether they are causal, correlational, or consequential.

The picture is more encouraging from the smaller group of studies that have used the fMRI signal as a predictive variable. Stice and colleagues (70) demonstrated that the blunting of the striatal response to the receipt of chocolate milkshake predicts weight gain over the subsequent 6 mo. This blunting of response was also related to polymorphisms of the Taq 1A allele (53) and more recently to a multilocus score of different dopamine-related genes (71). Food cue-related activity in the NAcc was shown to relate to subsequent snack food consumption in healthy women, and neither of these was related to hunger or explicit wanting or liking for the snack. However, a relation with BMI was only seen in women with lower self-control scores (72). Burger and Stice (73) presented women with repeated exposures to cues predicting imminent milkshake receipt. Subjects with the greatest increase in VP responsivity to food reward cues and greatest decrease in caudate response to the milkshake had significantly larger increases in BMI over the subsequent 2 y. Indeed the decreased caudate response to milkshake was shown to negatively correlate with BMI (74). In adolescents greater striatal activation to food advertisements was shown to correlate with weight gain over the subsequent year (75). Collectively, these studies indicate the potential value of fMRI as a tool to study vulnerabilities to weight gain. They also urge caution in drawing direct links

between altered brain responses and obesity, given that even here there seem to be other mediators such as impulsivity and self-control.

In summary, we have encouraging findings of reward dysfunction in obesity, but the lack of consistency does not allow us to make firm conclusions about its nature at present. Although some of these inconsistencies may relate to experimental differences, a much more important factor is likely to be the inherent heterogeneity of the obese phenotype in these studies. More precise phenotypes are needed in which specific mechanisms can be examined and also for newer methods that can be used in experimental settings less restrictive and more ecologically valid than the MRI scanner.

### The Control of Hedonic Food Intake: Cognitive Control

Cognitive control is the ability to orchestrate thought and action in accordance with internal goals (76). Despite liking and wanting being go systems embedded in environments where highly rewarding foods are widely available, individuals are able to control their hedonic intake (to varying degrees) in line with ethical motivations, religious beliefs, and health and fitness goals. Critical here is the ability to self-regulate consumption (i.e., resist immediate food rewards) to achieve/maintain long-term goals (77).

A widely held view of food-related decision making is that we are rational, reflective, and goal-directed decision makers. According to neuroeconomic models this involves first assigning goal values to all options under consideration and then selecting the one with the highest goal value (78). This is implemented by a set of the critical nodes in the PFC:

the OFC integrates internal state information with the sensory and reward aspects of foods, the dlPFC codes longer-term attributes such as health and the expected taste reward from the foods, and the ventromedial PFC computes the goal values from these inputs (79, 80) and sends this output to effector circuits (such as the motor cortex) that implement the decision. The dlPFC is also a key area for executive functions, for example, inhibitory control, working memory, cognitive flexibility, and planning (81–83). Inhibitory control is closely related to the personality trait of impulsivity, defined as behavior characterized by poor planning, premature actions, that may be risky or inappropriate to the context, without due consideration of the (often undesirable) consequences (84). As Dalley et al. (84) have astutely pointed out, this encompasses multiple components: acting without due consideration of the available evidence (reflection impulsivity), failing to inhibit actions (impulsive action), accepting smaller immediate rewards over larger delayed rewards (impulsive choice/delay discounting), and behavior that puts the individual at risk of harm. Although there are different perspectives on how these functions and their elements are conceptualized (85), in considering cognitive control of food intake, we can think of the interplay between executive control and impulsivity as a core aspect of self-regulation, with executive control keeping longer-term goals and consequences in mind and reining in the tendency to impulsive choice and actions.

Inhibitory control and trait impulsivity are the most studied areas in the human literature. By using questionnaire measures of trait impulsivity or laboratory measures such as the stop-signal reaction task, it has been shown that obese adults and children have higher impulsivity (86–87), and this relates to greater intake, weight gain, and poorer response to weight reduction treatments (88–90). Obese individuals show steeper delay discounting, even with monetary rewards (91). A recent systematic review of executive function studies in obese adults found overall an executive impairment, but the variability in the measures used did not permit the determination of a consistent pattern (92). A systematic review of studies in children and adolescents is more compelling. Once again, there is the issue of the variability of measures used, but inhibitory control in particular emerges as a strong factor. Two points are particularly striking. First, impairments in executive function are seen in obese children from a young age. Second, poorer executive function is related to BMI later in childhood and adolescence. Better inhibitory control (particularly from a young age) seems to protect individuals from future weight gain. Studies of self-regulation and the ability to delay gratification in young children have shown that better performance on these measures is predictive of lower subsequent weight gain in adolescence and adulthood (93–95). Further, the degree to which an individual is able to develop this capacity can determine their ability to lose weight and more critically maintain weight loss. Obese individuals show lower levels of dlPFC activation in response to food (96, 97) and higher levels of disinhibited eating (98). However,

formerly obese individuals who successfully maintain their weight loss show greater dlPFC activation in response to food (99, 100), lower levels of disinhibited eating, and greater dietary restraint (101–104), suggesting that these mechanisms can be successfully learned.

