# Roles of "Wanting" and "Liking" in Motivating Behavior: Gambling, Food, and Drug Addictions

**M.J.F. Robinson, A.M. Fischer, A. Ahuja, E.N. Lesser and H. Maniates**

**Abstract** The motivation to seek out and consume rewards has evolutionarily been driven by the urge to fulfill physiological needs. However in a modern society dominated more by plenty than scarcity, we tend to think of motivation as fueled by the search for pleasure. Here, we argue that two separate but interconnected subcortical and unconscious processes direct motivation: "wanting" and "liking." These two psychological and neuronal processes and their related brain structures typically work together, but can become dissociated, particularly in cases of addiction. In drug addiction, for example, repeated consumption of addictive drugs sensitizes the mesolimbic dopamine system, the primary component of the "wanting" system, resulting in excessive "wanting" for drugs and their cues. This sensitizing process is long-lasting and occurs independently of the "liking" system, which typically remains unchanged or may develop a blunted pleasure response to the drug. The result is excessive drug-taking despite minimal pleasure and intense cue-triggered craving that may promote relapse long after detoxification. Here, we describe the roles of "liking" and "wanting" in general motivation and review recent evidence for a dissociation of "liking" and "wanting" in drug addiction, known as the incentive sensitization theory (Robinson and Berridge 1993). We also make the case that sensitization of the "wanting" system and the resulting dissociation of "liking" and "wanting" occurs in both gambling disorder and food addiction.

**Keywords** "Wanting" · "Liking" · Motivation · Incentive salience · Sensitization · Addiction · Gambling · Obesity · Overconsumption

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## Contents



## 1 Introduction

Most people enjoy eating fatty, salty, and sugary foods. Many of us happily indulge in the occasional opportunity to gamble or get a thrill from visiting a casino. Others manage to recreationally use psychoactive drugs (such as alcohol), even in large quantities, without allowing them to consume their lives. Yet for each of these activities you can find countless examples of people who overindulge, even to the point of serious adverse consequences detrimental to their work, family, or health. In some instances, the enjoyment provided by these activities steadily declines, and all that is left is the unrelenting desire to carry on. Motivational structures of the brain provide the initial spark to seek out and consume the resources needed to survive, yet these systems can be hijacked by stimuli that surpass what is typically encountered in nature and may lead people astray, often with devastating consequences. It is in these moments, when the dichotomy between our survival needs and our wants is greatest, that the complexity of the system is exposed, and we can gain insights into its function.

## 2 "Liking" and "Wanting"

While we typically want the things that we like and like the things that we want, these concepts are not synonymous. The intuitive nature of these words helps nurture understanding of relatively complex motivational concepts. The fact that our language developed to have these two separate words shows how important the distinction between these ideas is to motivation. In 1993, Terry Robinson and Kent Berridge at the University of Michigan refined the use of the words in the context of motivational research (Robinson and Berridge 1993). They posited that the brain contains two distinct systems; one system responsible for hedonic pleasure, or "liking," and another separate yet interconnected system responsible for "wanting," or what Robinson and Berridge termed incentive salience. To ease discussion of

these concepts, we will refer to "wanting" (with quotation marks) as a specific subcomponent of the colloquial understanding of the word wanting. Wanting (without quotation marks) typically refers to conscious, cognitive desire, while we will use "wanting" to refer to the visceral feeling of desire. Similarly, "liking" refers to the core process of hedonic pleasure and is deemed separate from the subjective experience of conscious pleasure.

When you take a bite into your favorite food, the look, taste, texture, and smell of the food come together to comprise the pleasure experienced from the affective hedonic impact or "liking" aspects of the food. This "liking" component associated with attaining a reward goes beyond mere sensory properties. Rewards such as food possess clear sensory components of taste and smell. However, separate brain circuits account for how much a food is "wanted" or "liked." For example, the once-liked sweet taste of chocolate ice cream can become strongly disliked if paired with violent sickness, despite retaining its sweet sensory properties (Garcia et al. 1985; Rozin 2000; Reilly and Schachtman 2009; Berridge et al. 2010). The converse seems anecdotally true of the bitter taste of beer or coffee, as these tastes often become desired and pleasant with repeated exposure and cultural norms. Further, both "wanting" and "liking" can be strongly modulated by internal physiological states. Hunger will make foods more desired and pleasurable (Cabanac 1971), whereas satiation can dampen the pleasure elicited by chocolate in a self-proclaimed chocoholic (Small et al. 2001; Lemmens et al. 2009), a dynamic shift in hedonic tone referred to as "alliesthesia" (Cabanac 1971).

"Wanting," or incentive salience, is the acquisition of a visceral and unconscious desire for a reward. The motivational value given to that reward can be conferred to cues and objects related to the reward or its retrieval (Bindra 1978) transforming them into "wanted" incentives. Noticing cues that predict food (or monetary gains) can help one accrue more rewards and, therefore, evolutionary fitness (Hollis 1984). In turn, these cues are imbued with incentive salience and become capable of triggering motivation and bursts of reward-seeking (Holmes et al. 2010; Peciña and Berridge 2013). For example, the smell of freshly brewed coffee or the distinct lights and layout of a casino may prompt the need for a pick-me-up or create the urge to play. Three fundamental characteristics apply to cues or conditioned stimuli (CSs) that have been imbued with incentive salience. First, these cues become "motivational magnets." Attention and behavior is "drawn" to them, like a magnet, making such cues difficult to ignore. Experimentally, we can see this demonstrated during Pavlovian conditioned approach (PCA) or autoshaping, where an animal will sniff, lick, and even bite inedible objects such as a protruding metal lever because it has repeatedly predicted delivery of a tasty edible reward (Brown and Jenkins 1968; Hearst and Jenkins 1974; Boakes et al. 1978; Robinson et al. 2014c). This irrational behavior, referred to as sign-tracking, is often evolutionarily adaptive behavior similar to that prompted by the nature of the reward, but appears irrational due to the arbitrary nature of the stimulus (such as an inedible metal lever).

Secondly, beyond simply attracting attention, reward-related cues can become the focus of motivation and themselves act as reinforcers. They may even foster new behaviors that increase interaction and contact with these cues. In a laboratory

setting, animals will display this type of behavior, known as conditioned reinforcement (Robbins et al. 1983), when they are first trained to associate a cue with a reward and then given the opportunity in a novel task to work for a presentation of that cue alone. The animal is no longer receiving a reward that has any innate value like food (unconditioned stimulus, or UCS); all that generates and sustains their behavior is the cue that was once associated with the UCS reward. In our daily lives, this phenomenon can be seen in routine behaviors like walking by our favorite bakery simply to experience the aroma of freshly baked goods or when a recent ex-smoker might linger around other smokers for the opportunity to experience the smell of second-hand smoke.

Finally, a reward-associated cue attributed with incentive salience can trigger sudden surges in effort to obtain a reward. Experimentally, we see this in a task called Pavlovian-to-instrumental transfer (PIT) that measures cue-induced peaks in "wanting," seen as surges in effort to obtain a previously available reward. For example, many people report needing a cup of coffee to start their day. But on days when they do not have time to go and buy coffee, the simple sight or smell of someone else's coffee nearby can trigger a powerful enough urge, on top of what might be already strong motivation, to go and get coffee. Here, cues become powerful enough to direct and sometimes dictate behavior.

Although cortical influences are now responsible for cognitive processes we use to consciously determine our behavior, these cortical inputs are an evolutionarily more recent addition to motivated behavior (Swanson 2000; Cardinal et al. 2002; Bernard et al. 2005; Swanson 2005). It is likely that incentive salience developed in living organisms that lacked higher level cortical functioning to guide them toward activities like feeding, drinking, and procreating. For example, animals lacking any clear cortical structures, such as the Atlantic cod and the cuttlefish, show evidence of incentive salience attribution in the form of sign-tracking (Purdy et al. 1999; Nilsson et al. 2008). Nevertheless, not all behavior is determined by subcortical systems. There are likely earlier-evolved reflexes that are now suppressed in order to let cortical mechanisms guide behavior. Despite this, it appears that we sometimes still rely on these primitive brain systems to provide a motivational spark toward fulfilling our biological needs (Robinson and Berridge 1993). Thus, many of our conscious wants arise from the subcortical "wanting" system, often despite any cognitive awareness of their subcortical origin.

Beyond cognitive intentions to seek out reward, most people believe that rewards are "wanted" and desired because they produce a conscious experience of pleasure. Although pleasure is a fundamental component of human existence, our ability to accurately discern its inner workings is limited (James 1884). Pleasure is generally described as a purely subjective experience, but evidence suggests that subjective pleasure is only one of the components of reward that is experienced (Berridge et al. 2009; Dai et al. 2010; Litt et al. 2010). Instead rewards can influence behavior even in the absence of conscious awareness (Fischman and Foltin 1992; Winkielman et al. 2005). For example, Fischman and Foltin showed that recovering addicts would consistently choose a very low dose of cocaine over an injection of saline, despite reporting no more subjective feelings of pleasure than with saline, no

cardiovascular responses, and indicating that they thought they were sampling both options equally (Fischman and Foltin 1992). Similarly, a study by Winkielman and colleagues showed that subliminal presentations of happy faces made thirsty participants rate, pour and drink more of a sweet beverage despite reports of their conscious feelings remaining unaffected (Winkielman and Berridge 2003; Winkielman et al. 2005). Instead, these rewards may provoke unconscious pleasure or "liking" reactions that may be more objective as they do not rely on self-report and are typically contiguous with the experience of the hedonic stimulus. In contrast to conscious subjective pleasure, "liking" is an implicit response to hedonic stimuli that can be measured in behavior and physiology even in the absence of conscious liking. It is measured using a technique called taste reactivity that exploits objective "liking" reactions to sweet tastes (Grill and Norgren 1978). This method examines orofacial affective expressions, which are homologous across species, including humans, rats, and apes (Steiner et al. 2001; Berridge and Kringelbach 2008). Specifically, sweet tastes elicit positive "liking" responses such as lip licking and rhythmic tongue protrusions, whereas bitter tastes such as quinine produce negative "disliking" expressions such as gapes and headshakes.

Beyond a psychological dissociation, pleasure "liking" also appears to possess a more restrictive limbic brain circuit, both anatomically and neurochemically, which may predispose us more to states of desire than to states of pleasure (see Fig. 1). The "liking" and "wanting" systems in the brain have some structural and neurochemical overlap, but also separate substrates (Berridge et al. 2009, 2010; Castro et al. 2015). While both systems are contained within certain common mesolimbic structures, the "liking" components, or hedonic "hot spots," are only small subregions of these greater mesolimbic structures, including the nucleus accumbens and ventral pallidum (Berridge and Robinson 2003; Berridge et al. 2010). These hedonic "hot spots" were so named (Berridge 2003; Smith et al. 2007) for their ability to elicit positive facial hedonic reactions ("liking") to a sweet solution when neurochemically stimulated (such as by opioid and endocannabinoid neurotransmitters, but not dopamine stimulation). These increases in hedonic pleasure are restricted to stimulation of the small hedonic "hot spots" and cannot be readily elicited by stimulation of neighboring areas in the remaining mesolimbic system (Smith and Berridge 2007; Smith et al. 2007). These hot spots seem to function as a cooperative network that requires a unanimous vote to engender a "liking" response. While stimulation of just one hot spot will typically recruit others, pharmacologically inhibiting activity in one hot spot will prevent an enhancement of "liking" from opioid stimulation in one of the other hot spots (Smith and Berridge 2007; Castro and Berridge 2014). In contrast, "wanting" can be increased by raising dopamine levels in any part of the mesolimbic system (including those hot spots) and does not seem to require simultaneous activity from other motivation centers. "Wanting" can also be evoked by opioid stimulation (and certain other neurotransmitters) within the hot spots (in addition to the aforementioned effects of opioids on "liking"). For example, the opioid agonist DAMGO will enhance "liking" in the cubic millimeter hot spot of the accumbens medial shell, which makes up only 10 % of the entire nucleus accumbens (Peciña 2005; Smith and

