2 Drug Addiction as Incentive Sensitization

Kent C. Berridge and Terry E. Robinson

In this chapter we present a brief overview of the incentive-sensitization theory of addiction. This description is excerpted from our previous articles on the topic (Robinson & Berridge, 1993, 2003, 2008). We then offer a few additional comments on related issues that we hope might be relevant to philosophical analyses, some excerpted from essays on the concept of incentive salience for philosophers and psychologists (Berridge, 2009; Berridge & Aldridge, 2008).

Addiction and Incentive Sensitization

At some time in their lives most people try a potentially addictive drug—for example, alcohol. However, few become addicts. Even relatively few people who try "hard drugs," such as cocaine or heroin, go on to become addicts. Addiction refers specifically to a pathological and arguably compulsive pattern of drug-seeking and drug-taking behavior, which occupies an inordinate amount of an individual's time and thoughts, and persists despite adverse consequences. Addicts also find it difficult to quit taking drugs, even when they express a strong desire to do so. Finally, if they do manage to abstain, addicts remain highly vulnerable to relapse for long periods of time, well after symptoms of withdrawal have disappeared.

Presumably people initially experiment with drugs because of their pleasant consequences, but what is responsible for the transition from casual or experimental drug use to drug abuse and, eventually, the symptoms of addiction? Over the last 20 years or so there has been increasing recognition that drugs themselves can change the brains of susceptible individuals in complex ways and that these drug-induced changes in the brain contribute to the transition to addiction. Furthermore, some of these

brain changes, especially those related to mesolimbic sensitization, are very persistent and far outlast other changes associated with tolerance and withdrawal (Hyman, Malenka, & Nestler, 2006; Kalivas & Volkow, 2005; Robinson & Berridge, 2003).

Drug-induced changes in the brain alter a number of different psychological processes in parallel, contributing to multiple symptoms of addiction. We suggested in the *Incentive-Sensitization Theory of Addiction*, originally published in 1993, that the most important of these psychological changes is a persistent *"sensitization" or hypersensitivity to the incentive motivational effects of drugs and drug-associated stimuli* (Robinson & Berridge, 1993). *Incentive sensitization* produces a bias of attentional processing toward drug-associated stimuli; it also produces pathological motivation for drugs themselves (compulsive "wanting"). The intensified "wanting" or incentive salience is especially focused on drugs in addicts, in part by Pavlovian associative mechanisms, because an addictive drug is a stimulus that both potently activates the mesolimbic brain system and initiates neurobiological events that enduringly sensitize that system. Importantly, the intensified "wanting" for drugs is not matched by an intensification of "liking" for the same drugs. The dissociation occurs because brain "liking" mechanisms are somewhat separable from "wanting" mechanisms, even for the same reward (Berridge, 2007; Berridge & Robinson, 1998). Only "wanting" systems sensitize, and so "wanting" can increase and become quite intense due to sensitization, regardless of whether a drug still remains "liked" after many repeated uses.

After sensitization of brain mesolimbic systems, excessive "wanting" can be triggered by drug-associated cues or their mental representations, especially in contexts where drugs have been taken before, or in other specific situations such as when one is under stress and similar circumstances. Specific contexts, stimuli, or mood states can facilitate the expression of a sensitized "wanting" response. When combined with impaired executive control over behavior, perhaps due to drug-induced prefrontal cortex dysfunction, incentive sensitization culminates in the core symptoms of addiction (Robinson & Berridge, 1993, 2000, 2003). The concept of incentive sensitization has drawn considerable interest in the past 15 years as an explanation of addiction. Here we summarize this view of addiction, based on past articles, and raise some current issues.

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What Is Drug Sensitization?

In its most generic sense, a pharmacologist would define sensitization as simply any increase in a drug effect that occurs after repeated exposures to the drug. However, in both neurobiological and psychological terms, a more specific form of drug sensitization is central to the incentive-sensitization theory. Incentive sensitization refers to particular neurobiological changes in brain mesolimbic dopamine systems and in related structures belonging to the same larger brain circuit that mediate the psychological function of incentive salience ("wanting"). Measured neurobiologically, sensitization is associated with an increase in the ability of drugs to elevate dopamine neurotransmission in brain regions that receive dopamine inputs, such as the nucleus accumbens, and with changes in the physical structure of neurons in the dopamine-related circuits (Boileau et al., 2006; Robinson & Kolb, 1999). Measured psychologically, incentive sensitization is associated with increases in "wanting" for specific rewards triggered especially when the sensitized individual encounters cues related to those rewards and is expressed in behavioral seeking and sometimes in subjective ratings of rewards (Tindell, Berridge, Zhang, Peciña, S., & Aldridge, 2005; Vezina, 2004; Vezina & Leyton, 2009; Volkow et al., 2008; Wyvell & Berridge, 2001). In a nutshell, we think that the core features of addiction result from sensitization of brain systems that mediate the incentive motivational effects of drug rewards and drug cues—which leads to pathological motivation for drugs in addicts.

Why do only some drug users become addicts? Not all individuals are equally susceptible to sensitization—some are much more vulnerable than others. Individual susceptibility to sensitization is determined by many factors: genetic factors, hormonal factors, gender differences, previous drug experiences, and previous experiences with major stresses in life (Robinson & Becker, 1986; Robinson & Kolb, 2004; Samaha, Yau, Yang, & Robinson, 2005). Sensitization is also influenced by factors related to the drug itself. Drugs such as heroin, cocaine, amphetamine, alcohol, and nicotine can all induce sensitization, although not necessarily to the same degree. Once induced, sensitization to one drug often crosses to other drugs too. More sensitization is produced by exposure to high doses of drug than to low doses. The repeated but intermittent use of drugs induces greater sensitization than a single dose or even continuous exposure to a drug, and sensitization is further facilitated if periods of use are interspersed with periods

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of abstinence—as is typically the case during the development of addiction. For example, the induction of sensitization would presumably be facilitated in someone who regularly indulged in drug parties of high consumption on weekends but abstained during the week. Sensitization is also influenced by the speed with which drugs reach the brain (related to route of administration) and is facilitated by having extended access to drugs that leads to increased intake.

Once neural sensitization occurs, the brain's mesolimbic dopamine system becomes hyperreactive to drugs. The system is not c*onstantly* hyperactive in a stable fashion, but it can be put temporarily into a hyperactive state by exposure to the drug again or by exposure to drug-related cues: that is, it is hyperreactive to particular stimuli. Furthermore, the effects of drug cues and drugs themselves can interact, such that a small amount of drug can potentiate the influence of drug cues (Caggiula, Donny, Palmatier, Liu, Chaudhri, & Sved, 2009).

