IS ADDICTION A BRAIN DISEASE?

The incentive-sensitization view

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The ‘addiction is a brain disease’ model

The phrase ‘brain disease’ burst into modern discussions of addiction in 1997, introduced by a Science article by Alan Leshner, then director of the U.S. National Institute on Drug Abuse (Leshner, 1997; see Chapter 2, this volume). The title of Leshner’s article declared “Addiction is a brain disease, and it matters.” Leshner called on policy makers to discard traditional blame-based approaches to addiction, and to replace incarceration with treatment. He argued, “What does matter tremendously is whether or not a drug causes what we now know to be the essence of addiction: compulsive drug seeking and use, even in the face of negative health and social consequences” (p. 46). Further, “The addicted brain is distinctly different from the nonaddicted brain, as manifested by changes in brain metabolic activity, receptor availability, gene expression, and responsiveness to environmental cues” (p. 46). Yet Leshner also added a caveat: “Of course, addiction is not that simple. Addiction is not just a brain disease. It is a brain disease for which the social contexts in which it has both developed and is expressed are critically important” (p. 46). Leshner’s proposal seems reasonably nuanced, but its nuances sometimes may be forgotten.

Criticisms of the brain disease model

In recent years, a number of critics have contested the view that addiction should be viewed as a brain disease (Lewis, 2015, 2017, 2018; Pickard et al., 2015; Pickard, 2017; Satel & Lilienfeld, 2017; Szelavitz, 2017; Heather et al., 2018). Such critics list several reasons for challenging the brain disease concept. For example, many addicts may not regard themselves to have a disease. Recovering addicts may never feel themselves to be fully cured, as returned to their pre-addictive state again, but rather live in a third state that requires continual effort to remain drug-abstinent. Similarly, critics note that to view addicts as passive medical patients neglects the need for their active agency in efforts to overcome drug use, and that a disease label perhaps even causes some to fatalistically resign themselves to addiction. Encouraging fatalism could make less likely the personal act of self-re-invention needed in order to successfully give up drugs. Also, critics note that drug use is promoted by disadvantaged life situations and by particular social networks, resulting in higher likelihood of addiction. And critics point out that brain mechanisms important in addiction, such as mesolimbic dopamine systems, are also brain mechanisms of ordinary desires that are shared by everyone, such as love or hunger. Some may therefore conclude, for example, as Marc Lewis put it, “If addiction is a disease, then so apparently is love” (Lewis, 2017, p. 12).

I believe many of the critics’ points are valid (and a few overlap with Leshner’s original caveats). Yet I still believe that brain disease can be a reasonable label for addiction. The validity of these caveats...
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and critics’ points is not inconsistent with a modern notion of addiction as brain disease, as will be explained here. In particular, if the incentive-sensitization theory is a valid explanation of addiction, as I believe it is, then brain disease can be a legitimate label for the incentive-sensitization changes in brain and mind that cause excessive and narrowly focused ‘wants’ in addiction. The essential disease features of incentive-sensitization are: 1) the extremity of the neural changes in mesolimbic systems and resulting psychological extremity of addictive temptations, which are well beyond the range experienced in normal life; and 2) the deleterious consequences that result from repeatedly facing, and sometimes giving in, to such extreme temptations. That is, the mesocorticolimbic neural changes of incentive-sensitization add an arguably compulsive motivational intensity to addiction, and are sufficiently extreme and destructive to be viewed as pathological.

But I also believe that this neural and psychological ‘disease’ remains entirely compatible with the person’s ability to make choices. The disease quality of incentive-sensitization in addiction doesn’t replace choice or free will, it powerfully distorts those choices. Finally, I am persuaded by many writers on addiction, both historical and contemporary, that escape from addiction requires enormously effortful acts of personal agency and self-reinvention (James, 1902; Lewis, 2015; Pickard, 2017). Recovery is never passively received at the hands of a medical professional – or anyone else. It is the unusually tempting nature of this incentive-sensitization ‘brain disease’ that requires such active efforts to overcome.

The nature of disease?