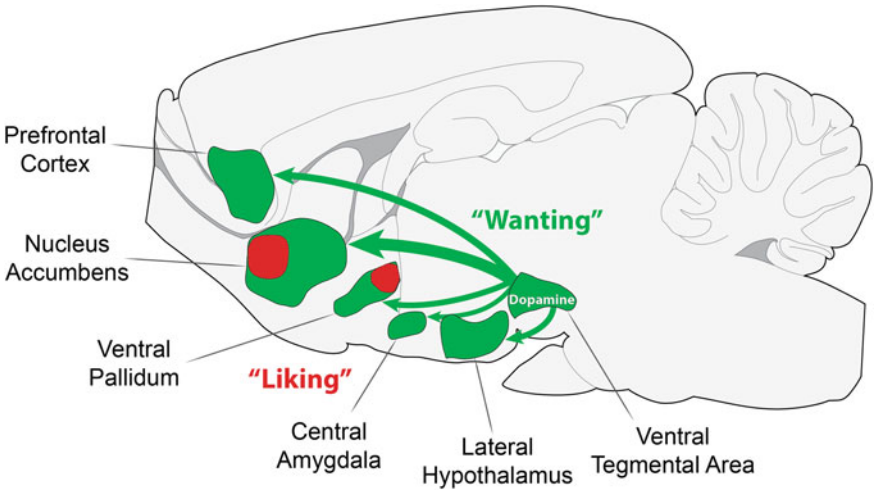


**Fig. 1** Mesocorticolimbic circuitry of "liking" and "wanting." This sagittal view of a rodent brain depicts structures and circuitry underlying "liking" (*red*) and "wanting" (*green* and *red*). The nucleus accumbens medial shell contains a hedonic hot spot in the rostral half, where opioid and related stimulation increases "liking" reactions to sucrose taste. The caudal half of the ventral pallidum contains a similar opioid hedonic hot spot. The ventral tegmental area projects dopaminergic afferents to the above labeled areas, which when stimulated increase "wanting" and the attribution of incentive salience, including the areas that contain hedonic hot spots. Sagittal section adapted from Paxinos and Watson (2007)

Berridge 2007; Berridge et al. 2010). In contrast, the same DAMGO microinjection will potently enhance "wanting" in the entire nucleus accumbens (Peciña 2005). Some of the neural structures and pathways involved in "liking" and "wanting" are illustrated in Fig. 1.

Evidence for the existence of distinct neural pathways governing "liking" and "wanting" suggests that in some instances it might be possible to experience "wanting" without "liking" or vice versa. The earliest example of "wanting" without "liking" came from laboratory studies examining the impact of electrical stimulation of the lateral hypothalamus, a part of the brain that activates mesolimbic pathways and dopamine release (Berridge and Valenstein 1991). When electrically stimulated in such a fashion, animals eat voraciously but show no increase in their "liking" responses. Instead, they display a moderate increase in "disliking" to a sucrose solution, as if it became slightly unpleasant. Similar results have been found in mutant mice that have their dopamine transporter knocked down, which leads to excessive synaptic dopamine (Peciña et al. 2003), or in rats following amphetamine or drug sensitization-induced elevation of dopamine release (Wyvell and Berridge 2000; Tindell et al. 2005). More recently, studies have shown that stimulation of areas such as the central nucleus of the amygdala either pharmacologically using DAMGO or optogenetically will increase "wanting" for specific rewards and their cues independently of any changes in "liking" (Mahler and Berridge 2009;

DiFeliceantonio and Berridge 2012; Robinson et al. 2014b). In humans, studies show that dopamine levels are more highly correlated with subjective ratings of "wanting" a reward than with pleasure ratings of that same reward (Volkow et al. 2002; Leyton et al. 2002). In fact, certain highly addictive drugs such as nicotine are exceedingly "wanted" despite producing little to no feelings of pleasure or euphoria (Benowitz 1996; West 2009; Isomura et al. 2014).

Conversely, "liking" without "wanting" can also occur, specifically when dopaminergic transmission is disrupted. For example, in mutant mice that lack the ability to produce any dopamine in their brains, sweet solutions or food rewards will still be liked and preferred over water due to their hedonic impact (Cannon and Palmiter 2003; Robinson et al. 2005). Similarly, drugs that block dopamine transmission, such as the dopamine antagonist pimozide, or treatments (6-OHDA) that destroy over 99 % of mesolimbic and neostriatal dopamine afferents do not disrupt positive "liking" facial reactions to the taste of sucrose (Peciña et al. 1997; Berridge and Robinson 1998). However, these drugs do disrupt "wanting," in that the animals lack the motivation to feed themselves and display life-threatening aphagia and adipsia. In humans, drugs that block dopamine function completely fail to reduce the subjective ratings of pleasure people give to an addictive drug, such as amphetamine or methamphetamine (Brauer and De Wit 1997; Wachtel et al. 2002; Leyton 2010), yet diminish craving and cue-induced craving (Berger et al. 1996). Similarly, studies in which dopamine transmission was decreased by interfering with dopamine synthesis (acute phenylalanine/tyrosine depletion; APTD) show that the pleasurable and mood altering effects of a wide range of abused substances, such as alcohol (Leyton et al. 2000; Barrett et al. 2008), tobacco (Casey et al. 2006; Munafò et al. 2007), amphetamine (Leyton 2007), and cocaine (Leyton et al. 2005), remain intact, while traits related to "wanting" such as cocaine-induced confidence and drug craving are dramatically reduced (Leyton et al. 2005). These results demonstrate that both "wanting" and "liking" can occur independently, and since "liking" is controlled by a smaller portion of the brain and requires collective activation of different hot spots (making it easier to disrupt), it may be a more fragile and less critical component of motivated behavior than "wanting" (Fig. 1). That survival may be almost impossible in the total absence of "wanting," but not in the absence of "liking" may be evidence for this claim.

Natural rewards such as food, water, and sex all generate pleasure, while also triggering the release of mesolimbic dopamine and activating our "wanting" system (Hernandez and Hoebel 1988; Pfaus et al. 1990). In drug, food, and gambling addictions, we see evidence of hypersensitive "wanting" systems taking salience attribution to maladaptive levels, often with very little change in pleasure responding (Robinson and Berridge 2008; Rømer Thomsen et al. 2014; Robinson et al. 2015b). As such we often talk about how drugs of abuse hijack our natural "wanting" system and send it into overdrive. In the three following sections, we will examine the evidence and the insight that the incentive salience theory can provide in three types of addictive behavior: drug abuse, gambling disorder, and overeating and obesity. We will pay close attention to explaining what roles both "liking" and "wanting" may play in the development and maintenance of each addiction. We

begin with drug addiction, as it has been the most extensively studied and provides the groundwork for explaining some of the changes seen in gambling and food addiction.

## 3 Drug Addiction

The symptoms and behaviors that characterize drug addiction can vary greatly from person to person, depending on the drug of choice, the circumstances of use and individual differences between users (Robinson and Berridge 1993; Cadet et al. 2014). Nevertheless, all cases of drug addiction possess three common, significant characteristics that a complete theory of drug addiction must explain (Hollis 1984; Robinson and Berridge 1993). These characteristics highlight the fractioning of the natural bond between "liking" and "wanting," which we believe occurs in multiple forms of addiction. They are as follows:

1. An increased intake and desire for the drug over time, often to the point of intense cravings.
2. Persistent and recurring bouts of craving, frequently triggered by drug-paired cues, that posses the ability to promote relapse, even long after drug-taking has ceased.
3. The dissociation of the pleasure generated by the drug, which tends to decrease or remain unchanged over time, from the desire for the drug, which increases over time and becomes hyper-responsive to drugs and drug stimuli.

The incentive sensitization theory of addiction aims to incorporate and explain these three tenets (Robinson and Berridge 1993; Holmes et al. 2010; Peciña and Berridge 2013). In this theory, Terry Robinson and Kent Berridge posit that repeated drug use causes the mesolimbic dopamine system of the brain responsible for the generation of "wanting" to experience **incentive sensitization,** which in turn leads to the symptoms of drug addiction. Incentive sensitization is defined as an increase in the sensitivity of the neural circuits responsible for the attribution of **incentive salience** ("wanting") to a drug—a process that occurs as a consequence of gradual and progressive neurological changes induced by repeated drug use. The attribution of incentive salience is mediated by dopamine projections to the nucleus accumbens and striatum from the ventral tegmental area and substantia nigra (Robinson and Berridge 2003). Sensitization of this neural circuitry over time, as a consequence of repeated drug consumption, elicits a greater dopaminergic response, and as a result, the incentive salience for the drug and its cues steadily increases. This means that the desire for a particular drug and the ability of its associated cues to trigger craving escalate with repeated drug consumption.

According to the incentive sensitization theory, an individual would first have to consume a potentially addictive drug. This initial behavior would likely be prompted by a desire to experience the expected pleasure ("liking") associated with being under the influence of the drug or by societal pressure to use the substance.

This sensation of euphoria or drug "liking" will likely initially prompt sporadic use that may evolve into repeated use over time. Each drug experience will incur surges in dopaminergic activity in the mesolimbic reward system. Over time, these recurring surges in dopamine release from repeated consumption will cause sensitization of mesolimbic dopamine pathways. The result is an enhanced dopaminergic response to the same initial dose of the drug (Robinson et al. 1988; Kalivas and Duffy 1990; Vezina 1993, 2004), in the form of enhanced dopamine overflow (Kalivas and Duffy 1993; Vanderschuren and Kalivas 2000; Vanderschuren et al. 2001), dopamine D1 receptor supersensitivity (Henry and White 1991; Hu et al. 2002), and enhanced intracellular mechanisms such as induction of immediate early genes (Hiroi et al. 1997). Greater dopamine signaling will result in an increase in the incentive salience assigned to the drug and its cues, which in turn will cause the drug to be "wanted" more. This process occurs independently of the pleasure produced by the drug and is not necessarily tied to "liking" (which may sometimes decrease with increased consumption) (Wyvell and Berridge 2000; Tindell et al. 2005). Due to the increasing incentive salience of the drug and its cues, the user is motivated to approach and consume the drug even more, which will only sensitize the brain further. Thus, a progressive increase in drug "wanting" and consumption occurs, without any paralleled increase in drug "liking," sometimes even despite "liking" the drug less. As a result, the drug becomes compulsively "wanted," in that the urge to consume may contradict cognitive wants to abstain (see Berridge and Robinson 2011), and drug-associated cues are able to trigger intense cravings, that may result in bouts of drug-seeking. In many instances, these urges to seek out and take drugs are appeased by top-down cognitive control, meaning that more often than not, cue-triggered impulses to take drugs are quashed by the knowledge of the undesired consequences. Yet in this war between subcortical impulses and cognitive intentions, it only takes the loss of a single battle in favor of subcortical "wanting" for relapse to occur, and the war to be lost (Berridge and Robinson 2011).

It has been suggested that compulsive drug-seeking might originate from a physical need for the drug or a powerful motivation to avoid the unpleasant symptoms of drug withdrawal (Wikler 1973; Khantzian 1985; Koob et al. 1989; Koob 1996). According to this view, drug-taking and the resulting dopamine release would satisfy a need, thereby satiating the user and reducing motivation to take more drug. This is counter-intuitive, as it implies that an addict would only take drugs to satisfy a need (and not beyond), when some of the hallmarks of addiction are a tendency to escalate the amount of drug taken and to regularly take more drug than intended (American Psychiatric Association 2013). Instead, the incentive sensitization theory suggests that dopaminergic activity produces incentive motivation for a reward and that a heightened/sensitized dopaminergic response to drug-taking events explains why a small hit of the drug triggers a greater urge for more drug, rather than producing any form of satiation or reduction in motivation (Robinson and Berridge 1993). The process of incentive sensitization is illustrated in Fig. 2.