Thus, our theory suggests that sensitization of mesolimbic systems may create unusually strong (compulsive) levels of "wanting" for drugs or other addictive incentives. A sensitized brain responds with extra incentive salience to reward cues just as a brain that has been drugged with amphetamine does—even if the sensitized brain has no drug on board at that moment (Leyton, 2007; Tindell et al., 2005; Vezina, 2004; Wyvell & Berridge, 2001). An addict, on encountering the right drug cue, would "want" the cued reward at that moment because of excessive incentive salience—even if the person cognitively expected not to like it very much and eventually did not like it much in the end. And crucially, sensitization may last years after an individual stops taking any drugs (Boileau et al., 2006; Paulson, Camp, & Robinson, 1991; Vezina & Leyton, 2009).

Traditional Withdrawal-Based Explanations of Addiction

How does incentive sensitization compare to other explanations for addiction? The most intuitive explanation for addiction has long been simply the traditional view that drugs are taken first because they are pleasant and then that after repeated drug use, drugs are then taken also to avoid the unpleasant withdrawal symptoms that would ensue upon the cessation of use (Koob & Le Moal, 2006). Compulsive drug taking is maintained, by

this view, to avoid unpleasant withdrawal symptoms. This two-sided hedonic hypothesis has gone by many different names: pleasure-pain; positive-negative reinforcement; opponent processes; hedonic homeostasis; hedonic dysregulation; reward allostasis, and others (Koob & Le Moal, 2006; Solomon, 1977). No matter what the name, these hypotheses posit the same basic explanatory logic: addictive drugs are taken initially simply to achieve pleasant drug "highs," and after addiction, to escape withdrawal "lows."

We believe that drug pleasure and withdrawal, which no one doubts contribute to reasons why people take drugs, are unlikely to be a complete explanation of addiction. Everyone agrees that addicts sometimes take drugs chiefly for pleasure and sometimes to escape withdrawal or other dysphoric states (e.g., life stresses). However, there are several major problems with hedonic/withdrawal theories as full explanations of drug addiction. One of the most striking problems is that drug withdrawal actually may be much less powerful at motivating drug-taking behavior than people generally think. Relative to positive incentive processes caused directly by drugs themselves and by their cues, withdrawal states are not especially potent in motivating drug-seeking behavior (Stewart, 2004). For example, in animal studies Stewart and colleagues examined what causes rats to "relapse" into drug-seeking behavior if they previously were dependent on cocaine or heroin but have been drug-free for some time (Shalev, Grimm, & Shaham, 2002; Stewart, 2004). Stewart, Shaham, and colleagues measured lever-pressing to obtain drug infusions under extinction conditions after activating brain mesolimbic systems or instead by inducing an aversive withdrawal state. To activate mesolimbic systems (to produce, we suggest, a resurgence of incentive salience), the rats were simply given a small injection of their old drug prior to the test (called a priming injection). To induce the negative withdrawal state, the rats where given naltrexone (an opioid antagonist drug that blocks opioid receptors in the brain and that induces "precipitated withdrawal" symptoms in the relatively fragile brain of an individual who was recently heroin dependent). Precipitated withdrawal is clearly a negative state, and so it would be expected by any withdrawal-based hypothesis of addiction that was predicated on escape from unpleasant distress to be a very powerful cause for reactivating drug-seeking behavior (Koob & Le Moal, 2006; Solomon, 1977).

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But in fact a priming cocaine or heroin injection turns out to be far more effective at reinstating drug-seeking behavior than naltrexone administration (Shalev et al., 2002; Stewart, 1992, 2004). The free cocaine-heroin injection would have been mostly pleasant in valence, rather than aversive, making reinstatement harder to explain in terms of escape from distress. Withdrawal was relatively ineffective at directly motivating drug taking, and further studies have shown that withdrawal remains ineffective unless individuals have already learned before that they can escape withdrawal by taking the drug (Hellemans, Dickinson, & Everitt, 2006). That is, withdrawal is a state individuals can learn to avoid (Kenny, Chen, Kitamura, Markou, & Koob, 2006), but withdrawal may not be very powerful at directly motivating drug taking without that previous learning. Furthermore, withdrawal symptoms are maximal within a few days after the cessation of drug use, but the susceptibility to reinstatement continues to grow for weeks to months (Grimm, Hope, Wise, & Shaham, 2001). The finding that drug withdrawal can be relatively weak at motivating drug seeking is counterintuitive to many and is a direct contradiction of the opponent-process prediction. But the laboratory finding fits with the reports of some human addicts who say that their sick feelings of withdrawal are quite different from their most intense feelings of drug craving. As one heroin addict explained to a researcher studying craving, "No doc, craving is when you want it—want it so bad you can almost taste it . . . but you ain't sick . . . sick is, well sick" (Childress, McLellan, Ehrman, & O'Brien, 1988).

Another major problem for withdrawal theories is explaining why addicts so often relapse into drug taking again even after they have long been free from withdrawal symptoms. After only a few weeks of drug abstinence the symptoms of withdrawal dissipate, and they therefore can no longer be a powerful motivating factor, whether learned or direct. Yet elimination of withdrawal symptoms does not protect against future relapse, as the many recidivist graduates of detoxification programs can attest. One reply by withdrawal theorists to explain this comes from *conditioned* opponent theories, which suggest that associative conditioning causes predictive drug cues to elicit conditioned tolerance and conditioned withdrawal symptoms (Kenny et al., 2006; Schull, 1979). Conditioned withdrawal effects have sometimes been found in studies of human drug addicts as well as in animal studies, and in principle these

could prompt relapse long after unconditioned withdrawal symptoms have subsided. However, many human addicts report that cues often fail to elicit conditioned withdrawal. Plus, drug cues often elicit quite different effects, such as conditioned feelings of a drug high or feelings of drug craving by themselves (O'Brien, Childress, McLellan, Ehrman, & Ternes, 1988). Indeed, one report found that only 27.5% of heroin addicts experienced conditioned withdrawal, and of these, only 5% indicated this was a reason for relapse (McAuliffe, 1982). In conclusion, neither unconditioned withdrawal nor conditioned feelings of withdrawal seems to be sufficiently strong or reliable to serve as the principal explanation for relapse.

