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Binge eating, overeating and food addiction: Approaches for examining food overconsumption in laboratory rodents

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Abstract

Overeating ranges in severity from casual overindulgence to an overwhelming drive to consume certain foods. At its most extreme, overeating can manifest as clinical diagnoses such as binge eating disorder or bulimia nervosa, yet subclinical forms of overeating such as emotional eating or uncontrolled eating can still have a profoundly negative impact on health and wellbeing. Although rodent models cannot possibly capture the full spectrum of disordered overeating, studies in laboratory rodents have substantially progressed our understanding of the neurobiology of overconsumption. These experimental approaches range from simple food-exposure protocols that promote binge-like eating and the development of obesity, to more complex operant procedures designed to examine distinct 'addiction-like' endophenotypes for food. This review provides an overview of these experimental approaches, with the view to providing a comprehensive resource for preclinical investigators seeking to utilize behavioural models for studying the neural systems involved in food overconsumption.

Keywords

Palatable food; Self-administration; Obesity; Overeating; Preclinical model; Feeding

1. Introduction

In an environment where palatable foods are abundant and easily accessible, a multitude of factors play a role in why individuals overconsume. Understanding how these factors are encoded in the brain is thus an important step in determining why we often overeat beyond

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our energy requirements. To date, significant attention has focused on homeostatic feeding, whereby food intake is driven by nutritional need for survival and is governed by metabolic and satiety signals from the gut. However, in an environment rich in easily accessible palatable foods, the signals to eat or to stop eating are complex and extend beyond the control of the homeostatic system.

Critically, overconsumption of food in the absence of compensatory behaviour (such as purging or excessive exercise) can result in obesity (Duffey and Popkin, 2011; Swinburn et al., 2009), which has significant deleterious health consequences for the individual and imposes significant costs to society more broadly (Collaborators et al., 2017). Moreover, overconsumption is a core characteristic of eating disorders associated with binge eating, including binge eating disorder (BED) and bulimia nervosa (BN) (American Psychiatric Association et al., 2013), and is a feature of more subclinical forms of overeating such as loss-of-control eating and emotional eating (Anversa et al., 2021).

In an effort to better understand the neurobiology of overeating, there has been a recent proliferation of preclinical studies seeking to test non-homeostatic feeding outcomes in laboratory animals, particularly rodents. Collectively, these approaches have advanced our understanding of the basic mechanisms and neural systems involved in food overconsumption. Here, we provide an overview of these paradigms, with a particular focus on those paradigms that provide behavioural endpoints with relevance to loss-of-control eating. We seek to provide a comprehensive touchstone for preclinical investigators interested in studying food overconsumption and its behavioural, neurological and metabolic consequences.

1.1. How well can we model disordered eating in animals?

Animal models of human disease have proven of enormous value in identifying the basic mechanisms underlying various diseases and informing the development of more effective treatments. Within many areas of medical research, both clinicians and basic scientists enjoy the benefit of working within a coherent pathophysiological taxonomy. Sometimes, disease classification can be made at a molecular or cellular level and, therefore, more confidence exists with respect to the face and construct validity of animal models. However, the field of psychiatry is somewhat compromised in this respect, and is ultimately reliant upon classification criteria provided by the Diagnostic and Statistical Manual of Mental Disorders —Fifth Edition (DSM—V (Diagnostic and Statistical Manual of Mental Disorders : DSM-5, 2013)) and The International Classification of Diseases and Related Health Problems, Tenth revision (ICD-10 (World Health, 2004)), making the extrapolation of these diagnostic categories to laboratory animals challenging. Furthermore, modelling human psychiatric disorders in animals, including eating disorders and compulsive eating, is particularly challenging as it is almost impossible to capture the full spectrum of a psychiatric disorder in a single paradigm that can be performed in a rodent. Despite these challenges, the reward and feeding systems in the brain that underlie eating behaviour are highly conserved among species; eating is essential for survival and thus the circuits underlying ingestive behaviour have been maintained across evolution. In this way, laboratory animals offer a valuable model for studying both homeostatic feeding and reward, and thus significant progress has

been made in determining the biological basis of these processes (for recent reviews, see (Rossi and Stuber, 2018; Bulik et al., 2022; Guleken and Uzbay, 2022; Brown et al., 2022)).

Various paradigms exist that distinguish between consummately and appetitive components of reward. Indeed, under the right set of experimental parameters, rodents are capable of exhibiting patterns of food overconsumption that mimic some aspects of human conditions. Here, we provide a detailed overview of these procedures, as well as give some discussion to the construct, face and predictive validity of these models. Ultimately, as noted above, the multifaceted and complex nature of both the aetiology and behavioural symptoms of disordered eating means that animal models cannot recapitulate a particular disorder in its entirety. Thus, here we attempt to highlight the utility of these models, while simultaneously discussing their associated shortcomings. By means of clarification, the term 'animal model' is typically used to refer to the animal itself, either genetically engineered or the product of artificial selection (intentional or unintentional, as in the case of most common laboratory inbred rodents). Here, we seek to focus on approaches that promote patterns of food overconsumption that resemble disordered eating in humans, as well as behavioural assays/tests that can be used to quantify these outcomes.

2. Approaches to evaluating aberrant feeding behaviour in rodents

2.1. Free access/consummately/preference approaches

The most basic approach for assessing the rewarding properties of food in rodents is one that simply measures consumption of the specific food in question. This can occur in the home cage, in which case food must be weighed daily (which is both labour-intensive and prone to error), or the use of metabolic cages which provide automatic quantification of food intake (but may be associated with higher levels of stress and are therefore not recommended for chronic studies (Kalliokoski et al., 2013)). In the former, food can be weighed daily or less frequently depending on how critical it is that precise daily intake data is obtained for the study. Animals can also be examined for their preference to consume a specific reinforcer over another. In the case of liquid reinforcers such as sucrose, Ensure™ or an oil emulsion, the alternative liquid is often water. In the case of solid food, the alternative is often a control food that is as similar as possible to the test food in terms of micro and macronutrients except for the specific levels of the reinforcer in question. The consumption of the test substance/solution versus that of a control substance/solution can be compared and relative preference determined (Boggiano et al., 2007; Klump et al., 2013). When measured correctly, food intake and preference provide valuable information regarding consummately behaviour, particularly when compared to control food or liquids.

2.2. Paradigms that promote binge-like eating

The presence of 'binge eating' is central to the diagnosis of BED and BN and also occurs among individuals with an anorexia nervosa-binge eating/purge phenotype (American Psychiatric Association et al., 2013). Despite the wide prevalence of binge eating across the spectrum of eating disorders, there continues to be debate over how best to define binge eating, which in turn raises questions about how best to study this behaviour in laboratory animals. According to the DSM—V (American Psychiatric Association et al.,

2013), a binge is defined by both (a) eating a large amount of food during a discrete period of time (e.g. 2 h); and (b) a sense of loss of control over eating during the episode. As such, models of binge-like eating in rodents must seek to recapitulate these phenomena - i.e. eating over-and-above what is normally consumed by animals in the same amount of time, and ideally in a manner whereby a loss of control over behaviour can be observed. The cornerstone of promoting binge-like eating in laboratory animals is the utilization of intermittent or limited access to a particular food reward; this has been reliably shown to promote a gradual escalation of food intake across sessions, culminating in vigorous consumption of large amounts of food during the period of time in which food is available (Corwin et al., 1998).

There is some debate as to how important the size of the binge is when it comes to diagnosing binge eating. Given evidence that indicates that perceived loss of control is the key driver of the eating disorder pathology (Pratt et al., 1998), the concept of a 'subjective' versus 'objective' binge encapsulates the idea that is the individual's subjective assessment of loss of control over eating behaviour which is the defining characteristic of a binge (American Psychiatric Association et al., 2013). Recapitulating this phenomenon in animals is difficult, however the escalation of intake that characterizes limited/intermittent food exposure paradigms is often argued to reflect a progressive 'loss of control' (Goeders et al., 2009). Important also is the antecedent or driver of the binge-like eating episode: specific environmental conditions elicit binge eating in humans and these can be recapitulated in animals, including stress or negative emotion (acute or chronic – this being the most common driver of binge eating in humans (Anversa et al., 2021)), as well as availability of the food (e.g. intermittent periods of deprivation of access to palatable food or overall caloric restriction). For an elegant examination of the different approaches used to model components of binge-eating behaviour with the strongest clinical relevance, see (Hildebrandt and Ahmari, 2021). Below, we provide an overview of the most common approaches used to examine binge-like eating in rodents.

2.2.1. Binge models: limited access—Historically, the vast majority of studies examining binge eating in rodents have employed limited access paradigms, whereby animals are given free access to highly palatable food in their home cage for limited periods of time throughout either the circadian cycle (e.g. 1 h per day) or week (e.g. 3 times per week). This is often combined with periods of caloric restrictions which causes even more pronounced binge-like behaviour. Early work by Corwin and colleagues showed that intermittent access to vegetable shortening caused binge-like intake by rodents (Corwin et al., 1998; Corwin and Wojnicki, 2006). Under this intermittent protocol (2 h binge sessions, Monday, Wednesday, Friday), escalation of intake is observed, such that by the ~5th session rats consume around double what was initially consumed during initial binge sessions (typically this equates to 40-80 kcal in 2 h). Although no food restrictions were used, the authors discovered that binge rats compensate for the binge intake by restricting their consumption of standard chow on non-binge days relative to controls (Corwin and Buda-Levin, 2004). Corwin and colleagues also showed that animals maintained on this intermittent (Monday, Wednesday and Friday) schedule consumed more sweetened fat than animals that received daily 2 h access, suggesting that more episodic and restricted access

results in more pronounced binge-like behaviour (Corwin et al., 1998). Others have utilized an array of access schedules with success: varied exposure lengths from as short as 30 min to as long as 24 h have been demonstrated to successfully elicit binge-like eating, though typically an exposure period of between 1 and 4 h is optimal for promoting maximal binge-like intake (Kreisler et al., 2018).

Since the early work of Corwin and colleagues, evidence has accumulated demonstrating behavioural attributes in rodents exposed to intermittent access schedules that are reminiscent of behavioural features of binge-eating disorder. An elegant study by Furlong and colleagues (Furlong et al., 2014) showed that 1 h of access daily to sweetened condensed milk accelerates habitual control of behaviour compared to continuous access (see below for an overview of procedures to test habitual behaviour). Further, seminal work by Avena and colleagues showed intermittent access to a sugar solution results in the development of addiction-like behaviours (Avena et al., 2008): after several days of daily 12 h access, rats showed an escalation in their daily intake and binge-like consumption of a sugar solution, especially during the first hour of access. In addition, the rats changed their feeding pattern by taking larger meals of sugar within the limited access compared to continuous access control rats.

2.2.2. Binge models: caloric restriction—Boggiano (formally Hagan) and colleagues (Hagan and Moss, 1997) were the first to explore the effects of long-term food restriction and refeeding cycles (mimicking dieting behaviours) on subsequent eating behaviour. These authors reported that even up to 30d after resuming full feeding, rats with a history of restriction continue to exhibit persistent binge-like eating. In the years since, this finding has been recapitulated by several groups and it is now well-established that cycles of caloric restriction facilitate the development of binge-like eating behaviour in rodents (for recent reviews on this topic, see (Hildebrandt and Ahmari, 2021; Rehn et al., 2022)). Restriction is typically between 50 and 85% of daily intake and performed in cycles. Furthermore, by combining schedules of intermittent or limited access with cycles of caloric restriction, binge-like eating is further enhanced (Bello et al., 2009; Bello et al., 2019). Indeed, binge-eating prone rats subjected to restriction-refeeding cycles of chow and palatable food have been shown to tolerate higher amounts of foot-shock to gain access to palatable foods compared to non-cycled rats (Oswald et al., 2011). Further, repeated patterns of restriction and refeeding of homecage chow has been shown to impair the performance of goal-directed actions as well as the ability to reject a pre-fed food when it is offered alone (Ahn and Phillips, 2012; Parkes et al., 2017).

