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A unified framework for addiction: Vulnerabilities in the decision process

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Abstract: The understanding of decision-making systems has come together in recent years to form a unified theory of decision-making in the mammalian brain as arising from multiple, interacting systems (a planning system, a habit system, and a situation-recognition system). This unified decision-making system has multiple potential access points through which it can be driven to make maladaptive choices, particularly choices that entail seeking of certain drugs or behaviors. We identify 10 key vulnerabilities in the system: (1) moving away from homeostasis, (2) changing allostatic set points, (3) euphorigenic "reward-like" signals, (4) overvaluation in the planning system, (5) incorrect search of situation-action-outcome relationships, (6) misclassification of situations, (7) overvaluation in the habit system, (8) a mismatch in the balance of the two decision systems, (9) over-fast discounting processes, and (10) changed learning rates. These vulnerabilities provide a taxonomy of potential problems with decision-making systems. Although each vulnerability can drive an agent to return to the addictive choice, each vulnerability also implies a characteristic symptomology. Different drugs, different behaviors, and different individuals are likely to access different vulnerabilities. This has implications for an individual's susceptibility to addiction and the transition to addiction, for the potential for relapse, and for the potential for treatment.

Keywords: Addiction; decision making; dopamine; frontal cortex; gambling; hippocampus; striatum

1. Introduction

Addiction can be operationally defined as the continued making of maladaptive choices, even in the face of the explicitly stated desire to make a different choice (see the *Diagnostic and Statistical Manual of Mental Disorders* [*DSM-IV-TR*], American Psychiatric Association 2000; *International Classification of Diseases* [*ICD-10*], World Health Organization 1992). In particular, addicts continue to pursue drugs or other maladaptive behaviors despite terrible consequences (Altman et al. 1996; Goldstein 2000; Koob & Le Moal 2006; Lowinson et al. 1997). Addictive drugs have been hypothesized to drive maladaptive decision-making through pharmacological interactions with neurophysiological mechanisms evolved for normal learning systems (Berke 2003; Everitt et al. 2001; Hyman 2005; Kelley 2004a; Lowinson et al. 1997; Redish 2004). Addictive behaviors have been hypothesized to drive maladaptive decision-making through interactions between normal learning systems and the reward distribution of certain behaviors (Custer 1984; Dickerson & O'Connor 2006; Dowling et al. 2005; Parke & Griffiths 2004; Redish et al. 2007; Wagenaar 1988). However, how those interactions drive maladaptive decision-making remains a key, unanswered question.

Over the last 30 years, a number of theories have been proposed attempting to explain why an agent might continue to seek a drug or maladaptive behavior. These theories can be grouped into the following primary categories: (1) *opponent processes*, based on changes in homeostatic and allostatic levels that change the needs of the agent (Becker & Murphy 1988; Koob & Le Moal 1997; 2001; 2005; 2006; Solomon & Corbit 1973; 1974); (2) *reward-based processes* and *hedonic components*, based on pharmacological access to hedonically positive signals in the brain (Kalivas & Volkow 2005; Volkow et al. 2003; 2004; Wise 2004); (3) *incentive salience*, based on a sensitization of motivational signals in the brain (Berridge & Robinson 1998; 2003; Robinson & Berridge 1993; 2001; 2003; 2004); (4) *non-compensable dopamine*, based on a role of dopamine as signaling an error in the prediction of the value of taking an action, leading to

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an overvaluation of drug-seeking (Bernheim & Rangel 2004; Di Chiara 1999; Redish 2004); (5) *impulsivity*, in which users make rash choices, without taking into account later costs (Ainslie 1992; 2001; Ainslie & Monterosso 2004; Bickel & Marsch 2001; Giordano et al. 2002; Odum et al. 2002); (6) *situation recognition and categorization*, based on a misclassification of situations that produce both gains and losses (Custer 1984; Griffiths 1994; Langer & Roth 1975; Redish et al. 2007; Wagenaar 1988); and (7) *deficiencies in the balance between executive and habit systems*, in which it becomes particularly difficult to break habits through cognitive mechanisms either through over-performance of the habit system (Robbins & Everitt 1999; Tiffany 1990) or under-performance of flexible, executive, inhibitory systems (Gray & McNaughton 2000; Jentsch & Taylor 1999; Lubman et al. 2004) or a change in the balance between them (Bechara 2005; Bickel et al. 2007; Everitt et al. 2001; Everitt & Wolf 2002). (See Table 1.)

Although each of these theories has been attacked as incomplete and unable to explain all of the addiction data, the theories are not incompatible with each other. We argue, instead, that each theory explains a different vulnerability in the decision-process system, capable of driving the agent to make an addictive choice. Thus, the set of theories provides a constellation of potential causes for addictive choice behavior. Each different drug of abuse or maladaptive behavior is likely to access a subset of that constellation of potential dysfunction. Individual differences are likely to define the importance of each vulnerability for an individual's dysfunction. Successful treatment depends on treating those vulnerabilities that are driving the individual's choice. The identification of addiction as vulnerabilities in the biological decision-making system means that understanding addiction will require an understanding of how animals (including humans) make decisions.

The understanding of decision processes has come together in recent years to form a unified theory of decision-making arising from multiple interacting systems (Cohen & Squire 1980; Daw et al. 2005; Dickinson 1980; 1985; Nadel 1994; O'Keefe & Nadel 1978; Packard & McGaugh 1996; Redish 1999; Squire 1987). Briefly, a decision can arise from a flexible planning system capable of the consideration of consequences or from a less flexible habit system in which actions are associated with situations (Daw et al. 2005; Redish & Johnson 2007). Behavioral control can be transferred from one system to the other depending on the statistics of behavioral training (Balleine & Dickinson 1998; Colwill & Rescorla 1990; Killcross & Coutureau 2003; Packard & McGaugh 1996). Both systems also require a recognition of the situation in which the agent finds itself (Daw et al. 2006; Redish et al. 2007; Redish & Johnson 2007). These processes provide multiple access points and vulnerabilities through which the decision process can be driven to make maladaptive choices.

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2. Scope of the work

Addiction is a complex phenomenon, with causes that can be identified from many perspectives (Volkow & Li 2005a; West 2001), including social (Davis & Tunks 1991), environmental (DeFeudis 1978; Dickerson & O'Connor 2006; Maddahian et al. 1986; Morgan et al. 2002), legal (Dickerson & O'Connor 2006; Kleber et al., 1997; MacCoun 1993), as well as psychological and neurobiological (Goldman et al. 1987; 1999; Heyman 1996; 2000; Koob & Le Moal 2006; Redish 2004; Robinson 2004; Robinson & Berridge 2003; Tiffany 1990), economic (Ainslie 1992; 2001; Becker & Murphy 1988; Bernheim & Rangel 2004; Hursh 1991; Hursh et al. 2005), and genetic (Crabbe 2002; Goldman et al. 2005; Hiroi & Agatsuma 2005) perspectives. All of these perspectives have explanatory power as to the causes of addiction, and all of them provide suggested methods of treatment of addiction. However, a thorough treatment of addiction from all of these perspectives is beyond the scope of a paper such as this one. In this target article, we address an explanation for addictive decisions based on animal learning theory, the neuroscience of learning and memory, human decision-making, and neuroeconomics, which we argue have converged on a unified theory of decision-making as arising from an interaction between two learning systems (a quickly learned, flexible, but computationally expensive-to-execute *planning* system and a slowly learned, inflexible, but computationally inexpensive-to-execute *habit* system).

2.1. Our goals

The goal of this target article is to lay out a novel explanation for addiction as "vulnerabilities" in an established decision-making system. Although many of the vulnerabilities that we describe can be identified closely with current theories of addiction (see, e.g., Table 5), those theories have generally arisen from explanations of specific experiments and have all been attacked as incomplete. Our article is the first to identify them as "failure points" in a unified decision-making system. This theory has implications for the taxonomy of addiction, both drug-related and behavioral, as well as implications for prevention

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Table 1. *Theories of addiction*

Opponent processes	Changes in allostatic and homeostatic needs	*a*
Hedonic processes	Pharmacological access to hedonically positive signals	*b*
Incentive salience	Sensitization of motivational signals	*c*
Noncompensable DA	Leading to an overvaluation of drug-seeking	*d*
Impulsivity	Overemphasis on a buy-now, pay-later strategy	*e*
Illusion of control	Misclassification of wins and losses	*f*
Shifting balances	Development of habits over flexible systems	*g*

Related References:
a. Solomon and Corbit (1973; 1974); Koob and Le Moal (1997; 2001; 2005; 2006).
b. Kalivas and Volkow (2005); Volkow et al. (2003, 2004); Wise (2004).
c. Berridge and Robinson (1998; 2003); Robinson and Berridge (1993; 2001; 2003; 2004).
d. Bernheim and Rangel (2004); Di Chiara (1999); Redish (2004).
e. Ainslie (1992; 2001); Ainslie and Monterosso (2004); Bickel and Marsch (2001); Reynolds (2006).
f. Custer (1984); Griffiths (1994); Langer and Roth (1975); Redish et al. (2007); Wagenaar (1988).
g. Everitt and Wolf (2002); Everitt et al. (2001); Nelson and Killcross (2006); Robbins and Everitt (1999).

and treatment. These implications are addressed at the end of the article.