Disease is not a sharply defined concept, even in medicine (Wakefield, 2020). When we hear the term ‘brain disease’, we may think of damage to neurons or pathological lesions that actually produce holes in the brain. In some extreme cases of drug addicts, lesion-type neuronal damage in prefrontal cortex is indeed known to occur (Ersche et al., 2013). That prefrontal damage doesn’t create the addiction itself, but it impairs cognitive regulation of motivational impulses, including addictive impulses, producing further downward spirals. Still, such cortical damage may be relatively rare, and I agree with brain disease critics that it is unfair to consider most addicts as significantly brain damaged.

However, there are other forms of neural pathology that don’t involve damage, but instead involve extreme changes in the values of parameters that govern neuronal functions, and consequently alter psychological processes mediated by those brain systems. One of those neural pathologies is mesolimbic neural sensitization, described later in this chapter, which is induced by drugs in particularly susceptible individuals. It is the extremity of those changes in neural-psychological parameter values within dopamine-related mesolimbic systems that causes problems. The changes are pathological partly in the sense that nonaddicts do not have parameters that extreme, and in the sense that those extreme values cause bad consequences. These incentive-sensitization changes in addicts make drug use especially hard to quit – much harder than for other individuals who may use the same drugs and live in similar social situations but remain less susceptible to developing mesolimbic sensitization, and so do not become addicted.

Brain diseases are not unique in resulting from extreme changes in cell signaling parameters. Physiological diseases of the body also can arise similarly from extreme parameter changes in cellular function. For example, insulin-resistant diabetes results when cells throughout the body become less sensitive to circulating levels of insulin. Insulin normally would cause those cells to take up glucose from the bloodstream and store it, but when insulin receptors in the cellular membrane become resistant or relatively insensitive to insulin signals, the cells fail to perform that function, even if blood insulin levels are high. That cellular failure carries deleterious downstream consequences. In short, extreme changes in the parameters controlling cellular signaling can disrupt normal function in body or brain in maladaptive ways, and so qualify as diseases. In my view, addiction as mesolimbic incentive-sensitization is a disease in much the same way.
Similarly, addiction is not the only disease requiring an individual’s active agency and effort to overcome. Many bodily diseases, including insulin-resistant diabetes, require lifestyle changes in diet or exercise to manage the symptoms, which may be difficult and demand effort to succeed. And success in making that effort may well depend on a person’s social support, both in addiction and those other diseases.

Thus, addiction shares important features with many other diseases of body and mind (Wakefield, 2020). As Szalavitz has put it:

All mental illnesses occur in a social context and are to some degree, socially constructed. This doesn’t mean they aren’t as real or as deserving of empathetic and respectful treatment as any other problem that can bring you to the hospital. So, call it whatever you like – so long as you recognize that addiction is far more like ADHD or depression than it is like cancer or pneumonia and requires a panoply of social, medical and psychoeducation options.

(S zalavitz, 2017, p. 85)

**Incentive-sensitization of ‘wanting’ as a mechanism of compulsive addiction**

Addiction is a brain disease of temptation and of the brain mechanisms of choice itself. In particular, sensitization of brain dopamine-related ‘wanting’ systems, which assign incentive salience to reward-related cues and acts, creates amplification of addictive temptations to a level more intense than most nonaddicts ever face. The intensity of these addictive temptations interacts with normal mechanisms of choice but imposes a formidable degree of difficulty for a recovering addict who is trying to practice continual abstinence. Successful abstinence requires the right choice every time in facing a long series of intense temptations – and many of us would fail that test, given the levels of temptation involved in addiction.

Addiction has special features that make it different from ordinary desires. Drugs are the focus of addiction, but the essence of addiction is not in the drugs themselves. Rather, the essence of addictive temptation is in the addict’s own sensitized brain response to drug cues, psychologically manifest as excessive cue-triggered ‘wanting’. Evidence increasingly suggests that similar forms of incentive-sensitization can arise endogenously in the brains of particularly susceptible individuals to cues for gambling, sex, food, shopping, etc., resulting in behavioral addictions.