2.2.3. Binge models: stress—When protocols involving periods of caloric restriction followed by free access are combined with exposure to a stressor, pronounced binge-like eating is observed. The success of this type of protocol reflects the key role that stress/emotion plays in driving binge-like eating behaviour. Early studies of stress-induced binge-eating used a tail-pinch as the stressor, which often needs more than one session to alter feeding in rodents (Antelman and Szechtman, 1975; Antelman et al., 1975; Meadows et al., 1988; Aso-Someya et al., 2018). Administered chronically, the tail-pinch has been shown by some studies to induce overeating (e.g. 16 days of 10–15 min of tail-pinch) (Rowland and

Antelman, 1976), whereas others report the opposite (i.e. a supression of intake) (Goebel-Stengel et al., 2014; Hawkins et al., 2002). There has been a decline in the use of the tail-pinch stressor in recent years, which can potentially be attributed to the development of models that have higher face validity. Physical stressors, including footshock, have been used to induce binge-like eating, typically when repeated cycles of stress are applied in combination with caloric restriction or intermittent access to palatable food (discussed in (Boggiano and Chandler, 2006)). However, as with tail pinch stress, footshock has also been shown to reduce food intake (Kuriyama and Shibasaki, 2004). This is likely due to the complex relationship between stress and food intake: the typical response to severe stress is an anorectic response (Stammers et al., 2020), however if the stress is mild to moderate it is more likely to increase food intake (Goebel-Stengel et al., 2014; Rutters et al., 2009). Cifani and colleagues introduced a novel form of psychological stress – frustration – which has proven to be mild enough to consistently generate a robust bingeing response (Micioni Di Bonaventura et al., 2020). This approach similarly consists of periods of intermittent access combined with cyclic caloric restriction, except instead of being physical in nature, the ‘stressor’ is a frustrative experience: the food reward is placed in a cup whereby the rat can see and smell it but not access it for 15 min. This is followed by subsequent access to the highly palatable food reward where robust binge eating is consistently observed (Cifani et al., 2009).

Anversa and colleagues adapted this emotional stress protocol to mice and developed a model that does not require caloric restriction (Anversa et al., 2020). This protocol involves repeated cycles of exposure to the frustrative stressor (food reward is placed in a tea strainer in the homecage) and despite no history of caloric restriction, female mice will binge up to 1.5 g of chocolate/peanut butter chips in 15 min following exposure to the stressor (over half their daily caloric intake). This amount of food consumed is 70% higher compared to control mice who had the same access to food without the frustrative experience. The comparison of these two groups allows researchers to discern true ‘bingeing’ i.e. an amount of food consumed over and above what would be typically consumed in the same period of time – this is an advantage over standard limited access models which do not allow the same comparison. Interestingly, in the procedure developed by Anversa and colleagues, male mice do not exhibit the same response to this ‘emotional’ stressor, consuming similar amounts to control (no stress) mice. This observation adds face validity to this approach as it recapitulates a sex difference commonly observed in humans, whereby overeating is more commonly driven by stress and/or negative affect in females compared to males (Anversa et al., 2021).

2.3. Operant procedures

There are several ‘costs’ associated with seeking and consuming food, including the money and effort required to purchase the food, as well the negative consequences associated with overeating (e.g. stigma, embarrassment), and it might be argued that the free access procedures in rodents described above fail to adequately account for such imposts. In contrast, operant self-administration procedures allow precise experimental control over the relationship between a response and the food reinforcer, thus allowing for modifications of the ‘cost’ of obtaining a food reward. This is typically achieved by altering the number of

operant responses required to earn a food pellet, or by pairing the delivery of food with an aversive stimulus (e.g. footshock). Thus, at the most basic level, operant self-administration models provide information regarding the reinforcing efficacy of a particular substance (e.g. food, drugs). These paradigms also provide the opportunity to examine the role of classical conditioning in food seeking behaviour, as food can be paired with both discriminative and discrete stimuli to model different aspects of craving and relapse. Here, we provide a brief overview of operant paradigms commonly used to both induce and measure dysregulated feeding behaviour.

2.3.1. Fixed and progressive ratio schedules—Under fixed/progressive ratio schedules, animals are trained to make an operant response (typically a lever press or a nose poke) to receive a food reward (typically a pellet or a liquified palatable solution). Under fixed ratio (FR) schedules of reinforcement, the delivery of food reward is contingent on a fixed number of responses (e.g. a FR1 schedule requires one lever press to earn a reward; an FR3 schedule requires three lever presses to earn a reward, etc.). In contrast, under a progressive ratio (PR) schedule, the 'cost' of the reward is progressively increased over a number of trials to determine the maximal effort the subject is willing to exert for the reward (Hodos, 1961). The final ratio completed by the subject within a determined amount of time defined as the 'breaking point' and is commonly used as a proxy for the subject's motivation to earn the reward. Because PR schedules promote high levels of responding while also limiting the number of reinforcers earned, this paradigm avoids confounds associated with satiation during the tests (as in low-effort FR schedule; also see section on behavioural economics approaches, below) (Wojnicki et al., 2010).

Although dysregulated feeding is typically induced via the home cage paradigms described above, there are some examples of low-effort FR schedules being utilized to promote overeating. For example, rats allowed to self-administer chocolate flavoured high-sucrose (45%) pellets on an FR1 schedule for 1 h/day for 15d develop behaviours reflective of binge eating, including an escalation of intake and increased rate and regularity of sustained food responding, compared to rats allowed to self-administer regular chow (Cottone et al., 2012). Similarly, rats allowed short (1 h) or extended (6 h) daily access to highly palatable milk chocolate Ensure™ on an FR1 schedule exhibit greater 30-min caloric intake compared to ad libitum or chow access (Curtis et al., 2019). Higher-effort FR or PR schedules can also be used to measure motivation for food following induction of binge-like eating. For example, higher breakpoints for fat reward are observed in rats given intermittent home cage access to vegetable shortening compared to daily access groups (Wojnicki et al., 2010), and a similar trend is observed for chocolate Ensure™ in rats given extended (6 h) operant access to this type of food (Curtis et al., 2019).

2.3.2. Random ratio (RR) and random interval (RI) schedules—Certain operant reinforcement schedules have been shown to promote goal-directed vs. habitual patterns of food seeking (typically assessed on a devaluation procedure, discussed below). Under a random interval (RI) schedule, food reinforcement is delivered, on average, after n amount of time, contingent on a lever press. This schedule minimizes the perceived correlation between behaviour and reward, and promotes patterns of responding for food that are

impervious to outcome devaluation (i.e. responding is habitual) (Tantot et al., 2017). In contrast, under a random ratio (RR) schedule, a food reinforcer is delivered on average after n lever presses, a schedule that maintains a strong correlation between behaviour and outcome and maintains responding that is suppressed when the outcome (food) is devalued (ie. responding is goal-directed) (Derusso et al., 2010). Interestingly, when trained on a RI schedule, rats maintained on a high fat diet (HFD) exhibit reduced motivation (PR breakpoint) for a food reward, but develop habitual food seeking more quickly compared to controls. However, these deficits are abolished when HFD rats are subsequently trained on a RR schedule, indicating that the manifestation of aberrant feeding behaviours involves a complex coordination of goal-directed actions and habits that are dependent on reinforcement schedule (Tantot et al., 2017).

2.3.3. Behavioural economics—Behavioural economics has recently emerged as a powerful quantitative analysis of food self-administration behaviour. In this approach, which has also been successfully used to examine a range of different reinforcers (Bentzley et al., 2013; Bentzley et al., 2014; James et al., 2019a; Pantazis et al., 2021; Zimmer et al., 2012; James and Aston-Jones, 2022), consumption of a food reinforcer is examined across several ‘prices’, either by progressively changing the fixed ratio requirement to earn a food reward (Freeman et al., 2020; Giannotti et al., 2022), or by maintaining an FR1 schedule but successively decreasing the volume of reward (in the case of liquid sucrose, for example (Batten et al., 2020a)). An exponential demand equation (Hursh and Silberberg, 2008) is then applied to consumption data to compute demand curves, from which several key indices can be derived. Q_0 is an experimentally derived measure of food consumption when cost approaches zero, and is therefore a measure of consummatory behaviour under unrestricted conditions (sometimes referred to as the ‘hedonic set point’, or demand intensity) (Bentzley et al., 2013; Freeman et al., 2020). By contrast, demand elasticity, denoted by α, refers to the price sensitivity of consumption and indicates an animal’s willingness to ‘work’ to maintain their preferred level of consumption (Bentzley et al., 2013; Freeman et al., 2020). This approach has several advantages over the other operant measures of food motivation described above. For example, α values from demand curves self-normalize for differences in food consumption, and therefore are not dependent on factors such as palatability or baseline differences in consumption (Freeman et al., 2020). Moreover, demand elasticity is remarkably stable across sessions within an individual (Freeman et al., 2020), allowing for repeated assessment of a pharmacologic treatment on drug motivation. The behavioural economics paradigm is also highly translational; demand elasticity for food and other reinforcers is readily measured in humans via a hypothetical purchasing task, and the α and Q_0 parameters are derived using an identical approach to that used in rats (Buscemi et al., 2021; Epstein et al., 2018a; Epstein et al., 2018b; Murphy et al., 2016; Stojek et al., 2015; Stojek and MacKillop, 2017).

As noted above, the self-normalizing nature of demand elasticity permits direct comparisons of the motivational properties of various palatable foods regardless of baseline differences in their consumption. This approach is therefore extremely useful in determining the motivational properties of food reward in obese vs. lean rats, where baseline consumption is significantly different across groups. Indeed, Batten et al. (Batten et al., 2020a) recently

reported that obesity-prone rats have lower demand elasticity (higher motivation) for liquid sucrose and saccharin solutions compared to obese-resistant rats, indicating differences in reward processes in these rats that is independent of their intake under free access conditions. Moreover, Freeman and colleagues used a behavioural economics approach to show that although female rats have higher hedonic set points (Q_0 values; kcal normalized to body weight) than male rats for three types of palatable food pellets, they do not differ in their motivation to work for these foods (demand elasticity) (Freeman et al., 2020). Interestingly, demand indices (α and Q_0) for food are associated with total food consumption history, but not cued 'relapse' of food seeking or food choice (Heinsbroek et al., 2021). In light of evidence that α is negatively correlated with several addiction behaviours for drugs of abuse (Bentzley et al., 2014; James et al., 2019a; James et al., 2019b; Fragale et al., 2020; Fragale et al., 2019; Mohammadkhani et al., 2019), it might be expected that α for food might have some predictive value for problematic feeding patterns, however this remains to be comprehensively tested. It will be interesting for future studies to test whether baseline differences in Q_0 and α can predict, for example, animals most likely to be categorized as addiction-prone on operant models of 'food addiction' (discussed below) or to show exaggerated intake in a binge paradigm.