We think that a better explanation for such anomalies comes from a distinction between "liking" and "wanting" that is posited by the incentive-sensitization theory but overlooked by traditional pleasure and withdrawal accounts of addiction. Many potentially addictive drugs initially produce feelings of pleasure (euphoria), encouraging users to take these drugs again. However, with the transition to addiction there sometimes appears to be a decrease in the role of drug pleasure. Some people would argue that the hedonic impact of the drugs undergoes tolerance, so that a stable drug dose induces less of a high. How can it be that drugs come to be "wanted" more and more even if they become "liked" less and less? According to incentive-sensitization theory the reason for this paradox is because repeated drug use sensitizes only the neural systems that mediate the motivational process of incentive salience ("wanting"), but not neural systems that mediate the pleasurable effects of drugs ("liking"). Thus, with repeated drug use the degree to which drugs are "wanted" increases disproportionately to the degree to which they are "liked," and with the development of addiction, this dissociation between "wanting" and "liking" gets progressively greater (figure 2.1). The dissociation between "wanting" and "liking" solves the puzzle that otherwise has led some neuroscientists to conclude that, "one prominent prediction of an incentive-sensitization view would be that with repeated use, addicts would take less drug" (Koob & Le Moal, 2006). Of course, incentive sensitization actually predicts that "wanting" drugs more intensely should make addicts take more drug—not less.

In a related but opposite way the separation of "wanting" from "liking" also frees the control of addiction from being driven solely by the negative affective dysphoria that often follows cessation of drug use, at least for a

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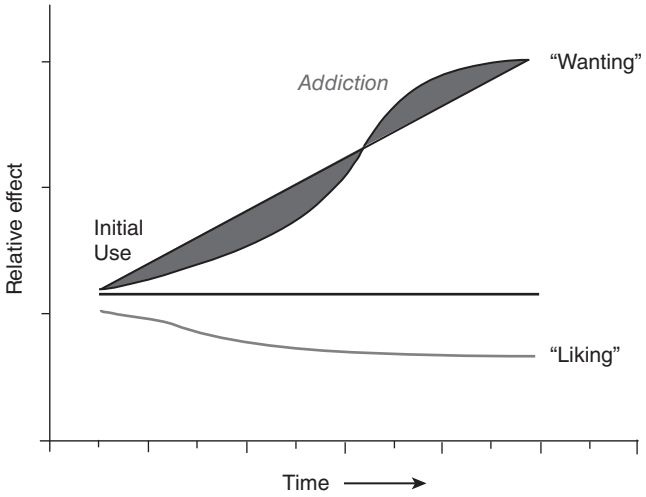

Figure 2.1
Incentive-sensitization model of addiction. Schematic model of how "wanting" to take drugs may grow over time independently of "liking" for drug pleasure as an individual becomes an addict, due to sensitization of brain mesolimbic systems. Modified from Robinson and Berridge (1993).

few days or weeks. Withdrawal states may well contribute to drug taking while they last (Koob & Le Moal, 2006). But addiction typically persists long after withdrawal states dissipate. Sensitization-related changes in the brain, which can persist long after withdrawal ends, provide a mechanism to explain why addicts continue to "want" drugs and are liable to relapse even after long periods of abstinence and even in the absence of a negative affective state.

Aberrant Learning as an Explanation of Addiction?

There is now considerable evidence that in both animals and humans the brain's nucleus accumbens (NAcc) and dopamine-related circuitry are involved in some aspect of reward learning, which has prompted the speculation that in addicts *drugs may alter learning processes* to somehow cause the transition to addiction (Hyman et al., 2006; Robbins, Everitt, & Nutt, 2008; Schultz, 2006). For example, cues that *predict* the availability of rewards can powerfully activate NAcc-related circuitry (Childress et al.,

2008; Day & Carelli, 2007; Tindell et al., 2005; Volkow et al., 2006), sometimes even better than the reward itself (Schultz, 2006). Further, repeated exposure to drugs of abuse facilitates some forms of learning (Nelson & Killcross, 2006; Phillips, Harmer, & Hitchcott, 2002) and triggers some of the same types of neuroadaptations in reward-related neurons as seen in learning (Hyman et al., 2006). Several researchers have hypothesized, therefore, that the transition to addiction results from the ability of drugs to promote *aberrant learning* (Hyman et al., 2006; Redish, 2004; Robbins, Everitt, et al., 2008; Schultz, 2006).

How Does Incentive-Sensitization Theory Contrast to Learning Accounts of Addiction?

Everyone agrees that learning plays a role to guide aspects of addicted behavior, but it has become popular among some to actually refer to addiction as a "learning disorder" (Hyman, 2005). Is aberrant learning per se a chief cause of addiction? We suggest that thinking about addiction as a disorder of learning may not be quite accurate. Learning is only one part of the reward process—and probably not the one that contributes most to the pathological pursuit of drugs in addicts.

Perhaps the most influential type of "learning hypothesis" suggests that compulsivity arises in addiction because drugs facilitate the learning of especially strong automatic stimulus-response (S-R) *habits* and that by their nature S-R habits confer compulsivity to behavior (Belin, Jonkman, Dickinson, Robbins, & Everitt, 2009; Berke & Hyman, 2000; Everitt, Dickinson, & Robbins, 2001; Hyman et al., 2006; Robbins, Everitt, et al., 2008; Tiffany, 1990). After all, some would argue, is an automatic habit not a compulsion if it is performed independently of a person's intentions? We think not. Instead we think a confusion may be involved in calling a pure habit "compulsive" (Robinson & Berridge, 2003). Automatic S-R habits do not become compulsive merely by virtue of being extremely well learned. The defining feature of habits is that they tend to be performed autonomously when one is thinking of something else, without having to think about them. However, habits do not intrude and impose themselves when one is consciously trying to do something else—at worst, they slip in only when one's attention wanders. That is, automatic habits appear only when there is no countervailing purpose to act otherwise. In a classic example

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of habit at work, William James wrote of going upstairs to his bedroom to dress formally for dinner and removing his clothes while thinking about one of his intellectual projects. Suddenly he found that he had put on his pajamas and nearly climbed into bed (James, 1890). "Oops, silly me!" A habit explanation of addiction must rely on similar absentmindedness to create that cognitive vacuum. "Oops, silly me, I took drugs again!" is how the habit theory must construe an addict's experience of relapse. But absentminded drug taking followed by surprise is surely not an accurate account of most instances of addictive relapse.

And no matter how many times an action is repeated, repetition or "stamping in" cannot by itself make a habit compulsive. Strong S-R habits do not necessarily lead to compulsive behavior: tying your shoe, brushing your teeth, and similar acts are not performed compulsively by most people, even after having been performed more than 10,000 times. Few people think obsessively or compulsively about doing one of these things again. For an action to acquire compulsive properties requires something motivational. A compulsive psychological trait is characterized by pathological motivation—that is, something like incentive salience (Robinson & Berridge, 2003). A similar point has been made concerning the compulsive feature of rituals in obsessive-compulsive disorder (OCD). For example, Boyer and Lienard argue that in OCD compulsiveness and automaticity are quite different and, in fact, nearly opposites (Boyer & Lienard, 2008). They write: "Note that [compulsive OCD] ritualized behavior in the sense used here is the opposite of routinized behavior, which people can accomplish 'without thinking'" (293). We agree, and think the same distinction can be applied to compulsive drug use versus drug habits performed "without thinking."