Do these cognitive impairments cause obesity or vice versa? This is unlikely to be straightforward, given the multiple mechanisms involved in the development of obesity. However, these may be interacting mechanisms (i.e., poorer inhibitory control causes overeating) which worsens the cognitive impairment (105). The determinants of these mechanisms likely extend into the prenatal period. Feeding rat mothers a diet rich in fatty, sugary, and salty snacks during pregnancy and lactation enhances the preference for junk food and increases the propensity for obesity in the offspring (106). Extensive animal work shows the deleterious effect of overeating, particularly of high-fat and -carbohydrate foods, on brain structure and function [for a review see (107)]. Of particular note is the finding that rats fed a Western diet exhibited cognitive impairments even before developing substantial excess body weight gain (108). Less direct evidence comes from the human studies that show an association between obesity and decreased brain volume (109, 110) and the association between obesity and later life cognitive decline and dementias (111).

Although there is strong focus on goal-directed decision making in food choice and intake, given that we make several food-related decisions everyday [as many as 200–250 by some estimates (112)], it is extremely unlikely that every single decision is a considered goal-directed one. In fact, it is likely that many of these decisions are more habitual, driven by internal (e.g., hunger, stress) and external (e.g., advertisements, foods) cues without much deliberation (80, 113). This is certainly a more rapid and efficient way to make these decisions but a less flexible one [although it is possible that cognitive control mechanisms can be triggered unconsciously (114, 115)]. We emphasize this point because these cognitive control mechanisms may, to some extent, be enduring personality traits and cognitive styles that endow individuals with varying degrees of control over their habitual choices and intake, thus determining their weight trajectories perhaps even from early childhood. However, they can also be successfully learned as demonstrated by formerly obese individuals who maintain their weight loss.

### **Loss of Control over Hedonic Food Intake: FOA**

At perhaps the other extreme from using strong cognitive control for weight loss and maintenance is the idea of FOA, inherent in which is loss of control over intake. Two ideas in the literature are key as to what FOA is (70, 116). The first is that certain foods, specifically highly palatable foods rich in fat and sugar, are addictive and like drugs of abuse activate brain reward systems and induce patterns of overeating that resemble drug addiction. The second is that certain individuals (with obesity) show a pattern of food-related behavior characterized by loss of control over intake and compulsive consumption despite adverse

consequences, which strongly resembles the behavioral syndrome of drug addiction. We shall consider both of these in turn but emphasize that they are not mutually exclusive.

Can certain foods be potentially addictive? Rats allowed intermittent access to high-sugar and high-fat foods develop escalating, binge-like eating (117, 118). Enforced abstinence from sugar and administration of the opioid antagonist naloxone results in a withdrawal syndrome with a behavioral (enhanced anxiety, teeth chattering, forepaw tremor, and head shakes) (119) and neural profile (low levels of dopamine and high levels of acetylcholine in NAcc) similar to that seen in drug withdrawal (119, 120). This is not seen in animal models of intermittent access to fat (118). Importantly, these animals do not become obese (121) because their daily intake remains unchanged, but a larger proportion of it occurs during the intermittent access period (117, 118). However, when fat and sugar are combined in cafeteria diets with foods such as bacon and cheesecake, animals increase their intake and gain weight (122–124). Their eating becomes compulsive, and they continue to seek food despite aversive consequences such as electric foot shock (122–124).

What neural mechanisms underlie these changes? In animals bingeing on high sugar and fat, even those who are sham fed (food is consumed orally but is removed immediately via a gastric cannula), the enhanced dopamine release in the NAcc that occurs with food exposure fails to habituate with loss of novelty (125–127). Animals on cafeteria diets show reductions in presynaptic dopamine and, although palatable foods still produce a dopamine response, the response to standard chow is blunted (128). In the sugar-bingeing and the cafeteria diet animals, striatal dopamine D2 receptor values fall (119, 122). In the latter animals, brain self-stimulation thresholds (the minimum intensity of electrical stimulation in the lateral hypothalamus that will maintain self-administration of the stimulation by the animal) increase and remain elevated 2 weeks after cessation of the diet. This indicates early and persistent alteration of reward thresholds (122), suggestive of the development of a reward deficiency state similar to drug addiction (129). The overall picture shows strong similarities to animal models of drug addiction. An important conceptual issue to consider is that, although these changes occur in areas implicated in drug addiction, in drug addiction they are thought to represent a hijacking of the food reward circuitry by drugs of abuse, so it is not surprising to see similar areas here. However, Carelli et al. (130, 131) have shown that distinct populations within the accumbens respond to food and drug rewards, but we do not have sufficient spatial resolution to detect these subpopulations with human neuroimaging.