2.3.4. Extinction/reinstatement procedures—Persons often relapse to unhealthy eating habits shortly after attempting to control their food intake through dieting (Kramer et al., 1989). Attempts to understand this phenomenon have primarily utilized an adapted version of the extinction-reinstatement model, which was originally developed to study drug relapse behaviour in rats and consists of three discrete phases (for comprehensive reviews, see (Calu et al., 2014; Nair et al., 2009)). In the *training* phase, rats are trained daily to lever press for palatable food pellets on an FR schedule (typically FR1). Pellet delivery is often paired with the presentation of a discrete stimuli such as light + tones associated with the food's acute rewarding effects. Once responding is stable, rats transition to the *extinction* phase, whereby lever presses are no longer rewarded with pellet delivery or discrete cues, resulting in a gradual reduction in lever pressing behaviour. In the *reinstatement* phase, extinguished lever pressing is reinstated by presenting the animal with food-related cues, food priming and/or stress (described below). Reinstatement testing is conducted in the absence of food rewards, and thus reinstatement of lever pressing is considered an assessment of relapse to food seeking (as opposed to consumption) and thus a proxy of craving. Notably, in some studies, rats are food restricted during the extinction and reinstatement phases (~75% of daily intake) to mimic human dieting while abstaining from palatable foods; this does not appear to affect cued reinstatement behaviour (Cason and Aston-Jones, 2013), but is reported to result in stronger primed and stress-induced reinstatement (Nair et al., 2009).

Cued reinstatement: In a discrete cued paradigm, reinstatement is typically elicited by presenting rats with a single, non-contingent cue delivery at the beginning of the session; responses on the active lever then elicit cue delivery in a contingent manner. In a discriminative stimulus paradigm, reinstatement is elicited by presenting rats with non-contingent stimuli that previously indicated food availability (e.g. white noise, house light, olfactory or tactile stimuli; DS+). Other discriminative stimuli that previously indicated

the absence of food availability (DS−) fail to reinstate responding. Both discrete and discriminative cues reliably reinstate extinguished responding in rats trained to lever respond for palatable foods, including sucrose pellets and sweetened condensed milk (James et al., 2018; McGlinchey et al., 2016; Brown et al., 2016; Jupp et al., 2011; Grimm et al., 2002; Ghitza et al., 2007; Cervo et al., 2007; Martin-Fardon et al., 2018; James et al., 2012; Martin-Fardon and Weiss, 2014); it is unclear how this behaviour might be altered in rodents exposed to the limited/restricted access binge models described above. Note that this procedure is distinct from cue-potentiated feeding, whereby food-sated rats will increase their food consumption after presentation of conditioned stimuli previously paired with food while rats were food restricted (Holland and Petrovich, 2005; Cole et al., 2020). The latter phenomenon is an interesting approach for examining pathological consumption patterns that override internal regulatory signals (Holland and Petrovich, 2005; Cole et al., 2020); however, the effect of diet exposure and binge-like eating on these outcomes is not known. Context-induced reinstatement: Food-associated contexts/environments can also potently renew palatable food seeking. In the ‘renewal’ or ‘ABA’ design, rats are trained to self-administer food in one context (A), before lever pressing is extinguished in a different non-food context (B). During the reinstatement test, exposure to the original food self-administration context (A) reinstates palatable food (e.g. sucrose) seeking behaviour (Bossert et al., 2006; Hamlin et al., 2006). These outcomes have not been explicitly explored in rodents with a history of binge-like eating. Food primed reinstatement: Food priming is modelled by a non-contingent delivery of a small number of food pellets, either before/at the beginning of the test session (Dias et al., 2004; Duarte et al., 2004; Ghitza et al., 2006; Shaham et al., 1997), at fixed intervals throughout the session (Sun and Rebec, 2005), or during parts of the session (e.g. first 10-20min (McFarland and Kalivas, 2001; Nair et al., 2008)). In rats with a history of binge-like eating, food priming elicits reinstatement of extinguished chocolate seeking (de Jong et al., 2013) and exacerbates the extent to which contextual cues promote food overconsumption (Boggiano et al., 2009). Stress reinstatement: Reinstatement of food seeking can be elicited by exposure to pharmacological stressors, most commonly the alpha 2-adrenergic receptor antagonist yohimbine administered immediately prior to the test session (Ghitza et al., 2007). Interestingly, intermittent footshock (typically considered a psychological stressor) is not effective at reinstating food seeking behaviour in rats trained to self-administer regular food pellets or a sucrose solution (Ahmed and Koob, 1997; Buczek et al., 1999); it is unclear how stress affects reinstatement in animals that have undergone other approaches that promote binge-like eating.

2.4. Approaches to measuring ‘compulsive’ eating and food seeking

Compulsion is a transdiagnostic psychiatric symptom that can be defined as repetitive acts that one feels they have to perform while being aware that these acts are not in line with their overall goal (George et al., 2022). Thus, compulsive actions involve motivational conflict (George et al., 2022); in the context of BED and other eating disorders, this might involve the competing urge to overconsume food and the desire to refrain from eating due to concerns over negative health and social outcomes (Moore et al., 2017). To explore this concept in laboratory rodents, Johnson & Kenny (Johnson and Kenny, 2010) developed a procedure in which rats were conditioned to associate a light (conditioned stimulus, CS)

with the delivery of footshock, before palatable food consumption was measured in the presence of the CS alone. Presentation of the CS was sufficient to suppress food intake in rats exposed to regular chow and restricted access to a palatable diet, but had no effect in rats with a history of extended palatable food access (and excessive weight gain), a finding the authors interpreted as reflecting compulsive-like eating behaviour in the latter group. Since this publication, several other studies have utilized the cue-induced suppression of feeding task to assess compulsive eating in alternate models. Most notably, Velazquez-Sanchez et al. (Velázquez-Sánchez et al., 2015) reported that male rats trained to self-administer a sugary, highly palatable diet (on a schedule that promotes binge-like escalation of intake) perseverated in their responding for food despite the presence of an aversive CS. Another study showed that binge-eating rats spent more time in a chocolate-paired compartment despite the presence of conditioned stimuli predicted footshock, compared to non-binge-eating controls (Heal et al., 2016). An alternative approach measures the willingness of animals to consume food in the middle of the light zone of a light/dark conflict apparatus. Teegarden & Bale (Teegarden and Bale, 2007) used this assay to show that mice withdrawn from a high-fat diet were more likely to endure the aversive environment to gain access to palatable food, compared to a high-carbohydrate control group. Cottone et al. (Cottone et al., 2012) used the same task to show that rats with a history of binge-like intake of palatable food exhibit higher food consumption in the light zone compared to non-bingeing chow controls. These same authors reported enhanced food consumption in the light/dark test in high-impulsive rats, which exhibit several other exacerbated binge-related behaviours (Velázquez-Sánchez et al., 2014). We note that preclinical studies have tended to operationalize ‘compulsivity’ as continued reward seeking “despite negative consequences” (or potential negative consequences): it was recently argued that this might reflect experimental convenience rather than construct validity (George et al., 2022), and thus alternative approaches might need to be considered to better understand this construct as it applies to eating disorders. For an overview of alternative assays to examine compulsive eating, we refer readers to an excellent book chapter on this topic (Moore et al., 2019).

2.5. Outcome devaluation as a test of habitual food seeking

It has been proposed that overeating and associated disorders can be explained in part by inflexible or ‘habitual’ feeding patterns (Tomasi and Volkow, 2013). Habits are developed to automate regularly occurring and reinforced behaviour (such as feeding), allowing one to focus on other things in their environment. Habits do not rely on outcome expectancy and thus are not immediately sensitive to changes in the value of the earned outcome (Hart et al., 2014). Habitual actions can be dissociated from goal-directed behaviours using an outcome-devaluation task (or contingency degradation), whereby the outcome (food) is paired with illness (e.g. lithium chloride injections) or animals are allowed to consume the outcome to satiety prior to testing (Hart et al., 2014). Performance of an action (typically lever pressing) that previously resulted in the now ‘devalued’ outcome is then measured under extinction conditions (i.e. in the absence of the outcome); persistent responding for the devalued outcome is said to reflect ‘habitual’ control of food seeking. Rats exposed to paradigms that promote binge-like intake of palatable foods, including sweetened condensed milk and a 10% sucrose solution, fail to reduce their responding for a devalued food outcome, indicating a shift towards habitual food seeking behaviour (Furlong et al., 2014;

Kendig et al., 2013). Similarly, compared to rats with continuous food access, rats exposed to repeated cycles of restriction and re-feeding show equal choice for valued and devalued rewards (Kendig et al., 2013).

2.6. Three-criteria approach to studying 'food addiction'

Significant recent attention has been given to the notion that some foods possess 'addictive' qualities (Gearhardt et al., 2009; Gearhardt and Schulte, 2021; Schiestl et al., 2021), and thus there has been some interest in adapting approaches designed to study drug behaviours to study behaviours reflective of 'food addiction'. Most notable is the so-called '3 criterion' model, which was first developed to examine the presence/absence of 3 distinct drug-related endophenotypes in an individual animal (Deroche-Gamonet et al., 2004). To this end, Valazquez-Sanchez et al. (Velázquez-Sánchez et al., 2014) examined rats' propensity to exhibit BED-related behaviours, including i) consumption of large amounts of palatable food in a short period of time, measured using a daily operant task for palatable vs regular chow diet), ii) high motivation for palatable food, as measured by a PR task, and iii) consume palatable food despite negative consequences, as measured by the light/dark conflict test. Rats were then grouped based on the number of positive criteria (0, 1, 2 or 3 criterion), with '3-criterion' rats being considered to exhibit 'food addiction'. Interestingly, rats with a history of operant responding for palatable food were more likely to be classified as 3-criterion, whereas those that responded for regular chow were more likely to be classified as 0-criterion. In a separate study, Brown and colleagues (Brown et al., 2017) examined the extent to which diet-induced obesity is related to food addiction behaviours. Rats were given 8w access to a palatable diet and then assessed for PR responding, palatable food intake during an FR5 operant task, as well as persistence of responding during a signalled period of food non-availability. Diet-induced obese prone (top third weight gainers) rats exhibited significantly increased addiction like behaviours across all three criteria, compared to diet-induced obese resistant (bottom third weight gainers) rats.

More recently, a similar approach has been utilized to examine the expression of 'food addiction' behaviours in mice (Domingo-Rodriguez et al., 2020; Inbar et al., 2020). In one study, mice were categorized as 'addicted' or 'non-addicted' based on their responding on a PR test and during signalled periods of food unavailability, as well as on a task where food delivery was paired with a footshock. Mice were considered 'positive' for an addiction-like criterion if they scored above the 75th percentile of the normal distribution of a control group. Mice that achieved 2–3 criteria were classified as 'addicted' and those that achieved 0 or 1 criteria were classified as 'non-addicted'. 'Addicted' mice were more likely to make more non-reinforced lever presses during time out periods following pellet delivery, and exhibited reduced conditioned suppression of feeding. It is worth noting that the 3-criterion approach relies on retrospective analysis of behavioural data; its value as a predictor of future behavioural outcomes is unclear. Moreover, we note that several biological markers have been found to differentiate 0–1 vs. 2–3 criterion animals (Brown et al., 2017), and that some of these biomarkers can differentiate persons with 'food addiction' (García-Blanco et al., 2022). Again, it is unclear if these biomarker profiles can prospectively predict susceptibility to 'food addiction' or if they represent a biological adaptation in response to chronic food overconsumption.