Beyond compulsion, addictive behavior also displays a high degree of targeted flexibility, which requires a completely different explanatory mechanism from S-R habits, and which again suggests a motivational component. Habit cannot explain why an addict waking up in the morning with no drug spends the day engaging in a complex series of behaviors that may never have been performed in quite the same way before—scamming, stealing, negotiating—all seemingly motivated to procure drug. Addicts do what they have to do and go where they have to go to get drugs, even if actions and routes that never have been performed before are required. Such focused yet flexible behavior in addiction shows patho-

logical motivation for drugs that cannot be explained by evoking S-R habits, which by their nature consist of stereotyped inflexible actions triggered by specific stimuli. Indeed, a strict S-R habit theory would require the addict, on waking up in the morning with no drug available, to engage *automatically* in exactly the same old sequence of habitual actions he used previously to get drugs, whether the actions were currently effective or not. Yet addicts in the real world are not S-R automatons; they are, if nothing else, quite resourceful.

On the other hand, everyone must agree that S-R associations involved in habits are responsible for the automatized habits and rituals involved in *consuming* drugs once they have been obtained, and we also agree that treatment with drugs facilitates the development of S-R habits in animals (Miles, Everitt, & Dickinson, 2003; Nelson & Killcross, 2006), perhaps via recruitment of the dorsal striatum (Everitt et al., 2008; Robbins, Ersche, & Everitt, 2008). We further agree that habits may be especially prominent in standard self-administration animal models, where only a single response is available to be performed (e.g., press a lever) thousands of times in a very impoverished environment to earn injections of drugs. Thus we applaud efforts to understand the neural basis of habits that are a prominent feature of *drug consumption behavior* in addicts.

How Does Learning Interact with Incentive Sensitization?

As we reject aberrant learning as an explanation of addiction, it is incumbent on us to explain how learning might interact with incentive sensitization. The central thesis of the incentive-sensitization theory of addiction (Robinson & Berridge, 1993) is that repeated exposure to potentially addictive drugs can, in a way that is not reducible to learning, persistently change brain cells and circuits in susceptible individuals and under particular circumstances. After it has developed, there is no question that the *expression* of sensitization is powerfully *modulated* by learning—but sensitization is not caused by associative learning (Anagnostaras & Robinson, 1996; Anagnostaras, Schallert, & Robinson, 2002). The sensitized brain circuits normally regulate the attribution of incentive salience to stimuli, a psychological process involved in motivated behavior. The nature of these neuroadaptations is to render these brain circuits hypersensitive ("sensitized") in a way that results in pathological levels of incentive salience being attributed to drugs and drug-associated cues. Persistence of

incentive sensitization makes pathological incentive motivation ("wanting") for drugs last for years, even after the discontinuation of drug use. Sensitized incentive salience can be manifest in behavior via either implicit (as unconscious "wanting") or explicit processes (as conscious craving), depending on circumstances.

Although learning is not identical to "wanting," learning is still an important contributor to the operation of incentive salience mechanisms. The specific *focus* on drugs in particular in addicts is produced by an interaction between incentive-salience mechanisms with associative learning mechanisms that normally direct motivation to specific and appropriate targets. Learning specifies the object of pathological desire via associations to that object gained from past experiences and also modulates the expression of neural sensitization at particular places or times (and not others). Yet it is important to note that learning per se is not enough for pathological motivation to take drugs. We argue that pathological motivation arises from the sensitized and nonassociative adaptations in brain circuits that mediate incentive-motivational processes (i.e., incentive sensitization). The fact that learning can modulate the expression of those changes is why neural sensitization is often expressed in behavior only in contexts in which drugs have been previously experienced (Badiani & Robinson, 2004; Vezina & Leyton, 2009). The exact nature of associative contextual control over the expression of sensitization needs further study, but we suggest this contextual control provides an additional mechanism for why addicts will "want" drugs most particularly when they are in drug-associated contexts.

As further testimony to the difference between learning and incentive salience, we note that by spreading beyond the learned focus of "wanting" on drug targets, incentive sensitization can also sometimes spill over in animals or humans to other targets such as food, sex, gambling, and others (Fiorino & Phillips, 1999; Mitchell & Stewart, 1990; Nocjar & Panksepp, 2002; Taylor & Horger, 1999). For example, treatment with dopaminergic medications in some patient populations can lead to a "dopamine dysregulation syndrome" (DDS) that is manifest not only by compulsive drug use but also sometimes by "pathological gambling, hypersexuality, food bingeing . . . and punding, a form of complex behavioral stereotypy" (Evans et al., 2006; Lawrence, Evans, & Lees, 2003).

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Other Addictions?

Does incentive sensitization apply to any other form of addiction beyond drugs? This question remains difficult to answer. As indicated above, there is some reason to believe that overactivation of brain dopamine circuits can power certain human cases of excessive "wanting" to have sex, to binge eat, gamble, and so forth. The clearest cases involve use of drugs. What is not known so far is whether sensitization-type states ever emerge in any brains in the *absence* of the person having taken any drugs or medications (with the exception of repeated intermittent exposures to intense stress, for which there is some evidence for sensitization induction). Such emergence is within the realm of possibility, but it is not yet an established fact. In support of this possibility, for example, some researchers have suggested that when rats are exposed to patterns of alternating periods of dieting interspersed with access to sugary treats, their brains may undergo changes that overlap with drug sensitization (Avena & Hoebel, 2003). If so, some plausibility is gained by the hypothesis that excessive "wanting" might power episodes of binge eating in some people, to the extent that similar changes might occur in them either by related environmental exposures or even spontaneously in a gene-related fashion (Kessler, 2009).

It is conceivable then that sensitization or sensitization-like processes could contribute to cases of pathological motivation for gambling, sex, food, and other addictions. But it must be cautioned that to our knowledge at present no actual evidence exists that such sensitization-like processes actually occur spontaneously in the brains of any particular individuals. Perhaps the closest cases so far in this direction come from suggestions that some obese binge eaters have inherited gene variants that may predispose their brains toward excessive mesolimbic activations, including stronger dopamine activation (Davis et al., 2009). Still, more evidence is needed. Until and unless such evidence does appear, the extension of incentive sensitization to other types of addiction remains essentially speculative.

