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Determinants of choice, and vulnerability and recovery in addiction

R.J. Lamb^{a,b,*}, David R. Maguire^b, Brett C. Ginsburg^{a,b}, Jonathan W. Pinkston^{a,c}, and Charles P. France^{a,b}

^aUniversity of Texas Health Science Center at San Antonio, Department of Psychiatry, 7703 Floyd Curl Drive San Antonio, TX 78229-3900

^bUniversity of Texas Health Science Center at San Antonio, Department of Pharmacology, 7703 Floyd Curl Drive San Antonio, TX 78229-3900

^cUniversity of North Texas, Department of Behavioral Analysis 360 G Chilton, Hall, Avenue C Denton TX 76208

Abstract

Addiction may be viewed as choice governed by competing contingencies. One factor impacting choice, particularly as it relates to addiction, is sensitivity to delayed rewards. Discounting of delayed rewards influences addiction vulnerability because of competition between relatively immediate gains of drug use, *e.g.* intoxication, versus relatively remote gains of abstinence, *e.g.* family stability. Factors modifying delay sensitivity can be modeled in the laboratory. For instance, increased delay sensitivity can be similarly observed in adolescent humans and non-human animals. Similarly, genetic factors influence delay sensitivity in humans and animals. Recovery from addiction may also be viewed as choice behavior. Thus, reinforcing alternative behavior facilitates recovery because reinforcing alternative behavior decreases the frequency of using drugs. How reinforcing alternative behavior influences recovery can also be modeled in the laboratory. For instance, relapse risk decreases as abstinence duration increases, and this decreasing risk can be modeled in animals using choice procedures. In summary, addiction in many respects can be conceptualized as a problem of choice. Animal models of choice disorders stand to increase our understanding of the core processes that establish and maintain addiction and serve as a proving ground for development of novel treatments.

Keywords

Delay Discounting; Differential Reinforcement of Alternative Behavior; Vulnerability; Recovery

*Corresponding author at: Psychiatry MC 7792, UTHSCSA 7703 Floyd Curl Drive, San Antonio, TX 78229-3900. Tel.: 210-567-5483.

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1.0 Introduction

Addiction is a phenomenon science struggles to both define and treat. Most commonly, the word addiction pertains to the habitual use of licit and illicit substances threatening the individual and society, and these threats may include direct health effects, such as cardiovascular or liver disease, or effects such as loss of employment or social relationships. Prevalence of regular drug use is high in the US; a recent survey indicated that over 21 million Americans, or about 8% of the population meet the criteria for substance abuse or dependence (SAMHSA, 2014), and the economic burden exceeds several hundred billion dollars annually (NDIC, 2011). Numbers that do not even take into account the almost 1 in 5 American adults who smoke tobacco.

Additionally, addiction is often characterized by compulsions or inability to stop using drugs, despite the individual expressing a desire to stop (see Belin et al, 2016). Health risk, habitual usage, and compulsion have helped identify addiction as a phenomenon, but the responsible processes remain elusive. The prevailing scientific view is of addiction as a brain disease, best understood as a change in molecular, cellular, or circuit mechanisms (Leshner 1997), a view that contains some face and construct validity. Appealing to changes in brain circuits may help reconcile the continued drug use despite the person's expressed desire to stop, and certainly, it is difficult to understand how such extensive behavior change could not be accompanied by changes in the brain.

However, an alternative to the conceptualization of addiction as a brain disease has continued to gain momentum; in this view, addiction is not *best* understood as a brain disease, but as a choice disorder (Heyman 2009; Vuchinich & Tucker 1988). The term "choice" has the usual problems inherent in adopting common language to describe behavior (see Chiesa, 1994, Chapter 2 ; Skinner, 1938 pp. 6–8), especially because this term has such a loaded societal meaning when applied to addiction. In a scientific context, "choice" simply refers to engaging in one activity out of several possibilities. When studying choice the important question is what are the determinants of the relative probabilities of various behaviors, *i.e.*, what are the determinants of choice? Conceptualizing addiction as a choice disorder focuses study on the determinants of drug choice. Proponents of addiction as a choice disorder do not deny the role of molecular or neural processes in the production of behavior. No one would maintain the brain was not involved in behavior nor that biologic factors might bias the choice that occurs in a given circumstance, but again the argument is how to *best* frame the relevant processes (see also Szasz, 1974). When addiction is viewed as a choice disorder, addiction is the outcome of poor options in the environment, devalued rewards, and/or the ease of access to drugs relative to other goods (see, Heyman, 2009; Hursh & Roma, 2013; Madden & Bickel, 2010; Schaler, 2002; Vuchinich & Tucker 1988); and how these interact with the history and biology the individual brings to this environment.

