OPINION

Obesity and the brain: how convincing is the addiction model?

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Abstract | An increasingly influential perspective conceptualizes both obesity and overeating as a food addiction accompanied by corresponding brain changes. Because there are far-reaching implications for clinical practice and social policy if it becomes widely accepted, a critical evaluation of this model is important. We examine the current evidence for the link between addiction and obesity, identifying several fundamental shortcomings in the model, as well as weaknesses and inconsistencies in the empirical support for it from human neuroscientific research.

Obesity, which has a profound impact on personal well-being and on the demand for health care, is at pandemic levels[1]. Central to weight gain is the development of an energy imbalance, a situation that arises as a result of complex interactions between an individual's biology and environmental factors[1,2]. Clinicians, researchers and politicians recognize the importance of understanding how the brain interacts with an obesogenic environment and the corresponding potential for neuroscience to develop our understanding of the causes and consequences of obesity. The messages now emerging from the neuroscientific research community may therefore have an unprecedented impact on policy development.

A fast-growing consensus is that obesity might be understood within the same neurobiological framework as addiction and that research, investigations, treatments and policy should be shaped accordingly[3]. Essentially, the view is that obesity results from an addiction to food that strongly resembles addiction to drugs, both behaviourally and in terms of underlying neural processes. This idea is exerting a tremendous influence on the field of obesity research and has driven cogent, although unsuccessful, arguments for the inclusion of obesity or overeating as a category in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-V)[4,5]. Although there has been debate about the validity of arguments for phenotypic similarity between overeating and addiction — and questions over whether such a model can generate realistic goals for policymakers[3] — one area that has not yet been critically scrutinized is the human neuroscience work that is often cited in support of the addiction model and that provides a pervasive framework for design and inference in human studies of overeating.

In this Perspective article, we describe how the addiction model has been applied to obesity and overeating and critically review each of the five main lines of research that are usually invoked to support this conflation. At the outset, it is important to acknowledge that the food-addiction literature has largely adopted the clinical model of addiction as defined by the DSM-IV. Although this model has clinical validity, in the addiction research literature it has been supplemented, and to an extent superseded, by powerful neurobiological models that have decomposed the clinical syndrome in terms of its core cognitive processes and their possible neural substrates (BOX 1). This approach, which is based on a growing understanding of the neurobiology of addiction, is welcome and — as we discuss — may offer new ways of identifying overlap between obesity and addiction. However, this article is primarily concerned with the existing arguments in favour of addiction as a model for obesity, arguments that draw on clinical definitions.

Obesity and addiction: two views

The addiction model has been applied to obesity in a number of ways. Central to each is the idea that someone can become a 'food addict'. What might this mean? Two broad ideas have been discussed. The first is that certain foods (those high in fat, salt and sugar[6–8]) are akin to addictive substances insofar as they engage brain systems and produce behavioural adaptations comparable to those engendered by drugs of abuse. This in itself is not surprising, given that current addiction models suggest that addictive drugs hijack the brain circuitry subserving the motivation for and enjoyment of, among other things, food[9,10]. What the putatively addictive foods are has yet to be fully defined. The case has been made that processed foods — as opposed to unrefined foods — are addictive because they have nutrient profiles, such as very high sugar content or combinations of high sugar and high fat, that are not found in naturally occurring foods[3,6]. However, this classification (processed versus unrefined foods) is very broad and imprecise, and it would ultimately be important to specify in more detail a particular substance or a level of nutrient (for example, a fat percentage) that would distinguish an addictive food from a non-addictive one. Sugar addiction, for example, has been demonstrated in animals, but not in humans. Indeed, the validity of sugar addiction as a concept that could apply to humans has been criticized[11].

A second view is that food addiction is a behavioural phenotype that is seen in a subgroup of people with obesity and resembles drug addiction. This view draws on the parallels between the DSM-IV criteria for a substance-dependence syndrome and observed patterns of overeating (TABLE 1). A quantitative measure of the features of the syndrome has recently been developed in the form of the Yale Food Addiction Scale (YFAS)[5,12–14]. However, although there seem to be some similarities between these two phenotypes, the overlap is only partial (TABLE 1). A related, but narrower, view asserts that a food-addiction phenotype is most apparent in individuals with binge-eating disorder (BED), which is