2.7. Experimental considerations

2.7.1. The choice of food: influence of macronutrients—The rewarding effects of drugs of abuse are due to specific pharmacological actions at receptors or other drug targets such as transporters. With repeated use, drugs of abuse cause long lasting cellular, molecular and neuronal adaptations across the central nervous system which ultimately result in 'addiction'. In the case of food, no particular pharmacological target exists, though it is specifically foods high in fat and sugar that are typically consumed in excess (Kales, 1990; Hetherington et al., 1994; Drewnowski et al., 1987; Guertin, 1999; Gleaves et al., 1993). This specific combination of fat and refined sugar is not found in naturally occurring unrefined foods that humans have historically eaten, and thus our brains respond uniquely to this combination of macronutrients (Thanarajah et al., 2019; DiFeliceantonio et al., 2018). Therefore, it is possible that, due to evolutionary pressure, the simultaneous consumption of both fat and sugar could be perceived as more rewarding than the consumption of either macronutrient alone (Thanarajah et al., 2019; DiFeliceantonio et al., 2018). Indeed, using an auction task in parallel with fMRI imaging, DiFeliceantonio and colleagues showed that in a human laboratory setting, people are willing to pay more for fat + carbohydrate foods compared foods high in *either* fat or carbohydrates, even when those foods are equally familiar and liked, and this overvaluation is associated with great recruitment of dorsal striatum (DiFeliceantonio et al., 2018), a brain region implicated in the shift from casual to compulsive use of addictive drugs (Everitt and Robbins, 2013). These data suggest that simultaneous activation of fat and carbohydrate signaling pathways produces a supra-physiologic reward response in the brain that renders high-fat/high-sugar foods more rewarding than high-fat or high-sugar alone (DiFeliceantonio et al., 2018). Consistent with this proposal is the observation that rodents will typically regulate their caloric intake and body weight when given access to fat or carbohydrate alone, but rapidly gain weight under conditions of unrestricted access to fat and carbohydrate together (Johnson and Kenny, 2010; Adolph, 1947; Beilharz et al., 2014).

Because of this, studies examining the effects of diet must give critical consideration to the macronutrients of experimental substance. Many studies utilize highly palatable, calorie-dense foods that are high in fat, sugar, or both, either from a formulated diet from commercial vendors (e.g. Research Diets, Bio-Serv) (Freeman et al., 2020) or readily-available 'junk food' (e.g. Oreo cookies, Reeses' peanut butter cups, chocolate) (Anversa et al., 2020; Presby et al., 2020). Other studies have utilized a 'cafeteria diet', in which a combination of highly palatable sweet and savoury foods are provided (e.g. cheesecake, meat pie, noodles) that typify a highly processed, highly caloric, western 'junk food' diet (Hansen et al., 2004; Fam et al., 2022; Kendig et al., 2022; Tajaddini et al., 2022). The appeal of the latter is strong face validity, however the non-standardised format of the diet does not allow for direct comparisons across studies based on specific macronutrient combinations – this is important, as saturated fats have different effects on dopamine signaling in the brain and alter HPA axis function compared to monounsaturated fats (Hryhorczuk et al., 2016; Hryhorczuk et al., 2017). Notably, the 'junk foods' typically overconsumed in modern society are generally high in saturated fats (Pressler et al., 2022), and thus studies that include saturated fats in their experimental diets could be argued to have enhanced face validity.

2.7.2. Caloric restriction—Studies of famine victims and semistarvation experiments have shown that experiences with food restriction can cause long-lasting changes in eating behaviour. Notably, participants in the Minnesota study, which involved 24 weeks of semistarvation followed by 12 weeks of controlled refeeding, showed persistent behavioural and personality changes towards food including the development of binge eating and purging behaviour, as well as difficulties in reading hunger cues, even after 5 months of refeeding. Semistarvation has also been linked to the development of body image concerns (Franklin et al., 1948; Polivy et al., 1994). Thus, food restriction is a common tool utilized in animal studies to induce aberrant forms of eating behaviour. The converse of food deprivation is the sham feeding model, whereby a gastric fistula is used to induce drainage of consumed foods before it enters the intestine. This minimizes contact of food with gastric and intestinal mucosa, producing a reversible, acquired deficit in satiation (Davis and Campbell, 1973; Mook, 1963). As expected, these rats eat abnormally large meals, and an escalation in binge-like eating behaviour is observed with repeated cycles (Casper et al., 2008). As noted above, many models rely on bouts of food restriction in their protocol to observe dysregulated feeding behaviour. Conveniently, this pattern of repeated periods of food restriction appropriately models the cycles of dieting exercised by many individuals who suffer from disordered overeating behaviour. There is increasing evidence to suggest that repeated dieting-or ‘yo-yo’ dieting – results in increased risk of weight gain, development of obesity and can contribute to the development of dysregulated patterns of eating (Lowe et al., 2001; Amigo and Fernández, 2007). Indeed, evidence now exists which shows that caloric restriction reprogrammes stress and orexinergic pathways and promotes binge eating (Pankevich et al., 2010), and thus modelling this pattern of repeated periods of dieting is an important consideration for studies in this space. That said, it is equally important to have models that specifically focus on the bingeing behaviour itself, while avoiding the potential impacts that food restriction might have on the brain; indeed, this is the only way in which the field can disentangle the precise neural mechanisms underlying binge-eating per se. Further, not all individuals who display disordered overeating behaviour engage in these repeated dieting attempts, and thus it is important to have models that encompass all subpopulations and clinical scenarios.

2.7.3. Circadian influences—Binge eating episodes are more likely during the evening than in the daytime and persons with a late chronotype (so called ‘night owls’) are more prone to higher weight and unhealthy snacking as well as associated conditions such as Type 2 diabetes and cardiovascular disease (Raymond et al., 2003; Riccobono et al., 2020; Muscogiuri et al., 2021). Moreover, in the case of Night Eating Syndrome, excessive food intake occurs in the evening and is followed by morning anorexia (Stunkard et al., 1955). Thus, when modelling disorders of food overconsumption in laboratory animals, consideration should be given to the time of day in which feeding manipulations are made. Similar to other behavioural and physiological processes, feeding is tightly regulated by circadian clocks that induce daily rhythms that synchronize with light/dark cycles (Patton and Mistlberger, 2013). Although there are some individual differences in meal pattern, these variations are generally minor and are consistent across days (Brinkhof et al., 1998; Strubbe et al., 1986). To align with naturalistic feeding patterns, it is common for studies that utilize limited food access schedules (e.g. to induce binge-like eating) to be carried

out during or just prior to the dark (active) period (Bello et al., 2019; Anversa et al., 2020; Berner et al., 2009) although there are some examples of these models being carried out in the light.

Notably, food intake itself can act as an entrainment cue, such that peripheral and central clock gene rhythms are shifted to align with expected meal times. Indeed, when rodents are restricted to a 2-6 h mealtime, they exhibit a behavioural rhythm of food seeking behaviour that anticipates the daily mealtime (Mistlberger, 1994; Boulos et al., 1980; Stephan, 2002). Interestingly, there is some evidence that palatable foods can also induce behavioural entrainment in otherwise sated rats (ie. when regular chow is available ad libitum), indicating that this type of behavioural entrainment might drive the search and craving for palatable foods (Mendoza et al., 2005a; Mendoza et al., 2005b; Blancas et al., 2014; Flôres et al., 2016; Escobar et al., 2011). It is also notable that free access to high fat/highly palatable foods significantly disrupts behavioural rhythms such that patterns of activity become desynchronized from photic input, and the expression of circadian clock genes in both central and peripheral organs are severely disrupted (Kohsaka et al., 2007; Klöting et al., 2013; Mendoza et al., 2008). There is evidence that disruptions to the rhythmicity of the circadian cycle can itself contribute to dysregulated eating, metabolism and weight gain (Turek et al., 2005; Griebel et al., 2014) and thus the potential implications of food entrainment/photic desynchronization should be considered when employing both limited and unrestricted access models such as those outlined here. These data might also explain the high prevalence of sleep dysregulation in obesity, binge eating disorder and other eating disorders, for which a mechanistic link has yet to be fully characterized (reviewed in (Mehr and James, 2022)).

2.7.4. Relationship to weight gain and obesity—Eating in the absence of hunger in both adults and children is consistently associated with elevated body mass index (François et al., 2022). This is not surprising as, by definition, chronic overeating in the absence of compensatory behaviours such as purging, fasting or excessive exercise typically leads to weight gain in humans (Villarejo et al., 2012). This is further exacerbated by the highly caloric nature of the foods that people typically choose to overconsume; thus, weight gain and overeating are inextricably intertwined. This raises the question as to whether the preclinical investigation of disordered overeating behaviour should include subjects of higher weight. Several rodent models of diet-induced obesity exist which are useful tools in the study of hedonic eating behaviour as it relates to obesity. One important consideration in this regard is utilizing an approach whereby obesity is induced by excessive intake as opposed to metabolic factors. For example, the outbred Sprague-Dawley rat model of diet-induced obesity established by Barry Levin and colleagues yields diet-induced obese and diet-resistant subpopulations (Levin and Sullivan, 1989). Diet-induced obese rats exhibit increased food intake and subsequent weight gain when placed on an 8w high-fat high sugar diet compared to their diet-resistant counterparts. Further, they have been shown to have increased conditioned approach to food associated cues, lower demand elasticity and higher motivation for palatable foods, as well ‘addiction-like’ behaviour towards palatable foods (Brown et al., 2017; Narayanaswami et al., 2013; Robinson et al., 2015; Batten et al.,

2020b), thus representing an appropriate model for the study of excessive hedonic eating behaviour.

By contrast, application of a subpopulation split methodology to an inbred strain of mice reveals largely the opposite; one study published in this special issue found no relationship between the development of obesity and addiction-like behaviour towards high-fat/high-sugar food in mice on a C57BL/6 background (Horton et al., 2023), yet pre-existing higher motivation in obesity prone mice has also been observed (Inbar et al., 2020). Thus, it may be that metabolic factors play more of a role in the *differential* development of obesity in C57Bl/6 mice as compared to Sprague Dawley rats. As such, the choice of species and strain can be an important consideration for experimenters embarking on studies of aberrant feeding behaviour using subpopulation splits. Regardless, elegant work using animal models diet-induced obesity have generated a body of evidence which demonstrates that diet-induced obesity *per se* is associated with altered reward processing and decision-making in in both rats and mice (e.g. Johnson and Kenny, 2010; Matikainen-Ankney et al., 2022; Seabrook et al., 2022). Even two weeks of exposure to this type of diet is sufficient to impair sensory-specific satiety and stimulus-outcome learning (Reichelt et al., 2014). As such, one could argue that the research question becomes vitally important when determining whether to incorporate a model of obesity into experimental design.

Interestingly, many animal models of binge eating do not result in the subjects developing obesity (for example, see (Corwin et al., 1998)). Rodents excel at body weight homeostasis and thus, when exposed to intermittent palatable food schedules, can under-consume standard chow during non-binge periods to account for the increased calories consumed during binge access periods. This represents a potential criticism of rodent models of binge eating: while the vast majority of binge eating human subjects are obese (one study estimates lifetime prevalence of nearly 88% (Villarejo et al., 2012)), the same cannot be said for binge eating rodents. However, one could argue that the behaviour (i.e. bingeing) is the most crucial element of the paradigm for studies focused on understanding mechanisms of overeating. Of interest is the finding by Boggiano and colleagues that overconsumption of palatable food predicts binge-eating independent of susceptibility to obesity (Boggiano et al., 2007). That is, the propensity for binge eating was not related to the propensity to develop diet-induced obesity when Sprague-Dawley rats were placed on a continuous high fat diet. This is supported by the observation that the prevalence rates for obesity far exceed those of BED (Udo and Grilo, 2018). Nevertheless, to increase the translational relevance of preclinical research, experimenters should consider the integration of obesity and overeating models into their research.