Although we do not directly address the social, environmental, or policy-level theories, we believe that our proposed framework will have implications for these viewpoints on addiction. For example, changes in drug price, taxes, legality, and level of policing can change the costs required to reach the addictive substance or behavior (Becker et al. 1994; Grossman & Chaloupka 1998; Liu et al. 1999). The presence of casinos can provide cues triggering learned associations (Dickerson & O'Connor 2006). Acceptability of use and punishments for use will affect the relationship between rewards and costs (Goldman et al. 1987; 1999). Genetics will shape the person's vulnerabilities to the potential failure points noted further on and will have to be an important part of the individual's treatment plan (Goldman et al. 2005; Hiroi & Agatsuma 2005).

Before proceeding to the implications of this theory, we first need to lay out the unified model of the decision-making system (sect. 3). As we go through the components of this system, we point out the identifiable vulnerabilities as they arise. In section 4, we then return to each identified vulnerability in turn and discuss the interactions between that vulnerability and specific drugs and problematic behaviors. In section 5, we discuss the implications of this theory for individual susceptibility to addiction, for multiple pathways to relapse, and for the necessity of making available multiple appropriately guided treatment regimens. In section 6, we turn to social, political, and clinical implications, lay out open questions, and suggest future directions for addiction research. Finally, we include an appendix reviewing the known effects of six drugs and problematic behaviors, discussed in the light of the vulnerabilities identified in this article (A: cocaine; B: opiates; C: nicotine; D: alcohol; E: caffeine; and F: gambling).

3. Making decisions

Theories of how animals make decisions have been developed over the last 50 years in the fields of economics (Ainslie 1992, 2001; Becker & Murphy 1988; Bernheim & Rangel 2004; Bickel & Marsch 2001; Glimcher & Rustichini 2004; Petry & Bickel 1998), psychology and neuroscience (Daw 2003; Glimcher 2003; Hastie 2001; Herrnstein 1997; Heyman 1996; Kahneman et al. 1982; Kahneman & Tversky 2000; Sanfey et al. 2006; Slovic et al. 1977), and machine learning (Sutton & Barto 1998). These literatures have converged on the concept that decisions are based on the prediction of *value* or *expected utility* of the decision.[1] These terms can be defined as the total, expected, future reward, taking into account the probability of receiving the reward and any delay before the reward is received. In these analyses, costs are typically included as negative rewards, but they can also be included separately in some formulations. If the agent can correctly predict the value (total discounted[2] reward minus total expected cost) of its actions, then it can make appropriate decisions about which actions to take. The theories of addiction that have been proposed (Table 1) all have the effect of changing the prediction of value or cost in ways that make the agent continue to repeatedly return to seeking of the addictive drug or maladaptive behavior.

There are two potential methods from which one can derive the value of taking some action (Bernheim & Rangel 2004; Daw et al. 2005; Redish & Johnson 2007; Sutton & Barto 1998): *forward-search* and *caching*. In the first case (forward-search), one considers the possible consequences of one's actions – the agent realizes that if it takes this action in this situation, this will occur, and it will get this reward, but if it does something else, there will be different consequences, and it will get a different reward. In the other case (caching), the agent has learned to associate a specific action with a given situation – over time, the agent has learned that the best thing to do in this situation is to take this action. The forward-search system takes time to execute (because one has to mentally trace down possible paths), but is very flexible. That flexibility means that it is safe to learn quickly. Learning potential consequences of one's actions does not commit one to an action; rather it opens the possibility of considering the consequences of an action before selecting that action. In contrast, the caching system is very fast to execute (because one simply has to retrieve the best action for a given situation), but is very rigid. That inflexibility means that it would be dangerous to learn the stimulus-action relationships stored in the habit system too quickly.

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This dichotomy can be related to the question of when to stop a search process (Nilsson et al. 1987; Simon 1955). Incomplete search processes may be available in which temporarily cached values are accessed to cut off parts of the search tree, similar to heuristic search processes studied in the classic artificial intelligence literature (Nilsson et al. 1987; Rich & Knight 1991; Russell & Norvig 2002). Similarly, one can imagine that only some of the potential paths are searched in any decision. Finding an optimal solution takes time, and there is a tradeoff between search time and the optimality of the solution found (Simon 1955). From an evolutionary perspective, a quickly found, acceptable solution may be more efficient than a slowly found optimal solution (Gigerenzer 2001; Gigerenzer & Goldstein 1996; Simon 1955). A true caching system, however, does not entail a search process and should not be considered to be equivalent to a single step of the search process (Daw et al. 2005; Gigerenzer 2001). A single step of the search process would identify the consequence of that step, allowing changes in that consequence to change performance without relearning. In contrast, the caching system compares a stored value with an action taken in a given situation and does not identify the consequence during performance, which means that it cannot change its reactions to changes in the value of that consequence. This distinction can be seen in the devaluation literature, discussed further on.

A number of literatures have converged on a division between learning systems that match these two systems. In the animal navigation literature, these two systems are referred to as the *cognitive map* and *route* systems,[3] respectively (O'Keefe & Nadel 1978; Redish 1999). In the animal learning-theory literature, these systems can be identified as three separate systems, a Pavlovian learning system (situation-outcome, $S \xrightarrow{(a)} O$), an instrumental learning system (action-outcome, $\xrightarrow{a} O$), and a habit learning system ($S \xrightarrow{a}$).[4]

They have also been referred to as *cognitive* and *habit* learning systems (Mishkin & Appenzeller 1987; Poldrack & Packard 2003; Saint-Cyr et al. 1988; Yin & Knowlton 2006), and match closely the distinction made between *declarative* and *procedural* learning (Cohen & Eichenbaum 1993; Cohen & Squire 1980; Redish 1999; Squire 1987; Squire et al. 1984) and between *explicit* and *implicit* learning systems (Clark & Squire 1998; Curran 1995; Doyon et al. 1998; Ferraro et al. 1993; Forkstam & Petersson 2005; Knopman & Nissen 1987; 1991; Nissen et al. 1987; Willingham et al. 1989), as well as between *controlled* and *automatic* processing theories (Kahneman & Frederick 2002; Schneider & Chein 2003; Schneider & Shiffrin 1977). We argue that these diverse literatures have converged on a pair of decision-making systems, which can be understood as (1) a flexible, cognitive, planning system and (2) a rigid, automatic, habit-based system.

This dichotomy is related to the historical debate on "expectancies" in the classic animal learning theory literature (Bolles 1972; Hull 1943; 1952; Munn 1950; Tolman 1938; 1939; 1948). Tolman (1938; 1939; 1948) argued that animals maintain an expectancy of their potential future consequences (including an expectancy of any rewarding component), and that this provided for latent learning effects as well as fast changes in choices in response to changes in provided needs, whereas Hull (1943; 1952) argued that animals learn simple associations of stimuli and responses, allowing for the slow development of automation (Carr & Watson 1908; Dennis 1932). As noted by Guthrie (1935; see Balleine & Ostlund 2007; Bolles 1972), one implication of Tolman's cognitive expectancies theories would be a delay in choosing. Just such a delay is seen in early learning, particularly in tasks that require the planning system. At choice points, rats faced with difficult decisions pause and vicariously sample the different choices before committing to a decision (Brown 1992; Meunzinger 1938; Tolman 1938; 1939). This "vicarious trial and error" (VTE) behavior is abolished with hippocampal lesions (Hu & Amsel 1995), and is related to hippocampal activity on hippocampal-dependent tasks (Hu et al. 2006). Recent neural ensemble recording data have found that hippocampal firing patterns transiently represent locations ahead of the animal at choice points during VTE-like behaviors (Johnson & Redish 2007). Once tasks have been overtrained, these VTE movements disappear (Hu et al. 2006; Munn 1950; Tolman 1938), as do the forward representations (Johnson & Redish 2007), suggesting that VTE may be a signal of the active processing in the planning system (Buckner & Carroll, 2007; Johnson & Redish 2007; Tolman 1938; 1939).