Box 1 | **The addiction model for drugs of abuse**

Influential models of drug dependence have divided the *Diagnostic and Statistical Manual of Mental Disorders IV* (DSM-IV) behavioural syndrome into several core processes that are involved in the transition from drug-taking to drug dependence in the subgroup of individuals who develop the syndrome. This transition involves a shift from voluntary drug-taking, under ventral striatal and prefrontal control, to habitual and compulsive drug-seeking, driven predominantly by the dorsal striatum, with loss of executive control over this behaviour[75]. Trait impulsivity, which relates to lower levels of striatal D2 dopamine receptors (D2Rs), has been shown to increase the vulnerability to this process[44,76]. Lower levels of striatal D2Rs may indicate a reward-deficiency state that leads to greater drug-taking in an attempt to achieve the same level of reward. The transition from initial impulsivity to later compulsivity has been proposed to progress through a three-stage model of anticipation and/or preoccupation; binge and/or intoxication; and withdrawal and/or negative effect[77]. Furthermore, drugs of abuse are also thought to sensitize the mesolimbic dopaminergic systems, leading to an enhanced salience of, and consequent motivation towards, drug-related cues as well as to cravings induced by such cues[78]. Increasing drug intake leads to neural adaptations in the striatum (further decrease of D2Rs) that promote compulsive drug-seeking and impaired inhibitory control[79], whereas adaptations in the amygdala counter the negative states of dysphoria and withdrawal related to drug use[77]. These adaptations serve to perpetuate the syndrome.

characterized by recurrent episodes (binges) of uncontrolled, often rapid consumption of large amounts of food, usually in isolation, even in the absence of hunger. This eating persists despite physical discomfort, and binges are associated with marked distress and feelings of guilt and disgust[15]. Once again, there is an important caveat: although BED is associated with obesity[16], a substantial number of people who show binge-eating behaviour are not obese and most obese people do not have BED.

A closer look at the evidence

At a population level, one of the main drivers of the rise in prevalence of obesity seems to be increased availability of food, with a consequent imbalance between energy intake and expenditure[1]. A modest energy imbalance over a sustained period of time can account for the observed changes in the body mass index (BMI) distributions of populations[2,17]. This suggests that any loss of control of eating, which is important to the idea of obesity as addiction, is very subtle in most of the obese population. Moreover, in considering unhealthy food choices and consumption, we cannot ignore social circumstances. For example, limited family budgets direct choice to more obesogenic foods[18]. However, as we note above, although obesity per se is often linked to addiction, a more nuanced view suggests that if food addiction produces obesity, it is likely to do so only in certain individuals with disordered eating behaviours such as BED[15,19,20]. Here, we consider both perspectives.

There are five key pieces of evidence cited in support of the addiction model: first, a clinical overlap between obesity (or, more specifically, BED) and drug addiction[15]; second, evidence of shared vulnerability to both obesity and substance addiction; third, evidence of tolerance, withdrawal and compulsive food-seeking in animal models of overexposure to high-sugar and/or high-fat diets[21]; fourth, evidence of lower levels of striatal dopamine receptors (similar to findings in patients with drug addiction) in obese humans[22]; and fifth, evidence of altered brain responses to food-related stimuli in obese individuals compared with non-obese controls in functional imaging studies. Below, we consider each of these in turn.

Table 1 | **Modelling food addiction on substance dependence**

DSM-IV criteria for substance dependence	Proposed food-addiction equivalent*	Comment
Tolerance: increasing amounts of drug are required to reach intoxication	Tolerance: increasing amounts of food are required to reach satiety	Not a convincing equivalent to drug tolerance because it assumes an equivalence between satiety and intoxication. In addition, key characteristics of binges are eating in the absence of hunger and to the point of physical discomfort (beyond satiety)
Withdrawal symptoms on drug discontinuation, including dysphoria and autonomic symptoms such as shakes and sweats	Distress and dysphoria during dieting	No convincing evidence of a human withdrawal syndrome for foods
Persistent desire for and unsuccessful attempts to cut drug use	Persistent desire for food and unsuccessful attempts to curtail the amount of food eaten	This criterion requires the application of severity and impairment thresholds to be meaningful
Larger amounts of drug taken than intended	Larger amounts of food eaten than intended	This criterion requires the application of severity and impairment thresholds to be meaningful
A great deal of time is spent on getting the drug, using the substance or recovering from it	A great deal of time is spent eating	It is difficult to apply this criterion because of the easy availability of foods in most developed societies
Important social, occupational or recreational activities are given up or reduced because of substance abuse	Activities are given up through fear of rejection because of obesity	A strict equivalence would require engagement in eating to the exclusion of other activities
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	This criterion requires the application of severity and impairment thresholds to be meaningful

*Data in second column are taken from REFS 5,14. DSM-IV, *Diagnostic and Statistical Manual of Mental Disorders IV*.