**Individual differences: why only some drug users become addicts**

Not everyone who takes drugs develops mesolimbic incentive-sensitization, and so many users do not become addicted. Even fewer individuals develop behavioral addictions, such as compulsive gambling. There are enormous individual differences in vulnerability to developing incentive-sensitization, even when people take drugs at the same doses, due to underlying individual differences in genes, steroid hormone fluctuations, previous stress exposures, etc. (Robinson & Becker, 1986; Flagel et al., 2009; Villaruel & Chaudhri, 2016). Non-sensitized individuals may still become dependent on drugs, and develop withdrawal symptoms upon ceasing drug use, yet become free if they can outlast withdrawal symptoms and emotional malaise, which fades over weeks or months. These are the majority of individuals who consume drugs of abuse, but can eventually give the drugs up (Heyman, 2009).

However, some individuals are more highly vulnerable to develop incentive-sensitization changes in their brain mesolimbic systems (Robinson & Berridge, 1993; Berridge & Robinson, 2016). These are the individuals most likely to become compulsive addicts, and their addiction doesn’t go away when withdrawal ends. Neurally, in human functional magnetic resonance imaging (fMRI) studies, the brain signature for addiction in the sense of incentive-sensitization is mesocorticolimbic hyper-reactivity to the addictive cues in nucleus accumbens, neostriatum, ventral tegmentum, amygdala or limbic cortical regions (Childress et al., 2008; Volkow
et al., 2008; Leyton & Vezina, 2014; Prisciandaro et al., 2014; Tomasi et al., 2014; Young et al., 2014; Regier et al., 2016; Devoto et al., 2020; Wiers et al., 2020). An incentive-sensitization fMRI signature is hyper-reactive to drug cues in both of two ways: 1) more intense brain activations triggered by addictive cues than by other reward cues in the same individual; and 2) more intense brain activations triggered by the addictive cues in sensitized individuals than the same cues trigger in other drug users who are not addicts. This is an fMRI signature often observed in drug addicts (Childress et al., 2008; Volkow et al., 2008; Leyton & Vezina, 2014; Wiers et al., 2020).

The brain signature identity of incentive-sensitization relates also to why a smaller minority of especially vulnerable people can develop forms of behavioral addictions to gambling, sex, or other non-drug incentives, whether or not they’ve been exposed to drugs. These people may be so vulnerable to mesolimbic incentive-sensitization that they may develop it spontaneously to produce behavioral addictions of gambling, sex, food, etc., whether or not they’ve taken addictive drugs. In the past decade, a large body of neuroimaging evidence has emerged that some individuals with behavioral addictions, such as compulsive gambling, sex addiction, binge eating, etc., share the incentive-sensitization brain signature of mesolimbic hyper-reactivity to cues for their particular addiction (Davis & Carter, 2009; Gearhardt et al., 2011; O’Sullivan et al., 2011; Hartston, 2012; Linnet et al., 2012; Ray et al., 2012; Voon et al., 2014; Stice & Yokum, 2016; Devoto et al., 2018; Stice & Burger, 2019).

**Prognosis and relapse**

Individuals who show mesolimbic hyper-reactivity to reward cues in fMRI studies have been reported to be more likely to give into temptations than other individuals (Lopez et al., 2014). Mesolimbic hyper-reactivity to drug cues predicts a higher probability of subsequent relapse in both cocaine users (MacNiven et al., 2018) and alcoholics (Reinhard et al., 2015). Similarly, mesolimbic hyper-reactivity to cocaine cues is found in individuals with the longest histories of cocaine use (Prisciandaro et al., 2014).

Another marker of incentive salience is behavioral attribution to drug cues makes those cues ‘wanted’, attractive, hard to ignore, and quickly able to capture attention – even involuntarily. As a result, a high degree of attentional capture by visual drug cues has sometimes been taken as a behavioral marker of incentive-sensitization, and has been reported to positively correlate with the intensity of craving for cocaine (Leeman et al., 2014). Higher attentional capture by drug cues has been reported to positively predict the likelihood of relapse into drug use in the following week (Marhe et al., 2013), and similarly to predict relapse three months later (Marissen et al., 2006).