The differing views (brain disease vs choice disorder) are not just a matter of perspective, but they lie at the center of how best to study, understand, and ultimately treat addiction. The brain disease conceptualization seeks to understand addiction as the result of brain dysfunction in an otherwise normal world; the choice-disorder conceptualization seeks to

understand addiction as normal neural functioning in an otherwise dysfunctional world. In parallel, treatments borne out of the brain disease conceptualization seek to correct dysfunctional circuits, correct imbalanced neurotransmitters, *etc.*, while the choice-disorder view centers on “choosing” as the *prima facie* focus of treatment. In other words, providing the circumstances for better choices. Contingency management (CM) approaches, for example, have seen wide success in the treatment of substance abuse problems for a variety of drugs (Bigelow & Silverman, 1999, Higgins et al 1991; Lamb et al 2010; Petry et al 2012; Stitzer et al 1992) by arranging more immediate, tangible reinforcement for abstinence. Among the guiding principles in CM is that delayed outcomes, such as those that follow years of healthy choices, weakly motivate behavior, in contrast to immediate rewards, which are more powerful motivators. Therefore by providing more immediate reward for healthy choices (abstinence), those alternatives may be chosen more frequently.

Continued understanding of the role environmental, genetic, and neural factors play in disorders of choice will require the continued development of sophisticated laboratory models. The purpose of this paper is to review work on some of these pre-clinical models developed in our laboratories. The models grew out of the conceptualization of addiction as a choice-disorder, and they can be used to study processes that may be involved in the vulnerability to and the recovery from addiction. The present conceptualization and the models derived from it may have great translational utility. The remainder of the paper first discusses how individual differences in how the delay to alternative rewards affect behavior may result in individual differences in vulnerability to addiction; and how these processes might be modeled in animals. Next, how recovery can be modeled in animals when addiction is viewed as a choice is discussed. Finally, the paper concludes that conceptualizing addiction as choice is a paradigm that furthers translational research into addiction and is a natural extension of the earlier paradigm shift of conceptualizing addiction as reinforced behavior (Schuster 1976; Griffiths et al 1980).

2.0 Delay Discounting & Choice

The consequences of behavior often differ along multiple dimensions, with magnitude and delay being among the most salient. Other things equal, individuals prefer larger rewards over smaller and rewards that are delivered sooner over those that are delivered later (e.g., Catania 1963; Chung and Herrnstein 1967). Predicting which options an individual is likely to choose becomes more complicated when these dimensions conflict, for example, when the choice is between a smaller reward delivered sooner and a larger reward delivered later. Given that many choices involve consequences differing in both magnitude and delay, elucidation of how these dimensions interact is critical for predicting and controlling behavior, and the delay discounting framework has been tremendously useful in this regard. According to the delay discounting framework, the effectiveness of a behavioral consequence decreases as the delay to its presentation increases (Rachlin et al., 1991; Green and Myerson, 2004). The decrease in effectiveness of a reward with delay to its receipt is often assessed by examining at what delay to the larger reward the choice of a larger over a smaller reward switches to the choice of the smaller over the larger reward. Individuals differ in the delay at which this switch occurs (Odum 2011). Individuals who discount more rapidly than others are likely to switch from choosing larger delayed rewards to smaller

sooner reward after shorter delays than those who discount less rapidly. These individual differences in the rate of discounting are thought to be important in understanding numerous problematic behaviors including addiction.

2.1 Rapid discounting and risk for addiction

Many studies show that those with substance use problems discount delayed rewards more rapidly than those without these problems. For instance, opioid abusers discount more rapidly than those who do not abuse opioids (Kirby et al 1999). Similarly, those who abuse cocaine discount more rapidly than those who do not (Heil et al 2006), and those with problematic alcohol use discount more rapidly than without alcohol problems (Petry 2002). Finally, people who smoke cigarettes discount more rapidly than those who do not (Mitchell 1999). Thus, those having problems with addiction appear to discount more rapidly than those not having problems with addiction, but why is this the case?