These two systems mirror the classical two-process theory in psychology (Domjan 1998; Gray 1975) and the more recent distinction between stimulus-stimulus (SS, $S \longrightarrow O$), stimulus-outcome (SO, SAO, $S \xrightarrow{a} O$), action-outcome (AO, $\xrightarrow{a} O$), and stimulus-response or stimulus-action (SA, $S \xrightarrow{a}$) (Balleine & Ostlund 2007; Dickinson 1985) (see Table 2). The first ($S \longrightarrow O$) entails the recognition of a causal sequence but does not entail an actual decision. The second ($S \xrightarrow{a} O$) is classical Pavlovian conditioning and entails an action taken in response to a situation in anticipation of a given outcome (Domjan 1998; Pavlov 1927; Rescorla 1988). The third ($\xrightarrow{a} O$) is classical instrumental conditioning (Balleine & Ostlund 2007; Domjan 1998; Ferster & Skinner 1957) and entails an action taken to achieve an outcome, even in the absence of an immediate stimulus. It is important to note, however, that action-outcome associations do still

Table 2. *Learning theory and decision-making*

System	Description	Learning Theory		Expectation
Observation	$S \longrightarrow O$	Pavlovian	S-S	$E(O)$
Planning	$S \xrightarrow{a} O$	Pavlovian with action	S-O	$E(O) \rightarrow E(V)$
Planning	$\xrightarrow{a} O$	Instrumental	A-O	$E(O) \rightarrow E(V)$
Habit	$S \xrightarrow{a}$	Habit	S-R	$E(V)$

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include stimuli in the form of the context (actions are not taken at all times but rather only within certain facilitating contexts).[5] The fourth ($S \xrightarrow{a}$) entails an association between a situation and an action and denotes habit learning (Domjan 1998; Hull 1943; 1952).

These four associations can be differentiated in terms of their expectancies (Table 2). $S \longrightarrow O$ associations entail an expectancy of an outcome, but with no decision, there is no necessary further processing of that outcome, although there is likely to be an emotional preparation of some sort. If an animal can do something to prepare for, produce, or change that outcome, then the association becomes one of situation-action-outcome ($S \xrightarrow{a} O$). If there is no immediate stimulus triggering the action, then the association becomes an $\xrightarrow{a} O$ association. Because $\xrightarrow{a} O$ associations continue to include a contextual gating component, the $\xrightarrow{a} O$ association is truly an $S \xrightarrow{a} O$ association. Although there are anatomical reasons to separate $\xrightarrow{a} O$ from $S \xrightarrow{(a)} O$ associations (Balleine & Ostlund 2007; Ostlund & Balleine 2007; Yin et al. 2005), for our purposes, they can be treated similarly: they both entail an expectancy of an outcome that must be evaluated to produce an expectancy of a value. This means they both require a planning component and can be differentiated from habit learning in which situations are directly associated with actions ($S \xrightarrow{a}$). In the $S \xrightarrow{a}$ association, situation-action pairs entail a direct expectancy of a value, which can then drive the action, even in the absence of a recognition of the outcome.

Following this distinction, we categorize these four association systems into three decision systems: an *observation* system, which does not make decisions and will not be discussed further; a *planning* system, which takes a given situation (derived from stimuli, context, or a combination thereof), predicts an outcome, and evaluates that outcome; and a *habit* system, which takes a given situation (derived from stimuli, context, or a combination thereof) and identifies the best remembered action to take.

These systems, of course, exist within overlapping and interacting structures (Balleine & Ostlund 2007; Corbit et al. 2001; Dayan & Balleine 2002; Devan & White 1999; Kelley 1999a; 1999b; Voorn et al. 2004; Yin et al. 2006; Yin & Knowlton 2006). The flexible planning system involves the entorhinal cortex (Corbit & Balleine 2000), hippocampus (O'Keefe & Nadel 1978; Packard & McGaugh 1996; Redish 1999), the ventral and dorsomedial striatum (Devan & White 1999; Martin 2001; Mogenson 1984; Mogenson et al. 1980; Pennartz et al. 2004; Schoenbaum et al. 2003; Yin et al. 2005), prelimbic medial prefrontal cortex (Jung et al. 1998; Killcross & Coutureau 2003; Ragozzino et al. 1999), and orbitofrontal cortex (Davis et al. 2006; Padoa-Schioppa & Assad 2006; Schoenbaum et al. 2003; 2006a; 2006b; Schoenbaum & Roesch 2005). The habit system involves the dorsolateral striatum (Barnes et al. 2005; Packard & McGaugh 1996; Schmitzer-Torbert & Redish 2004; Yin & Knowlton 2004; 2006), the infralimbic medial prefrontal cortex (Coutureau & Killcross 2003; Killcross & Coutureau 2003) as well as the parietal cortex (DiMattia & Kesner 1988; Kesner et al. 1989) (see Table 3).

3.1. Transitions between decision systems

Behavior generally begins with flexible planning systems but, for repeated behaviors, can become driven by the less-flexible (but also less computationally expensive) habit systems. Examples of this development are well known from our experiences. For example, the first time we drive to a new job, we need a travel plan; we pay attention to street-signs and other landmarks. But after driving that same trip every day for years, the trip requires less and less attention, freeing up resources for other cognitive processes such as planning classes, papers, or dinner. The flexible system, however, generally remains available, as when road construction closes one's primary route to work and one now needs to identify a new route. Errors

Table 3. *Two systems*

	Planning System	**Habit System**
Literature		
Animal navigation	Cognitive map	Route, taxon, response
Animal behavior	S-O, S-A-O, A-O	S-A, S-R
Memory systems	Cognitive	Habit
Learning and memory	Episodic (declarative)	Procedural
Cognition	Explicit	Implicit
Machine learning	Forward-search	Action-caching
Properties		
Flexibility	Flexible	Rigid
Execution speed	Slow	Fast
Learning speed	Quick	Slow
Devaluation?	Yes	No
Key Anatomical Structures		
Striatum	Ventral, dorsomedial striatum (accumbens, head of the caudate)	Dorsolateral striatum (caudate, putamen)
Frontal cortex	Prelimbic, orbitofrontal cortex	Infralimbic, other components?
Hippocampal involvement	Hippocampus (yes)	——— (no)
Dopaminergic inputs	Ventral tegmental area	Substantia nigra pars compacta

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can exist within both systems, as for example, a misjudged plan or a trip so automatic, that if one is not paying attention, one might accidentally find oneself having driven to work even though one planned to go somewhere else. This interaction is well-studied in the animal literature, including the overlaying of planning by habit systems (Dickinson 1980; Hikosaka et al. 1999; Packard & McGaugh 1996; Schmitzer-Torbert & Redish 2002), restoration of planning in the face of changes (Gray & McNaughton 2000; Isoda & Hikosaka 2007; Sakagami et al. 2006), and conflict between the two systems (Gold 2004; McDonald & White 1994; Packard 1999; Poldrack & Packard 2003; Redish et al. 2000).

Four well-studied examples in the animal literature are the transfer of place strategies to response strategies in the plus-maze (Chang & Gold 2004; Packard & McGaugh 1996; Yin & Knowlton 2004), the development of the regularity of behavioral paths (Barnes et al. 2005; Jog et al. 1999; Schmitzer-Torbert & Redish 2002), the disappearance of devaluation in animal learning studies (Adams & Dickinson 1981; Balleine & Dickinson 1998; Colwill & Rescorla 1985; Tang et al. 2007), and the inhibition of habitual responses in go/no-go tasks (Gray & McNaughton 2000; Husain et al. 2003; Isoda & Hikosaka 2007).

In the plus-maze, animals are trained to take an action that can be solved either by going to a specific place (Tolman et al. 1946) or by taking an action in response to being placed on the maze (Hull 1952). These algorithms can be differentiated by an appropriately designed probe trial (Barnes et al. 1980; Packard & McGaugh 1996; Restle 1957). Rats on this task (and on other similar tasks) first use a place strategy, which then evolves into a response strategy (McDonald & White 1994; Packard & McGaugh 1996; Yin & Knowlton 2004). Place strategies depend on hippocampal, as well as ventral and dorsomedial striatal integrity, while response strategies depend on dorsolateral striatal integrity (Packard & McGaugh 1996; Yin & Knowlton 2004; 2006; Yin et al. 2005).