Clinical overlap. Substance dependence is defined in the DSM-IV by the presence of characteristic patterns of behaviour (TABLE 1), and it has been suggested that similar patterns characterize obesity[5,6,14]. Although some features (persistent desire, unsuccessful attempts to cut down and continued use despite negative consequences) translate reasonably well from substance abuse to overeating[6,14], others do not. Tolerance and withdrawal are not convincingly observed in the human eating literature[14]. Furthermore, food, unlike drugs, is necessary for survival, is easy to obtain openly and does not (generally) provoke social opprobrium. As a result, it is difficult to apply criteria that relate to efforts expended in acquiring and consuming: such criteria are useful in addiction to separate use from abuse for purposes of a DSM-IV diagnosis, but have little value with respect to food.

As shown in TABLE 1, three criteria translate reasonably well from substance dependence to overeating. Crucially, drug dependence can be diagnosed if any three criteria are met. Extending this to food, an individual who ate more than intended (loss of control), dieted frequently and unsuccessfully (persistent attempts to cut down) and continued eating despite significant weight gain (continued use despite negative consequences) would meet the requisite criteria and be deemed a food addict. The YFAS has applied severity and impairment thresholds that must be met to satisfy the criteria[13]. Although this certainly may capture a pattern of eating behaviour that is abnormal, we question whether such an approach is sufficiently rigorous to constitute good grounds for assuming an addictive basis for overeating in research studies and in clinical policy decisions.

If we narrow our application of the concept to individuals with BED[15], who clearly have abnormal eating behaviour and a high prevalence of obesity[16], the argument becomes more convincing. We can recognize a behavioural syndrome more convincingly like that of drug addiction, entailing loss of control of eating, escalating consumption, compulsivity, restriction of activities, time spent in pursuing behaviour, and possibly consuming to ameliorate dysphoric and negative effects[23]. It seems that the face value of the food-addiction construct is strongest when it is applied to certain (although not all) individuals with BED[19]. Perhaps this highlights a key limitation of the current and pervasive DSM-IV-based model relating over-consumption to addiction. The syndrome as it is defined and measured captures a phenotype that may be too imprecise to evaluate rigorously (BOX 2).

Box 2 | **Towards a food-addiction model?**

We have argued that attempts to develop the food-addiction model by relating obesity to the current clinical definition of addiction (in the *Diagnostic and Statistical Manual of Mental Disorders IV* (DSM-IV)) have been unconvincing. A possible future direction that we feel offers more hope of identifying a convincing, useful clinical entity is to separate the consideration of a putative food-addiction model from both obesity and the DSM-IV criteria of substance dependence. This separation must be made for two reasons. First, food addiction, if it exists, may be a cause, a co-morbidity or possibly a consequence of obesity. Accordingly, food addiction may prevail in non-obese and not-yet-obese individuals. Therefore, obesity, particularly when assessed solely cross-sectionally by body-mass index (BMI), will be an unsatisfactory phenotype for food addiction. Second, the DSM-IV criteria for substance dependence translate poorly to food-related behaviours (TABLE 1) and, more importantly, these criteria aggregate core features (such as maintained use despite negative consequences) with markers of long-term use (such as tolerance) and severity of impairment (such as time spent in acquiring substance).

Future research into the possibility of food addiction would gain by becoming more focused and neuroscientifically driven in the following ways:

- By creating a more precise neurobehavioural definition of food addiction in which a core set of measurable behaviours is clearly defined (inability to control consumption, increased motivation to consume and persistent consumption despite negative consequences[75,80]). This would capture a range of problem-eating behaviours, including, but not restricted to, binge eating.
- By incorporating impulsivity, compulsivity and specific patterns of cognitive response as markers of vulnerability to and endophenotypes of the addiction[81].
- By applying current models of addiction that are based on recent empirical neuroscientific work. For example, demonstrating a transition from goal-directed food-seeking under voluntary control to compulsive habitual seeking and consumption driven by environmental cues[75].
- By relating more precise behavioural and cognitive phenotypes, rather than BMI, to neuroimaging findings and outcomes.

With these principles in mind, we believe that future work on food addiction could obviate the problems that have so far led to an inconsistent and contradictory literature.