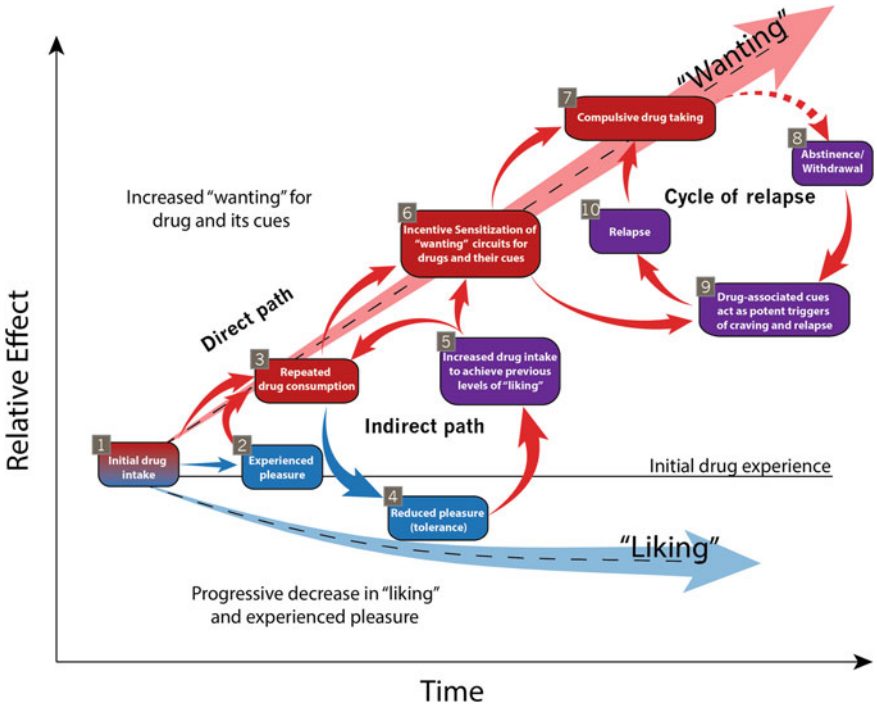


**Fig. 2** The incentive sensitization model of addiction. Addiction is characterized by a progressive dissociation of drug "wanting" and "liking" with increasing incentive salience being attributed to drugs and their cues. This schematic model suggests a "direct path" to addiction that develops with repeated and escalating drug consumption leading to incentive sensitization of "wanting" and compulsive drug-taking [Steps: *1-3-6-7*]. A separate contributing factor to this phenomenon is highlighted by the "indirect path" loop, which suggests that with repeated drug-taking the experienced pleasure and euphoria caused by the drug fails to increase and may sometimes even diminish, which prompts intake of larger and larger doses of drug, thus contributing to the sensitization of mesolimbic dopamine circuits [Steps: *3-4-5*]. Finally, compulsive drug-taking is often punctuated by periods of abstinence and withdrawal, which all too frequently result in relapse, often triggered by cue-induced craving. This "cycle of relapse" characterizes drug addiction as a chronic relapsing disorder [Steps: *7-8-9-10*]. Adapted with permission from Robinson and Berridge (1993), Berridge et al. (2009)

The neural changes involved in the process of incentive sensitization are long-lasting (Shuster et al. 1975; Paulson et al. 1991; Castner and Goldman-Rakic 1999). More importantly, these changes persist beyond the cessation of drug-taking and beyond withdrawal, which often only lasts 1–2 weeks (Khavari et al. 1975; Stinus et al. 1998; Gekht et al. 2003). Withdrawal is typically described as an intense negative emotional state accompanied by dysphoria, anxiety, and irritability. Withdrawal avoidance-based theories of addiction suggest that these unpleasant symptoms are the primary motivator for unrelenting drug-taking and relapse (Koob

et al. 1989). Although withdrawal may be a potent reason why many addicts relapse, it fails to explain why relapse frequently occurs even after withdrawal symptoms have subsided (Hunt et al. 1971). The persistence of incentive sensitization accounts for why drugs and their cues retain the ability to trigger craving and relapse for many years, even in "detoxified" addicts long after "recovery."

Finally, this entire process takes place independently of the pleasure induced by the drug, since the aforementioned sensitization affects only the motivational effects of the drug, but not to the euphoria it generates. Thus, the three facets of addiction outlined at the beginning of this section are addressed by the incentive sensitization theory.

The incentive sensitization theory also addresses the role of drug-related cues in addiction. Cues related to drug abuse (paraphernalia, contexts, etc.) can themselves take on added incentive salience through the process of sensitization. As a result, they are transformed into powerful "motivational magnets," able to induce cravings upon exposure and bring individuals into the proximity of drugs. Specifically, drug-related cues become increasingly capable of triggering increases in dopaminergic activity in the mesolimbic reward pathway resulting in excessive "wanting," even when presented in the absence of the drug (Leyton 2007; Vezina and Leyton 2009). A striking example of this can be seen with crack cocaine addicts, who when experiencing intense cravings will inspect the floor for any small, white specks and often try and smoke them, even when the specks are most likely dust or ordinary pebbles—a phenomenon known as "chasing ghosts" (Rosse et al. 1993).

In order to account for drug addiction, the incentive sensitization theory makes several verifiable assumptions. **Firstly**, the consumption of drugs must be able to affect areas of the brain involved in regulating "wanting," independent of influence from the brain's pleasure or "liking" systems. **Secondly**, excessive consumption of drugs should gradually render this neural circuitry hypersensitive to the motivational effects of said drugs. **Thirdly**, for this theory to apply to drug addiction more broadly, the neurological mechanism responsible for the attribution of incentive salience must be common to all addictive drugs. **Finally**, the neurobiological changes produced by excessive drug consumption must be long-lasting in order to account for instances of relapse occurring long after withdrawal symptoms have subsided. The next section will address all of these criteria and provide supporting experimental evidence.

## *3.1 Evidence for the Incentive Sensitization Theory*

Let us begin by addressing the assumption that the neural system sensitized by drug consumption is one that only regulates "wanting," and acts independently of "liking." Since dopamine is the primary neural substrate that controls "wanting," an increase in the release of dopamine in response to a particular stimuli can be interpreted directly as an increase in "wanting" for those stimuli. Supporting evidence for the diverging role of these two systems comes from manipulations of the

dopamine system in humans and animals that influences "wanting" while leaving "liking" intact. Drugs such as amphetamine, cocaine, methamphetamine, morphine, nicotine, alcohol, and even THC have been shown to increase transmission of dopamine in the nucleus accumbens and dorsal striatum (Robinson and Berridge 1993). A study by Di Chiara et al. further illustrated that while in humans, drugs of abuse such as cocaine, amphetamine, nicotine increase the concentration of dopamine in both the nucleus accumbens and the dorsal caudate nucleus, drugs that are typically not abused, such as antihistamines or antimuscarinic drugs, fail to show similar results (Di Chiara and Imperato 1988). Furthermore, drugs such as nicotine produce increases in dopamine transmission but fail to produce any reported "liking" or euphoria, suggesting the absence of any clear relationship between "liking" and the excessive "wanting" that leads to addiction (Rose et al. 2000; Caggiula et al. 2009; Balfour and Munafò 2015). The lack of any significant correlation between "liking" and "wanting" has also been shown for alcohol in humans (Hobbs et al. 2005; Ostafin et al. 2010). We can therefore suggest that a critical aspect of drug addiction is the sensitization of the mesolimbic dopaminergic system which results in an increase in dopaminergic response to drugs and their cues, and that these increases in incentive salience/"wanting" are independent of changes in "liking" (Ferrario et al. 2005; Ferrario and Robinson 2007; Robinson and Berridge 2008).

Our second assumption states that repeatedly consuming drugs that trigger activity in the "wanting" system gradually increases their incentive properties, which helps explain excessive drug use and the development of addiction. A study by Woolverton et al. reported that when rhesus monkeys were pretreated with methamphetamine injections, they became more likely to self-administer amphetamine if given the opportunity at a later time (Woolverton et al. 1984; Leyton 2010). This finding demonstrates that the initial exposure resulted in an "increased sensitivity to the reinforcing properties of the drug," because of which subjects were more motivated to consume the drug during subsequent trials as compared to controls. More recently, a study by Boileau et al. reported that when treated with three doses of amphetamine within the span of five days, healthy adult men demonstrated an increased release of dopamine in response to the third dose relative to the first (Berger et al. 1996; Boileau et al. 2006). When participants were re-tested a year later, they continued to demonstrate dopaminergic sensitization in brain areas such as the ventral striatum, which is involved in the regulation of "wanting." A similar sensitization of dopamine release has also been reported in Parkinson's patients who compulsively use dopaminergic drugs and exhibit dopamine dysfunction syndrome (DDS) (Leyton et al. 2000; Evans et al. 2006; Barrett et al. 2008). Studies like these establish that addictive drugs such as cocaine and amphetamine have the ability to produce sensitizing effects in the brain, especially in regard to how much they are "wanted" by the user.

Incentive sensitization theory also hinges on the idea that drug-induced sensitization occurs in a common neural network that is responsible for the attribution of incentive salience to all addictive drugs. One significant piece of evidence for this is a phenomenon known as **cross-sensitization.** Cross-sensitization, in the context of

drug use, refers to when sensitization to one drug will produce a sensitized response to other drugs (such as between heroin and cocaine). In cases of cross-sensitization of "wanting," an individual, as a result of excessively consuming one drug, is rendered hyper-responsive to the motivational effects of other drugs, including ones that may have never been previously consumed. A study by Horger et al. found that when rats were given nine daily injections of amphetamine or nicotine, they acquired a cocaine self-administration habit much quicker than control animals, thus demonstrating that the pretreated rats were more susceptible to the reinforcing effects of the cocaine (Horger et al. 1992; Casey et al. 2006; Munafò et al. 2007). Similarly, a study by Cunningham et al. found that rats who were given intra-accumbens treatment of certain opiates (such as morphine) later proved to be sensitized to the behavioral effects of amphetamine (Cunningham and Kelley 1992; Leyton 2007). Cross-sensitization and resulting hyper-responsivity of dopaminergic systems also occurs between drugs of abuse and natural rewards (Avena and Hoebel 2003a) and drugs of abuse and stress (at both behavioral and physiological levels) (Piazza et al. 1990; Cruz et al. 2011; Garcia-Keller et al. 2013). This latter finding highlights the important role that stress may play in relapse, whereby stressful life events can act as powerful triggers of drug cravings and a history of stressful life events may even predispose a person to drug addiction. These examples of cross-sensitization support the idea of an underlying neural circuitry common to all addictive drugs.

Finally, the neural changes that underlie sensitization appear to be long-lasting. A study by Paulson and colleagues showed that when rats were pretreated with amphetamine, they exhibited sensitization an entire year after the pretreatment was discontinued (Paulson et al. 1991). Likewise, other studies have reported that mice demonstrate behavioral or psychomotor sensitization, in the form of increased locomotor activity, up to 3 months after cocaine exposure (Shuster et al. 1977) and up to 8 months after morphine exposure (Shuster et al. 1975), while monkeys still display a sensitized response to amphetamine even 2 years post-treatment (Castner and Goldman-Rakic 1999). Studies like these confirm that the sensitizing effects seen in the brain as a result of repeated drug consumption are long-lasting, which in turn explains the constant temptation as well as the tendency to relapse seen in many recovering addicts.

## *3.2 The Role of "Liking," and Alternate Hypotheses of Addiction*

Initial drug consumption is often fueled by feelings of euphoria generated by taking the drug. In contrast to the sensitized response of the "wanting" system that develops in addicts toward drugs and their cues, the euphoria produced by drugs does not undergo the same transformation. There is no sensitization of "liking" systems in the brain. In fact, unlike "wanting," "liking" often undergoes a

phenomenon known as **tolerance**, which is the opposite of sensitization. In other words, repeated drug consumption causes "liking" to decrease, and with time, the same dose of drug is no longer able to generate as much pleasure as it once could. As a consequence, an addict may be driven to chase that initial high by progressively escalating the amount of drug consumed, which further causes greater and more rapid incentive sensitization (represented by the indirect path [3-4-5] in Fig. 2). This progression may especially be the case for drugs such as opiates (e.g., heroin and some prescription painkillers) that trigger a strong "liking" response and produce rapid tolerance (Cochin and Kornetsky 1964; Lamb et al. 1991). The implication of this pattern is particularly striking, as it means that an addict can reach a point where a drug causes very little pleasure, and yet he/she may go to great lengths to fulfill an inexplicable craving for it. Supporting evidence comes from a study showing tolerance to the euphoric effects of psychostimulant drugs in cocaine-dependent abusers despite enhanced drug-seeking (Volkow et al. 1997; Mendelson et al. 1998). Several studies have also demonstrated that drug self-administration can be maintained in the absence of any subjective pleasure (Lamb et al. 1991; Fischman and Foltin 1992; Hart et al. 2001) and that drugs such as morphine concomitantly generate both positive reinforcing and negative aversive effects (Stolerman 1985; Bechara et al. 1993). These results highlight the limited role of "liking" in drug addiction and shift the explanation toward "wanting." "Wanting" is thought to be to blame rather than cognitive wanting, as awareness of desire does not seem to play a large role in drug-taking (Lamb et al. 1991; Fischman and Foltin 1992). Such lack of cognitive awareness would explain why addicts often have little insight into their hunger for drugs and drug-associated cues (Childress et al. 2008; Goldstein et al. 2009) and why drug-taking persists despite adverse consequences and a cognitive intent to remain abstinent.