The association between rapid discounting and addiction could be because drug use increases the rate of discounting, because rapid discounting increases the risk of addiction, because some third factor causes both an increase risk for addiction and more rapid discounting, or because of some combination of these factors. Evidence exists for each of these first three viewpoints, which certainly makes the last of these four viewpoints the most likely. Animal models that allow us to examine these various viewpoints would aid us in examining the relative contribution of each of these pathways. The effects of drugs of abuse on delay discounting have been widely studied; and drugs of abuse affect discounting (see Perry & Carroll, 2008; Weafer et al., 2014; Winstanley et al, 2010; de Wit and Mitchell 2010). However, these effects are not entirely consistent with increases, no effect or decreases being observed even within a single class of abused drugs; and the determinants of this heterogeneity are unclear.

Animal models of how rapid discounting might place one at risk for addiction also exist. The relationship between drug choice and the delay to reward of alternative behavior has been modeled in monkeys (Maguire, Gerak & France 2013a). Monkeys were trained to respond on one lever for delivery of a food pellet and to respond on another lever to earn an intravenous injection of remifentanyl, a short acting mu opioid receptor agonist (*i.e.* a drug belonging to the same pharmacological class as morphine and heroin). Following food or remifentanyl delivery a time-out occurred. The time-out was sufficiently long and the actions of remifentanyl sufficiently short that the direct pharmacological actions of remifentanyl would be unlikely to affect subsequent responding. Then the delay between completion of the fixed-ratio on the food-lever and the delivery of food was varied, while remifentanyl was still immediately delivered following completion of the fixed-ratio on the other lever.

As can be seen in Figure 1, when the delay to food was zero, two of the three monkeys chose food more or less exclusively and the third monkey chose food on seven or eight of the ten choice trials. Thus, when food was immediately available following completion of the response requirement, remifentanyl consumption was either nil or at low levels. However, when the delay to food delivery was increased to two minutes, a different pattern emerged. The monkey who had chosen a modest number of remifentanyl deliveries when food was delivered immediately, almost exclusively chose remifentanyl when food delivery was

delayed two minutes. Similarly, one of the two monkeys who almost never chose remifentanil when food was immediately available, now chose remifentanil about two out of ten times. The last monkey still chose food almost exclusively, even when food delivery was delayed by two minutes (in fact, this monkey chose food even with a 4-min delay). Thus, the effects of delaying food delivery upon remifentanil choice differed among the three monkeys: One was greatly affected, one modestly and the third almost not at all. This study is but one of a small but growing literature exploring the impact of delay on drug taking and indicating that in nonhuman primates delaying delivery of an otherwise preferred reinforcer, whether food (Maguire et al., 2013a; Woolverton and Anderson, 2006; Huskinson et al. 2015) or a dose of drug (Maguire et al., 2013b; Maguire et al. 2015; Woolverton and Anderson, 2006; Woolverton et al., 2007), increases responding for a small and less preferred reward, including doses of drug. This difference in how the monkeys were affected presumably relates to differences in how rapidly each monkey discounted the rewarding effects of food, and the procedure just described provides a useful way of examining how delay and the rate of delay discounting interact to increase or reduce the likelihood of substance use.

2.2 Discounting in those at risk for addiction

There appears to be two dominant groups of individuals at risk for addiction and both appear to discount rapidly. Many individuals in their adolescence and young adulthood engage in dangerous substance use and other risky behavior outside the norms of older individuals (SAMSHA 2009; Moffitt 1993). This risky behavior, however, declines as adult roles are taken on (Moffitt 1993). There are parallel developmental trends in delay discounting. For example, adolescents tend to discount more rapidly than adults (Green et al 1994; Steinberg et al 2009). Thus, as alternative behaviors become more available and the effectiveness of the frequently delayed rewards of these alternatives increases, substance use and other risky behavior decline. Members of a second group appear to be poorly controlled by delayed rewards throughout their life and these individuals engage in levels of risky behavior outside of the norms of their age group throughout their life. This group displays conduct disorder when in primary school, began to abuse substances earlier, and are more likely to engage in criminal behavior (Moffitt 1993; Moffitt et al 2002). These two groups can be thought of those engaging in adolescence-limited-deviancy and those in engaging in life-course-persistent-deviancy (Loeber & Stouthammer-Loeber 1998; Moffitt 1993).