Shared vulnerabilities. Another observation linking obesity to drug addiction comes from family studies indicating that there may be shared genetic susceptibilities to the two conditions. A family history of alcoholism is associated with an increased risk of obesity[24], and BED is associated with increased levels of substance-use disorder in relatives[25]. The possible contribution of specific genetic variants has been explored[26–28]. The most widely studied of these has been the *Taq*1A minor (A1) allele of the dopamine receptor D2 (*DRD2*) gene, which has been associated with alcoholism[29]; substance-misuse disorders, including cocaine[30], smoking[31] and opioid dependence[32]; and obesity[33]. However, many studies, including large meta-analyses that addressed concerns about population stratification and sample size, have failed to replicate these findings[34–36]. Moreover, this polymorphism is located 10 kilobases downstream of the *DRD2* gene, and convincing evidence of an effect on the expression or function of the receptor is lacking, although an association with lower levels of D2 dopamine receptors (D2Rs) in the striatum, measured by positron emission tomography (PET), has been reported[37,38].

Obese individuals with BED have also been reported to have a higher prevalence of a gain-of-function allele (A118G) of the μ-opioid receptor (*OPRM1*)[33] that has been associated with increased sensitivity to reward, greater preference for sweet and fatty foods[39] and substance addiction[40,41]. Indeed, sensitivity to reward is a personality trait that has been associated with obesity and drug addiction. It has been argued that, as in drug addiction, obese individuals have lower reward sensitivity (the reward-deficiency hypothesis[42]), resulting in a compensatory overconsumption. However, the relationship between BMI and reward sensitivity is not straightforward, and in some people overeating occurs in the setting of an apparently enhanced sensitivity to the hedonic aspect of food[43]. Reward sensitivity may be mediated by the *OPRM1* and *Taq*1A allele polymorphisms mentioned above.

Another personality trait, impulsivity — the tendency to initiate behaviour without adequate forethought of its consequences — has been identified as a risk factor for substance addictions[44] (BOX 1). This trait has shown a modest association with the *Taq*1A polymorphism[45,46] and has been shown to be higher in obese and BED individuals, correlating with food intake[47–49].

It is possible, therefore, that there are some shared vulnerabilities between drug addiction and obesity. However, this does not in itself strongly support an argument that the same processes occur in each condition.

Evidence from animal models. By far the strongest evidence for a food-addiction syndrome comes from animal models[50]. Using highly palatable foods and highly structured intermittent-access regimes, it has been possible to induce an addiction-like phenotype in rats. Rats with intermittent access to high-sugar and high-fat foods develop escalating, binge-like eating behaviours[21,51], a phenomenon that seems to be related to the palatability of the foods rather than their macronutrient composition[52]. However, this escalation of sugar and fat intake is offset by decreases in intake of their normal food supply, so although these animals become 'addicted', they do not become obese[53]. A different picture is seen when fat and sugar are combined (as in 'cafeteria' diets, in which animals are fed on foods such as bacon, cheesecake and chocolate), whereupon increased consumption and weight gain occur in the context of eating that appears more compulsive[54].

In the case of sugar 'addiction', enforced abstinence is associated with enhanced motivation towards food[55]. Moreover, a withdrawal syndrome, which can be induced by challenge with the opioid antagonist naloxone or by enforced abstinence, has also been demonstrated[56]. The features of the syndrome — including teeth chattering, forepaw tremor and head shakes — along with their induction by administration of an opioid antagonist, indicate an opioid-mediated effect of the high-sugar diet. In these withdrawal states, levels of dopamine in the accumbens fall and acetylcholine levels rise[56]. However, such a withdrawal syndrome has not been demonstrated with high-fat and cafeteria diets[51].

How do these behavioural changes relate to altered neural substrates? In animals binge-eating on high-sugar diets, the dopamine release that occurs with food exposure fails to habituate with loss of novelty, even in those that are sham fed (food is consumed orally but not digested because it is removed immediately by a gastric cannula)[52,57]. In animals binge-eating on sugar and those fed a cafeteria diet, striatal D2R levels fall[54,58]. Moreover, in the animals of the latter group, 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, indicating early and persistent alteration of reward thresholds[54]. These findings suggest the development of a reward-deficiency state similar to that seen with drugs of abuse[59,60]. Reductions in presynaptic dopamine have also been shown in animals on cafeteria diets, and their dopamine activity is reduced in response to standard chow but not palatable food[61]. A complementary finding is that obesity-prone animals have been shown to have lower baseline levels of dopamine[62,63].