The incentive sensitization theory is not the only explanation that has been put forward to account for drug addiction. There are three other main reasons frequently suggested to explain addiction and relapse. The first has to do with drug euphoria or pleasure and suggests that addicts resume drug-taking to experience intense pleasure (Wise 1982). While drug pleasure or "liking" certainly accounts for initial patterns of drug use, as previously mentioned, tolerance frequently develops with repeated drug use (although not equally for all drugs) and addicts often report knowing that relapse will fail to lead to intense pleasure but rather to more misery. The second explanation has to do with drug habits and the belief that drug-taking distorts learning and creates such robust habits that relapse is inevitable (Hyman et al. 2006; Everitt et al. 2008; Koob and Volkow 2010). This approach fails to incorporate the dimension of excessive "wanting" and compulsion that accompanies drug-taking, which otherwise distinguishes it from regular habits like brushing one's teeth and tying one's shoelaces. Certainly habits facilitate the repeated drug use that is characteristic of drug addiction and contributes to incentive sensitization, but they are unable to explain the flexibility and resourcefulness that addicts display when procuring drugs, and thus account better for drug-taking than for the craving-driven drug-seeking that typifies drug addiction primarily as a relapsing disorder. Finally, the intense negative emotional state of withdrawal produced as a

result of drug abstinence is often suggested as the primary cause for relapse (Robinson and Berridge 1993; Koob and Volkow 2010). While withdrawal may be a potent reason many addicts do resume drug-taking, withdrawal is relatively short-lived and decays within days to weeks, depending on the drug (Wikler 1973; Khantzian 1985; Koob et al. 1989; Koob 1996). By contrast, relapse frequently occurs long after withdrawal has subsided, even many years later in fully detoxified individuals (Hunt et al. 1971). In fact, addicts often voluntarily undergo withdrawal in detoxification clinics to reduce tolerance and the monetary cost of their addiction (Kleber 2007; Robinson et al. 2013). In addition, certain drugs such as cocaine may produce relatively mild signs of physical withdrawal despite still being highly addictive, whereas certain pharmaceutical drugs such as sleeping pills induce high levels of tolerance and consequently withdrawal, and although they induce physical dependence, fail to produce some of the compulsive behavior seen in drug addiction (Graham and Vidal-Zeballos 1998; Wilkinson 1998). While all three of the aforementioned elements (pleasure, habit, withdrawal) are certainly present in most instances of drug abuse, they alone fall short of a full explanation that encompasses all aspects of addiction. Instead, incentive sensitization of "wanting" circuitry explains the escalation and compulsive pattern of drug-taking that occurs as addiction develops. It also accounts for the frequent incidence of relapse common to all addicts, which can often occur beyond withdrawal and in some cases for a lifetime. As an explanation for addiction, incentive sensitization theory is not limited to drugs of abuse. This divergence of "liking" and "wanting" can also be explored in the realm of gambling addiction.

## 4 Gambling

In the first four editions of the Diagnostic Statistical Manual of Mental Disorders (DSM), gambling disorder was classified as an impulse control disorder like kleptomania or pyromania. The 2013 release of the DSM-V, however, reclassified gambling disorder as a behavioral addiction (American Psychiatric Association 2013). Gambling disorder shares many characteristics with substance disorders, including the inability to cut down on gambling, continued gambling despite adverse consequences such as loss of money or job, and cravings for gambling (Potenza 2008). In this section, we will explore why gambling is attractive and potentially addictive, and if the transition from casual gambling to compulsive gambling can be explained by the same mechanisms that cause substance addiction.

Although few studies have specifically examined "wanting" and "liking" in gambling disorder, there is support for the idea that the incentive sensitization theory may apply to gambling disorder. The incentive sensitization theory posits that substance addictions cause drugs and their cues to take on increased salience and generate excessive motivation to consume more drug. In gambling addiction, gambling-related cues also seem to take on increased incentive salience, becoming motivational stimuli that drive behavior. One of the hallmarks of gambling, and

indeed of most games, is the presence of uncertainty (Costikyan 2013). Studies in rats suggest that uncertainty pertaining to the probability and magnitude of the reward outcome can cause attribution of additional incentive salience to reward-related cues. A recent study by Anselme, Robinson, and Berridge showed that rats exposed to an uncertain reward schedule (where both the chances of receiving a reward and the magnitude of this reward vary) direct significantly more of their attention and behavior to the reward cue than rats exposed to a certain reward schedule (Anselme et al. 2013). In other words, uncertain reward-related cues appear to become stronger "motivational magnets." This finding is paradoxical since it contradicts the idea that the motivational value of a cue should be monotonically related to its predictive value. It is consistent with the incentive salience theory, however, and highlights the dissociation that can occur between the predictive value of a cue, driven by cue learning (CS-UCS association), and the attribution of cue "wanting" (CS attraction) (Zhang et al. 2009). Furthermore, cues that predict reward with a large degree of uncertainty are also more likely to acquire incentive salience. For example, distal cues that are on the periphery of our attention are typically ignored under certain and predictable reward conditions, but when reward conditions are unpredictable, these cues attract more attention (Robinson et al. 2014a). In fact the degree of incentive enhancement that uncertainty imparts to reward-related cues is similar to that produced by psychomotor sensitization through repeated amphetamine administration (Robinson et al. 2015a). This may not come as a surprise considering that cues that predict an uncertain reward (50 % probability) produce a greater dopamine signal, originating from the ventral midbrain, during the anticipation of the uncertain outcome (Fiorillo et al. 2003), and that this dopaminergic signal appears to promote risk-seeking behavior, as evidenced in gambling (Fiorillo 2011).

The role of uncertainty in attributing excessive incentive value can also be seen in humans. A set of studies by Brevers indicate that problem gamblers exhibit attentional bias toward gambling-related cues as compared to healthy controls, suggesting that these stimuli also take on increased salience in human gamblers and may possess "motivational magnet" properties (Brevers et al. 2014a, b). Thus, cues related to uncertain reward seem to acquire incentive salience, just as drug-related cues take on increased salience in substance addictions. Casinos are full of both uncertain reward and potentially salient reward-related cues, like sounds and flashing lights, which likely increase the potential for gambling to become addictive and are reported by problem gamblers as a crucial part of the gambling experience (Dow Schüll 2012).

There is also direct evidence for (cross-)sensitization of the dopaminergic system under gambling-like conditions. Uncertainty causes cross-sensitization of the dopaminergic system, as seen by increased reactivity to a single dose of amphetamine, in the same way that repeated exposure to drugs of abuse sensitizes this system. Zack and colleagues found that rats exposed to maximally uncertain conditions showed the greatest locomotor response to an amphetamine challenge (Zack et al. 2014). In a similar study, Singer and his collaborators found that rats trained to press a lever for reward on a variable schedule showed a greater locomotor response

to amphetamine than those who were rewarded on a fixed schedule (Singer et al. 2012). As mentioned previously, heightened amphetamine-induced dopamine release in rats is associated with increased "wanting" but not increased "liking" (Wyvell and Berridge 2001). This implies that the escalating "wanting" that drives substance addictions may also be present in gambling disorder and is independent from "liking."

Cross-sensitization of dopaminergic systems from gambling has also been seen in humans. Boileau and colleagues found that problem gamblers have increased dopamine release in their dorsal striatum in response to amphetamine in comparison with healthy controls (Boileau et al. 2013). These results suggest that the escalating, sensitized "wanting" seen in rats exposed to uncertain reward is also present in human gamblers and possibly drives the transition from casual recreational gambling to compulsive gambling. Additionally, studies have found that problem gamblers have a sensitized dopaminergic response to gambling-related cues. Studies have correlated striatal dopamine release in problem gamblers with severity of problem gambling (Joutsa et al. 2012) and with self-reported levels of excitement during a gambling task (Linnet et al. 2011). However, certain studies instead report a blunted striatal dopamine response to cues in pathological gamblers (Miedl et al. 2012; Balodis et al. 2012). It has been suggested that such contradictory reports can be explained by the absence of familiar or relevant gambling cues during laboratory testing (Leyton and Vezina 2012), which when present instead produce an exaggerated striatal dopamine response (van Holst et al. 2012). This finding implies that while gambling-related cues take on increased incentive salience, other non-related or unfamiliar cues may become less important or even inhibit motivation. Similar arguments have been put forward to explain certain findings that suggest a role for dopamine deficiency across a variety of forms of addiction (Leyton 2007, 2014; Leyton and Vezina 2012, 2014).

Another key characteristic of addiction present in problem gamblers is their willingness to persist in gambling despite the negative consequences such as losing large amounts of money. A study by Linnet and colleagues found that problem gamblers have increased dopamine release in their ventral striatum as compared to healthy controls when they lost money in a gambling task, implying that loss still generates motivation in problem gamblers (Linnet et al. 2010). Additionally, a study by Clark and colleagues found that near misses (or almost winning) in a slot machine gambling task recruited areas of the brain that respond to wins. Participants in this study reported that near misses were significantly less pleasant than full misses, but triggered their urge to play more (Clark et al. 2009). These studies illustrate that although problem gamblers do not enjoy losses, they do find losses motivating, providing further evidence for a dissociation of "liking" and "wanting."

Lesion studies have implicated a number of brain regions involved in "liking" and "wanting" in gambling behavior. As previously mentioned, the nucleus accumbens is a component of the mesolimbic system with connections to prefrontal cortices and the dopaminergic neurons of the ventral tegmental area. Cardinal and Howes lesioned the nucleus accumbens core of rats and found that rats with these lesions were less likely to choose large uncertain rewards than controls when small certain rewards were also presented (Cardinal and Howes 2005). These results suggest that the nucleus accumbens core, a key component of the mesolimbic dopaminergic pathway, plays a role in mediating the desirability of uncertain reward.

Although further research is needed to fully understand the role of "liking" in human gambling, studies have supported the idea that "liking" is decreased in pathological gamblers. In a recent PET neuroimaging study, Mick and colleagues found reduced endogenous opioid release in pathological gamblers following an amphetamine challenge as compared to healthy controls. The problem gamblers also reported lower feelings of euphoria in response to the amphetamine challenge as compared to healthy controls (Mick et al. 2014). These results suggest that problem gamblers may experience a down-regulation in their "liking" system consistent with the incentive sensitization theory of addiction. Interestingly, opioid antagonists such as naltrexone (which is used to manage opioid and alcohol dependence) can help relieve gambling cravings and reduce problem gambling behaviors in some individuals. Although these results may at first seem controversial, as opioid-mediated "liking" seems to play less of a role in compulsive behavior than dopamine-mediated "wanting," there is increasing evidence that the opioid system is involved in regulating both "liking" and/or "wanting" in different regions of the brain (DiFeliceantonio et al. 2012; Castro and Berridge 2014).

Problem gambling, like substance addiction, seems to be rooted in the dysfunction or hijacking of the brain's natural reward system. This system drives animals to seek food, water, sex, and other rewards necessary for survival and propagating the species. It also likely evolved to make exploration and uncertainty motivating. Anselme posits that the motivational qualities of uncertainty are designed to compensate for the high rates of failure organisms experience when seeking resources (Anselme 2013). Resources are rarely fully predicted by external cues meaning that the appeal of uncertain cues may be a necessary requirement to overcome the unpleasantness of failure. If unpredictability were not motivating, the inevitable repeated failure experienced when seeking reward would extinguish behavior. The motivating qualities of uncertainty may therefore not be driven by pleasure or "liking," as could be argued in the case of food or sex, but instead by more primitive subcortical "wanting" systems. When purposefully programmed or designed as the outcome of a game or slot machine, uncertainty could drive the excessive "wanting" that arises below our conscious awareness and promote unhealthy gambling behavior.

## 5 Food Addiction

Here, we focus on the impact of highly palatable foods on the DA system (Genn et al. 2004; Avena et al. 2008; Tang et al. 2012) and examine how the incentive sensitization theory may explain food addiction and its associated health risks: obesity and binge eating.