The animal literature presents compelling proof of concept for the FOA model with the combination of high fat and sugar producing the most striking phenotype. This is important but unfortunately does not help us identify a putative agent which becomes an important issue as we move on to consider the human literature on FOA which is mainly based on the behavioral syndrome of FOA (132). This is modeled on the criteria for substance dependence from the Diagnostic and Statistical Manual of Mental Disorders,

Fourth Edition (DSM-IV) (136), which were translated into equivalents for food, but this translation is not entirely satisfactory (Table 2).

Three conceptual issues are important to consider [for a review see (116)]. The first issue is that DSM-IV substance dependence criteria (136) are defined as behavioral criteria for an addictive agent, and it is difficult to apply them without such an agent. The FOA literature considers hyperpalatable and/or highly processed foods to be key (137–139), although these are not an explicit part of the criteria. To refine this model and to develop interventions that are based on it, a more precise definition of the addictive agent(s) will be necessary to be able to say what composition of a common food, such as cheesecake, would make it hyperpalatable and addictive. The second issue is that, although these clinical criteria are behavioral, they have been validated by a large body of neuroscientific research that has examined their neural underpinnings, and this broader understanding is part of the clinical syndrome; that is, both the syndrome and the term addiction imply a specific set of underlying neural mechanisms. Behaviors that look like addiction would suggest, but do not on their own confirm, the possibility of an addiction syndrome (i.e., anatine morphology alone does not confirm anatine identity). We emphasize this because FOA does derive some legitimacy from comparisons with this broader understanding of drug addiction. The third issue is that drug addiction results from the combination of an addictive agent, an individual with vulnerabilities to drug addiction, and time. Only 15% of individuals who use drugs develop dependence (140). This is especially critical when the substance (food) is universally consumed (although not necessarily in the aforementioned hyperpalatable forms), but some individuals may develop a FOA. This is not easily examined in a body of work that, given the infancy of the field, is almost entirely cross-sectional in design. It is acknowledged that FOA is not a general mechanism to explain overeating and obesity, but one that may be relevant to specific subgroups with obesity (although theoretically an individual could be addicted to food and not, or not yet, be obese), the strongest candidate being binge eating disorder (BED) (141). However, the case has been made that such potentially addictive foods present a risk to the population at large (142).

The human model of FOA was operationalized in the now widely used Yale Food Addiction Scale (YFAS) for adults (139) and more recently for children (143). However, the scale has certain limitations [Table 2; for a review see (116)]. Without a clear addictive agent it is difficult to identify features of its consumption that discriminate use from abuse/addiction. The scale applies severity thresholds and an overall distress/impairment criterion to determine whether an individual is addicted. There is also a danger of circularity. The YFAS is designed to capture eating behaviors that may be addiction-like, so certain aspects of its validity hinge on the degree to which FOA is a valid model of disordered eating. The potential circularity is as follows: FOA exists because certain people are defined as food addicts on the YFAS; the YFAS is valid because it can identify FOA.

**TABLE 2** Comparison of the DSM-IV substance use criteria and the YFAS<sup>1</sup>

DSM-IV criteria for substance dependence	YFAS equivalent	Comment
Persistent desire for and unsuccessful attempts to cut drug use.	Persistent desire for food and unsuccessful attempts to cut down the amount of food eaten.	Without a clear agent or substance this criterion requires the application of severity and impairment thresholds to be meaningful. The YFAS asks about certain foods and gives examples of energy-dense and fast foods and does indeed apply severity and impairment thresholds.
Larger amounts of drug are taken than intended.	Larger amounts of food are eaten than intended.	As above.
Substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem caused or exacerbated by the drug.	Overeating is maintained despite knowledge of adverse physical and psychological consequences caused by excessive food consumption.	As above.
Great deal of time spent on getting, using, or recovering from using the substance.	Great deal of time is spent eating.	As above. Less useful to distinguish use from abuse or addiction for foods, given their easy availability in most developed societies.
Important social, occupational, or recreational activities are given up or reduced because of substance abuse.	Activities are given up because of overeating or recovering from overeating.	
Tolerance: increasing amounts of drug are required to reach intoxication.	Tolerance: increased amounts of food are required to get the same pleasure or relief from negative emotions.	Tolerance and withdrawal have not been demonstrated for any foods. The proposed equivalents are not convincing, particularly given that in substance dependence these relate to physiologic adaptations that occur with sustained substance use.
Withdrawal symptoms on drug discontinuation, including dysphoria and autonomic symptoms (such as shakes and sweats).	Withdrawal symptoms such as anxiety, agitation, or other physical symptoms.	Importantly, tolerance and withdrawal are not seen with all substances and may not be relevant to foods at all. However, despite being poorly characterized by the YFAS, these criteria are strongly endorsed by participants in studies that use this measure (133–135).