In tasks in which animals are provided a general task with specific cases that change from day to day or session to session, animals can learn the specific instantiations very quickly. In these tasks, behavioral accuracy improves quickly, followed by a slower development of a regularity in the actions taken by the animal (rats, Jog et al. 1999; Schmitzer-Torbert & Redish 2002; monkeys, Hikosaka et al. 1999; Rand et al. 1998; 2000; humans, Nissen & Bullemer 1987; Willingham et al. 1989). In these tasks, the early (accurate, flexible, and slower) behavior is dependent on hippocampal integrity and correlated to hippocampal activity (Ferraro et al. 1993; Johnson & Redish 2007; Knopman & Nissen 1987), whereas later (also accurate, but inflexible and faster) behavior is dependent on dorsolateral striatal integrity and correlated to dorsolateral striatal activity (Barnes et al. 2005; Doyon et al. 1998; Hikosaka et al. 1998; Jackson et al. 1995; Jog et al. 1999; Knopman & Nissen 1991).

The implication of multiple decision-making systems on the calculation of value can also be seen in the effect of these two decision systems on changes in the valuation of a reward (Adams & Dickinson 1981; Balleine & Dickinson 1998; Colwill & Rescorla 1985; Dickinson 1980; 1985). Classically, these differences are measured by (1) training an agent to take an action (or a sequence of actions) to receive a reward R, and then, (2) changing the value of reward R to the agent, usually in a different context. The value of a reward can be changed by providing excess amounts of the reward (satiation, Balleine & Dickinson 1998) or by pairing the reward with an aversive stimulus, such as lithium chloride (devaluation, Adams & Dickinson 1981; Colwill & Rescorla 1985; Holland & Rescorla 1975; Holland & Straub 1979; Nelson & Killcross 2006; Schoenbaum et al. 2006a). Finally, (3) the agent is provided the chance to take the action. If the action-selection process takes into account the current value of the reward, then the agent will modify its actions in response to the change, but if the action-selection process is an association between the situation and the action (hence does not take into account the value of the reward), the agent will not modify its response. Lesions to ventral striatum (Corbit et al. 2001; Schoenbaum et al. 2006c) and prelimbic medial prefrontal cortex (Killcross & Coutureau 2003) or orbitofrontal cortex (Ostlund & Balleine 2007; Schoenbaum et al. 2006a; 2006b) discourage devaluation, whereas lesions to dorsolateral striatum (Yin et al. 2004; Yin & Knowlton 2004; Yin et al. 2006) and infralimbic cortex (Coutureau & Killcross 2003; Killcross & Coutureau 2003) encourage devaluation processes. Lesions to entorhinal cortex (Corbit & Balleine 2000) and dorsomedial striatum (Adams et al. 2001; Ragozzino et al. 2002a; 2002b; Yin et al. 2005) disrupt flexibility in the face of predictability changes (contingency degradation), whereas lesions to dorsolateral striatum do not (Yin & Knowlton 2006).

It is important to note that not all transitions need be from planning strategies to habit strategies. Because planning strategies are flexible and learned quickly, while habit-based strategies are more rigid and learned more slowly, many tasks are solved in their early stages through the planning system and in their late stages through the habit system (Dickinson 1980; Hikosaka et al. 1999; Packard & McGaugh 1996; Restle 1957). But the habit system can also learn in the absence of an available planning system (Cohen & Squire 1980; Day et al. 1999; Knowlton et al. 1994; Mishkin et al. 1984). Under appropriate conditions, well-developed automated responses can be overridden by controlled (planning-like) systems as in go/no-go tasks (Goldman et al. 1970; Gray & McNaughton 2000; Isoda & Hikosaka 2007; Iversen & Mishkin 1970) or reversal learning (Hirsh 1974; Mackintosh 1974; Ragozzino et al. 2002a). Which system drives behavior at which time depends on parameters of the specific task (Curran 1995; McDonald & White 1994; O'Keefe & Nadel 1978; Redish 1999) and may even differ between individuals under identical experimental conditions. In many cases, identical behaviors can be driven by the two systems, and only specialized probe trials can differentiate them (Barnes 1979; Curran 2001; Hikosaka et al. 1999).

3.2. The planning system

The *planning* system requires recognition of a situation and/or context S, identification of the consequences of taking action a in situation S (recognition of a means of achieving outcome O), and the evaluation of the value of achieving outcome O. This system selects the most appropriate action by considering the potential consequences of that action. The key behavioral parameters involved in this system are fast storage and slow retrieval. As noted earlier, retrieval within this system can be slow

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because the calculation of value at each step requires processing through the consideration of possibilities. Because the consideration of possibilities does not commit one to a single choice, this system is flexible in its behavioral choices. Because the value of taking action *a* in situation *S* is calculated from the value of achieving expected outcome *O*, which is calculated online from the current needs of the agent, if the desire (need) for the outcome is changed (even in another context), the value calculation can reflect that change.

Computationally, the planning system is likely to require three interacting components: a *situation-recognition component*, which classifies the complex interaction of contexts and stimuli to identify the situation in which the animal finds itself; a *prediction component*, which calculates the consequences of potential actions; and an *evaluative component*, which calculates the value of those consequences (taking into account the time, effort, and probability of receiving reward).

The situation-recognition component entails a categorization process, in which the set of available cues and contexts must be integrated with the agent's memory so as to produce a classification of the situation. This system is likely to arise in cortical sensory and association systems through competitive learning (Arbib 1995; Grossberg 1976; Redish et al. 2007; Rumelhart & McClelland 1986). Mathematically, the cortical recognition system can be modeled with attractor network dynamics (Durstewitz et al. 1999; 2000; Kohonen 1984; Laing & Chow 2001; Redish 1999; Seamans & Yang 2004; Wilson & Cowan 1972; 1973), in which a partial pattern can be completed to form a remembered pattern through recurrent connections within the structure (Hebb 1949/2002; Hertz et al. 1991; Hopfield 1982). This *content addressable memory* provides a categorization process transforming the observed set of cues to a defined (remembered) *situation* that can be reasoned from (Redish et al. 2007).

The prediction component entails a prediction of the probability that the agent will reach situation s_{t+1}, given that it takes action a in situation s_t: $P(s_{t+1}|s_t, a)$. This functionality has been suggested to lie in the hippocampus (Jensen & Lisman 1998; 2005; Johnson & Redish 2007; Koene et al. 2003) or frontal cortex (Daw et al. 2005). The hippocampus has been identified with stimulus-stimulus associations (Devenport 1979; 1980; Devenport & Holloway 1980; Hirsh 1974; Mackintosh 1974; White & McDonald 2002), episodic memory (Cohen & Eichenbaum 1993; Ferbinteanu & Shapiro 2003; Ferbinteanu et al. 2006; Squire 1987), flexible behavior (Devenport et al. 1981b; Gray & McNaughton 2000), including flexible navigation behavior (the cognitive map, i.e., spatial associations between stimuli; O'Keefe & Nadel 1978), as well as in sequence learning (Agster et al. 2002; Cohen & Eichenbaum 1993; Fortin et al. 2002; Levy 1996; Levy et al. 2005) (see Redish [1999] for review). Similar functionality has been proposed to lie in the frontal cortex (Daw et al. 2005), which has long been associated with the ability to recategorize situations (Baddeley 1986; Clark & Robbins 2002; Dalley et al. 2004; Isoda & Hikosaka 2007; Jentsch & Taylor 1999; Quirk et al. 2006; Rushworth et al. 2007) with the storage of delayed events (Baddeley 1986; Fuster 1997; Goldman-Rakic et al. 1990) and the anticipation of reward (Davis et al. 2006; Fuster 1997; Watanabe 2007), as well as with sequence planning (Averbeck & Lee 2007; Kolb 1990; Mushiake et al. 2006; Owen 1997).