Relation of Incentive Sensitization to Cognitive Dysfunction

The incentive-sensitization theory focuses on sensitization-induced changes in incentive-motivational processes and related changes in the brain, but it is important to also acknowledge that myriad other brain

changes contribute to addiction as well, including damage or dysfunction in cortical mechanisms that underlie cognitive choice and decision making (Robinson & Berridge, 2000, 2003). Many important studies have documented that changes in executive functions, involving how alternative outcomes are evaluated and decisions and choices made, occur in both addicts and animals that take drugs (Bechara, 2005; Robbins, Ersche, et al., 2008; Schoenbaum & Shaham, 2008). We agree that impairment in executive control plays an important role in making bad choices about drugs, especially when combined with the pathological incentive motivation for drugs induced by incentive sensitization.

Unpacking Some Issues That Remain

Beyond addiction, there are a number of related issues that might be important to evaluation of our claims about the nature of "wanting," its relation to "liking," whether "wants" can be truly compulsive, and whether "wants" can be irrational. In the remainder of this chapter we briefly explore several of those additional issues that seem to us to be of potential interest to philosophers.

The Nature of Incentive Salience as a "Wanting" Module

Desire is not a unitary phenomenon but contains several neurological-psychological modules (figure 2.2). Incentive salience is a "wanting" module, that is, just one of several types of what is meant ordinarily by the word wanting (no quotes) (Berridge, 2007; Berridge & Aldridge, 2008; Robinson & Berridge, 1993). As a distinct module, incentive salience is psychologically most visible in its cue-triggered "wanting" and motivational magnet effects that cause individuals to be strongly attracted to particular reward stimuli. Importantly, "wanting" can occur even in the absence of conscious awareness of the reward. By comparison, cognitive wanting, in the more familiar sense of the word, is quite a different module of desire. If one has a cognitive want, one has a conscious desire for a specific reward—one knows what one wants. Cognitive wanting has declarative goals, involving explicit expectations of future outcomes. Incentive salience "wanting" has causes and targets but not explicit goals except to the degree that incentive salience can color cognitive desires. When the two forms of desire are congruent, "wanting" adds a visceral

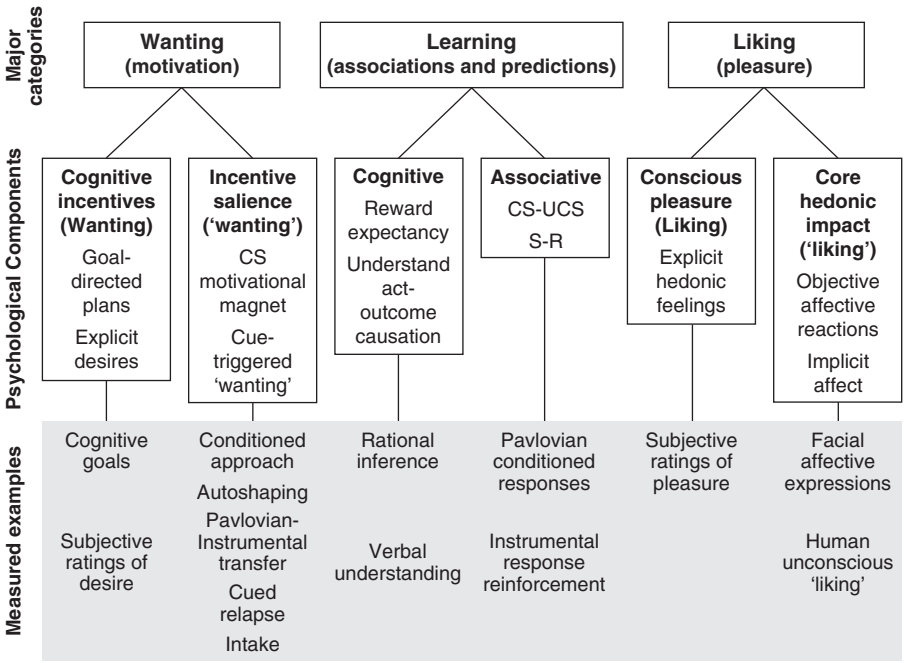

Figure 2.2
Components of liking, wanting, and learning in reward. The desire module of incentive salience is shown as a "wanting" module inside Wanting (motivation). The separate desire module of cognitive incentives (wanting without quotation marks) exists alongside, mediated by separable neural systems. The separate nature of these motivation modules underlies why a sensitized "want" can become compulsive. Modified from Berridge and Robinson (2003).

"oomph" to mental desires. Ordinarily "wanting" and wanting work together toward the same incentives, but in certain situations the two psychological processes can be momentarily dissociated. When this happens, "wanting" can manifest in seeking behavior that occurs somewhat irrationally and even in some cases unconsciously, as described further below.

Another way of distinguishing among modules of desire is through the concept of reward utility that stems from behavioral economics. Drawing on the terminology of Kahneman and colleagues, for example, utility comes in several forms: predicted, decision, experienced, and remembered (Kahneman, Wakker, & Sarin, 1997). Predicted utility is the expectation

of how much a future reward will be liked. Decision utility is what we actually decide to do, manifest in choice and pursuit. Experienced utility is what most people think of the term reward, being the hedonic impact experienced when the reward is gained. Remembered utility is the memory of how good a previous reward was in the past and, typically, the chief determinant of predicted utility.

In this framework, incentive salience "wanting" is a pure form of decision utility, which is distinct from other forms of utility and in some conditions can decouple from all the others. That is, "wanting" for an outcome is distinguishable from experienced utility (hedonic impact or "liking" the outcome), remembered utility of how nice the outcome was in the past, and forecast or predicted utility of how nice it will be in the future. For cognitive wants, by contrast, decision utility essentially becomes joined to forecast or predicted utility. That is, one wants an outcome to the degree one expects it to be good. This difference is part of what makes incentive salience "wanting" a unique module and quite different from cognitive wanting (no quotation marks). It is why we put quotation marks around "wanting" when referring to incentive salience.

Incentive salience "wants" are bound closely to percepts: the sights, sounds, or smells of rewards and their associated cues, or vivid images of those stimuli. Incentive salience typically is triggered as a phasic pulse or relatively brief peak upon encountering a reward or a physical reminder of the reward (a cue) (Tindell et al., 2005; Wyvell & Berridge, 2001; Zhang, Berridge, Tindell, Smith, & Aldridge, 2009). Incentive salience does not require a clear cognition of what is wanted and does not even need to be consciously experienced as a feeling of wanting, at least in some cases (although on occasions when it is brought into consciousness by additional neural machinery, "wanting" can considerably intensify feelings of desire). Perhaps a reason for the difference is that incentive salience is mediated chiefly by subcortical brain mechanisms, whereas cognitive forms of desire are more dependent on higher cortex-based brain systems. Incentive salience may have initially evolved in animals as a distinct "wanting" module to facilitate the pursuit of particular innate incentives. Possibly it gave an elementary form of goal directedness, which could guide behavior in the right direction toward appropriate rewards and cues in advance of experiencing the goals.