3. Conclusions

Overeating can manifest as clinical diagnoses such as binge eating disorder or bulimia nervosa. Moreover, other subclinical forms of overeating are associated with a range of negative health and psychiatric outcomes. Though preclinical approaches cannot possibly capture the full spectrum of disordered overeating, studies in rodents have significantly advanced our understanding of the neurobiology underlying distinct aspects of hedonic appetitive behaviour. For researchers embarking on investigations in this area, there are

several important considerations to take into account: the macronutrient composition of the food being studied, selection of appropriate control groups, the sex of the animals, deciding whether caloric restriction will be employed, controlling for circadian influences on behaviour, as well as identifying the precise overeating behaviour that one is attempting to model and how best to study this in a laboratory animal. As we outline here, there exists a variety of behavioural approaches to address the latter, including basic consumption studies and operant paradigms, through to more complex approaches that permit more nuanced examination of underlying motivational constructs, including demand elasticity and food seeking in the presence of aversive stimuli. Ultimately, the approach(es) selected must reflect the experimental question at hand, and one must consider the strengths – and perhaps more importantly – the limitations of the adopted strategy. We note that studies should also seek to identify the biological contributors to overeating across different stages of the disordered eating continuum, starting with high-risk periods associated with initiation of problematic eating patterns (e.g. adolescence, periods of high stress), through to the full manifestation of disease. Together, integration of these foci will hopefully lead to a better understanding of the distinct brain circuits and molecular adaptations that underlie binge eating, overeating, and even ‘food addiction’, thus enhancing our prospects of identifying novel therapeutic strategies to better treat these conditions.

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Abbreviations:

BED	Binge Eating Disorder
BN	Bulimia Nervosa
FR	Fixed Ratio
RI	Random Interval
RR	Random Ratio
PR	Progressive Ratio
HFD	High Fat Diet

References

Adolph EF, 1947. Urges to eat and drink in rats. Am. J. Phys 151, 110–125. 10.1152/ajplegacy.1947.151.1.110.

Ahmed SH, Koob GF, 1997. Cocaine- but not food-seeking behavior is reinstated by stress after extinction. Psychopharmacology 132, 289–295. 10.1007/s002130050347. [PubMed: 9292629]

Ahn S, Phillips AG, 2012. Repeated cydes of restricted food intake and binge feeding disrupt sensory-specific satiety in the rat. Behav. Brain Res 231, 279–285. 10.1016/j.bbr.2012.02.017. [PubMed: 22366270]

American Psychiatric Association, A., American Psychiatric, A., Force, D.S.M.T., 2013. Diagnostic and Statistical Manual of Mental Disorders : DSM-5.

Amigo I, Fernández C, 2007. Effects of diets and their role in weight control. Psychol. Health Med 12, 321–327. 10.1080/13548500600621545. [PubMed: 17510902]

Antelman SM, Szechtman H, 1975. Tail pinch induces eating in sated rats which appears to depend on nigrostriatal dopamine. Science 189, 731–733. 10.1126/science.1154024. [PubMed: 1154024]

Antelman SM, Szechtman H, Chin P, Fisher AE, 1975. Tail pinch-induced eating, gnawing and licking behavior in rats: dependence on the nigrostriatal dopamine system. Brain Res. 99, 319–337. 10.1016/0006-8993(75)90032-3. [PubMed: 1182545]

Anversa RG, et al. , 2020. A model of emotional stress-induced binge eating in female mice with no history of food restriction. Genes Brain Behav. 19, e12613 10.1111/gbb.12613. [PubMed: 31605459]

Anversa RG, et al. , 2021. A review of sex differences in the mechanisms and drivers of overeating. Front. Neuroendocrinol 63, 100941 10.1016/j.yfrne.2021.100941. [PubMed: 34454955]

Aso-Someya N, Narikiyo K, Masuda A, Aou S, 2018. The functional link between tail-pinch-induced food intake and emotionality and its possible role in stress coping in rats. J. Physio. Sci 68, 799–805. 10.1007/s12576-018-0596-6.

Avena NM, Rada P, Hoebel BG, 2008. Evidence for sugar addiction: behavioral and neurochemical effects of intermittent, excessive sugar intake. Neurosci. Biobehav. Rev 32, 20–39. 10.1016/j.neubiorev.2007.04.019. [PubMed: 17617461]

Batten SR, Hicks KB, Dwoskin LP, Beckmann JS, 2020a. Toward isolating reward changes in diet-induced obesity: a demand analysis. Physiol. Behav 213, 112729 10.1016/j.physbeh.2019.112729. [PubMed: 31678579]

Batten SR, Hicks KB, Dwoskin LP, Beckmann JS, 2020b. Toward isolating reward changes in diet-induced obesity: a demand analysis. Physiol. Behav 213, 112729 10.1016/j.physbeh.2019.112729. [PubMed: 31678579]

Beilharz JE, Maniam J, Morris MJ, 2014. Short exposure to a diet rich in both fat and sugar or sugar alone impairs place, but not object recognition memory in rats. Brain Behav. Immun 37, 134–141. 10.1016/j.bbi.2013.11.016. [PubMed: 24309633]

Bello NT, et al. , 2009. Repeated binge access to a palatable food alters feeding behavior, hormone profile, and hindbrain c-Fos responses to a test meal in adult male rats. Am. J. Physiol. Regul. Integr. Comp. Physiol 297, R622–R631. 10.1152/ajpregu.00087.2009. [PubMed: 19535681]

Bello NT, Yeh CY, James MH, 2019. Reduced sensory-evoked locus coeruleus-norepinephrine neural activity in female rats with a history of dietary-induced binge eating. Front. Psychol 10, 1966. 10.3389/fpsyg.2019.01966. [PubMed: 31551861]

Bentzley BS, Fender KM, Aston-Jones G, 2013. The behavioral economics of drug self-administration: a review and new analytical approach for within-session procedures. Psychopharmacology 226, 113–125. 10.1007/s00213-012-2899-2. [PubMed: 23086021]

Bentzley BS, Jhou TC, Aston-Jones G, 2014. Economic demand predicts addiction-like behavior and therapeutic efficacy of oxytocin in the rat. Proc. Natl. Acad. Sci. U. S. A 111, 11822–11827. 10.1073/pnas.1406324111. [PubMed: 25071176]

Berner LA, Bocarsly ME, Hoebel BG, Avena NM, 2009. Baclofen suppresses binge eating of pure fat but not a sugar-rich or sweet-fat diet. Behav. Pharmacol 20, 631–634. 10.1097/FBP.0b013e328331ba47. [PubMed: 19752722]

Blancas A, González-García SD, Rodríguez K, Escobar C, 2014. Progressive anticipation in behavior and brain activation of rats exposed to scheduled daily palatable food. Neuroscience 281, 44–53. 10.1016/j.neuroscience.2014.09.036. [PubMed: 25255933]

Boggiano MM, Chandler PC, 2006. Binge eating in rats produced by combining dieting with stress. Curr. Protoc. Neurosci 10.1002/0471142301.ns0923as36. Chapter 9, Unit9.23A.

Boggiano MM, et al. , 2007. High intake of palatable food predicts binge-eating independent of susceptibility to obesity: an animal model of lean vs obese binge-eating and obesity with and without binge-eating. Int. J. Obes 31, 1357–1367. 10.1038/sj.ijo.0803614.

Boggiano MM, Dorsey JR, Thomas JM, Murdaugh DL, 2009. The Pavlovian power of palatable food: lessons for weight-loss adherence from a new rodent model of cue-induced overeating. Int. J. Obes 33, 693–701. 10.1038/ijo.2009.57.

Bossert JM, Poles GC, Sheffler-Collins SI, Ghitza UE, 2006. The mGluR2/3 agonist LY379268 attenuates context-and discrete cue-induced reinstatement of sucrose seeking but not sucrose self-administration in rats. Behav. Brain Res 173, 148–152. 10.1016/j.bbr.2006.06.008. [PubMed: 16834996]

Boulos Z, Rosenwasser AM, Terman M, 1980. Feeding schedules and the circadian organization of behavior in the rat. Behav. Brain Res 1, 39–65. 10.1016/0166-4328(80)90045-5. [PubMed: 7284080]

Brinkhof MW, Daan S, Strubbe JH, 1998. Forced dissociation of food-and light-entrainable circadian rhythms of rats in a skeleton photoperiod. Physiol. Behav 65, 225–231. 10.1016/s0031-9384(98)00051-1. [PubMed: 9855470]

Brown RM, et al. , 2016. Orexin-1 receptor signalling in the prelimbic cortex and ventral tegmental area regulates cue-induced reinstatement of ethanol-seeking in iP rats. Addict. Biol 21, 603–612. 10.1111/adb.12251. [PubMed: 25899624]

Brown RM, et al. , 2017. Addiction-like synaptic impairments in diet-induced obesity. Biol. Psychiatry 81, 797–806. 10.1016/j.biopsych.2015.11.019. [PubMed: 26826876]

Brown RM, Dayas CV, James MH, Smith RJ, 2022. New directions in modelling dysregulated reward seeking for food and drugs. Neurosci. Biobehav. Rev 132, 1037–1048. 10.1016/j.neubiorev.2021.10.043. [PubMed: 34736883]

Buczek Y, Lê AD, Wang A, Stewart J, Shaham Y, 1999. Stress reinstates nicotine seeking but not sucrose solution seeking in rats. Psychopharmacology 144, 183–188. 10.1007/s002130050992. [PubMed: 10395000]

Bulik CM, et al. , 2022. Genetics and neurobiology of eating disorders. Nat. Neurosci 25, 543–554. 10.1038/s41593-022-01071-z. [PubMed: 35524137]

Buscemi J, Acuff SF, Minhas M, MacKillop J, Murphy JG, 2021. Identifying patterns of alcohol use and obesity-related factors among emerging adults: a behavioral economic analysis. Alcohol. Clin. Exp. Res 45, 828–840. 10.1111/acer.14569. [PubMed: 33724488]

Calu DJ, Chen YW, Kawa AB, Nair SG, Shaham Y, 2014. The use of the reinstatement model to study relapse to palatable food seeking during dieting. Neuropharmacology 76 (Pt B), 395–406. 10.1016/j.neuropharm.2013.04.030. [PubMed: 23660229]

Cason AM, Aston-Jones G, 2013. Role of orexin/hypocretin in conditioned sucrose-seeking in rats. Psychopharmacology 226, 155–165. 10.1007/s00213-012-2902-y. [PubMed: 23096770]

Casper RC, Sullivan EL, Tecott L, 2008. Relevance of animal models to human eating disorders and obesity. Psychopharmacology 199, 313–329. 10.1007/s00213-008-1102-2. [PubMed: 18317734]

Cervo L, Cocco A, Petrella C, Heidbreder CA, 2007. Selective antagonism at dopamine D3 receptors attenuates cocaine-seeking behaviour in the rat. Int. J. Neuropsychopharmacol 10, 167–181. 10.1017/s1461145705006449. [PubMed: 16426478]

Cifani C, Polidori C, Melotto S, Ciccocioppo R, Massi M, 2009. A preclinical model of binge eating elicited by yo-yo dieting and stressful exposure to food: effect of sibutramine, fluoxetine, topiramate, and midazolam. Psychopharmacology 204, 113–125. 10.1007/s00213-008-1442-y. [PubMed: 19125237]

Cole S, Keefer SE, Anderson LC, Petrovich GD, 2020. Medial prefrontal cortex neural plasticity, orexin receptor 1 signaling, and connectivity with the lateral hypothalamus are necessary in cue-potentiated feeding. J. Neurosci 40, 1744–1755. 10.1523/jneurosci.1803-19.2020. [PubMed: 31953368]

Collaborators GBDO, et al. , 2017. Health effects of overweight and obesity in 195 countries over 25 years. N. Engl. J. Med 377, 13–27. 10.1056/NEJMoa1614362. [PubMed: 28604169]

Corwin RL, Buda-Levin A, 2004. Behavioral models of binge-type eating. Physiol. Behav 82, 123–130. 10.1016/j.physbeh.2004.04.036. [PubMed: 15234600]

Corwin RL, Wojnicki FH, 2006. Binge eating in rats with limited access to vegetable shortening. Curr. Protoc. Neurosci 10.1002/0471142301.ns0923bs36. Chapter 9, Unit9.23B.