**Brain ups and downs in addiction**

Incentive-sensitization in brain dopamine-related circuitry of addicts distorts choices about drugs. Incentive-sensitization is experienced as a ‘software pathology’ in psychological craving and behavior, but has roots in underlying brain changes that are the ‘hardware pathology’. It is important to be clear about the nature of incentive-sensitization changes in neural function, and to distinguish them from other drug-induced changes. Two different forms of neural changes occur in the brains of addicts due to drug use, namely mesolimbic tolerance and mesolimbic sensitization. The two are almost opposite of each other, but these opposites do not cancel each other out, and rather can co-exist simultaneously because their cellular mechanisms lie in different molecular cascades within the neurons of dopamine-related brain circuits that can occur in parallel in the same brain.

In past decades, many engaged in addiction science and therapy have thought that receptor down-regulation and its suppressive brain changes – especially withdrawal – were the essence of addiction (Volkow et al., 2019; Koob, 2021). But there is reason to believe that the temporary neural suppressions are mostly a consequence of the addiction and of drug taking, rather than the essential cause
of the addiction that can persist (Leyton & Vezina, 2014; Berridge & Robinson, 2016). Even withdrawal dysphoria – unpleasant as it is – eventually goes away. Yet many addicts remain vulnerable to relapse afterwards. The problem of addiction is not solved when the brain suppressions go away.

**Incentive-sensitization as excessive ‘wanting’**

In my view, the second type of brain change induced in vulnerable individuals by a history of drug binges is more plausible as the cause of addiction and compulsive craving: incentive-sensitization or hyper-reactivity in mesolimbic systems of incentive salience (Robinson & Berridge, 1993, 2008; Berridge & Robinson, 2016). Elicited by drug cues or by thinking vividly about drugs, incentive-sensitization produces excessive ‘wanting’ to take drugs. In recent decades, evidence has mounted that mesolimbic incentive-sensitization is an underlying essential cause of compulsive addiction (Steketee & Kalivas, 2011; Leyton & Vezina, 2014; Berridge & Robinson, 2016). Mesolimbic hyper-reactivity creates a too-high pulse of dopamine stimulation, interacting with corticostriatal glutamate signals. Mesolimbic incentive-sensitization is caused in part by increased excitability in the midbrain neurons that stimulate dopamine neurons to fire, by increased dopamine release from the dopamine neurons themselves, and by increased sensitivity in the target forebrain neurons that receive interacting dopamine and glutamate signals (Paulson & Robinson, 1995; Robinson & Kolb, 1997; Steketee & Kalivas, 2011; Wolf, 2016; Hearing et al., 2018; Kawa et al., 2019).

Neural sensitization of mesolimbic systems is almost the exact opposite of tolerance. That is, neural sensitization makes brain mesolimbic dopamine systems hyper-responsive to drug cues that can initiate drug taking. A sensitized dopamine system is not hyper-active all the time, but rather momentarily hyper-re-active to particular cues or imagery of drug taking. The sensitized brain response to cues triggers the stronger urge to relapse and take drugs again.

**Drug ‘liking’ in addiction**

If drug addicts experienced intense enough drug pleasure to explain their addictive pursuit of drugs, more pleasure than nonaddicted users who took the same drugs but remained able to quit, there would be no need for further explanations. But evidence does not indicate that addicts like their drugs more than nonaddicted users; yet, addicts still want their drugs more.

The incentive-sensitization theory posits that only ‘wanting’ for drugs (that is, the psychological process of incentive salience) – and not ‘liking’ for drug pleasure (hedonic impact) – is amplified by neural sensitization of dopamine-related mesolimbic systems. Thus, sensitized addicts come to ‘want’ drugs more than they ‘like’ drugs. Yet, this dissociation can be misunderstood.

Some critics have suggested that if brain disease views of addiction such as incentive-sensitization were true, then drug ‘liking’ should strongly decline or even vanish completely in addicts (Pickard, 2020). However, disappearance or strong decline of ‘liking’ for drug pleasure was never claimed by the original incentive-sensitization theory of addiction (Robinson & Berridge, 1993), nor has it ever been claimed since by its proponents.