So

Incentive salience as a module is not the form of desire we are most aware of in daily life nor the type of desire that has been the greatest focus of philosophers. But incentive salience is important in daily life, needed to color conscious desires with motivational power, to make them compelling spurs to action—even though its effects may be more implicit than explicit. Indeed, incentive salience may be a crucial component of our most intense and visceral desires, and especially important in the pathological intensity of some addictions and compulsive desires.

Incentive salience can be viewed as a motivational transform of a brain signal corresponding to the perceived object of desire or its mental representation. When attributed to a stimulus representation, incentive salience transforms mere sensory shapes, smells, or sounds into attractive and attention-riveting incentives. Once attributed with incentive salience a percept becomes difficult to avoid noticing: the eyes naturally move toward the incentive; it captures the gaze and becomes motivationally attractive; and the rest of the body may well follow to obtain it. It is what distinguishes a mere stimulus from an *incentive stimulus*.

How can one tell if a stimulus is attributed with incentive salience? It has several distinguishing psychological features that help it to be recognized even in animal experiments as well as in human daily life. First, incentive salience gives a "motivational magnet" property to stimuli it is attributed to and makes those stimuli attractive and potently able to elicit approach toward them. Second, stimuli attributed with incentive salience are "wanted." in the sense that animals and people will work to get them. Incentive stimuli even support the learning of new actions to get them (i.e., they act as what psychologists call *conditioned reinforcers*). Incentive cues typically predict the reward to follow, although it is worth noting that the predictive and incentive properties of cues are dissociable, and only the incentive properties are due to incentive salience attribution (Flagel, Akil, & Robinson, 2009; Robinson & Flagel, 2009; Tindell et al., 2005; Zhang et al., 2009). Third, incentive salience also triggers momentary peaks of intense motivation to obtain a cued reward, often manifest as a "surge" in the instrumental action required to obtain the reward. Such features (reward cues becoming motivational magnets, cues as objects of desire, peaks of cue-triggered "wanting" for the actual reward) allow us to determine if a stimulus is or is not attributed with

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incentive salience in behavioral neuroscience experiments with animals as well as in people.

Can "Wanting" Be Compulsive?

It may seem mistaken to some readers to claim that sensitized "wanting" in an addict ever creates an actual *compulsion* to take drugs. In an illuminating argument, for example, Stephens and Graham have taken issue with our claim (Stephens & Graham, 2009). Their argument is reasonable and helpful to consider here.

Stephens and Graham write that "a motive or want does not qualify as compulsive or addictive in character or purport unless it contravenes or violates a contrary" (Stephens & Graham, 2009, 32). Defining compulsive, they draw on Aristotle's sense of an external force, such as a strong wind or of one being forcefully carried by outside hands to compel an outcome contrary to desire. In that sense, a compulsive "want" or motive seems self-contradictory. The "want" is part of the internal desire and not outside the person.

We agree with the Stephens and Graham (2009) analysis of compulsion. Still, we suggest that the possibility of a compulsive "want" arises from the complex dissociation among components of desire discussed above. The difference between incentive salience "wanting" versus cognitive wanting allows a compulsion to arise internally from within the individual (via sensitized incentive salience), as well as from without. A person's most central desire, from the philosophical stance, must surely be what the person cognitively wants—the willed-for goal (even when the goal is abstinence). A person has some choice over the cognitively prized goal but not so much choice over the "wanted" target of incentive salience. If desire is not unitary, one can "want" one thing at the same time as one cognitively wants a different thing. For example, an addict may sincerely want to abstain from taking drugs and know full well that the drug on offer at that moment will not be worth the cost of taking it. The sincere recovered addict cognitively desires not to take the drug, and in the most extreme cases he may even be said to in no sense cognitively desire to take it (e.g., when the only drug available is known not to be particularly hedonic because of its type, poor quality, or low dose; when the consequences of relapse can be expected to be distressing; etc.). But if drug cues are dangled in the right context, by our theory, the sensitized

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addict will be seized by a sudden pulse of cue-triggered "wanting" for drugs (although we note that the expression of "wanting" is subject to top-down modulatory control, and this provides a way to win many battles over compulsions; however, a single loss may mean not winning the war). This would not be compulsive in Stephen and Graham's sense if the pulse of "wanting" always momentarily corrupted the dominant cognitive desire to produce a judgment shift, so that "wanting" and wanting became aligned together to thwart earlier precommitment and produce relapse (Holton, 2009). But we suggest that the dominant cognitive desire need not necessarily switch in every case and that sensitized "wanting" can act in the absence of a strong cognitive desire (described below under unconscious "wanting")—and sometimes even against the cognitive desire. "Wanting" can act against a dominant cognitive intention or desire. That is one reason why we say when "wanting" is strong enough, it can take on compulsive properties.

In practice it is admittedly difficult to prove that "wanting" actually competes with and wins out over a dominant cognitive desire. But we think there is at least some suggestive evidence. One piece of evidence comes from animal neuroscience studies regarding the difference in neuropharmacological substrates of cue-triggered "wanting" versus cognitive wanting. For example, administration of a dopamine-blocking drug to a rat prevents the occurrence of cue-triggered "wanting" but does not seem to have any effect on the rat's more cognitive wants involving experience-derived goal expectations and understandings of the relation between its acts and the outcome (Dickinson, Smith, & Mirenowicz, 2000).

Another piece of evidence comes from the highly transient nature of cue-triggered "wanting," which often seems to occur as a fleeting burst that rests on a stable and unchanging baseline of more cognitive wanting. For example, even when a rat's brain is in a constantly elevated state of dopamine activation due to having received a recent (painless) microinjection of amphetamine into its brain, its excessive hyper-"wanting" is still expressed only momentarily on encounters with reward cues (Wyvell & Berridge, 2000, 2001). Before the cue comes, the dopamine-activated brain of the rat simply wants sugar in the ordinary sense, without necessarily showing any indication of elevation over normal levels. The next moment, when the cue comes, the dopamine-activated brain transiently "wants" sugar to an exaggerated degree, as well as more stably wanting to the

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original degree, according to the incentive salience hypothesis. On the cue's arrival, the rat engages in a frenzied burst of efforts to obtain the sugary reward, far above normal levels. Yet just a few moments after the cue ends, the rat returns to its earlier and lower predominant level of wanting. Finally again, moments later still, the cue is reencountered once more, and excessive and irrational "wanting" again takes control. It seems unlikely that mesolimbic activation altered rats' dominant expectation or stable cognitive want because the intense enhancement of pursuit typically lasted only while the cue stimulus was actually present, although amphetamine was present in the nucleus accumbens throughout the entire session.