Corwin RL, et al. , 1998. Limited access to a dietary fat option affects ingestive behavior but not body composition in male rats. Physiol. Behav 65, 545–553. 10.1016/s0031-9384(98)00201-7. [PubMed: 9877422]

Cottone P, et al. , 2012. Antagonism of sigma-1 receptors blocks compulsive-like eating. Neuropsychopharmacology 37, 2593–2604. 10.1038/npp.2012.89. [PubMed: 22713906]

Curtis GR, et al. , 2019. Short-and long-access palatable food self-administration results in different phenotypes of binge-type eating. Physiol. Behav 212, 112700. 10.1016/j.physbeh.2019.112700. [PubMed: 31614159]

Davis JD, Campbell CS, 1973. Peripheral control of meal size in the rat: effect of sham feeding on meal size and drinking rate. J. Comp. Physiol. Psychol 83, 379–387. 10.1037/h0034667. [PubMed: 4715303]

de Jong JW, Meijboom KE, Vanderschuren LJ, Adan RA, 2013. Low control over palatable food intake in rats is associated with habitual behavior and relapse vulnerability: individual differences. PLoS One 8, e74645. 10.1371/journal.pone.0074645. [PubMed: 24058616]

Deroche-Gamonet V, Belin D, Piazza PV, 2004. Evidence for addiction-like behavior in the rat. Science 305, 1014–1017. 10.1126/science.1099020. [PubMed: 15310906]

Derusso AL, et al. , 2010. Instrumental uncertainty as a determinant of behavior under interval schedules of reinforcement. Front. Integr. Neurosci 4 10.3389/fnint.2010.00017.

Diagnostic and Statistical Manual of Mental Disorders : DSM-5, 2013. American Psychiatric Association.

Dias C, Lachize S, Boilet V, Huitelec E, Cador M, 2004. Differential effects of dopaminergic agents on locomotor sensitisation and on the reinstatement of cocaine-seeking and food-seeking behaviour. Psychopharmacology 175, 414–427. 10.1007/s00213-004-1839-1. [PubMed: 15064914]

DiFeliceantonio AG, et al. , 2018. Supra-additive effects of combining fat and carbohydrate on food reward. Cell Metab. 28, 33–44.e33. 10.1016/j.cmet.2018.05.018. [PubMed: 29909968]

Domingo-Rodriguez L, et al. , 2020. A specific prelimbic-nucleus accumbens pathway controls resilience versus vulnerability to food addiction. Nat. Commun 11, 782. 10.1038/s41467-020-14458-y. [PubMed: 32034128]

Drewnowski A, Bellisle F, Aimez P, Remy B, 1987. Taste and bulimia. Physiol. Behav 41, 621–626. 10.1016/0031-9384(87)90320-9. [PubMed: 3441532]

Duarte C, et al. , 2004. Blockade by the cannabinoid CB1 receptor antagonist, rimonabant (SR141716), of the potentiation by quinelorane of food-primed reinstatement of food-seeking behavior. Neuropsychopharmacology 29, 911–920. 10.1038/sj.npp.1300370. [PubMed: 14694354]

Duffey KJ, Popkin BM, 2011. Energy density, portion size, and eating occasions: contributions to increased energy intake in the United States, 1977-2006. PLoS Med. 8, e1001050 10.1371/journal.pmed.1001050. [PubMed: 21738451]

Epstein LH, et al. , 2018a. Reinforcing value and hypothetical behavioral economic demand for food and their relation to BMI. Eat. Behav 29, 120–127. 10.1016/j.eatbeh.2018.03.008. [PubMed: 29656049]

Epstein LH, Stein JS, Paluch RA, MacKillop J, Bickel WK, 2018b. Binary components of food reinforcement: amplitude and persistence. Appetite 120, 67–74. 10.1016/j.appet.2017.08.023. [PubMed: 28847564]

Escobar C, et al. , 2011. Scheduled meals and scheduled palatable snacks synchronize circadian rhythms: consequences for ingestive behavior. Physiol. Behav 104, 555–561. 10.1016/j.physbeh.2011.05.001. [PubMed: 21565213]

Everitt BJ, Robbins TW, 2013. From the ventral to the dorsal striatum: devolving views of their roles in drug addiction. Neurosci. Biobehav. Rev 37, 1946–1954. 10.1016/j.neubiorev.2013.02.010. [PubMed: 23438892]

Fam J, Clemens KJ, Westbrook RF, Morris MJ, Kendig MD, 2022. Chronic exposure to cafeteria-style diet in rats alters sweet taste preference and reduces motivation for, but not 'liking' of sucrose. Appetite 168, 105742. 10.1016/j.appet.2021.105742. [PubMed: 34634373]

Flôres DE, Bettilyon CN, Yamazaki S, 2016. Period-independent novel circadian oscillators revealed by timed exercise and palatable meals. Sci. Rep 6, 21945. 10.1038/srep21945. [PubMed: 26904978]

Fragale JE, Pantazis CB, James MH, Aston-Jones G, 2019. The role of orexin-1 receptor signaling in demand for the opioid fentanyl. Neuropsychopharmacology 44, 1690–1697. 10.1038/s41386-019-0420-x. [PubMed: 31112988]

Fragale JE, James MH, Aston-Jones G, 2020. Intermittent self-administration of fentanyl induces a multifaceted addiction state associated with persistent changes in the orexin system. Addict. Biol e12946 10.1111/adb.12946. [PubMed: 32798290]

François M, Fernández-Gayol O, Zeltser LM, 2022. A framework for developing translationally relevant animal models of stress-induced changes in eating behavior. Biol. Psychiatry 91, 888–897. 10.1016/j.biopsych.2021.06.020. [PubMed: 34433512]

Franklin JC, Schiele BC, Brožek J, Keys A, 1948. Observations of human behavior in experimental semi starvation and rehabilitation. J. Clin. Psychol 4, 28–45. 10.1002/l097-4679(194801)4:1<28::AID-JCLP2270040103>3.0.CO;2-F. [PubMed: 18903450]

Freeman LR, Bentzley BS, James MH, Aston-Jones G, 2020. Sex differences in demand for highly palatable foods: role of the orexin system. Int. J. Neuropsychopharmacol 10.1093/ijnp/pyaa040.

Furlong TM, Jayaweera HK, Balleine BW, Corbit LH, 2014. Binge-like consumption of a palatable food accelerates habitual control of behavior and is dependent on activation of the dorsolateral striatum. J. Neurosci 34, 5012–5022. 10.1523/jneurosci.3707-13.2014. [PubMed: 24695718]

García-Blanco A, et al. , 2022. miRNA signatures associated with vulnerability to food addiction in mice and humans. J. Clin. Invest 132 10.1172/jci156281.

Gearhardt AN, Schulte EM, 2021. Is food addictive? A review of the science. Annu. Rev. Nutr 41, 387–410. 10.1146/annurev-nutr-110420-111710. [PubMed: 34152831]

Gearhardt AN, Corbin WR, Brownell KD, 2009. Preliminary validation of the Yale food addiction scale. Appetite 52, 430–436. 10.1016/j.appet.2008.12.003. [PubMed: 19121351]

George O, Ahmed SH, Gilpin NW, 2022. Are we compulsively chasing rainbows? Neuropsychopharmacology, 10.1038/s41386-022-01419-w.

Ghitza UE, Gray SM, Epstein DH, Rice KC, Shaham Y, 2006. The anxiogenic drug yohimbine reinstates palatable food seeking in a rat relapse model: a role of CRF1 receptors. Neuropsychopharmacology 31, 2188–2196. 10.1038/sj.npp.1300964.

Ghitza UE, et al. , 2007. Peptide YY3-36 decreases reinstatement of high-fat food seeking during dieting in a rat relapse model. J. Neurosci 27, 11522–11532. 10.1523/JNEUROSCI.5405-06.2007. [PubMed: 17959795]

Giannotti G, et al. , 2022. Oxytocin and orexin systems bidirectionally regulate the ability of opioid cues to bias reward seeking. Transl. Psychiatry 12, 432. 10.1038/s41398-022-02161-z. [PubMed: 36195606]

Gleaves DH, Williamson DA, Barker SE, 1993. Additive effects of mood and eating forbidden foods upon the perceptions of overeating and binging in bulimia nervosa. Addict. Behav 18, 299–309. 10.1016/0306-4603(93)90031-4. [PubMed: 8342442]

Goebel-Stengel M, Stengel A, Wang L, Taché Y, 2014. Orexigenic response to tail pinch: role of brain NPY(1) and corticotropin releasing factor receptors. Am. J. Physiol. Regul. Integr. Comp. Physiol 306, R164–R174. 10.1152/ajpregu.00335.2013. [PubMed: 24338440]

Goeders JE, Murnane KS, Banks ML, Fantegrossi WE, 2009. Escalation of food-maintained responding and sensitivity to the locomotor stimulant effects of cocaine in mice. Pharmacol. Biochem. Behav 93, 67–74. 10.1016/j.pbb.2009.04.008. [PubMed: 19376153]

Griebel G, Ravinet-Trillou C, Beeské S, Avenet P, Pichat P, 2014. Mice deficient in cryptochrome 1 (cry1 (−/−)) exhibit resistance to obesity induced by a high-fat diet. Front. Endocrinol 5, 49. 10.3389/fendo.2014.00049.

Grimm JW, Shaham Y, Hope BT, 2002. Effect of cocaine and sucrose withdrawal period on extinction behavior, cue-induced reinstatement, and protein levels of the dopamine transporter and tyrosine hydroxylase in limbic and cortical areas in rats. Behav. Pharmacol 13, 379–388. 10.1097/00008877-200209000-00011. [PubMed: 12394414]

Guertin TL, 1999. Eating behavior of bulimics, self-identified binge eaters, and non-eating-disordered individuals: what differentiates these populations? Clin. Psychol. Rev 19, 1–23. 10.1016/s0272-7358(98)00017-8. [PubMed: 9987581]

Guleken Z, Uzbay T, 2022. Neurobiological and neuropharmacological aspects of food addiction. Neurosci. Biobehav. Rev 139, 104760 10.1016/j.neubiorev.2022.104760. [PubMed: 35780976]

Hagan MM, Moss DE, 1997. Persistence of binge-eating patterns after a history of restriction with intermittent bouts of refeeding on palatable food in rats: implications for bulimia nervosa. Int. J. Eat. Disord 22, 411–420. 10.1002/(sici)1098-108x(199712)22:4<411::aid-eat6>3.0.co;2-p. [PubMed: 9356889]

Hamlin AS, Blatchford KE, McNally GP, 2006. Renewal of an extinguished instrumental response: neural correlates and the role of D1 dopamine receptors. Neuroscience 143, 25–38. 10.1016/j.neuroscience.2006.07.035. [PubMed: 16949214]

Hansen MJ, Jovanovska V, Morris MJ, 2004. Adaptive responses in hypothalamic neuropeptide Y in the face of prolonged high-fat feeding in the rat. J. Neurochem 88, 909–916. 10.1046/j.1471-4159.2003.02217.x. [PubMed: 14756812]

Hart G, Leung BK, Balleine BW, 2014. Dorsal and ventral streams: the distinct role of striatal subregions in the acquisition and performance of goal-directed actions. Neurobiol. Learn. Mem 108, 104–118. 10.1016/j.nlm.2013.11.003. [PubMed: 24231424]