Overeating is one of the primary causes of obesity. Excessive "wanting" and "liking" for food, especially refined hyper-palatable food, may play a role in overeating. The recent rise in hyper-palatable foods that often combine high levels of sugar, sodium and fat may result in exacerbated hedonic reactivity, leading to a magnification of both "liking" and "wanting" and consequently overconsumption (Berridge et al. 2009; Davis and Carter 2009). Alternatively, overconsumption of highly palatable foods could be triggered by an amplification of "wanting" resulting from the progressive sensitization of mesolimbic dopamine circuits due to repeated exposure to sweet rewarding foods. Such a phenomenon has been demonstrated in animals following exposure to 12-h cycles of bingeing and overconsumption of sugar interspersed with cycles of dieting (Avena and Hoebel 2003a). After 21 days of this regimen, animals showed a sensitized locomotor response to amphetamine, suggesting an underlying sensitization of the mesolimbic dopaminergic system. Conversely, sensitization of this system in rats by daily amphetamine treatment results in hyperphagia and overconsumption of a sugar solution (Avena and Hoebel 2003b).

Overeating may not have one single explanation. Evidence from genetic studies suggests that for obese individuals with a BMI above 30, the presence or absence of binge eating disorder (BED) may be an important factor in determining the relative role of "liking" and "wanting." Specifically, obese individuals without BED were found to be more likely to possess certain polymorphisms of the dopamine $D_2$ receptor that suggest excessive "wanting." Yet obese individuals who also display BED might constitute a specific population subtype that is prone to binge eating due to an additional hyperactivity of their "liking" response to food. This enhanced hedonic response to food, linked to particular polymorphisms in their mu-opioid receptor gene, combined with excessive "wanting," may give rise to particularly intense addiction-like tendencies toward food (Davis et al. 2009; Davis and Carter 2009). Research also shows that individuals with a genetic leptin deficiency develop obesity at an early age and show both intense cravings for food and high levels of nucleus accumbens activity in response to food stimuli, even following a meal. When treated with medication to restore leptin levels, however, urges and pleasure reports for food are greatly reduced, as is activity in the accumbens (Farooqi et al. 2007; Farooqi and O'Rahilly 2009). Leptin may therefore regulate the suppression of "liking" and "wanting" following satiety. The development of leptin insensitivity with repeated exposure to a junk food diet may promote obesogenic behaviors through its interactions with the dopaminergic system (Pandit et al. 2011; Sáinz et al. 2015). In contrast, during states of hunger it appears that the pleasurable component of food may be enhanced by changes in activity in both

opioid and endocannabinoid systems (Kirkham 2005, 2008). However, endocannabinoids also facilitate VTA dopamine which may trigger enhanced "wanting" for palatable foods independent of "liking" (Kirkham 2005; Cota et al. 2006).

The evidence of excessive "wanting" triggered by food in obese individuals suggests that food may act as an intensely potent reward, similar to certain drugs of abuse. This was examined in an experiment in which rats were given access to sugar water as well as to intravenous injections of cocaine. Results showed that over 90 % of the 132 rats in the experiment preferred to press the lever that allowed them access to the sugar solution instead of the lever that administered cocaine (Lenoir et al. 2007). This finding suggests that a commonly available and frequently ingested substance like sugar is strongly preferred over a "wanted" addictive substance like cocaine (which triggers a supranormal dopamine response), and may therefore be attributed with excessive incentive salience.

In addition, much like in drug addiction, the attractive and rewarding properties of hyper-palatable foods like sugar do not stay confined to the reward itself. Reward-related cues, in this case food cues, can be attributed with excessive incentive salience and become beacons that attract attention and trigger overconsumption. For example, overweight and obese individuals appear to direct greater attention to food-related cues than individuals of a normal weight, especially when food deprived (Nijs et al. 2010). In adolescents, it has been shown that the speed at which food stimuli attract attention is correlated with BMI (Yokum et al. 2011). Another study suggests that despite reduced hunger, obese individuals maintained increased attention to food images over non-food images, as compared to controls (Castellanos et al. 2009). In fact, many of the structures of the mesocorticolimbic dopamine system are also activated in people who have a healthy BMI and/or weight when confronted with food imagery (Tang et al. 2012)—much like how they are activated in drug addicts' brains when confronted with drug cues. A recent study suggests that food cues are excessively attractive only to a subpopulation of rats fed a junk food diet (Robinson et al. 2015b). In this model, rats were given free access to a human junk food diet, made of peanut butter, chocolate chip cookies, potato chips, and chocolate milk powder. Surprisingly only some of these animals (approximately 33–50 %) gained excessive amounts of weight, while the remaining animals maintained a steady weight gain, similar to that of animals provided with regular lab chow. The rats that over consumed junk food and displayed large amounts of weight gain initially displayed greater attraction and "wanting" for food-related cues, as seen by greater levels of cue-driven conditioned approach (e.g., sign-tracking), even before they were ever exposed to the junk food. Following extended access to the junk food diet, the animals that gained large amounts of weight perceived food cues themselves as a reward and were more willing to work simply for their presentation (conditioned reinforcement). This observation provides further evidence of excessive "wanting." This tendency for certain rats to over consume a palatable diet was not the result of a prior heightened pleasure response to sweet tastes, nor was it driven by increases in "liking" with repeated exposure to the junk food. If anything, chronic consumption of a palatable junk food diet led to an overall dampening of the "liking" reaction to increasingly

sweet tastes (Robinson et al. 2015b), a phenomenon reminiscent of the sometimes blunted "liking" response seen in drug addicts, and that may similarly be related to tolerance. Further, these results echo previous animal findings suggesting a decoupling of "liking" and "wanting" in obesity (Shin et al. 2011).

Similar evidence for a neural dissociation of "liking" and "wanting" for food and food-related cues has also been demonstrated in humans using neuroimaging evidence (Jiang et al. 2014), with particular emphasis of the role of the striatum in "wanting" for food and its cues. One study also found that fMRI reactivity in obese participants in response to images of high-calorie food in those regions associated with motivation (the insula, ventral tegmental area, putamen, and fusiform gyrus) was inversely predictive of long-term efficacy of a weight loss program, although all participants reported liking the food in the pictures (Murdaugh and Cook 2012). Specifically, if these areas were more active when the participant was shown a picture of high-calorie food than when he or she was shown a control picture, that participant would likely have little success with a 9-month weight loss program. These findings suggest that it is the cues for food, as opposed to the food itself, which play a key role in weight maintenance and also further highlight the importance of individual differences. Specifically, the degree of mesolimbic brain reactivity may differ among individuals and may support a certain predisposition to food and its cues, where excessive attraction to food cues in certain individuals may promote weight gain and its maintenance. In a recent study, Yokum and colleagues found that food commercials caused striatal activation, whereas commercials that did not prominently feature food did not elicit activity in the same neural structures. More importantly, the degree of striatal activation in response to food commercials was predictive of adolescent weight gain one year later (Yokum et al. 2014). These results are further supported by findings that suggest that over time, cues may actually become the dominant driver of food overconsumption. In a recent fMRI study, Burger and Stice demonstrated that with repeated exposure, activity in the caudate progressively increased in response to cues that predicted delivery of a milk shake, while activity in the putamen and ventral pallidum showed a simultaneous decrease following receipt of the milk shake reward (Burger and Stice 2014). Crucially, in a 2-year follow-up, those who showed the greatest ventral pallidum increase to cues and the greatest decrease in caudate response to the milk shake also showed the largest increase in BMI. This finding suggests that the ability of food advertisements and food cues in general to be attributed with incentive salience and trigger surges of "wanting" might be the driving force behind our increasing waistlines. In spite of this support for individual differences, there is evidence to suggest that extended access to a palatable junk food diet sensitizes the mesolimbic dopamine system and renders it hyper-responsive to injections of amphetamine independent of whether animals gained excessive amounts of weight or were able to control their intake on that diet (Robinson et al. 2015b). Therefore, regular intake of palatable junk food, even in the absence of any overt weight gain, can sensitize and increase reactivity of the systems associated with "wanting" and the attribution to incentive salience—potentially leading to progressive susceptibility to overconsumption. An additional factor of particular importance for binge eating is the role

of stress. Stress, and more specifically corticotropin-releasing factor (CRF) release, may produce cue-triggered peaks in "wanting," as it has been shown to induce surges in motivation for sugar-paired cues in the same manner as amphetamine microinjections into the nucleus accumbens shell (Peciña et al. 2006). This finding may explain how stress can provoke cue-triggered bursts of binge eating, and in this particular case, powerful sugar-seeking.

Historically, our strong drive for sugar was rooted in its scarcity and its importance in providing energy and nutrition for the brain. However, sugar as a reward has changed, both in its form and availability, and so has the environment in which we live. Today's food is designed, packaged, and presented in a manner that is a far cry from how it was when our distant ancestors expended energy foraging and competing with other animals for resources. Supermarkets and cafeterias have negated the need to forage, yet the neural systems responsible for motivation and "wanting" continue to reward consumption. Food today, especially that containing highly rewarding ingredients such as sugar, fat, and salt, is readily available. These ingredients are refined and modified to enhance their rewarding and sensory properties. Sugar, for example, is now omnipresent in our food (Gearhardt et al. 2011), with a 30 % increase in intake over the past four decades (Elliott et al. 2002; Johnson et al. 2007), and is increasingly present in the absence of fiber, which usually slows down its absorption and dampens any possible spike in blood sugar (Gearhardt et al. 2013; Schulte et al. 2015). In addition, advertisement campaigns now generate a slew of food-related cues that may trigger intense motivation to seek food, driving people to consume more food than may be dictated by physiological needs (Kelly et al. 2008; Harris et al. 2009). Food advertisements are tailored to attract our attention with increasingly tempting visuals of food. Neural systems that direct our incentive motivation cannot evolve rapidly enough to temper the temptation provided by the ever-increasing amount of persuasive cues for food we are bombarded with daily, whether we are physiologically hungry or not.

While there is still an ongoing debate as to whether food addiction can be considered a legitimate concept, there is little doubt that the overconsumption of palatable foods is a growing problem in Western society. Part of this problem results from the refinement and engineering of hyper-palatable foods that contain large quantities of often both sugar and fat and trigger strong initial hedonic "liking" responses. A more prominent role in the obesity epidemic seems to be played by the exacerbated "wanting" reactions elicited by these foods and their cues. Hyper-palatable foods activate mesolimbic dopamine reward pathways, spurring on motivation and attributing the food and its cues with incentive salience. The incessant bombardment of our brain by food advertisements triggers powerful urges to consume these foods beyond our caloric needs and often in spite of reduced pleasure.

## 6 Concluding Remarks

The incentive sensitization theory helps explain excessive drug-taking, gambling, and eating by allowing for a psychological and neural differentiation between "liking" and "wanting." According to this theory, the psychological and biological process responsible for the attribution of "wanting" to a reward may become dissociated from the hedonic "liking" experience generated by that same reward. The incentive sensitization theory states that in a non-addicted person, these "liking" and "wanting" systems may function in tandem so that a person may "like" what he or she "wants" and "want" what is "liked." In an addict's brain, however, these two systems become decoupled, so that a person feels excessive motivation for the reward and its cues, often despite a decrease in enjoyment. This theory of motivation was created to explain the progressive and incremental development of drug addiction and its persistence. Many of its principle tenets such as the dissociation of "liking" and "wanting," the sensitization of the mesolimbic dopamine system, and the incentive sensitization of the reward and its cues may possibly help provide an explanation for other addictive behaviors such as gambling, sex, Internet, shopping, and food addiction.