The evaluative component allows the calculation of value with each predicted outcome. Anatomically, the evaluative component is likely to include the amygdala (Aggleton 1993; Dayan & Balleine 2002; Phelps & LeDoux 2005; Rodrigues et al. 2004; Schoenbaum et al. 2003), the ventral striatum (nucleus accumbens) (Daw 2003; Kelley 1999a; 1999b; Kelley & Berridge 2002; Mogenson 1984; Pennartz et al. 1994; Stefani & Moghaddam 2006; Wilson & Bowman 2005) and associated structures (Tindell et al. 2004; 2006), and/or the orbitofrontal cortex (Feierstein et al. 2006; Padoa-Schioppa & Assad 2006; Plassmann et al. 2007; Sakagami & Pan 2007; Schoenbaum et al. 2003; 2006a; Volkow et al. 2003). Neurons in the ventral striatum show reward correlates (Carelli 2002; Carelli et al. 2000; Carelli & Wondolowski 2003; Lavoie & Mizumori 1994; Martin & Ono 2000; Miyazaki et al. 1998) and anticipate predicted reward (Martin & Ono 2000; Miyazaki et al. 1998; Schultz et al. 1992; Yun et al. 2004). Neurons in the ventral pallidum are associated with the identification of hedonic signals (Tindell et al. 2004; 2006). Both the hippocampus and prefrontal cortex project to ventral striatum (Finch 1996; McGeorge & Faull 1989; Swanson 2000), and ventral striatal firing patterns reflect hippocampal and prefrontal neural activity (Goto & Grace 2005a; 2005b; Kalivas et al. 2005; Martin 2001; Pennartz et al. 2004). Neurons in the orbitofrontal cortex encode parameters relating the value of potential choices (Padoa-Schioppa & Assad 2006; Schoenbaum & Roesch 2005).

These structures all receive strong dopaminergic input from the ventral tegmental area. Neurophysiologically, dopamine signals in the ventral striatum – measured by neural recordings from dopaminergic projection neurons (Schultz 1998; 2002) and from voltammetry signals in the ventral striatum itself (Roitman et al. 2004; Stuber et al. 2005) – show increased firing to unexpected rewards and to unexpected cues predicting rewards. In computational models of the habit system, these signals have been hypothesized to carry value-prediction error information (see further on). Much of the data seems to support a similar role for dopamine from ventral tegmental sources (de la Fuente-Fernandez et al. 2002; Ljungberg et al. 1992; Roitman et al. 2004; Stuber et al. 2005; Ungless et al. 2004). However, detailed, anatomically instantiated computational models are not yet available for the planning system. Theories addressing dopamine's role in the planning system have included motivation and effort (Berridge 2006; Berridge & Robinson 1998; 2003; Niv et al. 2007; Robbins & Everitt 2006; Salamone & Correa 2002; Salamone et al. 2005; 2007) and learning (Ikemoto & Panksepp 1999; Reynolds et al. 2001). An important open question, however, is to what extent dopamine is carrying the actual signal of motivation (Berridge 2007) and to what extent dopamine's effects are dependent on corticostriatal synapses (Anagnostaras et al. 2002; Li et al. 2004; McFarland & Kalivas 2001; McFarland et al. 2003; Nicola & Malenka 1998; Reynolds & Wickens 2002). Finally, dopamine in the prefrontal cortex has also been hypothesized to have a role in controlling the depth of the categorization process (Durstewitz et al. 1999; 2000; Redish et al. 2007; Seamans et al. 2001; Seamans & Yang 2004; Tanaka 2002; 2006).

Neuropharmacologically, these systems, particularly the ventral striatum, are also highly dependent on mechanisms

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involving opioid signaling. Opioid signaling has been hypothesized to be involved in hedonic processes (Berridge & Robinson 1998; 2003; Kelley et al. 2002). Consistent with these ideas, Levine and colleagues (Arbisi et al. 1999; Levine & Billington 2004) report that opioid antagonists directly interfere with the reported qualia of hedonic pleasure in humans eating sweet liquids, without interfering in taste discrimination. We have suggested that the multiple opioid receptors in the mammalian brain (μ, κ, δ; De Vries & Shippenberg 2002; Herz 1997; 1998) are associated with an evaluation process identifying positive (euphorigenic, signaled by μ-opioid activation) and negative (dysphorigenic, signaled by κ-opioid signaling) evaluations (Redish & Johnson 2007). Whereas μ-receptor agonists are rewarding, euphorigenic, and support self-administration, κ-receptor agonists are aversive, dysphoric, and interfere with self-administration (Bals-Kubik et al. 1989; Chavkin et al. 1982; De Vries & Shippenberg 2002; Herz 1997, 1998; Kieffer 1999; Matthes et al. 1996; Meyer & Mirin 1979; Mucha & Herz 1985).[6]

We have also proposed that part of the evaluation mechanism occurring during the search process (calculating the expected value from the agent's needs and the expected outcomes given a $S \xrightarrow{(a)} O$ relation) may also involve the opioid system (Redish & Johnson 2007). This would predict a release of μ-opioid agonists (e.g., enkephalins) in anticipation of extreme rewards. Rats placed in a drug-associated location show a dramatic increase in released enkephalin in the nucleus accumbens relative to being placed in a saline-associated compartment, presumably in anticipation arising from the drug-associated compartment (Mas-Nieto et al. 2002).[7]

3.2.1. Potential vulnerabilities in the planning system. The planning system provides potential failure points in changes in the definition of the perceived needs N of the animal, in incorrect identification of satisfaction of that need (mimicking reward), in incorrect evaluation of the expected value of the outcome, and in incorrect search of the $S \xrightarrow{(a)} O$ relationships themselves, as well as a potential failure point in misclassification of situations.

Vulnerability 1: Homeostatic changes: Changing the definition of the needs N

Vulnerability 2: Allostatic changes: Changing the definition of the needs N

Organisms have evolved to maintain very specific levels of critical biological parameters (temperature, hormonal levels, neurotransmitter levels, etc.) under large challenge variations. Because these specific levels ("set-points") can change under contextual, biological, social, and other factors, such as with a circadian or seasonal rhythm, some authors have suggested the term *allostasis* over the more classic term *homeostasis*, reserving homeostasis for a constant set point (Koob & Le Moal 2006). Drugs and other manipulations can change the needs of an animal either by moving the system away from the homeostatic set-point itself (say, in a withdrawal state after drug use), requiring drugs to return the system to homeostasis, or by changing the system's desired set-point itself, thus requiring drugs to achieve the new inappropriate set-point (Koob & Le Moal 2006). In either case, these changes will change the perceived needs of the agent, and will thus change the evaluated value of expected outcomes.

Vulnerability 3: Overvaluation of the expected value of a predicted outcome – mimicking reward

As noted earlier, the planning system requires a component that directly evaluates the expected outcome. This evaluation process is, of course, a memory process that must take into account the history of experience with the expected outcome. This means that there must be a biological signal that recognizes the value of outcomes when the agent achieves the outcome itself (thus satisfying the perceived need). This signal is likely to be related to the qualia of euphoric pleasure and dysphoric displeasure (Berridge & Robinson 1998; 2003). We can thus identify this signal with subjective hedonic signals. It is likely that when the agent searches the consequences of the potential $S \xrightarrow{(a)} O$ action-sequence, the same evaluative process would be used, which could implicate these same signals in craving (Redish & Johnson 2007). This signal is likely to be carried in part by endogenous opioid signals (Berridge & Robinson 1998; 2003; Kelley et al. 2002), potentially in the ventral basal ganglia (Tindell et al. 2004; 2006). Additionally, the memory of value depends on the remembered values of experiences, which tend to be remembered as generally more positive than they really were due to biases in representation (Kahneman & Frederick 2002; Schreiber & Kahneman 2000). Social factors can also affect remembered values of actual dysphoric events (Cummings 2002; Goldman et al. 1999; Jones et al. 2001).

Vulnerability 4: Overvaluation of the expected value of a predicted outcome in the planning system

In fact, any mechanism by which the value of a predicted outcome is increased will have vulnerabilities leading the planning system to over-value certain outcomes. At this point, computational models of the planning system are insufficiently detailed to lead to specific predictions or explanations of the mechanisms by which outcomes are over-valued, but experimental evidence has suggested a role for dopamine release in the nucleus accumbens as a key component (Ikemoto & Panksepp 1999; Robinson & Berridge 1993; Roitman et al. 2004; Salamone et al. 2005; see Robinson & Berridge 2001; 2003, for reviews). The orbitofrontal cortex has also been implicated in the evaluation of potential rewards (Padoa-Schioppa & Assad 2006; Sakagami & Pan 2007; Schoenbaum & Roesch 2005), and incorrect signals arriving from the orbitofrontal cortex could also drive overvaluation of expected drug- or behavior-related outcomes (Kalivas & Volkow 2005; Schoenbaum et al. 2006a; Volkow et al. 2003). Changes in activity in the orbitofrontal cortex (Stalnaker et al. 2006; Volkow & Fowler 2000) and the ventral striatum (Carelli 2002; German & Fields 2007b; Peoples et al. 1999) are likely to play important roles in this vulnerability.