Hawkins MF, et al. , 2002. Behavioral responses to stress following central and peripheral injection of the 5-HT(2) agonist DOI. Pharmacol. Biochem. Behav 73, 537–544. 10.1016/s0091-3057(02)00822-5. [PubMed: 12151027]

Heal DJ, Goddard S, Brammer RJ, Hutson PH, Vickers SP, 2016. Lisdexamfetamine reduces the compulsive and perseverative behaviour of binge-eating rats in a novel food reward/punished responding conflict model. J. Psychopharmacol 30, 662–675. 10.1177/0269881116647506. [PubMed: 27170676]

Heinsbroek JA, et al. , 2021. A common limiter circuit for opioid choice and relapse identified in a rodent addiction model. Nat. Commun 12, 4788. 10.1038/s41467-021-25080-x. [PubMed: 34373454]

Hetherington MM, Altemus M, Nelson ML, Bernat AS, Gold PW, 1994. Eating behavior in bulimia nervosa: multiple meal analyses. Am. J. Clin. Nutr 60, 864–873. 10.1093/ajcn/60.6.864. [PubMed: 7985626]

Hildebrandt BA, Ahmari SE, 2021. Breaking it down: investigation of binge eating components in animal models to enhance translation. Front. Psychiatry 12, 728535. 10.3389/fpsyt.2021.728535. [PubMed: 34484010]

Hodos W, 1961. Progressive ratio as a measure of reward strength. Science 134, 943–944. 10.1126/science.134.3483.943. [PubMed: 13714876]

Holland PC, Petrovich GD, 2005. A neural systems analysis of the potentiation of feeding by conditioned stimuli. Physiol. Behav 86, 747–761. 10.1016/j.physbeh.2005.08.062. [PubMed: 16256152]

Horton AL, et al. , 2023. Addiction-like behaviour towards high-fat high-sugar food predicts relapse propensity in both obesity prone and obesity resistant C57BL/6 J mice. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 121, 110654. 10.1016/j.pnpbp.2022.110654.

Hryhorczuk C, et al. , 2016. Dampened mesolimbic dopamine function and signaling by saturated but not monounsaturated dietary lipids. Neuropsychopharmacology 41, 811–821. 10.1038/npp.2015.207. [PubMed: 26171719]

Hryhorczuk C, et al. , 2017. Saturated high-fat feeding independent of obesity alters hypothalamus-pituitary-adrenal axis function but not anxiety-like behaviour. Psychoneuroendocrinology 83, 142–149. 10.1016/j.psyneuen.2017.06.002. [PubMed: 28623763]

Hursh SR, Silberberg A, 2008. Economic demand and essential value. Psychol. Rev 115, 186–198. 10.1037/0033-295X.115.1.186. [PubMed: 18211190]

Inbar D, Gendelis S, Mesner S, Menahem S, Kupchik YM, 2020. Chronic calorie-dense diet drives differences in motivated food seeking between obesity-prone and resistant mice. Addict. Biol 25, e12753 10.1111/adb.12753. [PubMed: 31012232]

James MH, Aston-Jones G, 2022. Orexin reserve: a mechanistic framework for the role of orexins (hypocretins) in addiction. Biol. Psychiatry 10.1016/j.biopsych.2022.06.027.

James MH, Yeoh JW, Graham BA, Dayas CV, 2012. Insights for developing pharmacological treatments for psychostimulant relapse targeting hypothalamic peptide systems. J. Addict. Res. Ther S4, 008. 10.4172/2155-6105.S4-008.

James MH, McGlinchey EM, Vattikonda A, Mahler SV, Aston-Jones G, 2018. Cued reinstatement of cocaine but not sucrose seeking is dependent on dopamine signaling in prelimbic cortex and is associated with recruitment of prelimbic neurons that project to contralateral nucleus accumbens core. Int. J. Neuropsychopharmacol 21, 89–94. 10.1093/ijnp/pyx107. [PubMed: 29165565]

James MH, Bowrey HE, Stopper CM, Aston-Jones G, 2019a. Demand elasticity predicts addiction endophenotypes and the therapeutic efficacy of an orexin/hypocretin-1 receptor antagonist in rats. Eur. J. Neurosci 50, 2602–2612. 10.1111/ejn.14166. [PubMed: 30240516]

James MH, et al. , 2019b. Increased number and activity of a lateral subpopulation of hypothalamic orexin/hypocretin neurons underlies the expression of an addicted state in rats. Biol. Psychiatry 85, 925–935. 10.1016/j.biopsych.2018.07.022. [PubMed: 30219208]

Johnson PM, Kenny PJ, 2010. Dopamine D2 receptors in addiction-like reward dysfunction and compulsive eating in obese rats. Nat. Neurosci 13, 635–641. 10.1038/nn.2519. [PubMed: 20348917]

Jupp B, Krivdic B, Krstew E, Lawrence AJ, 2011. The orexin$_1$ receptor antagonist SB-334867 dissociates the motivational properties of alcohol and sucrose in rats. Brain Res. 1391, 54–59. 10.1016/j.brainres.2011.03.045. [PubMed: 21439948]

Kales EF, 1990. Macronutrient analysis of binge eating in bulimia. Physiol. Behav 48, 837–840. 10.1016/0031-9384(90)90236-w. [PubMed: 2087515]

Kalliokoski O, et al. , 2013. Mice do not habituate to metabolism cage housing–a three week study of male BALB/c mice. PLoS One 8, e58460. 10.1371/journal.pone.0058460. [PubMed: 23505511]

Kendig MD, Boakes RA, Rooney KB, Corbit LH, 2013. Chronic restricted access to 10% sucrose solution in adolescent and young adult rats impairs spatial memory and alters sensitivity to outcome devaluation. Physiol. Behav 120, 164–172. 10.1016/j.physbeh.2013.08.012. [PubMed: 23954407]

Kendig MD, et al. , 2022. Adolescent exposure to a solid high-fat, high-sugar ‘cafeteria’ diet leads to more pronounced changes in metabolic measures and gut microbiome composition than liquid sugar in female rats. Appetite 172, 105973. 10.1016/j.appet.2022.105973. [PubMed: 35192913]

Klöting I, Bahr J, Wilke B, Lange J, 2013. Light rhythm and diet differently influence facets of the metabolic syndrome in WOKW rats. Lab. Anim 47, 31–35. 10.1258/la.2012.011095. [PubMed: 23287511]

Klump KL, Racine S, Hildebrandt B, Sisk CL, 2013. Sex differences in binge eating patterns in male and female adult rats. Int. J. Eat. Disord 46, 729–736. 10.1002/eat.22139. [PubMed: 23625647]

Kohsaka A, et al. , 2007. High-fat diet disrupts behavioral and molecular circadian rhythms in mice. Cell Metab. 6, 414–421. 10.1016/j.cmet.2007.09.006. [PubMed: 17983587]

Kramer FM, Jeffery RW, Forster JL, Snell MK, 1989. Long-term follow-up of behavioral treatment for obesity: patterns of weight regain among men and women. Int. J. Obes 13, 123–136. [PubMed: 2663745]

Kreisler AD, Mattock M, Zorrilla EP, 2018. The duration of intermittent access to preferred sucrose-rich food affects binge-like intake, fat accumulation, and fasting glucose in male rats. Appetite 130, 59–69. 10.1016/j.appet.2018.07.025. [PubMed: 30063959]

Kuriyama H, Shibasaki T, 2004. Sexual differentiation of the effects of emotional stress on food intake in rats. Neuroscience 124, 459–465. 10.1016/j.neuroscience.2003.12.012. [PubMed: 14980395]

Levin BE, Sullivan AC, 1989. Glucose-induced sympathetic activation in obesity-prone and resistant rats. Int. J. Obes 13, 235–246. [PubMed: 2744935]

Lowe MR, Foster GD, Kerzhnerman I, Swain RM, Wadden TA, 2001. Restrictive dieting vs. “undieting”: effects on eating regulation in obese clinic attenders. Addict. Behav 26, 253–266. 10.1016/S0306-4603(00)00106-4. [PubMed: 11316380]

Martin-Fardon R, Weiss F, 2014. Blockade of hypocretin receptor-1 preferentially prevents cocaine seeking: comparison with natural reward seeking. Neuroreport 25, 485–488. 10.1097/WNR.0000000000000120. [PubMed: 24407199]

Marti n-Fardon R, Cauvi G, Kerr TM, Weiss F, 2018. Differential role of hypothalamic orexin/hypocretin neurons in reward seeking motivated by cocaine versus palatable food. Addict. Biol 23, 6–15. 10.1111/adb.12441. [PubMed: 27558790]

Matikainen-Ankney BA, et al. , 2022. Nucleus accumbens D(1) receptor-expressing spiny projection neurons control food motivation and obesity. Biol. Psychiatry 10.1016/j.biopsych.2022.10.003.

McFarland K, Kalivas PW, 2001. The circuitry mediating cocaine-induced reinstatement of drug-seeking behavior. J. Neurosci 21, 8655–8663. 10.1523/jneurosci.21-21-08655.2001. [PubMed: 11606653]

McGlinchey EM, James MH, Mahler SV, Pantazis C, Aston-Jones G, 2016. Prelimbic to accumbens core pathway is recruited in a dopamine-dependent manner to drive cued reinstatement of cocaine seeking. J. Neurosci 36, 8700–8711. 10.1523/jneurosci.1291-15.2016. [PubMed: 27535915]

Meadows P, Phillips JH, Davey GC, 1988. Tail-pinch elicited eating in rats (Rattus norvegicus) and hamsters (Mesocricetus auratus). Physiol. Behav 43, 429–433. 10.1016/0031-9384(88)90115-1. [PubMed: 3194461]

Mehr JB, James MH, 2022 Nov 23. Sleep disruption as a potential contributor to the worsening of eating disorder pathology during the COVID-19-pandemic. J. Eat. Disord 10(1), 181. 10.1186/s40337-022-00704-9. [PubMed: 36424635]

Mendoza J, Angeles-Castellanos M, Escobar C, 2005a. A daily palatable meal without food deprivation entrains the suprachiasmatic nucleus of rats. Eur. J. Neurosci 22, 2855–2862. 10.1111/j.1460-9568.2005.04461.x. [PubMed: 16324120]

Mendoza J, Angeles-Castellanos M, Escobar C, 2005b. Entrainment by a palatable meal induces food-anticipatory activity and c-Fos expression in reward-related areas of the brain. Neuroscience 133, 293–303. 10.1016/j.neuroscience.2005.01.064. [PubMed: 15893651]

Mendoza J, Pévet P, Challet E, 2008. High-fat feeding alters the clock synchronization to light. J. Physiol 586, 5901–5910. 10.1113/jphysiol.2008.159566. [PubMed: 18936083]

Micioni Di Bonaventura MV, Micioni Di Bonaventura E, Polidori C, Cifani C, 2020. In: Frank, Guido KW, Berner, Laura A (Eds.), Binge Eating: A Transdiagnostic Psychopathology. Springer International Publishing, pp. 85–101.

Mistlberger RE, 1994. Circadian food-anticipatory activity: formal models and physiological mechanisms. Neurosci. Biobehav. Rev 18, 171–195. 10.1016/0149-7634(94)90023-x. [PubMed: 8058212]

Mohammadkhani A, et al. , 2019. Orexin-1 receptor signaling in ventral pallidum regulates motivation for the opioid remifentanil. J. Neurosci 10.1523/jneurosci.0255-19.2019.

Mook DG, 1963. Oral and postingestional determinants of the intake of various solutions in rats with esophageal fistulas. J. Comp. Physiol. Psychol 56, 645–659. 10.1037/h0044824.