## References

American Psychiatric Association (2013) American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5®). American Psychiatric Association, Arlington

Anselme P (2013) Dopamine, motivation, and the evolutionary significance of gambling-like behaviour. Behav Brain Res 256C:1–4. doi:10.1016/j.bbr.2013.07.039

Anselme P, Robinson MJF, Berridge KC (2013) Reward uncertainty enhances incentive salience attribution as sign-tracking. Behav Brain Res 238:53–61. doi:10.1016/j.bbr.2012.10.006

Avena NM, Hoebel BG (2003a) A diet promoting sugar dependency causes behavioral cross-sensitization to a low dose of amphetamine. Neuroscience 122:17–20

Avena NM, Hoebel BG (2003b) Amphetamine-sensitized rats show sugar-induced hyperactivity (cross-sensitization) and sugar hyperphagia. Pharmacol Biochem Behav 74:635–639

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. doi:10.1016/j.neubiorev.2007.04.019

Balfour DJK, Munafò MR (2015) The role of mesoaccumbens dopamine in nicotine dependence. 24:1–172. doi:10.1007/978-3-319-13482-6_3

Balodis IM, Kober H, Worhunsky PD et al (2012) Diminished frontostriatal activity during processing of monetary rewards and losses in pathological gambling. Biol Psychiatry 71:749–757. doi:10.1016/j.biopsych.2012.01.006

Barrett SP, Pihl RO, Benkelfat C et al (2008) The role of dopamine in alcohol self-administration in humans: individual differences. Europ Neuropsychopharmacol 18:439–447. doi:10.1016/j.euroneuro.2008.01.008

Bechara A, Martin GM, Pridgar A, van der Kooy D (1993) The parabrachial nucleus: a brain stem substrate critical for mediating the aversive motivational effects of morphine. Behav Neurosci 107:147–160

Benowitz NL (1996) Pharmacology of nicotine: addiction and therapeutics. Annu Rev Pharmacol Toxicol 36:597–613. doi:10.1146/annurev.pa.36.040196.003121

Berger SP, Hall S, Mickalian JD et al (1996) Haloperidol antagonism of cue-elicited cocaine craving. Lancet 347:504–508

Bernard LC, Mills M, Swenson L, Walsh RP (2005) An Evolutionary Theory of Human Motivation. Genet Soc Gen Psychol Monogr 131:129–184. doi:10.3200/MONO.131.2.129-184

Berridge KC (2003) Pleasures of the brain. Brain Cognit

Berridge KC, Ho C-Y, Richard JM, DiFeliceantonio AG (2010) The tempted brain eats: pleasure and desire circuits in obesity and eating disorders. Brain Res 1350:43–64. doi:10.1016/j.brainres.2010.04.003

Berridge KC, Kringelbach ML (2008) Affective neuroscience of pleasure: reward in humans and animals. Psychopharmacology 199:457–480. doi:10.1007/s00213-008-1099-6

Berridge KC, Robinson TE (2003) Parsing reward. Trends Neurosci 26:507–513

Berridge KC, Robinson TE (1998) What is the role of dopamine in reward: hedonic impact, reward learning, or incentive salience? Brain Res Rev 28:309–369

Berridge KC, Robinson TE (2011) Drug Addiction as Incentive Sensitization. In: Poland J, Graham G (eds) Addict & Responsibility. MIT Press, Cambridge, pp 21–54

Berridge KC, Robinson TE, Aldridge JW (2009) Dissecting components of reward: 'liking', "wanting", and learning. Curr Opin Pharmacol 9:65–73. doi:10.1016/j.coph.2008.12.014

Berridge KC, Valenstein ES (1991) What psychological process mediates feeding evoked by electrical stimulation of the lateral hypothalamus? Behav Neurosci 105:3–14

Bindra D (1978) How adaptive behavior is produced: a perceptual- motivational alternative to response-reinforcement. Behav Brain Sci 1:41–91

Boakes RA, Poli M, Lockwood MJ, Goodall G (1978) A study of misbehavior: token reinforcement in the rat. J Exp Anal Behav 29:115–134

Boileau I, Dagher A, Leyton M et al (2006) Modeling sensitization to stimulants in humans: an [11C]raclopride/positron emission tomography study in healthy men. Arch Gen Psychiatry 63:1386–1395. doi:10.1001/archpsyc.63.12.1386

Boileau I, Payer D, Chugani B, et al (2013) In vivo evidence for greater amphetamine-induced dopamine release in pathological gambling: a positron emission tomography study with [$^{11}$C]-(+)-PHNO. Mol Psychiatry 19:1305–1313. doi:10.1038/mp.2013.163

Brauer LH, De Wit H (1997) High dose pimozide does not block amphetamine-induced euphoria in normal volunteers. Pharmacol Biochem Behav 56:265–272

Brevers D, Bechara A, Hermoye L et al (2014a) Comfort for uncertainty in pathological gamblers: a fMRI study. Behav Brain Res 278C:262–270. doi:10.1016/j.bbr.2014.09.026

Brevers D, Koritzky G, Bechara A, Noël X (2014b) Cognitive processes underlying impaired decision-making under uncertainty in gambling disorder. Addict Behav 39:1533–1536. doi:10.1016/j.addbeh.2014.06.004

Brown PL, Jenkins HM (1968) Auto-shaping of the pigeon's key-peck. J Exp Anal Behav 11:1–8. doi:10.1901/jeab.1968.11-1

Burger KS, Stice E (2014) Greater striatopallidal adaptive coding during cue–reward learning and food reward habituation predict future weight gain. Neuroimage 99:122–128. doi:10.1016/j.neuroimage.2014.05.066

Cabanac M (1971) Physiological role of pleasure. Science 173:1103–1107

Cadet JL, Bisagno V, Milroy CM (2014) Neuropathology of substance use disorders. Acta Neuropathol 127:91–107. doi:10.1007/s00401-013-1221-7

Caggiula AR, Donny EC, Palmatier MI et al (2009) The role of nicotine in smoking: a dual-reinforcement model. Nebr Symp Motiv 55:91–109

Cannon CM, Palmiter RD (2003) Reward without dopamine. J Neurosci 23:10827–10831

Cardinal RN, Howes NJ (2005) Effects of lesions of the nucleus accumbens core on choice between small certain rewards and large uncertain rewards in rats. BMC Neurosci 6:37. doi:10.1186/1471-2202-6-37

Cardinal RN, Parkinson JA, Hall J, Everitt BJ (2002) Emotion and motivation: the role of the amygdala, ventral striatum, and prefrontal cortex. Neurosci Biobehav Rev 26:321–352

Casey KF, Benkelfat C, Young SN, Leyton M (2006) Lack of effect of acute dopamine precursor depletion in nicotine-dependent smokers. Europ Neuropsychopharmacol 16:512–520. doi:10.1016/j.euroneuro.2006.02.002

Castellanos EH, Charboneau E, Dietrich MS et al (2009) Obese adults have visual attention bias for food cue images: evidence for altered reward system function. Int J Obes (Lond) 33:1063–1073. doi:10.1038/ijo.2009.138

Castner SA, Goldman-Rakic PS (1999) Long-lasting psychotomimetic consequences of repeated low-dose amphetamine exposure in rhesus monkeys. Neuropsychopharmacol 20:10–28. doi:10.1016/S0893-133X(98)00050-5

Castro DC, Berridge KC (2014) Opioid Hedonic Hotspot in Nucleus Accumbens Shell: Mu, Delta, and Kappa Maps for Enhancement of Sweetness "Liking" and "Wanting". J Neurosci 34:4239–4250. doi:10.1523/JNEUROSCI.4458-13.2014

Castro DC, Cole SL, Berridge KC (2015) Lateral hypothalamus, nucleus accumbens, and ventral pallidum roles in eating and hunger: interactions between homeostatic and reward circuitry. Front Syst Neurosci 9:1–17. doi:10.3389/fnsys.2015.00090

Childress AR, Ehrman RN, Wang Z et al (2008) Prelude to passion: limbic activation by "unseen" drug and sexual cues. PLoS ONE 3:e1506. doi:10.1371/journal.pone.0001506

Clark L, Lawrence AJ, Astley-Jones F, Gray N (2009) Gambling near-misses enhance motivation to gamble and recruit win-related brain circuitry. Neuron 61:481–490. doi:10.1016/j.neuron.2008.12.031

Cochin J, Kornetsky C (1964) Development and loss of tolerance to morphine in the rat after single and multiple injections. J Pharmacol Exp Ther 145:1–10

Costikyan G (2013) Uncertainty in Games. MIT Press, Cambridge

Cota D, Barrera JG, Seeley RJ (2006) Leptin in energy balance and reward: two faces of the same coin? Neuron 51:678–680. doi:10.1016/j.neuron.2006.09.009

Cruz FC, Marin MT, Leão RM, Planeta CS (2011) Stress-induced cross-sensitization to amphetamine is related to changes in the dopaminergic system. J Neural Transm 119:415–424. doi:10.1007/s00702-011-0720-8

Cunningham ST, Kelley AE (1992) Evidence for opiate-dopamine cross-sensitization in nucleus accumbens: studies of conditioned reward. Brain Res Bull 29:675–680

Dai X, Brendl CM, Ariely D (2010) Wanting, liking, and preference construction. Emotion 10:324–334. doi:10.1037/a0017987

Davis C, Carter JC (2009) Compulsive overeating as an addiction disorder. A review of theory and evidence. Appetite 53:1–8. doi:10.1016/j.appet.2009.05.018

Davis CA, Levitan RD, Reid C et al (2009) Dopamine for "wanting" and opioids for "liking": a comparison of obese adults with and without binge eating. Obesity 17:1220–1225. doi:10.1038/oby.2009.52

Di Chiara G, Imperato A (1988) Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. Proc Natl Acad Sci USA 85:5274–5278

DiFeliceantonio AG, Berridge KC (2012) Which cue to "want?" Opioid stimulation of central amygdala makes goal-trackers show stronger goal-tracking, just as sign-trackers show stronger sign-tracking. Behav Brain Res 230:399–408. doi:10.1016/j.bbr.2012.02.032

DiFeliceantonio AG, Mabrouk OS, Kennedy RT, Berridge KC (2012) Enkephalin surges in dorsal neostriatum as a signal to eat. Curr Biol 22:1918–1924. doi:10.1016/j.cub.2012.08.014

Dow Schüll N (2012) Addiction by Design: Machine Gambling in Las Vegas, 1st edn. Princeton University Press, Princeton

Elliott SS, Keim NL, Stern JS et al (2002) Fructose, weight gain, and the insulin resistance syndrome. Am J Clin Nutr 76:911–922

Evans AH, Pavese N, Lawrence AD et al (2006) Compulsive drug use linked to sensitized ventral striatal dopamine transmission. Ann Neurol 59:852–858. doi:10.1002/ana.20822

Everitt BJ, Belin D, Economidou D et al (2008) Neural mechanisms underlying the vulnerability to develop compulsive drug-seeking habits and addiction. Philos Trans R Soc, Biol Sci 363:3125–3135

Farooqi IS, Bullmore ET, Keogh J et al (2007) Leptin regulates striatal regions and human eating behavior. Science 317:1355. doi:10.1126/science.1144599

Farooqi IS, O'Rahilly S (2009) Leptin: a pivotal regulator of human energy homeostasis. Am J Clin Nutr 89:980S–984S. doi:10.3945/ajcn.2008.26788C

Ferrario CR, Gorny G, Crombag HS et al (2005) Neural and behavioral plasticity associated with the transition from controlled to escalated cocaine use. Biol Psychiatry 58:751–759. doi:10.1016/j.biopsych.2005.04.046

Ferrario CR, Robinson TE (2007) Amphetamine pretreatment accelerates the subsequent escalation of cocaine self-administration behavior. Eur Neuropsychopharmacol 17:352–357. doi:10.1016/j.euroneuro.2006.08.005

Fiorillo CD (2011) Transient activation of midbrain dopamine neurons by reward risk. Neuroscience 197:162–171. doi:10.1016/j.neuroscience.2011.09.037

Fiorillo CD, Tobler PN, Schultz W (2003) Discrete coding of reward probability and uncertainty by dopamine neurons. Science 299:1898–1902. doi:10.1126/science.1077349

Fischman MW, Foltin RW (1992) Self-administration of cocaine by humans: a laboratory perspective. Ciba Found Symp 166:165–180

Garcia J, Lasiter PS, Bermudez-Rattoni F, Deems DA (1985) A general theory of aversion learning. Ann N Y Acad Sci 443:8–21

Garcia-Keller C, Martinez SA, Esparza MA et al (2013) Cross-sensitization between cocaine and acute restraint stress is associated with sensitized dopamine but not glutamate release in the nucleus accumbens. Eur J Neurosci 37:982–995. doi:10.1111/ejn.12121

Gearhardt A, Roberts M, Ashe M (2013) If sugar is addictive…what does it mean for the law? J Law Med Ethics 41(Suppl 1):46–49. doi:10.1111/jlme.12038

Gearhardt AN, Davis C, Kuschner R, Brownell KD (2011) The addiction potential of hyperpalatable foods. CDAR 4:140–145. doi:10.2174/1874473711104030140

Gekht AB, Polunina AG, Briun EA, Gusev EI (2003) Neurological disturbances in heroin addicts in acute withdrawal and early post-abstinence periods. Zh Nevrol Psikhiatr Im S S Korsakova 103:9–15

Genn RF, Ahn S, Phillips AG (2004) Attenuated dopamine efflux in the rat nucleus accumbens during successive negative contrast. Behav Neurosci 118:869–873. doi:10.1037/0735-7044.118.4.869

Goldstein RZ, Craig ADB, Bechara A et al (2009) The neurocircuitry of impaired insight in drug addiction. Trends Cognit Sci 13:372–380. doi:10.1016/j.tics.2009.06.004

Graham K, Vidal-Zeballos D (1998) Analyses of use of tranquilizers and sleeping pills across five surveys of the same population (1985–1991): the relationship with gender, age and use of other substances. Soc Sci Med 46:381–395

Grill HJ, Norgren R (1978) The taste reactivity test. II. Mimetic responses to gustatory stimuli in chronic thalamic and chronic decerebrate rats. Brain Res 143:281–297

Harris JL, Bargh JA, Brownell KD (2009) Priming effects of television food advertising on eating behavior. Health Psychol 28:404–413. doi:10.1037/a0014399

Hart C, Ward A, Haney M et al (2001) Methamphetamine self-administration by humans. Psychopharmacology 157:75–81. doi:10.1007/s002130100738

Hearst ES, Jenkins HM (1974) Sign tracking: the stimulus-reinforcer relation and directed action. Psychonmic Soc, Austin

Henry DJ, White FJ (1991) Repeated cocaine administration causes persistent enhancement of D1 dopamine receptor sensitivity within the rat nucleus accumbens. J Pharmacol Exp 258:882–890

Hernandez L, Hoebel BG (1988) Feeding and hypothalamic stimulation increase dopamine turnover in the accumbens. Physiol Behav 44:599–606

Hiroi N, Brown JR, Haile CN et al (1997) FosB mutant mice: loss of chronic cocaine induction of fos-related proteins and heightened sensitivity to cocaine's psychomotor and rewarding effects.