Vulnerability 5: Incorrect search of $S \xrightarrow{(a)} O$ relationships

The prediction component of the planning system is also a memory process, requiring the exploration of

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multiple consequences from situation *S*. If a drug or other process were to increase the likelihood of retrieving a specific $S \xrightarrow{(a)} O$ relationship, then one would expect this to limit the set of possibilities explored, which would appear as a cognitive blinding to alternatives (Redish & Johnson 2007). Because action-decisions in the planning system must be made through the comparison of available alternatives, this vulnerability would also mean that when an agent is returned to situation *S*, it would be more likely to remember the availability of outcome *O* than other potential outcomes, which would make it more likely to remember the high value associated with outcome *O* (see *Vulnerabilities 3* and *4*), and thus more likely to experience craving in situation *S*. This craving would then lead to a recurring search of the same $S \xrightarrow{(a)} O$ path, which would appear as a cognitive blinding or obsession. This process could also lead to an increase in attention to drug-related cues, which has been seen in both alcohol and heroin addicts (Lubman et al. 2000; Schoenmakers et al. 2007).

Vulnerability 6: Misclassification of situations

In order to retrieve an $S \xrightarrow{(a)} O$ relation, the agent must recognize that the situation it is in is sufficiently similar to a previous one to successfully retrieve the relation, predict the outcome, and evaluate it. The $S \xrightarrow{(a)} O$ relations are, of course, dependent on the predictability of the outcome for a given situation, and therfore are sensitive to *contingency degradation*, in which the predictability of an outcome from a given situation-action pair is decreased (thus changing the $S \xrightarrow{(a)} O$ relationship; Corbit & Balleine 2000; Corbit et al. 2002; Devenport & Holloway 1980). These relationships can be misunderstood either by *over-categorization*, in which two situations that are actually identical are miscategorized as different, or by *over-generalization*, in which two situations that are actually separate are miscategorized as the same.

Over-categorization. Thus, for example, if gambling losses are not recognized as occurring in the same situation as previous gambling wins, an agent can potentially (incorrectly) learn two $S \xrightarrow{(a)} O$ relations, one leading from situation S_1 to a winning outcome and one leading from situation S_2 to a losing outcome. If the agent can identify cues that separate situation S_1 from situation S_2, then it will (incorrectly) predict that it can know when it will achieve a winning outcome. This has been referred to as "the illusion of control" (Custer 1984; Griffiths 1994; Langer & Roth 1975; MacKillop et al. 2006; Redish et al. 2007; Wagenaar 1988).

Over-generalization. An inability to recategorize situations (by recognizing actual changes) can lead to the perseveration of responses and an inability to switch responses in the face of failures and losses. Many drug users and pathological gamblers show failures to reverse or switch action-selection choices in response to novel adverse conditions (Bechara et al. 2001; Clark & Robbins 2002; Everitt et al. 1999; Grant et al. 2000; Jentsch et al. 2002; Verdejo-Garcia et al. 2006). Developing abilities to recategorize situations has been suggested as one means of treating addictions (McCaul & Petry 2003; Sylvain et al. 1997). Simulated agents with deficiencies in the ability to recategorize cues find difficulty in breaking cue-addiction associations[8] (Redish et al. 2007).

3.3. The habit system

In contrast to the complexity of the planning system, the habit system entails a simple association between situation and action. Thus, the habit system requires recognition of a situation *S*, and a single, identified action to take within that situation. This simplicity allows the habit system to react quickly. However, this simplicity also makes the habit system rigid. A learned association essentially commits the agent to take action *a* in situation *S*. This means that it would be dangerous to store an association that was not reliable. Therefore, habit associations should only be stored after extensive experience with a consistent relation.

In contrast to the planning system, the habit system does not include any consideration of the potential outcome (i.e., there is no *O* term in the $S \xrightarrow{a}$ relation; Table 2). Therefore, in contrast to the planning system, the habit system does not include a prediction of available outcomes and cannot evaluate those potential outcomes online. Hence, it cannot take into account the current perceived needs (desires) of the agent. The habit system is still sensitive to the overall arousal levels of the agent. Thus, a hungry rat will run faster and work harder than a satiated rat (Bolles 1967; Munn 1950; Niv et al. 2007). However, because the habit system does not reflect the current desires of the agent, the habit system will not modify responses when a reward is devalued. Similarly, the habit system cannot select multiple actions in response to a single situation.[9] This means that in navigation, the habit system can only take a single action in response to a given situation. For example, a rat with a damaged planning system cannot decide to turn left for water when it is thirsty on one day and turn right for food when it is hungry on the next day.[10]

Computationally, there are very good models of how the habit system might work. These models have generally been based on the *temporal difference* instantiation of *reinforcement learning* (Daw 2003; Daw et al. 2005; 2006; Dayan et al. 2000; Doya 2000b; Montague et al. 1996; Redish 2004; Schultz et al. 1997; Suri & Schultz 1999; Sutton & Barto 1998). In the simplest version of this model, each situation-action pair is associated with a value (termed $Q(S, a)$; Sutton & Barto 1998).[11] When an agent takes an action from a situation, the agent can compare the expected value of taking action *a* in situation *S* (i.e., $Q(S, a)$) with the observed value (the reward received minus the cost spent plus the value of being in the state the agent ended up in):

$$(1) \qquad \delta = R(t) - C(t) + \gamma \max_a [Q(S_{new}, a)] - Q(S_{old}, a)$$

where $R(t)$ is the reward observed, $C(t)$ the cost spent, $\max_a[Q(S_{new}, a)]$ the most value one can get from the situation the agent finds itself in (S_{new}), and $Q(S_{old}, a)$ is the estimated value of taking action *a* in the situation the agent was in (S_{old}). By updating $Q(S_{\text{old}}, a)$ by δ, the agent moves its estimate $Q(S_{old}, a)$ closer to its true value; γ is a discounting parameter ($\gamma < 1$) which ensures that the time required to reach future rewards is taken into account (Daw 2003; Sutton & Barto 1998). These models can be trained to learn complex situation-action sequences.

The slow development of a habit association has been most studied in contrast to the fast planning system.

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Lesions or inactivation of the dorsolateral striatum (Yin & Knowlton 2004; Yin et al. 2004; Yin et al. 2006) and the infralimbic cortex (Coutureau & Killcross 2003; Killcross & Coutureau 2003) prevent the loss of devaluation with experience. Lesions or inactivation of the dorsolateral striatum (McDonald & White 1994; Packard & McGaugh 1992; 1996; Potegal 1972; White & McDonald 2002; Yin & Knowlton 2004) or the parietal cortices (DiMattia & Kesner 1988; Kesner et al. 1989) shift rats from response strategy to map strategies in navigation tasks.

As in the planning system, the habit system requires a situation-recognition component, in which the set of cues and contexts is integrated with the agent's memory to classify the situation, to allow retrieval of the correct $S \xrightarrow{a}$ association. As with our discussion in the planning system, we suggest that cortical sensory and association systems classify situations through competitive learning processes (Arbib 1995; Grossberg 1976; Redish et al. 2007; Rumelhart & McClelland 1986). Although there are no neurophysiological data suggesting that this situation categorization system is anatomically separate from that used for the planning system, the identification of the habit system with networks involving dorsal and lateral aspects of striatum, and the planning system with networks involving more ventral and medial aspects of striatum, suggest that the specific cortical systems involved may differ. The $S \xrightarrow{a}$ association itself, including the mechanisms by which the situation signals are finally categorized to achieve a single action decision, have been hypothesized to include the afferent connections from cortex to dorsolateral striatum (Beiser et al. 1997; Houk et al. 1995; Samejima et al. 2005; Wickens 1993; Wickens et al. 2003).

Neuropharmacologically, the habit system receives strong dopamine inputs from the substantia nigra pars compacta (SNpc). The dopamine signal has been well studied in the primate (Bayer & Glimcher 2005; Ljungberg et al. 1992; Mirenowicz & Schultz 1994; Schultz 1998; 2002; Waelti et al. 2001). Like the dopamine neurons in the ventral tegmental area, dopamine neurons in SNpc increase firing in response to unexpected increases in expected value (via unexpected rewards or via cues that lead to an increased expectation of reward), and decrease firing in response to unexpected decreases in value (via lack of expected reward or via cues that lead to a decrease in the expectation of reward). This signal has been identified with the value-error signal δ in the temporal difference reinforcement learning algorithm (Barto 1995; Montague et al. 1995; 1996; Schultz et al. 1997), which can provide dopamine a role in training up $S \xrightarrow{a}$ associations. Dopamine has been shown to be critical to the learning of habitual $S \xrightarrow{a}$ associations (Faure et al. 2005). However, the role of dopamine in learning and performance is still controversial (Berridge 2007; Cagniard et al. 2006; Frank et al. 2004; Niv et al. 2007).