<sup>1</sup> DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; YFAS, Yale Food Addiction Scale.

The YFAS is nevertheless a popular research tool, and numerous studies have used it to examine the prevalence of FOA in different populations. We focus here on the studies that have sought to validate the model and to examine its mechanisms. Much of this work focused on an association with BED (133, 141), which is classified as an eating disorder in the DSM. BED is characterized by recurrent episodes (binges) of uncontrolled, often rapid consumption of large amounts of food, usually in isolation, even in the absence of hunger. Eating persists despite physical discomfort, and binges are associated with marked distress, guilt, and disgust. Binges can be triggered by negative mood states that are not necessarily ameliorated by the binge (144). Here, we have a behavioral syndrome, more convincingly like that of drug addiction, including loss of control of eating, escalating consumption, and possibly consuming to ameliorate dysphoric and negative effects (145). It appears that the face validity of the FOA construct is strongest when it is applied to certain (although not all) individuals with BED (133, 141). An important caveat is that, although BED is associated with obesity, a substantial number of people who show binge eating behavior are not obese, and most obese people do not have BED (146). Three studies found

high values of comorbidity between BED and FOA as defined by the YFAS as follows: 72% (141), 56.8% (133), and 41.5% (134). The considerable overlap between FOA and BED and also other eating disorders such as anorexia and bulimia nervosa (147–149) raises the following important question: is FOA a unique nosological entity?

Determining the underlying mechanisms may help answer this question. Davis and colleagues (150) found that participants who met YFAS criteria for FOA showed a distinct composite genetic index of dopamine signaling, suggesting that these individuals may have some degree of up-regulation in the dopamine system, a finding complemented by the demonstration that the genetic profile's effect on YFAS scores was mediated by craving, bingeing, and emotion. The evidence most cited in support of the model however comes from the field of neuroimaging, from PET and fMRI studies of obese individuals. The first and most influential finding was the demonstration of lower values of striatal D2 receptors in obese individuals than in control participants, a pattern similar to that seen in drug-dependent individuals (151). This study compared severely obese individuals (BMI > 40 kg/m<sup>2</sup>) with controls (BMI < 30 kg/m<sup>2</sup>) and there was a considerable overlap between the groups. Since then,

this finding has been replicated twice with different approaches (152, 153), although at least 3 studies have failed to replicate it (154–156). The 1 study that specifically looked at individuals with BED did not find any difference in D2 receptor binding in this group compared with non-BED obese individuals (157). With the use of PET, Guo et al. (158) showed that increasing BMI is related to increased D2 receptor binding in the dorsal striatum and decreased binding in the ventromedial striatum. As already described in the functional neuroimaging section, no single mechanism has been consistently implicated in obesity, let alone an addictive one. To date only 1 study has specifically examined people phenotyped with the YFAS and found that individuals with higher FOA scores showed greater responses to anticipation of food in the anterior cingulate cortex, OFC, and amygdala (159). However, these findings were not entirely as predicted, and some of these effects were driven by a decreased response to the control taste rather than an increased response to the food. More importantly, 46 of 48 subjects did not qualify for a YFAS diagnosis of FOA, so the scores were treated as a continuous variable and the sample was divided into high and low scorers in the analyses. Interpretation of these findings therefore depends on the validity of the scale and the extent to which the scores do represent a real continuous variable, and any conclusions must necessarily be tentative.

In summary, the animal evidence for the FOA model is supportive. The human evidence is still preliminary, and this may relate to the relative infancy of the field (69, 160, 161). Nevertheless, it is a compelling idea and perhaps most importantly offers an explanation for individuals who struggle to control their food intake and casts their difficulties in a more sympathetic light to others (162). Some investigators have suggested recently that instead of FOA, it may be more useful to think of an eating addiction (163) more akin to behavioral addictions, although some of the conceptual concerns raised in this section may apply here too.