In summary, highly controlled conditions for short periods of time can produce sugar dependence in rats, although this is not associated with obesity. Conversely, the combination of high fat and high sugar can produce a compulsive overeating syndrome, accompanied by obesity and the development of a negative anhedonic state. In both situations, there is a corresponding reduction in D2Rs. Notably, researchers who have carried out experiments evaluating food addiction in animals are at pains to point out that there are important differences between the effects of foods and drugs (for example, dopamine release in response to drugs persists across multiple administrations, whereas dopamine release induced by palatable foods ceases when the food is no longer novel or the animal is no longer hungry[21]). The necessity for highly specific food presentation in order to engender addictive behaviours is also an important consideration[64]. Given that the environments of humans are much more variable than those of laboratory animals, the degree to which models of food addiction in animals may extend to human obesity has yet to be explored.

Dopamine receptor studies in human obesity. In 2001, a landmark PET study demonstrated reduced striatal D2R binding in a group of obese individuals[22]. Importantly, D2R levels were negatively correlated with BMI. The ensuing inference, that obesity is characterized by striatal hypofunction, is consistent with a reward-deficiency account of overeating[22]. The idea is that overeating arises because there is less hedonic value in food, leading to compensatory overconsumption. Complementing this was the observation that D2R binding correlated with prefrontal metabolism[65], suggesting that striatal hypofunction is compounded by reduced inhibitory control. This work has been important in developing the addiction model of obesity, although such correlative, cross-sectional observations do not tell us whether the receptor changes occur as a consequence of, rather than a cause of, increased BMI. More importantly, subsequent PET studies have not produced consistent findings.

In studies on normal-weight participants, the act of consuming food was initially shown to be associated with a reduction in dopamine binding in the dorsal striatum to a degree that correlated with subjectively rated meal pleasantness[66]. However, in a subsequent study, the presence of food in the mouth was not associated with a significant change in striatal dopamine binding, although high levels of dietary restraint were associated with greater food-induced alterations in dopamine-receptor availability in the dorsal striatum[67]. Furthermore, using an elegant combination of drug challenge (methylphenidate compared with placebo) and stimulus presentation (food and neutral non-food stimuli), it was shown that food stimulation alone does not always have an impact on D2R striatal binding and that, although food stimulation combined with a methylphenidate challenge is associated with reduced dopamine binding, the same is true for the combination of methylphenidate and a neutral non-food stimulus (and, moreover, binding changes produced by the food–methylphenidate combination do not differ significantly from those found with a food–placebo combination)[68]. In short, PET data relating to dopamine binding and food consumption in normal-weight people are inconsistent, although this may be due, in part, to the different methodological approaches used, such as consuming versus tasting food.

Given the variability in dopamine responsivity to food stimuli in normal-weight humans, it is perhaps unsurprising that the picture in obesity is also inconsistent. Even in the first study, which showed reduced D2R availability in morbidly obese individuals (BMI range 42–60), there was considerable overlap with binding measures in healthy-weight controls[22]. In a more recent study[69], a comparable striatum-based analysis showed no difference in baseline dopamine-binding measures between overweight or obese individuals and normal-weight controls (although a subsequent voxel-wise analysis showed a thalamic difference that extended into the striatum). The negative correlation between BMI and striatal dopamine binding was not replicated. There are, of course, numerous reasons why one might expect differences between the original sample, which consisted of a group of people with a BMI of more than 40, and the more recent one, in which mean BMI was much less. For example, peripheral metabolic profiles might be

quite different, as might food intake. But the fact remains that reduced D2R binding is not a consistent correlate of BMI or obesity and, as such, this does not, as is usually claimed, provide consistent evidence in favour of the addiction hypothesis.

Perhaps the inconsistency is a consequence of the phenotypic complexity of obesity. However, a study focusing specifically on differences between binge eaters and BMI-matched controls[20] demonstrated neither a correlation between receptor binding and BMI nor group differences that accord with an addiction model. In BED, the combination of a food stimulus and methylphenidate was associated with reduced dopamine binding in the caudate, whereas in non-binge-eating obese individuals only the combination of a non-food stimulus and methylphenidate produced a significant change. Other studies examining the impact of bariatric surgery have also produced conflicting results, suggesting both decreases and increases in receptor binding subsequent to surgery[70,71].

In short, the message emerging from PET ligand studies is rather more complex than is frequently asserted. Although it has been shown that dopamine ligand binding is reduced in obese individuals, this finding has not been replicated, and studies involving challenges with dopamine-stimulating drugs and food-related stimuli produce complex results that do not corroborate an addiction model. Nor does a narrowing of the phenotypic question to BED do anything to clarify matters.