Cellularly, neurons in the dorsal striatum have been found to represent key parameters of the temporal difference reinforcement learning algorithm: for example, situation-action associations (Barnes et al. 2005; Carelli & West 1991; Daw 2003; Gardiner & Kitai 1992; Hikosaka et al. 1999; Hikosaka et al. 2006; Jog et al. 1999; Kermadi et al. 1993; Kermadi & Joseph 1995; Matsumoto et al. 1999; Miyachi et al. 1997; Schmitzer-Torbert & Redish 2004; Tremblay et al. 1998); reward delivery (Daw 2003; Schmitzer-Torbert & Redish 2004; White & Hiroi 1998;); and value signals (Daw 2003; Kawagoe et al. 2004; Nakahara et al. 2004). These signals develop in parallel with the development of automated behaviors (Barnes et al. 2005; Itoh et al. 2003; Jog et al. 1999; Samejima et al. 2005; Schmitzer-Torbert & Redish 2004; Tang et al. 2007), through an interaction with dopamine signals (Arbuthnott & Wickens 2007; Centonze et al. 1999; Picconi et al. 2003; Reynolds & Wickens 2002). Functional imaging data from humans playing sequential games show similar correlates to value, δ, and other parameters of these models (McClure et al. 2003; 2004; O'Doherty 2004; O'Doherty et al. 2004; Seymour et al. 2004; Tanaka et al. 2004a).

3.3.1. Potential vulnerabilities in the habit system. The primary failure point of the habit system is the overvaluation of a habit association through the delivery of dopamine (Bernheim & Rangel 2004; Di Chiara 1999; Redish 2004). As with the planning system, a misclassification of the situation can also provide a potential vulnerability in the habit system (see *Vulnerability 6*).

Vulnerability 7: Overvaluation of actions

With natural rewards, once the value of the reward has been correctly predicted, the value-error term δ is zero and learning stops (Rescorla & Wagner 1972; Schultz & Dickinson 2000; Waelti et al. 2001). However, when dopamine is produced neuropharmacologically, sidestepping the calculation of δ, each receipt of the drug induces a positive δ signal, the value associated with taking action a in situation S continues to increase, producing an overvaluation (Redish 2004). Because the $S \xrightarrow{a}$ association is a habitual, automatic association, choices driven by $S \xrightarrow{a}$ relationships will be unintentional, robotic, perhaps even unconscious.

3.4. Interactions between planning and habit systems

Generally, the planning system is engaged early; but with experience, behavioral control in repetitive tasks is transferred to the habit system. This has been observed in the navigation (O'Keefe & Nadel 1978; Packard & McGaugh 1996; Redish 1999), animal conditioning (Balleine & Dickinson 1998; Dickinson 1985; Yin et al. 2006), and human learning (Jackson et al. 1995; Knopman & Nissen 1991; Poldrack et al. 2001) literatures. However, in tasks which require behavioral flexibility, behavioral control can remain with the planning system, even in highly trained animals (Gray & McNaughton 2000; Killcross & Coutureau 2003; McDonald & White 1994; Morris et al. 1982; White & McDonald 2002).

For many tasks, both systems can drive behavior in the absence of the other (Cohen & Squire 1980; Nadel 1994; O'Keefe & Nadel 1978; Squire 1987), but some tasks can only be solved by one system or the other. For example, the water maze requires a flexible response to reach a hidden platform and requires hippocampal integrity to be learned quickly (Morris et al. 1982; for a review, see Redish 1999). If the flexibility of the required response is decreased (by, for example, starting the animal in the same location each trial), then the hippocampus no longer becomes necessary to reach the platform (Eichenbaum et al. 1990). Other tasks, such as mirror-writing or the serial reaction time task, require the slow recognition

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of regularities in situation-action associations, and they are learned at similar speeds by patients with damaged and intact planning systems (Cohen & Squire 1980; Ferraro et al. 1993; Knopman & Nissen 1987). Patients with damaged lateral striatal systems are impaired on these habit-based tasks (Doyon et al. 1998; Ferraro et al. 1993; Knopman & Nissen 1991; Smith et al. 2000; Yin & Knowlton 2006). For some tasks, the planning system can "train up" the habit system, potentially through replay events occurring during subsequent sleep states (Buzsáki 1996; Hoffmann & McNaughton 2002; Marr 1971; Pavlides & Winson 1989; Redish 1999; Redish & Touretzky 1998; Wilson & McNaughton 1994). This transfer of information between systems can explain observations of incomplete retrograde amnesia with certain lesions (consolidation, Cohen & Squire 1980; Nadel & Bohbot 2001; Nadel & Moscovitch 1997; Redish 1999; Squire 1987) but predicts that "consolidated memories" will be less flexible than unconsolidated memories (Redish & Touretzky 1998).

The question of which system drives behavior when the two are put into conflict has only begun to be addressed computationally (Daw et al. 2005) and experimentally (Isoda & Hikosaka 2007), but there is a large literature on *behavioral inhibition*, in which a changed, novel, or potentially dangerous or costly behavior is inhibited (Gray & McNaughton 2000). This system seems to involve the prefrontal (Sakagami et al. 2006) and/or the hippocampal system (Gray & McNaughton 2000), depending on the specific conditions involved. Whether the interaction entails the planning system overriding a developed habit (Gray & McNaughton 2000) or an external system that mediates control between the two (Isoda & Hikosaka 2007) is still unresolved. Whether such an external mediator can be identified with executive control (presumably, in the prefrontal cortex, Baddeley 1986; Barkley 2001; Barkley et al. 2001) is still a matter of open research.

Vulnerability 8: Selective inhibition of the planning system

The habit system is inflexible, reacts quickly, "without thinking," whereas the planning system is highly flexible and allows the consideration of possibilities. The habit and planning systems consist of different anatomical substrates. Pharmacological agents that preferentially impair function in structures involved in the planning system or preferentially enhance function in structures involved in the habit system would encourage the automation of behaviors. A shift back from habits to planned behaviors is known to involve the prefrontal cortex (Dalley et al. 2004; Husain et al. 2003; Isoda & Hikosaka 2007; Iversen & Mishkin 1970), and has been hypothesized to involve executive function (Barkley 2001; Barkley et al. 2001; Tomita et al. 1999). If pre-existing dysfunction exists within the inter-system control or if pharmacological agents disrupt this inter-system control, then the agent would develop habits quickly and would have difficulty disrupting those established habits. This vulnerability is distinguishable from the specific planning and habit vulnerabilities by its disruption of function of the planning system and/or its disruption of the inter-system conflict resolution mechanism. Thus, the other vulnerabilities affecting the planning system lead the planning system to make the incorrect choice; *Vulnerability 8* makes it difficult for the planning system to correct a misguided habit system (Bechara 2005; Bechara et al. 2001; Bickel et al. 2007; Gray & McNaughton 2000; Jentsch & Taylor 1999; Lubman et al. 2004; Verdejo-Garcia et al. 2006).

3.5. Summary: Decision-making systems

The decision-making system in the mammal is hypothesized to consist of two subsystems: a *planning* system, based on the evaluation of potential possibilities (e.g., $S \xrightarrow{(a)} O$ relationships), and a *habit* system, based on the association of specific actions with specific situations (e.g., $S \xrightarrow{a}$ associations), both of which require a *situation-recognition* system, in which observed cues are categorized into situations (e.g., the S terms in the previous formulations). Correct decision-making depends on the integrity of each of these systems (see Figure 1).

3.6. Additional failure points

The eight vulnerabilities identified so far are certainly an incomplete list of the potential failure points of the decision-making system. The description of the decision-making system is, by necessity, incomplete. For example, we have not addressed the question of discounting and impulsivity. Nor have we addressed the question of learning rates.