By the nature of the classification of the two groups, the two groups differ in their prognosis: Adolescence-limited-deviancy would be expected to end with the coming of adulthood and conversely life-course-persistent-deviancy would be expected to persist throughout life. Certainly, some individuals who would have been expected to cease their problematic behavior in adulthood will continue to engage in this problematic behavior in adulthood because the problematic behavior in adolescence was sufficient given their circumstances to impede the emergence of alternative behavior competing with substance use and other risky behavior in adulthood (Moffitt 1993). Conversely, some individuals who would have been expected to be doomed to life-course-persistent-deviancy will because of fortunate circumstances avoid this fate. However, for the most part the prognosis of the two groups is

vastly different. There is also reason to suspect that etiologies of risk, of their rapid discounting, differ between the two groups.

The risk for life-course-persistent-deviancy appears to have a large genetic component (see Kendler et al 2003), while almost by definition the risk for adolescence-limited-deviancy will have a developmental etiology. In line with these assertions, there appears to a large genetic component to rapid discounting (Anokhin et al 2011; Anokhin et al 2015), and adolescents as a group discount more rapidly than adults to an extent unlikely to be accounted for by an increased mortality of those who discount rapidly (Green et al 1994; Steinberg et al 2009). If both life-course-persistent and adolescence-limited deviancy are a result of the decreased effectiveness of delayed rewards at controlling behavior in each group, a differing etiology of risk between the two groups may indicate that the mechanism underlying rapid discounting in each group also differs. The potential for multiple mechanisms controlling the rate of discounting is consistent with the multiple processes shown to contribute to discounting: working memory (Bobova et al., 2009); timing (Galtress et al., 2012); reward sensitivity (Locey & Dallery, 2009); as well as distinct brain regions/neurotransmitter systems (MacKillop, 2013; Monterosso et al., 2007; Stanger et al., 2013). Animal models of the rapid discounting seen in life-course-persistent and adolescence-limited deviancy might help us to discover the mechanisms underlying the rapid discounting seen in each group; and thus, aid in developing ways of ameliorating the consequences of this rapid discounting in each group, and in particular mouse models might be especially useful given the powerful tools for studying genetic factors in mice. Further, development is rapid in the mouse and adolescence spans a relatively short-period, postnatal days 28–42, which facilitates longitudinal and other types of studies.

And in fact, mice can be used to study delay discounting with procedures that typically take 40–60 sessions (*e.g.*, Helms et al 2006). However, studies aimed at identifying genetic loci require a high throughput that is facilitated by procedures that can be completed more rapidly. This is even more true of studies aimed at examining adolescence in the mouse that require procedures that can be completed within two-weeks.

Adriani and Laviola (2003) developed a delay discounting task that allows mice to choose between a smaller reward and a larger reward for one week. Then, during the following week, the delay to the larger reward systematically increases from 1 to 100 s. The primary measure is the percentage of larger, later reward choices as the delay increases.

The procedure has been used to examine choice in two inbred strains commonly used in studies of behavioral genetics the DBA/2J (D2) and C57BL/6J (B6) mouse strains (Pinkston & Lamb 2011). This procedure has also been used to compare responding of adult and adolescent B6 mice (Pinkston & Lamb 2011). Mice were trained to break a photo-beam on one side of the chamber to obtain a smaller dipper of milk delivered after a one-second delay and to break a photo-beam on the other side to obtain a larger dipper of milk also delivered after a one-second delay. After one week of this training, the delay to the larger dipper of milk was increased across days and the percentage of choices that were for the larger dipper of milk tracked. This procedure provides a limited, but rapid, measure of discounting that proved useful in differentiating the different strains and age groups.