Functional neuroimaging. Functional neuroimaging is an important tool in testing the addiction model, which predicts that functional responses to foods and food-related stimuli in key reward-related brain regions should be consistently perturbed. This is not the case. Although studies exploring brain responses to food and food-related stimuli in normal-weight people have shown largely consistent activation in reward circuitry (including the amygdala, insula and striatum), the pattern emerging from studies comparing obese individuals and binge-eaters with controls is most remarkable for its variability and inconsistency (TABLE 2). A more specific prediction, based on the reward-deficiency hypothesis, is an enhancement of anticipatory responses and a reduction of consummatory responses to food rewards in obese individuals[72]. However, studies that explicitly distinguish between anticipation- and consumption-related brain activity are rare, and their results are equivocal.

TABLE 2 summarizes key findings from functional neuroimaging studies of children, adolescents and adults that explored brain responses to food-related stimuli (typically images) and to anticipation and consumption

Table 2 | **Summary of the findings of studies exploring altered brain responses in people with obesity or altered eating patterns**

Brain region	Response to presentation of food images				Response to cues signalling imminent presentation of food/juice reward (anticipation)				Response to consumption of reward			
	Obese	BED	BMI	FA	Obese	BED	BMI	FA	Obese	BED	BMI	FA
Regions associated with the reward circuitry												
Striatum	2 ↑[83,84], 1 ↓[85], 1 ↔[86]	2 ↔[87,88]	1 ↑[89], 1 ↓[90], 3 ↔[85,91,92]	NA	1 ↑[93], 1 ↔[94]	NA	NA	1 ↑[95]	5 ↔[93,94,96–98]	1 ↓[99], 1 ↔[100]	1 ↓[94]	1 ↔[95]
Midbrain	4 ↔[83–86]	2 ↔[87,88]	5 ↔[85,89–92]	NA	2 ↔[93,94]	NA	NA	1 ↔[95]	1 ↑[96], 4 ↔[93,94,97,98]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]
PFC (orbital)	1 ↑[86], 3 ↔[83–85]	1 ↑[87], 1 ↔[88]	3 ↑[90–92], 1 ↓[89], 1 ↔[85]	NA	2 ↔[93,94]	NA	NA	1 ↑[95]	1 ↑[96], 4 ↔[93,94,97,98]	1 ↓[99], 1 ↔[100]	1 ↔[94]	1 ↓[95]
PFC (lateral)	3 ↑[84–86], 1 ↔[83]	2 ↔[87,88]	1 ↑[85], 1 ↓[92], 3 ↔[89–91]	NA	1 ↑[93], 1 ↔[94]	1 ↑[101]	NA	1 ↔[95]	1 ↑[93], 2 ↓[97,98], 2 ↔[94,96]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]
PFC (medial)	2 ↑[84,86], 1 ↓[85], 1 ↔[83]	1 ↑[87], 1 ↔[88]	1 ↓[92], 4 ↔[85,89–91]	NA	1 ↑[94], 1 ↔[93]	NA	NA	1 ↑[95]	5 ↔[93,94,96–98]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]
Amygdala	4 ↔[83–86]	2 ↔[87,88]	5 ↔[85,89–92]	NA	2 ↔[93,94]	NA	NA	1 ↑[95]	1 ↑[93], 4 ↔[94,96–98]	1 ↓[99], 1 ↔[100]	1 ↔[94]	1 ↔[95]
Gustatory cortex (AI/FO)	1 ↑[83], 3 ↔[84–86]	1 ↑[87], 1 ↓[88]	3 ↑[89,90,92], 2 ↔[85,91]	NA	1 ↑[94], 1 ↔[93]	NA	NA	1 ↔[95]	3 ↑[93,94,96], 2 ↔[97,98]	2 ↓[99,100]	1 ↔[94]	1 ↔[95]
Hippocampus/PHG	2 ↑[84,86], 1 ↓[85], 1 ↔[83]	2 ↔[87,88]	1 ↓[85], 4 ↔[89–92]	NA	1 ↑[93], 1 ↔[94]	NA	NA	1 ↔[95]	5 ↔[93,94,96–98]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]
Brain regions not associated with the reward circuitry												
Thalamus	1 ↓[85], 3 ↔[83,84,86]	2 ↔[87,88]	5 ↔[85,89–92]	NA	2 ↔[93,94]	NA	NA	1 ↔[95]	5 ↔[93,94,96–98]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]
Rolandic operculum	4 ↔[83–86]	2 ↔[87,88]	5 ↔[85,89–92]	NA	2 ↑[93,94]	NA	NA	1 ↔[95]	2 ↑[93,94], 3 ↔[96–98]	2 ↔[99,100]	1 ↔[94]	1 ↔[95]

The table shows responses that were elevated (↑) or reduced (↓) in groups of obese individuals or those with binge-eating disorder (BED) relative to controls. No group difference is signified by '↔'. Numbers before the arrows indicate the number of studies. The table also shows studies reporting positive (↑), negative (↓) or no (↔) reported group difference between neural activity and body mass index (BMI) or food addiction (FA) scores. AI, anterior insula; FO, frontal operculum; NA, no reports available (at the time of writing); PFC, prefrontal cortex; PHG, parahippocampal gyrus.