Moore CF, Sabino V, Koob GF, Cottone P, 2017. Pathological overeating: emerging evidence for a compulsivity construct. Neuropsychopharmacology 42, 1375–1389. 10.1038/npp.2016.269. [PubMed: 27922596]

Moore CF, Cheng JE, Sabino V, Cottone P, 2019. In: Cottone, Pietro, Sabino, Valentina, Moore, Catherine F, Koob, George F (Eds.), Compulsive Eating Behavior and Food Addiction. Academic Press, pp. 359–388.

Murphy CM, Owens MM, Sweet LH, MacKillop J, 2016. The substitutability of cigarettes and food: a behavioral economic comparison in normal weight and overweight or obese smokers. Psychol. Addict. Behav 30, 857–867. 10.1037/adb0000223. [PubMed: 27736143]

Muscogiuri G, et al. , 2021. Chronotype and cardio metabolic health in obesity: does nutrition matter? Int. J. Food Sci. Nutr 72, 892–900. 10.1080/09637486.2021.1885017.

Nair SG, Golden SA, Shaham Y, 2008. Differential effects of the hypocretin 1 receptor antagonist SB 334867 on high-fat food self-administration and reinstatement of food seeking in rats. Br. J. Pharmacol 154, 406–416. 10.1038/bjp.2008.3. [PubMed: 18223663]

Nair SG, Adams-Deutsch T, Epstein DH, Shaham Y, 2009. The neuropharmacology of relapse to food seeking: methodology, main findings, and comparison with relapse to drug seeking. Prog. Neurobiol 89, 18–45. 10.1016/j.pneurobio.2009.05.003. [PubMed: 19497349]

Narayanaswami V, Thompson AC, Cassis LA, Bardo MT, Dwoskin LP, 2013. Diet-induced obesity: dopamine transporter function, impulsivity and motivation. Int. J. Obes 37, 1095–1103. 10.1038/ijo.2012.178.

Oswald KD, Murdaugh DL, King VL, Boggiano MM, 2011. Motivation for palatable food despite consequences in an animal model of binge eating. Int. J. Eat. Disord 44, 203–211. 10.1002/eat.20808. [PubMed: 20186718]

Pankevich DE, Teegarden SL, Hedin AD, Jensen CL, Bale TL, 2010. Caloric restriction experience reprograms stress and orexigenic pathways and promotes binge eating. J. Neurosci 30, 16399–16407. 10.1523/jneurosci.1955-10.2010. [PubMed: 21123586]

Pantazis CB, James MH, O'Connor S, Shin N, Aston-Jones G, 2021. Orexin-1 receptor signaling in ventral tegmental area mediates cue-driven demand for cocaine. Neuropsychopharmacology. 10.1038/s41386-021-01173-5.

Parkes SL, Furlong TM, Black AD, Balleine BW, 2017. Intermittent feeding alters sensitivity to changes in reward value. Appetite 113, 1–6. 10.1016/j.appet.2017.02.009. [PubMed: 28189750]

Patton DF, Mistlberger RE, 2013. Circadian adaptations to meal timing: neuroendocrine mechanisms. Front. Neurosci 7, 185. 10.3389/fnins.2013.00185. [PubMed: 24133410]

Polivy J, Zeitlin SB, Herman CP, Beal AL, 1994. Food restriction and binge eating: a study of former prisoners of war. J. Abnorm. Psychol 103, 409–411. 10.1037/0021-843X.103.2.409. [PubMed: 8040513]

Pratt EM, Niego SH, Agras WS, 1998. Does the size of a binge matter? Int. J. Eat. Disord 24, 307–312. 10.1002/(sici)1098-108x(199811)24:3<307::aid-eat8>3.0.co;2-q.

Presby RE, Rotolo RA, Yang JH, Correa M, Salamone JD, 2020. Lisdexamfetamine suppresses instrumental and consummatory behaviors supported by foods with varying degrees of palatability: exploration of a binge-like eating model. Pharmacol. Biochem. Behav 189, 172851 10.1016/j.pbb.2020.172851. [PubMed: 31931017]

Pressler M, et al. , 2022. Dietary transitions and health outcomes in four populations - systematic review. Front. Nutr 9, 748305 10.3389/fnut.2022.748305. [PubMed: 35252289]

Raymond NC, Neumeyer B, Warren CS, Lee SS, Peterson CB, 2003. Energy intake patterns in obese women with binge eating disorder. Obes. Res 11, 869–879. 10.1038/oby.2003.120. [PubMed: 12855757]

Rehn S, Raymond JS, Boakes RA, Leenaars CHC, 2022. A systematic review and meta-analysis of animal models of binge eating - part 1: definitions and food/drink intake outcomes. Neurosci. Biobehav. Rev 132, 1137–1156. 10.1016/j.neubiorev.2021.10.036. [PubMed: 34742923]

Reichelt AC, Morris MJ, Westbrook RF, 2014. Cafeteria diet impairs expression of sensory-specific satiety and stimulus-outcome learning. Front. Psychol 5 10.3389/fpsyg.2014.00852.

Riccobono G, et al. , 2020. Night eating syndrome, circadian rhythms and seasonality: a study in a population of Italian university students. Riv Psichiatr 55, 47–52. 10.1708/3301.32719. [PubMed: 32051626]

Robinson MJ, et al. , 2015. Individual differences in cue-induced motivation and striatal systems in rats susceptible to diet-induced obesity. Neuropsychopharmacology 40, 2113–2123. 10.1038/npp.2015.71. [PubMed: 25761571]

Rossi MA, Stuber GD, 2018. Overlapping brain circuits for homeostatic and hedonic feeding. Cell Metab. 27, 42–56. 10.1016/j.cmet.2017.09.021. [PubMed: 29107504]

Rowland NE, Antelman SM, 1976. Stress-induced hyperphagia and obesity in rats: a possible model for understanding human obesity. Science 191, 310–312. 10.1126/science.1246617. [PubMed: 1246617]

Rutters F, Nieuwenhuizen AG, Lemmens SG, Born JM, Westerterp-Plantenga MS, 2009. Acute stress-related changes in eating in the absence of hunger. Obesity (Silver Spring, Md.) 17, 72–77. 10.1038/oby.2008.493. [PubMed: 18997672]

Schiestl ET, Rios JM, Parnarouskis L, Cummings JR, Gearhardt AN, 2021. A narrative review of highly processed food addiction across the lifespan. Prog. Neuro-Psychopharmacol. Biol. Psychiatry 106, 110152. 10.1016/j.pnpbp.2020.110152.

Seabrook LT, et al. , 2022. Disinhibition of the orbitofrontal cortex biases decision-making in obesity. Nat. Neurosci 10.1038/s41593-022-01210-6.

Shaham Y, Adamson LK, Grocki S, Corrigall WA, 1997. Reinstatement and spontaneous recovery of nicotine seeking in rats. Psychopharmacology 130, 396–403. 10.1007/s002130050256. [PubMed: 9160857]

Stammers L, et al. , 2020. Identifying stress-related eating in behavioural research: a review. Horm. Behav 124, 104752 10.1016/j.yhbeh.2020.104752. [PubMed: 32305343]

Stephan FK, 2002. The "other" circadian system: food as a Zeitgeber. J. Biol. Rhythm 17, 284–292. 10.1177/074873040201700402.

Stojek MMK, MacKillop J, 2017. Relative reinforcing value of food and delayed reward discounting in obesity and disordered eating: a systematic review. Clin. Psychol. Rev 55, 1–11. 10.1016/j.cpr.2017.04.007. [PubMed: 28478269]

Stojek MK, Fischer S, MacKillop J, 2015. Stress, cues, and eating behavior. Using drug addiction paradigms to understand motivation for food. Appetite 92, 252–260. 10.1016/j.appet.2015.05.027. [PubMed: 26022802]

Strubbe JH, Keyser J, Dijkstra T, Prins AJ, 1986. Interaction between circadian and caloric control of feeding behavior in the rat. Physiol. Behav 36, 489–493. 10.1016/0031-9384(86)90320-3. [PubMed: 3085115]

Stunkard AJ, Grace WJ, Wolff HG, 1955. The night-eating syndrome: a pattern of food intake among certain obese patients. Am. J. Med 19, 78–86. 10.1016/0002-9343(55)90276-X. [PubMed: 14388031]

Sun W, Rebec GV, 2005. The role of prefrontal cortex D1-like and D2-like receptors in cocaine-seeking behavior in rats. Psychopharmacology 177, 315–323. 10.1007/s00213-004-1956-x. [PubMed: 15309375]

Swinburn BA, et al. , 2009. Estimating the changes in energy flux that characterize the rise in obesity prevalence. Am. J. Clin. Nutr 89, 1723–1728. 10.3945/ajcn.2008.27061. [PubMed: 19369382]

Tajaddini A, Kendig MD, Prates KV, Westbrook RF, Morris MJ, 2022. Male rat offspring are more impacted by maternal obesity induced by cafeteria diet than females-additive effect of postweaning diet. Int. J. Mol. Sci 23 10.3390/ijms23031442.

Tantot F, et al. , 2017. The effect of high-fat diet consumption on appetitive instrumental behavior in rats. Appetite 108, 203–211. 10.1016/j.appet.2016.10.001. [PubMed: 27713085]

Teegarden SL, Bale TL, 2007. Decreases in dietary preference produce increased emotionality and risk for dietary relapse. Biol. Psychiatry 61, 1021–1029. 10.1016/j.biopsych.2006.09.032. [PubMed: 17207778]

Thanarajah SE, et al. , 2019. Food intake recruits orosensory and post-ingestive dopaminergic circuits to affect eating desire in humans. Cell Metab. 29, 695–706. e694. 10.1016/j.cmet.2018.12.006. [PubMed: 30595479]

Tomasi D, Volkow ND, 2013. Striatocortical pathway dysfunction in addiction and obesity: differences and similarities. Crit. Rev. Biochem. Mol. Biol 48, 1–19. 10.3109/10409238.2012.735642. [PubMed: 23173916]

Turek FW, et al. , 2005. Obesity and metabolic syndrome in circadian clock mutant mice. Science 308, 1043–1045. 10.1126/science.1108750. [PubMed: 15845877]

Udo T, Grilo CM, 2018. Prevalence and correlates of DSM-5–defined eating disorders in a nationally representative sample of U.S. adults. Biol. Psychiatry 84, 345–354. 10.1016/j.biopsych.2018.03.014. [PubMed: 29859631]

Velázquez-Sánchez C, et al. , 2014. High trait impulsivity predicts food addiction-like behavior in the rat. Neuropsychopharmacology 39, 2463–2472. 10.1038/npp.2014.98. [PubMed: 24776685]

Velázquez-Sánchez C, et al. , 2015. Seeking behavior, place conditioning, and resistance to conditioned suppression of feeding in rats intermittently exposed to palatable food. Behav. Neurosci 129, 219–224. 10.1037/bne0000042. [PubMed: 25798634]

Villarejo C, et al. , 2012. Lifetime obesity in patients with eating disorders: increasing prevalence, clinical and personality correlates. Eur. Eat. Disord. Rev 20, 250–254. 10.1002/erv.2166. [PubMed: 22383308]

Wojnicki FH, Babbs RK, Corwin RL, 2010. Reinforcing efficacy of fat, as assessed by progressive ratio responding, depends upon availability not amount consumed. Physiol. Behav 100, 316–321. 10.1016/j.physbeh.2010.03.004. [PubMed: 20298708]

World Health, O. (World Health Organization, Geneva, 2004).

Zimmer BA, Oleson EB, Roberts DCS, 2012. The motivation to self-administer is increased after a history of spiking brain levels of cocaine. Neuropsychopharmacology 37, 1901–1910. [PubMed: 22453139]