Proc Natl Acad Sci USA 94:10397–10402. doi:10.2307/43218?ref=no-x-route:2c8ba5cf31f36df291c5a2097b853938
Hobbs M, Remington B, Glautier S (2005) Dissociation of wanting and liking for alcohol in humans: a test of the incentive-sensitisation theory. Psychopharmacology 178:493–499. doi:10.1007/s00213-004-2026-0
Hollis KL (1984) The biological function of Pavlovian conditioning: the best defense is a good offense. J Exp Psychol Anim Behav Process 10:413–425
Holmes NM, Marchand AR, Coutureau E (2010) Pavlovian to instrumental transfer: a neurobehavioural perspective. Neurosci Biobehav Rev 34:1277–1295. doi:10.1016/j.neubiorev.2010.03.007
Horger BA, Giles MK, Schenk S (1992) Preexposure to amphetamine and nicotine predisposes rats to self-administer a low dose of cocaine. Psychopharmacology 107:271–276
Hu X-T, Koeltzow TE, Cooper DC et al (2002) Repeated ventral tegmental area amphetamine administration alters dopamine D1 receptor signaling in the nucleus accumbens. Synapse 45:159–170. doi:10.1002/syn.10095
Hunt WA, Barnett LW, Branch LG (1971) Relapse rates in addiction programs. J Clin Psychol 27:455–456
Hyman SE, Malenka RC, Nestler EJ (2006) Neural mechanisms of addiction: the role of reward-related learning and memory. Annu Rev Neurosci 29:565–598. doi:10.1146/annurev.neuro.29.051605.113009
Isomura T, Suzuki J, Murai T (2014) Paradise Lost: The relationships between neurological and psychological changes in nicotine-dependent patients. Addict Res Theor 22:158–165. doi:10.3109/16066359.2013.793312
James W (1884) What is an Emotion? Mind 9:188–205. doi:10.2307/2246769?ref=no-x-route:661c887760fcf4a1f23afb46f8f75b0a
Jiang T, Soussignan R, Schaal B, Royet J-P (2014) Reward for food odors: an fMRI study of liking and wanting as a function of metabolic state and BMI. Soc Cogn Affect Neurosci. doi:10.1093/scan/nsu086
Johnson RJ, Segal MS, Sautin Y et al (2007) Potential role of sugar (fructose) in the epidemic of hypertension, obesity and the metabolic syndrome, diabetes, kidney disease, and cardiovascular disease. Am J Clin Nutr 86:899–906
Joutsa J, Johansson J, Niemelä S et al (2012) Mesolimbic dopamine release is linked to symptom severity in pathological gambling. Neuroimage 60:1992–1999. doi:10.1016/j.neuroimage.2012.02.006
Kalivas PW, Duffy P (1990) Effect of acute and daily cocaine treatment on extracellular dopamine in the nucleus accumbens. Synapse 5:48–58. doi:10.1002/syn.890050104
Kalivas PW, Duffy P (1993) Time course of extracellular dopamine and behavioral sensitization to cocaine. I. Dopamine axon terminals. J Neurosci off J Soc Neurosci 13:266–275
Kelly B, Hattersley L, King L, Flood V (2008) Persuasive food marketing to children: use of cartoons and competitions in Australian commercial television advertisements. Health Promot Int 23:337–344. doi:10.1093/heapro/dan023
Khantzian EJ (1985) The self-medication hypothesis of addictive disorders: focus on heroin and cocaine dependence. Am J Psychiatry 142:1259–1264
Khavari KA, Peters TC, Baity PL, Wilson AS (1975) Voluntary morphine ingestion, morphine dependence, and recovery from withdrawal signs. Pharmacol Biochem Behav 3:1093–1096
Kirkham T (2008) Endocannabinoids and the neurochemistry of gluttony. J Neuroendocrinol 20:1099–1100. doi:10.1111/j.1365-2826.2008.01762.x
Kirkham TC (2005) Endocannabinoids in the regulation of appetite and body weight. Behav Pharmacol 16:297–313
Kleber HD (2007) Pharmacologic treatments for opioid dependence: detoxification and maintenance options. Dialogues Clin Neurosci 9:455–470
Koob GF (1996) Drug addiction: the yin and yang of hedonic homeostasis. Neuron 16:893–896
Koob GF, Stinus L, le Moal M, Bloom FE (1989) Opponent process theory of motivation: neurobiological evidence from studies of opiate dependence. Neurosci Biobehav 13:135–140

Koob GF, Volkow ND (2010) Neurocircuitry of addiction. Neuropsychopharmacology 35:217–238. doi:10.1038/npp.2009.110

Lamb RJ, Preston KL, Schindler CW et al (1991) The reinforcing and subjective effects of morphine in post-addicts: a dose-response study. J Pharmacol Exp Ther 259:1165–1173

Lemmens SGT, Schoffelen PFM, Wouters L et al (2009) Eating what you like induces a stronger decrease of "wanting" to eat. Physiol Behav 98:318–325. doi:10.1016/j.physbeh.2009.06.008

Lenoir M, Serre F, Cantin L, Ahmed SH (2007) Intense sweetness surpasses cocaine reward. PLoS ONE 2:e698. doi:10.1371/journal.pone.0000698

Leyton M (2010) The neurobiology of desire: dopamine and the regulation of mood and motivational states in humans. In: Kringelbach ML, Berridge KC (eds) Pleasures of the Brain. Oxford University Press, New York, pp 222–243

Leyton M (2007) Conditioned and sensitized responses to stimulant drugs in humans. Prog Neuropsychopharmacol Biol Psychiatry 31:1601–1613. doi:10.1016/j.pnpbp.2007.08.027

Leyton M (2014) What's deficient in reward deficiency? J Psychiatry Neurosci 39:291–293

Leyton M, Boileau I, Benkelfat C et al (2002) Amphetamine-induced increases in extracellular dopamine, drug wanting, and novelty seeking: a PET/[11C]raclopride study in healthy men. Neuropsychopharmacology 27:1027–1035. doi:10.1016/S0893-133X(02)00366-4

Leyton M, Casey KF, Delaney JS et al (2005) Cocaine craving, euphoria, and self-administration: a preliminary study of the effect of catecholamine precursor depletion. Behav Neurosci 119:1619–1627. doi:10.1037/0735-7044.119.6.1619

Leyton M, Vezina P (2012) On cue: striatal ups and downs in addictions. Biol Psychiatry 72:e21–e22. doi:10.1016/j.biopsych.2012.04.036

Leyton M, Vezina P (2014) Dopamine ups and downs in vulnerability to addictions: a neurodevelopmental model. Trends Pharmacol Sci 35:268–276. doi:10.1016/j.tips.2014.04.002

Leyton M, Young SN, Blier P et al (2000) Acute tyrosine depletion and alcohol ingestion in healthy women. Alcohol Clin Exp Res 24:459–464

Linnet J, Møller A, Peterson E et al (2011) Dopamine release in ventral striatum during Iowa Gambling Task performance is associated with increased excitement levels in pathological gambling. Addiction 106:383–390. doi:10.1111/j.1360-0443.2010.03126.x

Linnet J, Peterson E, Doudet DJ et al (2010) Dopamine release in ventral striatum of pathological gamblers losing money. Acta Psychiatr Scand 122:326–333. doi:10.1111/j.1600-0447.2010.01591.x

Litt A, Khan U, Shiv B (2010) Lusting while loathing: parallel counterdriving of wanting and liking. Psychol Sci 21:118–125. doi:10.1177/0956797609355633

Mahler SV, Berridge KC (2009) Which cue to "want?" Central amygdala opioid activation enhances and focuses incentive salience on a prepotent reward cue. J Neurosci 29:6500–6513. doi:10.1523/JNEUROSCI.3875-08.2009

Mendelson JH, Sholar M, Mello NK et al (1998) Cocaine tolerance: behavioral, cardiovascular, and neuroendocrine function in men. Neuropsychopharmacology 18:263–271. doi:10.1016/S0893-133X(97)00146-2

Mick I, Myers J, Stokes PRA, et al. (2014) Endogenous opioid release in pathological gamblers after an oral amphetamine challenge: a [$^{11}$C] carfentanil pet study. Eur Neuropsychopharmacol 1–4

Miedl SF, Peters J, Büchel C (2012) Altered neural reward representations in pathological gamblers revealed by delay and probability discounting. Arch Gen Psychiatry 69:177–186. doi:10.1001/archgenpsychiatry.2011.1552

Munafò MR, Mannie ZN, Cowen PJ et al (2007) Effects of acute tyrosine depletion on subjective craving and selective processing of smoking-related cues in abstinent cigarette smokers. J Psychopharmacol (Oxford) 21:805–814. doi:10.1177/0269881107077216

Murdaugh D, Cook E (2012) fMRI reactivity to high-calorie food pictures predicts short- and long-term outcome in a weight-loss program. Neuroimage

Nijs IMT, Muris P, Euser AS, Franken IHA (2010) Differences in attention to food and food intake between overweight/obese and normal-weight females under conditions of hunger and satiety. Appetite 54:243–254. doi:10.1016/j.appet.2009.11.004

Nilsson J, Kristiansen TS, Fosseidengen JE et al (2008) Sign- and goal-tracking in Atlantic cod (Gadus morhua). Animal Behavior 11:651–659. doi:10.1007/s10071-008-0155-2

Ostafin BD, Marlatt GA, Troop-Gordon W (2010) Testing the incentive-sensitization theory with at-risk drinkers: wanting, liking, and alcohol consumption. Psychol Addict Behav 24:157–162. doi:10.1037/a0017897

Pandit R, de Jong JW, Vanderschuren LJMJ, Adan RAH (2011) Neurobiology of overeating and obesity: the role of melanocortins and beyond. Eur J Pharmacol 660:28–42. doi:10.1016/j.ejphar.2011.01.034

Paulson PE, Camp DM, Robinson TE (1991) Time course of transient behavioral depression and persistent behavioral sensitization in relation to regional brain monoamine concentrations during amphetamine withdrawal in rats. Psychopharmacology 103:480–492. doi:10.1007/BF02244248

Paxinos G, Watson C (2007) The rat brain in stereotaxic coordinates, 6 edn. Elsevier, Amsterdam

Peciña S (2005) Hedonic hot spot in nucleus accumbens shell: where do μ-opioids cause increased hedonic impact of sweetness? J Neurosci 25:11777–11786. doi:10.1523/JNEUROSCI.2329-05.2005

Peciña S, Berridge KC (2013) Dopamine or opioid stimulation of nucleus accumbens similarly amplify cue-triggered "wanting" for reward: entire core and medial shell mapped as substrates for PIT enhancement. Eur J Neurosci. doi:10.1111/ejn.12174

Peciña S, Berridge KC, Parker LA (1997) Pimozide does not shift palatability: separation of anhedonia from sensorimotor suppression by taste reactivity. Pharmacol Biochem Behav 58:801–811