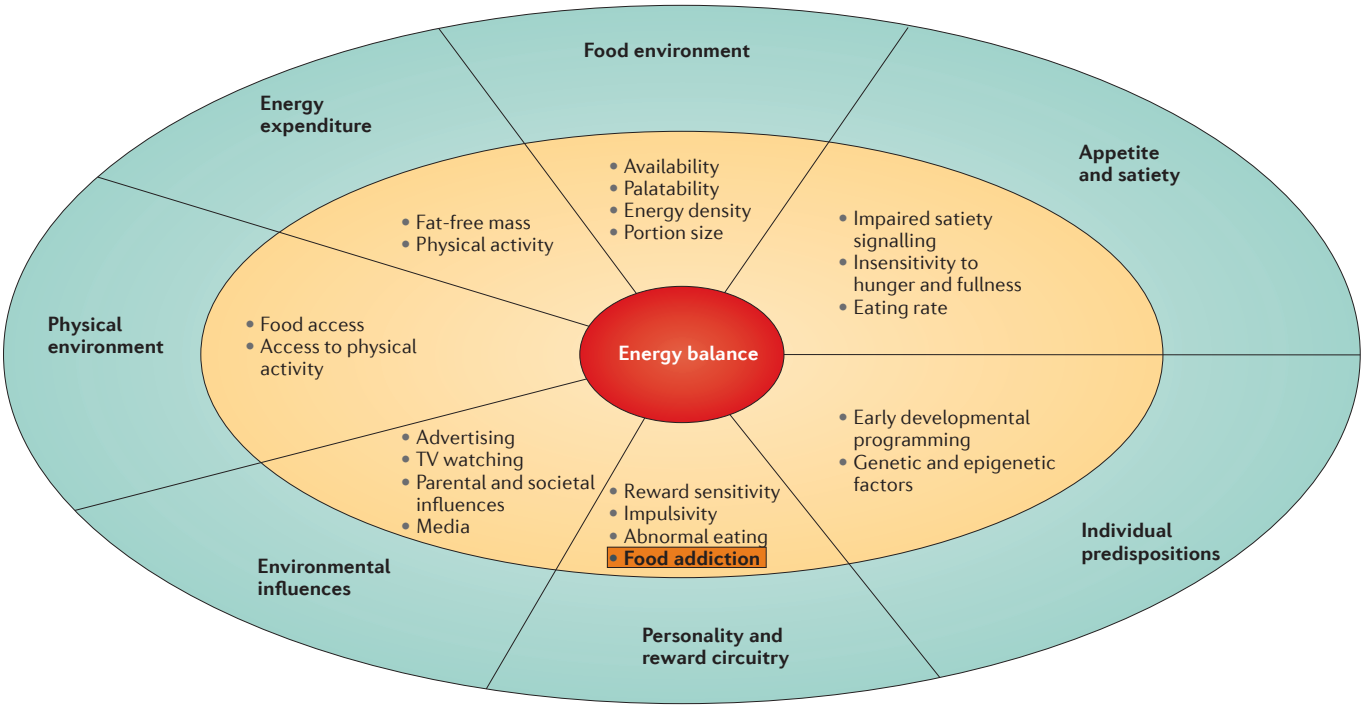

Figure 1 | **Mediators of energy balance and body weight.** The outer ring represents the major classes of mediators, the inner ring some of the individual mediators in each class. We suggest that food addiction is one of many factors in a more complex model of the obesity epidemic that require further exploration and refinement. The data on which the figure is based come from the Obesity Systems Map introduced by the UK Foresight programme 2007, a multidisciplinary effort to plan the UK response to obesity[82].

of actual food stimuli (typically milkshake). A number of approaches have been used to explore obesity and altered eating patterns. Case–control studies comparing obese individuals with normal-weight controls are typical and are complemented by analyses of the extent to which activity correlates with BMI and, in one study, with food-addiction score. Studies of binge eating (with bulimia nervosa or BED) have also been carried out. The findings shown in TABLE 2 indicate a striking lack of consistency across studies.