The neural mesolimbic mechanism for "wanting" seems to involve a synergy between dopamine levels and the external presence of a reward-related event or object. This seems separable from the cortex and other neural systems that mediate more stable cognitive goals and steady-state performance. Much more evidence is needed of course to convincingly resolve this issue, but we think such observations do seem compatible with the idea that cue-triggered bursts of "wanting" do not always lead to a shift in dominant cognitive desire but, rather, can overlay and override the stable desire at special moments.

Is Incentive Salience Intentional?

Intentionality seems to be an important part of many philosophical treatments of desire. Most cognitive desire has intentionality in the form of an explicit object of desire. Cognitive mental representations of a desired object can be imagined—its look or feel—and one can remember what it was like on previous occasions. Basically, one knows what one wants, and when one has a cognitive want, one always wants some goal in particular.

Incentive salience, by contrast, has a less stable relation to intentionality. We think "wanting" is intentional in some cases but not in others. At its most nonintentional, incentive salience may detach from the object of desire and be attributed too widely among stimuli, spewing indiscriminant "wanting" in directions that are inappropriate or completely general. The entire world can brighten up in a motivational sense on such occasions, taking on diffuse incentive properties. Thus, intentionality is not intrinsic to "wanting" but depends on mechanisms that focus the attribution of incentive salience to particular targets.

A special but odd form of intentionality seems involved when the cue for a reward becomes "wanted" as a motivational magnet, rather than only

the pleasant reward itself (Flagel et al., 2008; Mahler & Berridge, 2009; Robinson & Flagel, 2009; Tomie, 1996). When cues become the focus of desire, there is a slight distortion in the targeting of intentionality. No *reason* exists to desire the cue, only a neural and psychological *cause* and a target in the form of an external stimulus that is transformed into a "wanted" incentive. There is merely a psychological associative history and a neural mechanism that makes it desired. In some addiction situations an individual may become obsessively focused on the attractive cue. For example crack cocaine addicts are known to "chase ghosts," which means to compulsively pick up pebbles on the ground that somewhat resemble crack rocks (Rosse, Fay-McCarthy, Collins, Risher-Flowers, Alim, & Deutsch, 1993). They may even put the inert pebbles in their crack-smoking pipe and try to smoke them. Similarly, in animal experiments rats eagerly sniff and nibble a stark piece of metal when its appearance predicts that a food pellet will soon follow (figure 2.3) (Mahler & Berridge, 2009; Robinson & Flagel, 2009), and quail copulate with a bird-sized terrycloth object that predicts a subsequent sex partner in a manner perhaps related to human sexual fetishes (Koksal et al., 2004).

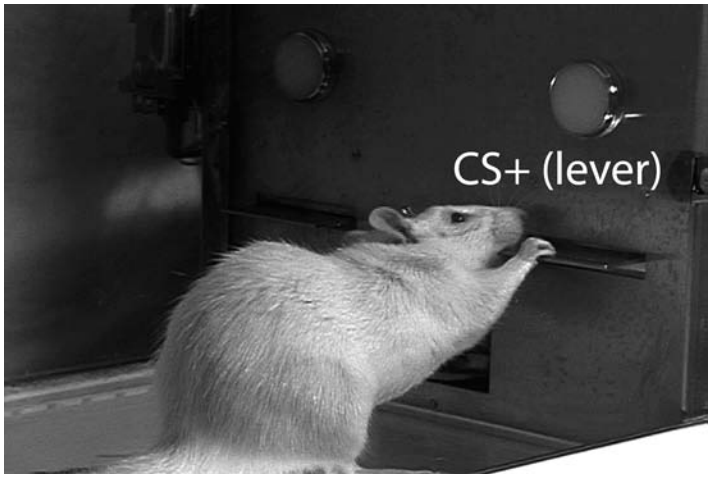

Figure 2.3
A cue as motivational magnet. This rat is trying to "eat" a metal lever, simply because it is a cue for sugar reward. Whenever the lever has previously been inserted through the wall into the chamber, it has predicted a sugar pellet to follow. Now whenever the lever is inserted, the rat approaches and nibbles on the lever. From Mahler and Berridge (2009); Robinson and Flagel (2009).

Least intentional of all may be cases when incentive salience is attributed indiscriminately to more than one thing at once. This may happen under conditions of intense activation of mesolimbic systems, for example, by electrical brain stimulation or a drug microinjection in some limbic structures, or perhaps even as a function of neural sensitization in certain cases. In such instances pathological incentive salience may simultaneously disrupt associative mechanisms that usually focus "wanting" on a particular target. As a result, one may "want" many different stimuli at the same time. Essentially everything perceived at that moment might become more attractive and "wanted." For example, some people who have been implanted with stimulation electrodes in their brain mesolimbic systems have been reported to describe the entire room as "brightening" in a motivational sense, so that they perceive everyone present as more interesting, more socially attractive, and even more romantically or sexually attractive, and at that moment they feel motivated to do quite a number of activities (Green, Pareira, & Aziz, 2010; Heath, 1996). Such indiscriminate "wanting" is powerfully motivational, but when everything is "wanted," then nothing in particular is. Does such an unfocused desire have intentionality at all?

Finally, we note that "wanting" mechanisms may also share a perhaps surprising link to dread. For example, we have found evidence that NAcc circuits are organized as an affective keyboard in which generators for desire versus dread are anatomically arranged at opposite ends and that some of the generators in the middle can generate desire and/or dread depending on circumstances (Reynolds & Berridge, 2008). We and others have suggested that such a mesolimbic dread may reflect a negatively valenced form of motivational salience, and we have postulated that this fearful salience may contribute to the paranoia of drug psychosis or schizophrenia by making the environmental stimuli it is attributed to become perceived as frightening (Berridge & Robinson, 1998; Kapur, 2003; Robinson & Berridge, 1993). Potential flickering between desire and dread, sometimes even directed to the same external object, may perhaps raise some questions regarding whether the want possesses stable intentionality.

Can "Wanting" Be Unconscious?

Another way in which incentive salience diverges from cognitive desire and intentionality is that incentive salience need not always be conscious.

There exist examples of unconscious core "wanting" in people ranging from drug addicts to ordinary college students. For instance, when given opportunity to work (press a button) for an intravenous cocaine dose too low to produce detectable physiological or subjective effects, drug addicts have been reported to say that the injection feels empty and completely devoid of any cocaine at all, yet they still work more to receive more of the same "empty" dose—all the while denying that they are doing so (Fischman & Foltin, 1992).