Figure 2A shows that adolescent B6 mice switch to choosing the more immediate smaller dipper of milk sooner than adult B6 as the delay to the larger dipper of milk increased (Pinkston & Lamb 2011). Figure 2B shows that adult D2 mice switch to choosing the more immediate smaller dipper of milk sooner than adult B6 as the delay to the larger dipper of milk increased (Pinkston & Lamb 2011). Thus, adolescent B6 mice might be used to model the rapid discounting that puts adolescents at risk for a variety of problems. Adolescent B6 mice might also be used to study the biologic and behavioral mechanisms behind this rapid discounting. It is difficult to draw firm conclusions about genetics when only two strains are used because any behavioral differences between the strains could be due to genetic or non-genetic differences (see Crabbe et al 1990). Still, as a first approximation, the present findings revealed differences between adolescents and between adults of these two strains, and the findings suggest several subsequent inquiries. Thus adult D2 & B6 mice might be used to study the genetic determinants of rapid discounting, as there are well-developed tools for this using D2 and B6 mice. Further, the adult D2 & B6 and adolescent B6 mice may be used to examine if developmentally determined and genetically determined rapid discounting results from the same mechanisms (in mice), and provide hypotheses about the similarity or dissimilarity in the two clinical risk groups.

The delay tolerance procedure used in these experiments has promise for understanding the sources of individual differences in delay discounting, and recently a variant of the procedure was used to compare discounting between males and female rats in adolescence and adulthood (Doremus-Fitzwater et al 2012). However, the quantitative information on important parameters of discounting provide by this procedure is limited. Recently, Pope et al 2015, published findings where mice choose between several pairs of smaller and large rewards in a rapidly alternating within-session procedure using signaled components that appears to result in rapid and stable choices. Such an approach may be an important for the exploring developmental changes in choice using mice as well as genetically determined differences in choice.

3. Modeling Recovery

Recovery from addiction can also be viewed within the conceptualization of choice. In this case, several strategies for reducing drug choice are apparent. First, one could reduce the effectiveness of drug at reinforcing behavior, and several pre-clinical studies have used choice procedures to study medications that might attenuate drug reinforcement (Ginsburg & Lamb 2014; Negus 2005; Weiss et al 1990). Another commonly used clinical strategy is the differential reinforcement of other behavior (DRO), *i.e.*, reinforcing the non-occurrence of drug use. This strategy is the basis of most contingency management treatments for substance abusers (Higgins et al 1991; Lamb et al 2010; Petry et al 2012; Stitzer et al 1992). There has also been some limited pre-clinical investigation of using DRO schedules to reduce drug-maintained behavior (Le Sage 2009). Another strategy that has seen less explicit clinical use is the differential reinforcement of alternative (DRA) behavior (Iguchi et al 1997), which is also implicit in several clinical treatments such as the community reinforcement approach (Azrin et al 1982) and likely plays a major role in unassisted recovery.

Recently, a DRA procedure has been adapted to examine recovery in a preclinical model (Ginsburg & Lamb 2013a, b). In this procedure, rats are trained on a multiple concurrent schedule. In the presence of one stimulus, responding on one lever delivers food following five responses and completion of five responses on another lever delivers ethanol. In the presence of another stimulus, completion of 150 responses on the food lever is required for food delivery, while still only five responses on the ethanol lever are required for ethanol delivery.

When the response requirement for food was 5 (FR 5), rats made a mean of 460 responses on the food lever compared to a mean of 6 when the response requirement for food was 150 (FR 150). Responding on the ethanol lever moved responding in the opposite direction. When the food FR was 5, rats made a mean of 2 responses on the ethanol lever compared to a mean of 62 responses when the food FR was 150. Thus, when the food FR was 150 responding was predominantly on the ethanol lever, and when the food FR was 5 responding was predominantly on the food lever. However, in both cases the availability of ethanol was unchanged. Thus, the first stimulus in which food is available under an FR5 could be used to model recovery and the stimulus in which food is available under an FR150 could be used to model excessive drinking.