Peciña S, Cagniard B, Berridge KC et al (2003) Hyperdopaminergic mutant mice have higher "wanting" but not 'liking' for sweet rewards. J Neurosci 23:9395–9402

Peciña S, Schulkin J, Berridge KC (2006) Nucleus accumbens corticotropin-releasing factor increases cue-triggered motivation for sucrose reward: paradoxical positive incentive effects in stress? BMC Biol 4:8. doi:10.1186/1741-7007-4-8

Pfaus JG, Damsma G, Nomikos GG et al (1990) Sexual behavior enhances central dopamine transmission in the male rat. Brain Res 530:345–348

Piazza PV, Deminiere JM, le Moal M, Simon H (1990) Stress- and pharmacologically-induced behavioral sensitization increases vulnerability to acquisition of amphetamine self-administration. Brain Res 514:22–26

Potenza MN (2008) The neurobiology of pathological gambling and drug addiction: an overview and new findings. Philos Trans Biol Sci 363:3181–3189

Purdy JE, Roberts AC, Garcia CA (1999) Sign tracking in cuttlefish (Sepia officinalis). J Comp Psychol 113:443–449

Reilly S, Schachtman TR (2009) Conditioned taste aversion: behavioral and neural processes. Oxford University Press, New York

Robbins TW, Watson BA, Gaskin M, Ennis C (1983) Contrasting interactions of pipradrol, d-amphetamine, cocaine, cocaine analogues, apomorphine and other drugs with conditioned reinforcement. Psychopharmacology 80:113–119

Robinson TE, Berridge KC (1993) The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain Res Brain Res Rev 18:247–291

Robinson TE, Berridge KC (2003) Addiction. Annu Rev Psychol 54:25–53. doi:10.1146/annurev.psych.54.101601.145237

Robinson TE, Berridge KC (2008) The incentive sensitization theory of addiction: some current issues. Philos Trans R Soc, Biol Sci 363:3137–3146. doi:10.1098/rstb.2008.0093

Robinson TE, Jurson PA, Bennett JA, Bentgen KM (1988) Persistent sensitization of dopamine neurotransmission in ventral striatum (nucleus accumbens) produced by prior experience with (+)-amphetamine: a microdialysis study in freely moving rats. Brain Res 462:211–222

Robinson S, Sandstrom SM, Denenberg VH, Palmiter RD (2005) Distinguishing whether dopamine regulates liking, wanting, and/or learning about rewards. Behav Neurosci 119:5–15. doi:10.1037/0735-7044.119.1.5

Robinson MJF, Robinson TE, Berridge KC (2013) Incentive salience and the transition to addiction. Elsevier, Amsterdam, pp 391–399

Robinson MJF, Anselme P, Fischer AM, Berridge KC (2014a) Initial uncertainty in Pavlovian reward prediction persistently elevates incentive salience and extends sign-tracking to normally unattractive cues. Behav Brain Res 266:119–130. doi:10.1016/j.bbr.2014.03.004

Robinson MJF, Warlow SM, Berridge KC (2014b) Optogenetic excitation of central amygdala amplifies and narrows incentive motivation to pursue one reward above another. J Neurosci 34:16567–16580. doi:10.1523/JNEUROSCI.2013-14.2014

Robinson MJF, Anselme P, Suchomel K, Berridge KC (2015a) Amphetamine-induced sensitization and reward uncertainty similarly enhance incentive salience for conditioned cues. Behav Neurosci. doi:10.1037/bne0000064

Robinson MJF, Burghardt PR, Patterson CM et al (2015b) Individual differences in cue-induced motivation and striatal systems in rats susceptible to diet-induced obesity. Neuropsychopharmacology, epub ahead of print:1–11. doi:10.1038/npp.2015.71

Robinson TE, Yager LM, Cogan ES, Saunders BT (2014c) On the motivational properties of reward cues: individual differences. Neuropharmacology 76 Pt B:450–459. doi:10.1016/j.neuropharm.2013.05.040

Rose JE, Behm FM, Westman EC, Johnson M (2000) Dissociating nicotine and nonnicotine components of cigarette smoking. Pharmacol Biochem Behav 67:71–81

Rosse RB, Fay-McCarthy M, Collins JP et al (1993) Transient compulsive foraging behavior associated with crack cocaine use. Am J Psychiatry 150:155–156

Rozin P (2000) Disgust. In: Lewis M, Haviland-Jones JM (eds) Handbook of emotions. Guilford, New York, pp 637–653

Rømer Thomsen K, Fjorback LO, Møller A, Lou HC (2014) Applying incentive sensitization models to behavioral addiction. Neurosci Biobehav Rev 45C:343–349. doi:10.1016/j.neubiorev.2014.07.009

Sáinz N, Barrenetxe J, Moreno-Aliaga MJ, Martínez JA (2015) Leptin resistance and diet-induced obesity: central and peripheral actions of leptin. Metab, Clin Exp 64:35–46. doi:10.1016/j.metabol.2014.10.015

Schulte EM, Avena NM, Gearhardt AN (2015) Which foods may be addictive? The roles of processing, fat content, and glycemic load. PLoS ONE 10:e0117959. doi:10.1371/journal.pone.0117959

Shin AC, Townsend RL, Patterson LM, Berthoud H-R (2011) "Liking" and "wanting" of sweet and oily food stimuli as affected by high-fat diet-induced obesity, weight loss, leptin, and genetic predisposition. AJP: Regulatory. Integr Comp Physiol 301:R1267–R1280. doi:10.1152/ajpregu.00314.2011

Shuster L, Webster GW, Yu G (1975) Increased running response to morphine in morphine-pretreated mice. J Pharmacol Exp Ther 192:64–67

Shuster L, Yu G, Bates A (1977) Sensitization to cocaine stimulation in mice. Psychopharmacology 52:185–190

Singer BF, Scott-Railton J, Vezina P (2012) Unpredictable saccharin reinforcement enhances locomotor responding to amphetamine. Behav Brain Res 226:340–344. doi:10.1016/j.bbr.2011.09.003

Small DM, Zatorre RJ, Dagher A et al (2001) Changes in brain activity related to eating chocolate: from pleasure to aversion. Brain 124:1720–1733

Smith KS, Berridge KC (2007) Opioid limbic circuit for reward: interaction between hedonic hotspots of nucleus accumbens and ventral pallidum. J Neurosci 27:1594–1605. doi:10.1523/JNEUROSCI.4205-06.2007

Smith KS, Mahler SV, Peciña S, Berridge KC (2007) Hedonic hotspots: Generating sensory pleasure in the brain. In: Kringelbach ML, Berridge KC (eds) Pleasures of the brain. Oxford University Press, Oxford, pp 1–35

Steiner JE, Glaser D, Hawilo ME, Berridge KC (2001) Comparative expression of hedonic impact: affective reactions to taste by human infants and other primates. Neurosci Biobehav Rev 25:53–74

Stinus L, Robert C, Karasinski P, Limoge A (1998) Continuous quantitative monitoring of spontaneous opiate withdrawal: locomotor activity and sleep disorders. Pharmacol Biochem Behav 59:83–89

Stolerman IP (1985) Motivational effects of opioids: evidence on the role of endorphins in mediating reward or aversion. Pharmacol Biochem Behav 23:877–881

Swanson LW (2000) Cerebral hemisphere regulation of motivated behavior. Brain Res 886:113–164

Swanson LW (2005) Anatomy of the soul as reflected in the cerebral hemispheres: neural circuits underlying voluntary control of basic motivated behaviors. J Comp Neurol 493:122–131. doi:10.1002/cne.20733

Tang DW, Fellows LK, Small DM, Dagher A (2012) Food and drug cues activate similar brain regions: a meta-analysis of functional MRI studies. Physiol Behav 106:317–324. doi:10.1016/j.physbeh.2012.03.009

Tindell AJ, Berridge KC, Zhang J et al (2005) Ventral pallidal neurons code incentive motivation: amplification by mesolimbic sensitization and amphetamine. Eur J Neurosci 22:2617–2634. doi:10.1111/j.1460-9568.2005.04411.x

van Holst RJ, Veltman DJ, Büchel C et al (2012) Distorted expectancy coding in problem gambling: is the addictive in the anticipation? Biol Psychiatry 71:741–748. doi:10.1016/j.biopsych.2011.12.030

Vanderschuren LJ, De Vries TJ, Wardeh G et al (2001) A single exposure to morphine induces long-lasting behavioural and neurochemical sensitization in rats. Eur J Neurosci 14:1533–1538

Vanderschuren LJ, Kalivas PW (2000) Alterations in dopaminergic and glutamatergic transmission in the induction and expression of behavioral sensitization: a critical review of preclinical studies. Psychopharmacology 151:99–120

Vezina P (1993) Amphetamine injected into the ventral tegmental area sensitizes the nucleus accumbens dopaminergic response to systemic amphetamine: an in vivo microdialysis study in the rat. Brain Res 605:332–337

Vezina P (2004) Sensitization of midbrain dopamine neuron reactivity and the self-administration of psychomotor stimulant drugs. Neurosci Biobehav Rev 27:827–839. doi:10.1016/j.neubiorev.2003.11.001

Vezina P, Leyton M (2009) Conditioned cues and the expression of stimulant sensitization in animals and humans. Neuropharmacology 56(Suppl 1):160–168. doi:10.1016/j.neuropharm.2008.06.070

Volkow ND, Wang G-J, Fowler JS et al (2002) "Nonhedonic" food motivation in humans involves dopamine in the dorsal striatum and methylphenidate amplifies this effect. Synapse 44:175–180. doi:10.1002/syn.10075

Volkow ND, Wang GJ, Fowler JS et al (1997) Decreased striatal dopaminergic responsiveness in detoxified cocaine-dependent subjects. Nature 386:830–833. doi:10.1038/386830a0

Wachtel SR, Ortengren A, de Wit H (2002) The effects of acute haloperidol or risperidone on subjective responses to methamphetamine in healthy volunteers. Drug Alcohol Depend 68:23–33

West R (2009) The multiple facets of cigarette addiction and what they mean for encouraging and helping smokers to stop. COPD 6:277–283. doi:10.1080/15412550903049181

Wikler A (1973) Dynamics of drug dependence: Implications of a conditioning theory for research and treatment. Arch Gen Psychiatry 28:611–616

Wilkinson CJ (1998) The abuse potential of zolpidem administered alone and with alcohol. Pharmacol Biochem Behav 60:193–202

Winkielman P, Berridge KC (2003) Irrational wanting and subrational liking: how rudimentary motivational and affective processes shape preferences and choices. Polit Psychol 24:657–680. doi:10.2307/3792260?ref=no-x-route:d779aaa6e949d52d4e89ed4f70b1996e

Winkielman P, Berridge KC, Wilbarger JL (2005) Unconscious affective reactions to masked happy versus angry faces influence consumption behavior and judgments of value. Pers Soc Psychol Bull 31:121–135. doi:10.1177/0146167204271309

Wise RA (1982) Neuroleptics and operant behavior: The anhedonia hypothesis. Behav Brain Sci 5:39–53

Woolverton WL, Cervo L, Johanson CE (1984) Repeated methamphetamine administration on methamphetamine self-administration in rhesus monkeys. Pharmacol Biochem Behav 21:737–741. doi:10.1016/S0091-3057(84)80012-X

Wyvell CL, Berridge KC (2000) Intra-accumbens amphetamine increases the conditioned incentive salience of sucrose reward: enhancement of reward "wanting" without enhanced "liking" or response reinforcement. J Neurosci 20:8122–8130

Wyvell CL, Berridge KC (2001) Incentive sensitization by previous amphetamine exposure: increased cue-triggered "wanting" for sucrose reward. J Neurosci 21:7831–7840

Yokum S, Gearhardt AN, Harris JL, et al. (2014) Individual differences in striatum activity to food commercials predict weight gain in adolescents. Obesity doi:10.1002/oby.20882

Yokum S, Ng J, Stice E (2011) Attentional bias to food images associated with elevated weight and future weight gain: an fMRI study. Obesity 19:1775–1783. doi:10.1038/oby.2011.168

Zack M, Featherstone RE, Mathewson S, Fletcher PJ (2014) Chronic exposure to a gambling-like schedule of reward predictive stimuli can promote sensitization to amphetamine in rats. Front Behav Neurosci 8:36. doi:10.3389/fnbeh.2014.00036

Zhang J, Berridge KC, Tindell AJ et al (2009) A neural computational model of incentive salience. PLoS Comput Biol 5:e1000437. doi:10.1371/journal.pcbi.1000437