Indeed, whether drug ‘liking’ declines at all in addiction was left open by the original theory proposal. For example, in that 1993 article, Terry Robinson and I devoted an endnote (note 5) to the question of what happens to drug ‘liking’ in addicts (Robinson & Berridge, 1993, pp. 275–276). We noted there that pleasure was often traditionally assumed to decrease in addiction neuroscience via receptor down-regulation and drug tolerance, based mostly on common observations that drug users often escalated their drug doses as they became addicted. That idea assumed addicts to need more drugs to attain the same pleasure. But we noted also that alternative explanations existed for dose escalation, such as that tolerance might grow to the aversive effects of drugs, which can occur at high doses of psychostimulants, alcohol, etc., and which limit how much drug can be taken. Growing tolerance
to aversive drug effects would allow doses to rise simply because they could, freed from punishment by unpleasant high-dose drug effects – even if drug pleasure remained constant. We concluded that “whether the subjective pleasurable effects show some tolerance or no change . . . , the development of an addiction is still characterized by an increasing dissociation between ‘wanting’ drugs and ‘liking drugs’” (Robinson & Berridge, 1993, p. 275). The dissociation still occurred because “‘wanting’ drugs . . . increases dramatically during addiction; ‘wanting’ evolves into craving. At the same time ‘liking’ drugs does not increase” (p. 276).

In real life, some addicts may enjoy their drugs as much as ever, some may report a moderate decline and a few may say they no longer get any significant pleasure from the drugs they take. The separation between ‘liking’ and ‘wanting’ systems in the brain makes each of these scenarios compatible with incentive-sensitization – as long as ‘wanting’ increases powerfully and selectively.

Returning to the critics’ characterization of addictive brain disease as involving ‘wanting in the absence of any liking’, it is true that such dramatic dissociations can be produced in the neuroscience laboratory (Warlow et al., 2020). That is, as a proof of principle demonstration of the potential independence of ‘wanting’ mechanisms, activating relevant brain mesolimbic systems can indeed produce ‘wanting for what hurts’ (Warlow et al., 2020). For example, compulsive attraction to an electrified shock-rod that gives only pain can be produced in rats by pairing activations of mesolimbic circuitry via amygdala stimulation during their voluntary encounters with the shock-rod. Consequently those rats become strongly motivated to seek out and repeatedly touch the noxious shock-rod, despite voluntarily subjecting themselves to shock after shock (Warlow et al., 2020). Conceivably, in extreme cases in addiction, something akin to ‘wanting what hurts’ might also apply. Thus, theoretically, incentive-sensitization should produce compulsive ‘wanting’ in an addict even if drugs are no longer ‘liked’. However, to say ‘even if’ is not to claim that drug pleasure usually disappears in addiction. Sensitized addicts may well often continue to like their drugs – they just don’t like the drugs as much they ‘want’ those drugs, and it is the excessive ‘wanting’ that powers their addiction.

**Temporary fluctuations in cue-triggered ‘wanting’**

Sensitized hyper-reactivity of incentive salience systems can be further amplified to even higher levels at certain moments in addicts temporarily by states of stress, emotional excitement, taking a hit of drug again, etc. (Berridge, 2012). For example, stressful situations activate brain CRF stress systems in amygdala and nucleus accumbens (which use corticotropin releasing factor as neurotransmitter), and stimulating those CRF systems recruits mesolimbic activation to strongly amplify incentive ‘wanting’ for reward (Baumgartner et al., 2021). Such moments of especially intense ‘wanting’ create special windows of heightened vulnerability to relapse, and may sometimes take the addict by surprise. Thus, a particularly strong cue-triggered ‘want’ in those states can create a stronger-than-usual urge, and perhaps prove irresistible to a recovering addict who has successfully resisted similar drug cues many times before. State-dependent amplification of incentive-sensitization hyper-reactivity is also a reason why many addicts find it so hard to stop at ‘just one hit’. That’s because having drugs on board at the moment further amplifies the incentive salience triggered by a related cue. State-dependent amplification is also a reason why emotionally stressful states – or even happy life stresses like winning the lottery – can promote vulnerability to relapse in addicts.