This experiment further studied how longer periods recovery (food FR 5) would affect subsequent extinction responding in the presence of the stimulus associated with excessive drinking (food FR 150). Rats were first exposed to 10 sessions in which the food FR was 150 and responding was predominantly for ethanol, then following 0, 1, 2 or 4 sessions of responding in the presence of the stimulus indicating the Food FR was 5 with ethanol still available at an FR5, responding for both food and ethanol were placed on extinction in the presence of the stimulus indicating the food FR was 150 (Ginsburg & Lamb 2013a). Figure 3A shows responding on the food lever before the completion of 5 responses on the ethanol lever during these test sessions. When 0, 1, or 2 sessions with the food FR equal to 5 preceded presentation of the stimulus indicating the food FR was 150 (analogous to re-exposing a recovering individual to drug-associated stimuli after a period of abstinence), rats still made fewer than 5 food-lever responses before completing 5 responses on the ethanol lever. However, when 4 sessions with the food FR equal to 5 preceded the test, responding on the food lever was more persistent and all of the rats would have earned food had the food FR still been 5.

These results indicate that the longer recovery is modeled in the rat (*i.e.*, the food FR is 5) the less likely the rat will “relapse” when exposed to stimuli previously occasioning ethanol responding. This decreasing relapse risk with increasing lengths of recovery parallels what is observed clinically (*e.g.*, Hunt, Barnett & Branch, 1971; Gilpin, Pierce & Farkas 1997.). To further explore this relationship, rats were given four sequential sessions in which the stimulus indicating that the Food FR was 5 and the stimulus indicating the Food FR was 150 alternated or four sequential sessions with only the stimulus indicating the Food FR was 5 (Ginsburg & Lamb 2013c). Following this a test session was conducted.

In this test session, both the stimulus indicating the food FR was 5 (8 kHz tone) and the stimulus indicating the Food FR was 150 (16 kHz tone) were presented. Additionally, on

half the trials these tones as well as intermediate tones (10, 12 & 14 kHz) were presented and responding was under extinction. This result was the generalization gradients shown in Figure 3B. In both conditions, the 8 kHz tone occasioned responding predominantly for food. When testing had been preceded by four days in which the two tones alternated, responding on the ethanol lever increased as a function of frequency reaching about 50% of the maximal level at around 12 kHz and a maximum of about 90% at the training stimulus of 16 kHz. When testing had been preceded by four days of only the stimulus indicating the food FR was 5, ethanol lever responding also increased as the frequency increased and 50% of the maximal level of ethanol responding also occur at about 12 kHz. However, the maximal level of ethanol responding was only about 40%, rather than about 90% as seen when the two stimuli had alternated.

The similar inflection point likely indicates the rats were similarly able to discriminate the tones in the two conditions. However the lower maximal level of responding following four “recovery” sessions likely indicates a decline in stimulus control, *i.e.*, the rats were attending less to these stimuli. This was hypothesized to occurred because the context of being in the operant chamber provided the rats with all the information needed for effective responding, and thus less attention to other stimuli, like the tone, was required (Ginsburg & Lamb 2013b).

4.0 Conclusions

Addiction may be conceptualized as a choice disorder (*e.g.* Heyman 2009), and this perspective may be modeled in the laboratory and explicitly tested. Several of the models, from among many, that can be used to examine the utility and validity of this conceptualization were reviewed in this paper. Such models may suggest new research questions or ways of understanding addiction. These, new questions or understandings provide ways of assessing the utility and veracity of the conceptualization and models. Finally, as the conceptualizations and models are necessarily more abstract than the clinical phenomenon itself, the conceptualizations and models bring our thinking about the clinical phenomenon into contact with a broader body of investigation that can then be applied to the phenomenon.

Conceptualizing addiction as resulting from the choice between other rewards and drug use suggests factors influencing the frequency of choosing drug use are key to understanding addiction. When this is modeled in monkeys, the results strongly suggest that as the delay to alternative rewards increases, drug use (if it remains available with little delay) will increase (Maguire et al 2013a). Further, this work suggests individuals vary in their sensitivity to the effects of delaying alternative rewards, with drug choice increasing rapidly with the delay to alternatives in some, but much more slowly in others. Thus, suggesting one reason those with substance abuse problems tend to discount more rapidly than those without substance abuse problems is that rapid discounting places one at risk for developing a substance abuse problem.