Of course, there are differences in tasks and stimuli across the studies and there are age and gender differences across the groups studied. But, given that the striatum, midbrain and prefrontal cortex are core components of the dopaminergic-reinforcement circuitry, the lack of consistent findings across a large set of studies militates strongly against the addiction model. If we consider the region of the anterior insula and frontal operculum that is sometimes referred to as the gustatory cortex, the inconsistency remains. Nor is observation of responses in the amygdala helpful in distinguishing obese individuals from normal-weight controls. The overwhelming message emerging from TABLE 2, even allowing for technical and participant differences, is that functional neuroimaging does not support the addiction model.

Functional neuroimaging allows us to measure not only regional responses but also inter-regional relationships. Alterations in these system-wide patterns have been assessed in association with external food sensitivity — the extent to which external food cues evoke the desire to eat[73] — and obesity[74]. Although intriguing observations have been made, particularly with respect to the regions described above (which constitute the 'reward circuitry'), it is too soon to judge whether connectivity studies will show a consistency that eludes regional measures.

There are two clear messages emerging from the functional neuroimaging literature on obesity and overeating. First, a growing body of work has not supported any single view of obesity and overeating. Second, even when analysis is confined to subgroups showing binge-eating behaviour, there has been no convincing or consistent pattern of abnormal responding in the reward circuitry. If the addiction model of overeating has currency beyond phenotypic similarities (which, as we argue above, are themselves weak), we would expect functional neuroimaging studies to identify core similarities. Why have they failed to provide any consistent insight into the behaviour of brain reward circuitry in overeating, let alone support for the addiction model? We find it hard to believe that such circuitry is unaltered. One possibility is that overeating and its consequences are just too complex to expect consistency when individuals are grouped simply according to BMI, or to binge-eating or food-addiction scores. Given that obesity and binge eating are complex phenotypes emerging for a host of genetic and environmental reasons, in failing to account for this complexity our capacity to identify group or factor-related differences is markedly reduced. Furthermore, both of these phenotypes have often been measured cross-sectionally, without taking into account the natural history of these conditions (BOX 2). We clearly need more precise behavioural, temporal, metabolic, genetic and cognitive profiling in such investigations. Moreover, the growing sophistication of cognitive neuroscientific models of addictive behaviours points to crucial process-specific alterations in regional responding. Dissecting out these processes will require more complex task-dependent measurements than are typically applied in overeating and obese individuals. In the future, those imaging studies that attempt to distinguish subtle processes and simultaneously take into account individual variability[27] will prove useful and important.

Conclusions and future directions

The view that overeating and obesity are directly related to addiction has provided impetus to a series of elegant studies testing this proposed link. Somehow, the view has emerged that, overall, these studies support the link. We challenge this view and argue that the work tells us three important things. First, the vast majority of overweight individuals have not shown a convincing behavioural or neurobiological profile that resembles addiction. Indeed, the enormous inconsistency emerging from a review of the neuroimaging literature tells us that in this highly heterogenous disorder, the application of a single model is likely to be more of a hindrance than a help to future research. Second, even when we refine the phenotype to characterize individuals who show obesity caused by BED, the evidence for an overlap with addiction is inconsistent and weak. Third, given the absence of good evidence, the ubiquitous influence of the addiction model of overeating and consequent obesity is remarkable. Now is a good time to question it and to acknowledge that adherence to it in the face of data that do not fit will lead to research that is too narrowly focused and, ultimately, misleading. Given the attention that is rightly paid to potential insights offered by neuroscience, there is an associated danger that clinical and policy recommendations will be misguided. We suggest that alternative approaches to exploring the brain's contributions to obesity be explored. Central to these is an explicit acknowledgement of the enormous heterogeneity of the condition, which requires further exploration and characterization. This characterization will, we anticipate, entail the use of cognitive neuroscience to provide useful phenotypic markers of the numerous pathways to obesity.

Our intention in this Perspective has been to urge caution against the hasty adoption of a model with limited applicability and supporting evidence. We do not deny that there may well be a place for an addiction model in the understanding of overeating and the spectrum of the obesity syndrome (FIG 1). However, successful development of such a model will demand a progression beyond existing clinical definitions of addiction to ideas that are guided by the developing neuroscientific literature (BOX 2). It will also demand sophisticated and precise delineations of altered eating behaviour in humans, and phenotypic markers that go well beyond simple cross-sectional measures such as BMI.

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Competing interests statement

The authors declare competing financial interests; see Web version for details.

DATABASES

Pathway Interaction Database: http://pid.nci.nih.gov

FURTHER INFORMATION

Behaviour and Health Research Unit:
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