**Neural mechanisms of tolerance and withdrawal**

Tolerance and withdrawal are largely due to neuronal down-regulation or suppression of mesolimbic dopamine receptors and related neurotransmitter receptors, as drugs cause bombardment of neurotransmitter receptors, and so the number of receptors becomes partially cut down in turn as a partial compensation to repeated over-stimulation.
(Volkow et al., 2019; Koob, 2021). Down-regulation of neurotransmitter receptors results in drug tolerance when drugs are taken again (needing higher doses of the drug to get high), and in withdrawal symptoms when the drug is stopped (due to inadequate receptor signaling from release of remaining endogenous neurotransmitter). Neurobiologically, dopamine down-regulation is known to be due to loss of the D2 type of dopamine receptors (and of other mesolimbic receptors, too, but D2 has been most studied). D2 receptor loss is a partial compensation to the too-high levels of dopamine stimulation that neurons encountered when the drug was repeatedly taken. Receptor bombardment with high levels of drug-induced dopamine release causes the receiving neurons to lose some of their D2 receptors, as a cellular attempt to rebalance to a normal level of dopamine signal. But most down-regulation is relatively temporary, requiring continued drug stimulation. Once drug taking stops, tolerance and withdrawal generally disappear over weeks or months. A few individuals — who may be especially predisposed to developing addictions — may naturally over-stimulate their D2 receptors with high dopamine release, and consequently undergo a more permanent suppression of D2 receptors as a partially compensating consequence.

**Neural mechanisms of incentive-sensitization**

Unlike tolerance and withdrawal, neural sensitization doesn’t go away when the person stops taking the drugs. Instead, neural sensitization grows and emerges with even more visibility. This is sometimes called ‘incubation of craving’: an actual increase in cue-triggered relapse that can emerge after a month or so of abstinence from drugs, despite disappearance of withdrawal symptoms by then (Pickens et al., 2011; Nicolas et al., 2019). Neural sensitization of dopamine systems renders addicts vulnerable for months or years to intense urges, especially when drug cues are encountered in stressed or emotionally excited states.

At a neuronal level, such sensitized hyper-reactivity to addictive cues is generated by a host of neurobiological changes in neurons at several locations in the mesolimbic circuitry. An early observation was that drug-induced sensitization causes mesolimbic dopamine neurons to release more dopamine in nucleus accumbens to a subsequent dose of drug than non-sensitized individuals release, even after a year of drug abstinence (Paulson & Robinson, 1995; Kawa et al., 2019). Subsequent studies showed that drug sensitization also caused long-lasting anatomical changes in the neurons that receive dopamine in nucleus accumbens or prefrontal cortex (Robinson & Kolb, 1997). Dendrites of those neurons act as the ‘receiving antennae’ for incoming neurotransmitter signals, with tiny protruding spines that are points of contact for input neurons. Drug sensitization causes physical changes in the number and arrangement of those dendritic spines, thus altering the processing of incoming signals. At a molecular level, mesolimbic sensitization can increase the number of AMPA glutamate receptors expressed on dendrites of neurons in the ventral tegmentum, nucleus accumbens and striatum, causing those neurons to be more highly excited by incoming signals (Steketee & Kalivas, 2011; Wolf, 2016; Hearing et al., 2018). AMPA refers to an excitatory type of receptor activated by glutamate neurotransmitter, and by the selective agonist drug that gives it the AMPA acronym: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid. Such increases in phasic excitability are possibly a mechanism explaining why sensitized mesolimbic dopamine neurons release larger pulses of dopamine to a drug, and why drug cues elicit more intense activations in nucleus accumbens and striatum.

**The nature of motivational compulsion**

Critics of the brain disease label sometimes note that normal love, normal hunger for palatable foods, normal sexual desire, and many other normal desires activate the same brain mesolimbic dopamine circuitry as is triggered in addiction. Those natural motives are why brain mesolimbic circuitry evolved. Similarly, some critics argue that addiction
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should not be called compulsive, because many addicts will modulate, postpone or even avoid drug use for some time in response to incentives or certain punishment (Stephens & Graham, 2009; Heather, 2017a). The ability of an addict to control drug use, even in the short term, they sometimes suggest, is incompatible with a meaning of compulsion as described by Aristotle: an external force such as an irresistibly strong wind that carries us away (Aristotle, 350BC/2009). It is also not the compulsion described by an alcoholic quoted by Benjamin Rush and William James, “Were a keg of rum in one corner of a room, and were a cannon constantly discharging balls between me and it, I could not refrain from passing before that cannon, in order to get at the rum” (Rush, 1812, p. 266; James, 1890, p. 543).