Understanding what causes vulnerable populations to rapidly discount delayed rewards could suggest ways to decrease their vulnerability. Preclinical models (*e.g.*, Pinkston &

Lamb 2011) may facilitate understanding what causes vulnerable populations to discount rapidly. For instance, such models could be used to better understand why the two major risk groups, adolescents and those with a family history of substance abuse, have a common phenotype that seems to put them at risk, rapid discounting, but differing etiologies and prognoses. Our understanding of the broader body of work on delay discounting suggests some possibilities. For instance, short-term memory has been suggested as a determinant of discounting rate (Killeen 2011) and those with poorer short-term memory discount more rapidly (Shamosh et al 2008). This would seem to be a possible mechanism for the rapid discounting of those with life-course-persistent deviancy, as poorer neuropsychological function is commonly found in this population (see Moffitt 1993). However, this is unlikely to explain the rapid discounting of adolescents (Green et al 1994; Steinberg et al 2009), as the short-term memory of adolescents appears to be at least as good as the short-term memory of adults (Brockmole & Logie 2013). This suggests that rapid discounting in adolescence results from some different factor such as how well reward amounts are differentiated. Such hypotheses generated from the broader body of investigation on discounting can be readily examined using preclinical models. Conceptualizing addiction as resulting from choice leads to examining how the known determinants of choice like delay influence drug choice. This in turn highlights the need to understand individual differences in the discounting of delayed rewards. Thus, viewing addiction as resulting from choice provides potential insights into addiction and through these insights ways of testing the models and conceptualization.

Viewing recovery as a result of choice behavior is similarly useful. This conceptualization has resulted in effective treatments involving reinforcing either the absence of drug use (Higgins et al 1991; Lamb et al 2010; Petry et al 2012; Stitzer et al 1992) or reinforcing alternative activities that may compete with drug use (Iguchi et al 1997). Also, this conceptualization has led to the realization that recovery does not involve putting drug-seeking in extinction or preventing drug access, but rather reducing drug-seeking while the contingencies of drug availability are relatively unaltered. In other words, drug-seeking is not reduced by delivering placebos instead of drugs or moving an individual to a world where drugs do not exist. Rather, other behaviors come to be chosen over drug-seeking and eventually supplant drug-seeking. Interestingly, models based on this conceptualization find that the likelihood of relapse-like behavior decreases with increasing lengths of recovery-like behavior (Ginsburg & Lamb 2013a, b). This is consistent with the clinical literature (e.g., Hunt, Barnett & Branch, 1971; Gilpin, Pierce & Farkas 1997), but not with models of recovery based on preventing drug access (see Ginsburg & Lamb 2015). Thus, suggesting the validity of the conceptualization and the model based upon it. Further, the degree of control by stimuli that had previously occasioned drug-use appeared to decline with increasing lengths of recovery-like behavior (Ginsburg & Lamb 2013c). This was hypothesized to occur because of decreased attention to the stimulus resulting from a decreasing need to attend as the length of time in which the only activity that occurred was the alternative (non-drug-seeking) activity. This decreased attention to the stimulus results in an increasing propensity for the context to occasion the alternative activity and a decreasing likelihood of attending to other stimuli. These findings also suggest why decreases in attentional bias toward drug-related stimuli are associated with decreased relapse risk (Field

& Cox 2008) and why attentional bias would be expected to decrease with increasing recovery.

Application of the conceptualization of addiction as choice disorder has resulted in several potentially useful models, and some insights into addiction. Application of these to the problem of addiction has greatly benefitted from basic research in the experimental analysis of choice behavior. Much of this research, however, has focused on the choice between the same reinforcer as the contingencies of its availability are varied. This research has produced valuable results and the use of a single reinforcer greatly simplifies examining how changing contingencies affects choices. However, the problems of greatest public health concern often involve choices in which the reinforcers are distinctly different. Understanding the extent to which choices between different reinforcers similarly or dissimilarly affect choice is an area of basic research that could have significant societal impact. Thus, while basic science research suggests ways that clinical problems can be conceptualized, more applied research also suggests useful avenues for future basic research.

In addition to these advantages of conceptualizing addiction as a choice disorder, this conceptualization has several specific advantages over the conceptualization of addiction as a brain disease. First, however, we need to acknowledge two important accomplishments achieved through the conceptualization of addiction as a brain disease. This conceptualization may have helped to reduce the stigmatization of addiction and thus, increased public support for treatment of and research on addiction. This conceptualization also was important in moving the discussion of addiction from one of morality to one of science. These are both important accomplishments that followed in part from the conceptualization of addiction as a brain disease and are to be applauded.