## Toward Future Research and Treatment Strategies

**The FOA perspective.** Preclinical studies may be the most rigorous way to determine what the addictive agent/food might be. Synthesizing the data from the growing number of YFAS studies may help determine which criteria are most informative and discriminatory. It may well transpire that a precise addictive agent may not be critical and that substance addiction is not the most appropriate human model for FOA. Longer-term prospective studies would help define the natural history of FOA and refine the phenotype. One valuable approach may be to study individuals who score highly on the YFAS as an extreme phenotype of FOA. Such work in extreme phenotypes could be performed in parallel in animal models and may offer critical insights into the syndrome and its underlying mechanisms.

What about potential interventions? If it could be established that certain foods are addictive, this could reasonably demand a policy response that would look at the important

issues of availability of and access to such foods, particularly in vulnerable groups such as children (142, 164). The issue is not that we lack evidence from other lines of health research to justify such policies, but that there are multiple challenges, including political will, industry agreement, issues of individual choice, and restricting access to particular groups and individuals. However, a confirmed FOA may change the picture because it invokes a specific model of state responsibility as for other substances (142). At the individual level, if FOA can be validated as a clinical disorder, it could suggest different treatment approaches for these individuals. These may include controlled consumption of or abstinence from specific foods, psychological treatments such as individual cognitive behavior therapy or 12-step programs to help individuals gain control over their eating. It is important to note that cognitive behavior therapy approaches for binge eating do not advocate avoidance or abstinence as addiction treatments do, but instead they focus on decreasing dietary restraint and enhancing the individual's sense of control over food (165).

**The cognitive control perspective.** Although a lot of research into the mechanisms of cognitive control have been done, large-scale intervention trials in overeating and obesity are few, though some of the preliminary evidence is compelling (166). Given the link between impulsivity and inhibitory control and obesity, this would be a good treatment target. Another potentially valuable strategy is to capitalize on the shared neurocognitive links between physical activity and eating behaviors. Habitual physical activity and healthy diet appear to share an interactive and reinforcing relation (167, 168), and physically active individuals were observed to exercise higher cognitive restraint of appetite (169). In addition, physical activity may potentially build cognitive resources or inhibitory control to down-regulate or reduce sensitivity to impulsive drives that underlie overeating (168). Aerobic fitness has been shown to correlate with cognitive control and its neural substrates in both children and adults (170). This hypothesis needs direct investigation to demonstrate this important additional benefit of physical activity. Finally, there is the possibility of modulating food reward via strategies based on cognitive enhancement, which include a growing list of nonpharmacologic options, such as foods/nutrients, physical activity, sleep, and computerized training (171). A key area of further research in this field is the identification of treatment targets and the development of interventions that can be evaluated, and this is an aspect of the field that is still at an early stage.

A particular appeal of successful cognitive control approaches is their potential to be developed as preventative public health interventions. The data on the role of early life inhibitory control in determining BMI strongly support the ongoing interest in intervening in childhood. The development of a validated treatment approach that could be included in school curricula as a group level intervention/training to improve inhibitory control, for example, could have an important population-level effect over time, not



only on weight but possibly on other health-related behaviors such as substance use.

## Conclusions

In this concluding paragraph we return to the food environment and particularly to food-related cues, which remain a relative constant whether we consider the addictive potential of certain foods or the ability to exercise cognitive control over intake. Such cues are ubiquitous, on television, street signs, and in the media. They can motivate consumption even in the absence of hunger and bias choices toward them (172). Advertising fosters associations between these cues and activities such as sport and socializing, and the relation between branding and advertising and food intake has been demonstrated (75, 173, 174). Although we may think of ourselves as rational arbitrators of food-related decisions, much of our food decisions are probably habitual, established by experience and driven by environmental cues (80, 113), which are not in short supply. The challenge for the individual is to control his or her intake in the face of an onslaught of such cues, and this would be particularly difficult for individuals with particular neurocognitive vulnerabilities such as poor inhibitory control. However, changing the food environment will be a major challenge that will require a collaborative effort by scientists, health care workers, industry, and lawmakers. Certainly, one appeal of the FOA idea is that, if this were to be conclusively demonstrated, it would provide an important and different impetus to this effort.

## Acknowledgments

We thank Kent C Berridge for providing valuable feedback on the manuscript and Chor San Khoo, Frances Coletta, Heather Steele, and Beth Bradley for their assistance in organizing the symposium at the ASN Scientific Sessions and Annual Meeting at Experimental Biology 2014. All authors read and approved the final manuscript.

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