There do exist forms of compulsive actions, created by certain brain stimulations or diseases, that can occur despite a conscious effort to suppress them in ways compatible with these notions. These might be experienced similar to the external ‘strong wind’ that feels entirely independent of the conscious individual, producing what might be called a compulsive automatic action. For example, electrical stimulation of the motor cortex can produce an involuntary movement of a hand, where the person feels the hand ‘has moved on its own’ (Penfield, 1975). Similarly, in ‘alien hand syndrome’, caused typically by stroke lesions of motor-related or parietal cortex, the affected hand may make intrusive reaching grasping movements that cannot be voluntarily suppressed, grabbing and pulling away objects against a person’s will (Hassan & Josephs, 2016).

Unlike these automatic compulsions, addiction does not compel action contrary to choice; instead, it carries choice with it. However, motivational compulsions also exist, and are able to carry choice with them. Motivational compulsions can be seen in addiction, in obsessive-compulsive disorder, and in certain other extreme situations. In my view, the critics who argue addiction to be not compulsive fail to recognize the nature of motivational compulsion. Motivational compulsion can remain responsive to incentives and punishments, yet eventually compel both choice and action.

To understand the nature of motivational compulsion, it may be analogous to the motivational consequences of prolonged starvation. Severe starvation is a state able to induce motivationally compulsive ‘wanting’ in almost anyone. You don’t have to be starved for delicious food cues to activate brain dopamine circuitry. But people who voluntarily starve for weeks begin to obsess about food, and to dream of food (Keys et al., 1950). Their brain dopamine circuitry is likely to react with higher intensity to food cues than in the rest of us, creating a more intense urge to eat than most of us ever experience in our well-fed lives. I believe that most of us would have to starve for weeks in order for food to evoke as intense a level of brain reaction as drug cues could trigger in a sensitized addict.

If the incentive-sensitization theory of addiction is correct, an addict who encounters drug cues in an emotionally excited state may experience super-strong ‘wanting’ similar to that of a starved brain’s reactions to palatable food. In the case of voluntary starvation, even those who are highly motivated to abstain from eating may fail to resist temptation repeated again and again. For example, a group of conscientious objectors during World War II volunteered in a University of Minnesota starvation study, aimed at finding how to best bring starved refugees and war victims back to health (Keys et al., 1950). Despite being strongly motivated to serve their country by continuing to starve, many of the volunteers defected from the study. But a recovering addict is asked to resist similar extreme temptation again and again, every time a drug cue or vivid imagery is encountered. A single defection may lead to a binge and spiral back into frequent drug use. It is no wonder that many addicts fail to resist such extreme temptation, when tested again and again. Although high incentive salience is not inherently pathological, to be condemned to undergo such intense temptation repeated frequently in life may be a form of pathology. Combined with the seriously damaging consequences of giving in to addictive temptation, it is no misnomer to call the excessive ‘wanting’ of incentive-sensitization a compulsive form of pathology – in short, a brain disease.
A motivational compulsion may be resisted once, twice or even many times – but perhaps not every time. There is a difference between the ‘wanting’ of ordinary hunger and that of incentive-sensitization. Motivational compulsion, produced by excessive incentive salience, is not an external wind, but it is an extreme intensity of temptation not faced by most of us in ordinary life. It is recurrent, varying in intensity and able to reach surprising heights on some occasions, making it extraordinarily difficult to resist every time. If success in escaping addiction requires resisting the temptation every time, then the addict is in an especially difficult situation.