However, there are significant problems caused by the conceptualization of addiction as a brain disease. Most importantly is the idea that at some point the brain is fundamentally altered, a switch is thrown so to speak that results in compulsive drug use or addiction; and thus, the cure to addiction rests in returning brain function to its pre-addiction state. This is problematic for several reasons. First, addictive behavior appears to be a lawful function of the experiences of the individual and the contingencies in operation (Griffiths et al 1980). Rather, than the function of a diseased, fundamentally altered brain. Second, as acknowledged even by the proponents of addiction as a brain disease, people suffering from addiction will still reliably choose not to take drug if the appropriate contingencies are arranged (Cohen et al 1971; Leshner 1997). Finally, this conceptualization is likely to lead to the mistaken notion that recovery occurs when the brain returns to the state present before addiction. Rather the brain accumulates changes as a function of experience and it is when the accumulated experiences moves one from choosing drug to not choosing drug that recovery occurs. Past experiences are not erased, but they become less influential. Risk is also not well handled by the conceptualization of addiction as a brain disease, while as we have seen, the conceptualization of addiction as a choice disorder can provide insight into the factors that increase risk. So, choosing between the two conceptualizations is not simply a matter of choosing one level of analysis over another. Further, the conceptualization of addiction as a choice disorder readily provides models of different aspects of addiction in a way that the conceptualization of addiction as a brain disease cannot.

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Highlights

- Addiction viewed as choice leads to useful translational models
- Delay discounting differences in monkeys influences their frequency of drug choices
- Some mice strains and adolescent mice discount rapidly modeling two major risk groups
- Reinforcing alternative behavior in rats reduces alcohol choices and models recovery
- Reinforcing other behavior longer reduces reinstatement by cues for ethanol taking

Figure 1.

Three monkeys responded on one lever to earn intravenous injections of 0.032 mg/kg remifentanyl and on another lever to earn food pellets. In each session, monkeys could choose to earn either remifentanyl or food on 10 occasions. The number of times out of ten, monkeys chose drug (remifentanyl) is plotted on the y-axis against the delay to the delivery of the food pellet on the x-axis. As delay to food delivery increased, remifentanyl choice increased in two of the three monkeys. This figure is adapted from Maguire, Gerak & France (2013)

Figure 2.

The Y-axis shows percent choice of the larger dipper (100 microliter) of 50% condensed milk as delay to its delivery increased across sessions (X-axis), while the delay to the smaller dipper (20 microliter) remained 1-s. Panel A shows the data for adult C57BL6/J mice and data for adolescent C57BL6/J mice (n=12), and Panel B shows percent choice for adult C57BL6/J and DBA2/J mice (n=14/strain). This figure is adapted from Pinkston & Lamb (2011).

Figure 3.

Panel A shows the number of responses made on the food lever before 5 responses occurred on the ethanol lever (X-axis) as a function of the number of preceding sessions rats ($n=5$) had responded under a concurrent food FR 5, ethanol FR 5 schedule. Responding had no programmed consequences and occurred in the presence of the stimulus signaling the concurrent food FR 150, ethanol FR 5 contingencies. The dotted gray line is at 5. Completion of 5 responses on the preceding days would have resulted in food delivery. Panel B shows the percent of responses made on the ethanol lever (left Y-axis) as the tone during

that trial varied from 8 kHz (the frequency signaling a concurrent food FR 5 ethanol FR 5 schedule) to 16 kHz (the frequency signaling a concurrent food FR 150, ethanol FR 5 schedule). Responding on these trials was not reinforced, but responding on intervening trials at either 8 or 16 kHz was reinforced. Under one condition in the preceding 4 sessions rats responded under a multiple concurrent food FR 5 ethanol FR 5, concurrent food FR 150, ethanol FR 5 schedule (open circles), and in the other condition in the preceding 4 sessions rats responded under a concurrent food FR 5, ethanol FR 5 schedule (closed triangles). This figure is adapted from Ginsburg & Lamb 2013a and Ginsburg & Lamb 2013c.