Similarly even for ordinary college students, Winkielman and colleagues found that unconscious "wanting" and "liking" could intensify a person's motivation to drink a subsequently encountered beverage without ever emerging into conscious awareness as subjective pleasure or desire (Winkielman & Berridge, 2004). The unconscious "wanting" was triggered by flashing subliminally brief visual presentations of happy emotional facial expressions that might activate brain limbic systems, as brief facial flashes (1/60 sec each), which could not be consciously seen or recognized later and did not cause any change in the person's ratings of his or her own positive or negative mood. But when the students were asked to subsequently judge a "new fruit-flavored beverage that was under development by a beverage company" and given a pitcher of the drink to pour, taste, and evaluate, their reactions to the drink were powerfully altered. When presented with the beverage, students found it more attractive after seeing subliminal happy faces, pouring and drinking 50% more of it. Further, they expressed willingness to pay four times more for the drink if it were sold when asked after the subliminal happy faces than after subliminal angry faces instead. We hypothesize that the subliminal happy faces activated incentive mesolimbic circuits of "wanting" in the brains of students who viewed them, which persisted for some minutes undetected as students evaluated their own mood. The "wanting" surfaced only when an appropriate target was finally presented in the form of a hedonically laden sweet stimulus that they could taste and choose to ingest or not.

Applying a related logic to cocaine addicts, Childress and colleagues induced limbic brain activation and positive affective psychological reactions by subliminal photos of drugs or sex (Childress et al., 2008). Subliminally brief photographs of scenes such as cocaine preparation or of erotic sexual scenes were flashed to the addicts. Although not consciously perceived, the photos activated brain limbic structures, including dopamine

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targets. The degree of limbic brain activation predicted the strength of positive affective reaction the same photos would elicit when the addict viewed them consciously for longer periods on another day, and reactions were measured in an emotional-cognitive conscious recognition task. Childress and colleagues suggested that *"*[b]*y the time the motivational state is experienced and labeled as conscious desire, the ancient limbic reward circuitry already has a running start"* (Childress et al., 2008, 4).

Such instances of unconscious "wanting" suggest that incentive salience can at least sometimes operate underneath conscious awareness. Mesolimbic "wanting" may run in parallel with ordinary (and more cortex-mediated) wanting. Usually they point in the same direction, but in cases of unconscious "wanting," only one of the mechanisms seems to be in operation. These cases may lack recruitment of the additional brain and psychological mechanisms needed to translate the core "wanting" process into a cognitive and conscious desire. An unconscious "want" seems difficult to reconcile with intentionality in the usual sense. To the degree that an unconscious "want" can be assigned to a malleable target, it does not have an explicit object of desire. It has only a stimulus target, which may to some degree depend on chance in the form of what happens to turn up next.

Can "Wanting" Be Irrational?

Ordinarily in optimal decisions, all subtypes of reward utility will be maximized together. But sometimes a decision is less than optimal, and then subtypes of utility may diverge from each other. A major contribution of Kahneman's utility taxonomy mentioned above has been to identify cases where predicted or remembered utility diverges from actual experienced utility (Kahneman, Fredrickson, Schreiber, & Redelmeier, 1993; Kahneman et al., 1997). Such divergence can lead to bad decisions on the basis of wrong expectations, called miswanting by Gilbert and Wilson (Gilbert & Wilson, 2000; Morewedge, Gilbert, & Wilson, 2005). If one has a distorted remembered utility because of memory illusions of various sorts, one will have a distorted predicted utility. Decisions made on the basis of false predicted utility are likely to turn out to fail to maximize eventual experienced utility. Or if predicted utility is distorted for reasons other than faulty memory, such as by inappropriate cognitive theories about what rewards will be like in the future, then decisions will again turn out wrong. In either

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case predicted utility will fail to match actual experienced utility, and the decision is liable to be wrong.

Thus, if decisions are guided principally by predictions about future reward (if decision utility equals predicted utility), then faulty predictions consequently entail that wrong decisions will be made (decision utility does not equal experienced utility). People may thus choose outcomes that they turn out not to like when their predictions about them are wrong. People choose them because they wrongly expect to like them in such cases (and perhaps because they wrongly remember having liked them in the past)—but then turn out not to like them after all.

The previously described mismatch captures much of what is discussed under the label of miswanting and decisions that fail to maximize utility. But Kahneman's taxonomy has a further use for an even more intriguing form of miswanting that we point to here, regarding the potential *irrationality* of incentive salience in addiction. This might be called "irrational miswanting" because it can lead to an outcome being "wanted" even when an outcome value is correctly predicted to be less than desirable (Berridge & Aldridge, 2008; Robinson & Berridge, 1993, 2003).

An irrational decision, we suggest, is to choose what you expect not to like. That is, a decision is irrational when its decision utility does not equal predicted utility. When decision utility is greater than predicted utility, if that can happen, then one might be said to choose what one does not expect to like (not only what one mistakenly expects to like). To choose what one does not expect to like is to choose in a way that is distinctly irrational, as we define irrationality.

If decision utility exists as a distinct psychological variable (with a somewhat separate neurobiological mechanism), it might sometimes dissociate from predicted utility—just as decision utility (together with predicted utility) sometimes dissociates from experienced utility. If at any time decision utility could grow above predicted utility, that could mean choosing an outcome that we actually expected not to like at the moment of decision (and that we not only expected not to like but also turned out not to like in the end). The conditions we expect to produce such excessive "wanting" would include when a sensitized addict encounters drug-related cues in an appropriate context. In addition, the potency of irrational "wanting" triggered by those cues would be especially exacerbated if the addict tried to take "just one hit." The presence of drug on board can prime

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mesolimbic systems and can amplify the response to drug cues, creating a surge of incentive salience in a way that might well precipitate a compulsive binge of further drug taking.

Conclusion

According to the incentive-sensitization theory, addiction involves drug-induced changes in many different brain circuits, and incentive sensitization of mesolimbic circuits is the most prominent of these for producing the distinguishing features of addiction. Bolstered by the evidence that has accumulated over recent years, we remain confident in concluding,

> that at its heart, addiction is a disorder of aberrant incentive motivation due to drug-induced sensitization of neural systems that attribute salience to particular stimuli. It can be triggered by drug cues as a *learned motivational response* of the brain, but it is not a disorder of aberrant learning per se. Once it exists, sensitized "wanting" may compel drug pursuit whether or not an addict has any withdrawal symptoms at all. And because incentive salience is distinct from pleasure or "liking" processes, sensitization gives impulsive drug "wanting" an enduring life of its own. (Robinson & Berridge, 2003, 44)

Sensitized "wanting" in an addict may motivate behavior independent of drug "liking" or withdrawal and independent of cognitive desires and intentions. Incentive sensitization can produce addictive features that make drug taking more compulsive than mere habits could ever achieve, and it may rise above expectations of drug value to become "wanted" to a degree that might even be called irrational. Such an addictive "want" has truly gained a destructive "life of its own." These phenomena of desire seem intriguing topics for philosophers and psychologists trying to understand the mind.

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