**Is compulsive incentive-sensitization compatible with free choice and agency?**

Yes: incentive-sensitization doesn’t override choice or free will. Sensitized ‘wanting’ creates only a probabilistic form of compulsion. On any given occasion, the person is free to say no to temptation, and may succeed in doing so despite the higher temptation. An addict truly committed to abstinence from drugs may succeed in saying no many times in a row. But success versus failure is probabilistic when temptations are very strong, and success in escaping addiction may require saying no every time a temptation occurs. Asking a starving person to resist the temptation of a modern feast – and to keep saying no to the next hundred offers of delicious food as weeks go on – seems rather a lot to ask. Many of us might fail that test in the end. Yet that test may be what we ask the addict with a sensitized brain dopamine system to pass.

The task is not insurmountable. Many addicts have passed the test and overcome the temptations. Overcoming such addictive temptations may well require a special act of personal agency by the addict in resolving to seek a better life (Lewis, 2015). But the task is difficult, and the situation deserves our empathy.

**Consequences of rejecting the ‘brain disease’ model?**

In this chapter, I have tried to make the case for why addiction can reasonably be considered a brain disease. Incentive-sensitization is pathological in the sense of involving extreme neuronal parameters. In addicts, this can produce motivationally compulsive ‘wants’, which are more intense than the ordinary temptations faced by most nonaddicts, and which carry life consequences that are destructive. Critics of the brain disease model, in my view, often caricature it as implying brain damage, external compulsion, pleasure elimination or personal passivity, or suggest that it denies social factors. Such criticisms are unfair, I believe, and mistake the nature of the motivational compulsions that are involved in addiction.

But beyond the merits of the argument, I suspect also that, if those who wish to banish the brain disease view of addiction ever succeeded, they would not like what would follow. Research into the nature and treatment of addiction would decline, and therapy development would be unlikely to progress much beyond the few strategies currently available (e.g., 12-step programs). And quite possibly, the result would be even worse. Quite possibly, in rejecting the disease view that encourages sympathy, society would also revert to the older ‘moral failing’ view and blame addicts for their choices. If so, therapy would decline, treatment would be less likely to be funded by government or insurance companies, and addicts might again become likely to face criminal incarceration rather than treatment.

Some might regard this forecast as overly dismal, and suggest that there is no reason why society cannot abandon the brain disease view, yet continue to be sympathetic and still support research or treatment (Lewis, 2015; Heather, 2017b; Pickard, 2017). After all, they might ask, why can’t society instead adopt a nuanced ‘addiction as choice’ view of addiction, recognize that addicts are responsible for their choices without assigning blame or criminal punishment, and still provide for therapy?

Well, good luck with that. I see no clear path to a more enlightened view of addiction as a form of choice that is able to promote societal support, if it refuses to recognize any pathological degree of compulsion that originally prompted the brain disease label.
Words, words . . .

It can be fun to argue about labels, such as which ones are the best to describe addiction. In my view, debates over whether addiction is brain disease often become simply about policing the words that others use, without advancing our understanding of addiction. Further, I think that arguments about labels – rather than focus on the actual features and mechanisms of addiction – also can too easily become traps that distract us from more important aims, such as identifying the most essential features and mechanisms of addiction, and thinking about better ways to help addicts.

Conclusion

Following are a few interesting issues for addiction. In what way is addiction compulsive, and in what way a choice? How do individuals differ in susceptibility to developing addiction? What are the crucial brain mechanisms underlying the transition to addiction, the essential mechanisms that cause addicts to be addicts? Are there are different ways of being addicted – or different types of addict – or does addiction always involve a common core of mechanisms? Why are some former addicts capable of controlled use and others not? What is the special act of agency necessary to escape from addiction? How can that act of agency be facilitated?

Less interesting than any of these is the semantic question of whether to call addiction a ‘disease’ or ‘choice’, ‘habit’ or ‘life stage’, or something else. All those words are just linguistic tools to be used in service of the stated questions.

In my view, we who study addiction should choose our words carefully to best capture the features, brain substrates or therapies of addiction we are trying to describe. With luck, we can use those words to reveal something new or useful about addiction. But let’s not mind too much the words that other people choose in their own quest to describe addiction, nor expend too much effort in trying to stop them from using ‘brain disease’ terms. They may be describing an aspect of reality, too. Addiction as a phenomenon is a hard nut to crack.

Better understanding of the nature of addiction and better therapy should be the focus of all our efforts – a difficult enough aim already, without wasting effort on squabbles over words.

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