Vulnerability 9: Over-fast discounting processes

Both the planning and habit systems need to take into account the probability and the delay before an expected goal will be achieved (Ainslie 1992; 2001; Mazur 2001; Stephens & Krebs 1987). In the planning system, this can be calculated online from the expected value of the expected goal given the searched sequence; in the habit system, this would have to be cached as part of the stored value function. The specific mechanism (and even the specific discounting function) are still a source of much controversy (for a review, see Redish & Kurth-Nelson [in press] in Madden et al. [in press]), but the long-term discounting of future rewards is well established. If an agent discounts too strongly, it will overemphasize near-term rewards and underemphasize far-future costs. Because addictions often

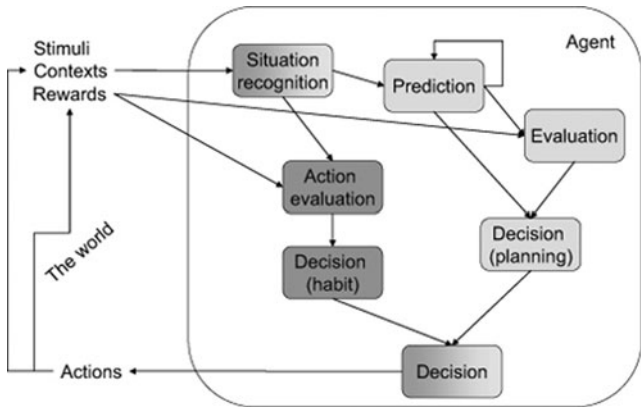


Figure 1. Structure of decision making in mammalian agents. Components of the more flexible, planning-based system are shown in light gray; components of the less flexible, habit-based system are shown in dark gray. Components involved in both are shown in gradient color.

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involve near-term pleasures and far-future costs, faster-than-normal discounting could drive an agent to underestimate the far-future costs and to choose those near-term pleasures. A number of studies have found that addicts discount faster than non-addicts (Alessi & Petry 2003; Bickel & Marsch 2001; Kirby et al. 1999; Madden et al. 1997; Madden et al. 1999; Odum et al. 2002; Petry 2001; Petry & Bickel 1998; Petry et al. 1998; Vuchinich & Simpson 1998).

Vulnerability 10: Changes in learning processes

Other unincorporated components include changes in learning processes (such as over-attention to cues or learning rates being too high or too low). More detailed models of each of the systems will be required before it will be possible to make strong claims about the consequences of such a potential failure point.

However, the hypothesis put forward in this paper that addiction is a consequence of falling victim to vulnerabilities (failure modes) in the decision-making system lays out a research paradigm with important consequences both for what (and how) research questions should be addressed as well as for drug-treatment paradigms and drug-control policies.

These vulnerabilities in the decision-making system may arise from individual predisposition (either due to genetic or social/environmental factors) as well as from drug- or behavior-driven interactions with the decision system. In the second half of this article, we address the interactions and implications of each of the previously identified vulnerabilities with drugs and behaviors of abuse as well as the policy and treatment consequences of the theory.

4. Addiction as vulnerabilities in decision-making

The unified framework for decision-making described above has potential access points through which it can be driven to make maladaptive choices, particularly choices which entail seeking of certain drugs or behaviors. Ten key vulnerabilities can be directly identified with this unified decision-making system as outlined earlier. They are summarized in Table 4 and related to the current theories in Table 5.

Some of these failure modes exist as prior conditions, making an agent more vulnerable to the addictive process, whereas other failure modes are driven by direct interactions with the drugs themselves.

4.1. Vulnerability 1: Deviations from homeostasis

A classic example of deviations from homeostasis that will produce changing needs is the well-known "crash" after the euphoria of an opiate experience (Koob & Le Moal 2006). These negative effects can occur after even a single dose of morphine (Azolosa et al. 1994; Harris & Gewirtz 2005; Koob & Le Moal 2006). Such a negative affect would drive an agent to attempt to compensate by returning to the positive qualia occurring during the drug use. Deviations from homeostasis also lead to the well-known withdrawal symptoms (Altman et al. 1996; Lowinson et al. 1997) seen in reaction to nicotine (Benowitz 1996; Hanson et al. 2003; Hughes & Hatsukami 1986), alcohol (Kiefer & Mann 2005; Littleton 1998; Moak & Anton 1999), opiates (Altman et al. 1996; Koob & Bloom 1988; Schulteis et al. 1997), and caffeine (Daly & Fredholm 1998; Evans 1998) addictions.

4.2. Vulnerability 2: Changes in allostatic set-points

Drug use, particularly repeated drug use, can also produce changes in the set-point itself (referred to as "changes in allostasis," most likely through long-term changes in receptor levels and changes in levels of endogenous ligands released during normal behaviors; Koob & Le Moal 2006). Animals given prolonged access to drugs, particularly access over many days to long periods of drug availability, develop greatly increased drug-intake levels (Ahmed & Koob 1998; 1999). This has been hypothesized

Table 4. *Failure modes in the decision-making system provide a taxonomy of vulnerabilities to addiction*

Failure Point	Description	Key Systems	Clinical Consequence
Vulnerability 1	Moving away from homeostasis	*Planning*	Withdrawal
Vulnerability 2	Changing allostatic set points	*Planning*	Changed physiological set points, craving
Vulnerability 3	Mimicking reward	*Planning*	Incorrect action-selection, craving.
Vulnerability 4	Sensitization of motivation	*Planning*	Incorrect action-selection, craving.
Vulnerability 5	Increased likelihood of retrieving a specific $S \xrightarrow{(a)} O$ relation	*Planning*	Obsession
Vulnerability 6a	Misclassification of situations: overcategorization	*Situation-recognition*	Illusion of control, hindsight bias
Vulnerability 6b	Misclassification of situations: overgeneralization	*Situation-recognition*	Perseveration in the face of losses
Vulnerability 7	Overvaluation of actions	*Habit*	Automated, robotic drug-use
Vulnerability 8	Selective inhibition of the planning system	*System-Selection*	Fast development of habit learning
Vulnerability 9	Overfast discounting processes	*Planning, habit*	Impulsivity
Vulnerability 10	Changes in learning rates	*Planning, habit*	Excess drug-related cue associations

Note. Because *Vulnerability 6* affects the situation S term in both planning and habit systems, we identify it as affecting "situation-recognition." *Vulnerability 8* affects the interaction between the planning and habit systems. *Vulnerabilities 9* and *10* can affect components of the planning and habit systems. Detailed models of the effects of these last two vulnerabilities on the systems are as yet unavailable.

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Table 5. *Relation between identified vulnerabilities and current theories of addiction*

Current Theory		Related Vulnerabilities
Homeostatic changes[a]	Deviations from homeostatic set-points drives the system to restore original homeostatic levels.	*Vulnerability 1*
Allostatic changes[b]	Changes in the homeostatic set-points drives the system to achieve incorrect homeostatic levels.	*Vulnerability 2*
Reward-based processing[c]	Pharmacological access to reward signals drives the return to those signals	*Vulnerability 3*
Incentive-salience[d]	Sensitization of motivational signals drives excess motivation for certain events	*Vulnerability 4*
Unmitigated craving[e]	Increased expectation of reward with experience drives craving	*Vulnerabilities 3, 4*
Noncompensable dopamine[f]	Excess positive value-error signals lead to an over-valuation of drug-seeking	*Vulnerability 7*
The illusion of control[g]	Incorrect expectations of control of situations leads to a willingness to gamble	*Vulnerability 6a*
Impulsivity[h]	Unwillingness to weigh future events leads to impulsive choices	*Vulnerabilities 8, 9*
Decreased executive function[i]	An inability to plan makes it difficult to break habits through cognitive mechanisms	*Vulnerabilities 6b, 8*
Alcohol expectancy theory[j]	Expectance of positive rewards are associated with alcohol consumption. These expectancies develop into automated processes under certain conditions	*Vulnerabilities 3, 8*

[a]Becker and Murphy (1988); Harris & Gewirtz (2005); Koob and Le Moal (2006).
[b]Becker and Murphy (1988); Koob and Le Moal (1997; 2001; 2005; 2006); Solomon and Corbit (1973; 1974).
[c]Kalivas and Volkow (2005); Volkow et al. (2003; 2004); Wise (2004).
[d]Berridge and Robinson (1998; 2003); Robinson and Berridge (1993; 2001; 2003; 2004).
[e]Drummond (2001); Goldman et al. (1987; 1999); Halikas (1997); Hommer (1999).
[f]Bernheim and Rangel (2004); Di Chiara (1999); Redish (2004).
[g]Custer (1984); Griffiths (1994); Langer and Roth (1975); Redish et al. (2007); Sylvain et al. (1997); Wagenaar (1988).
[h]Ainslie (1992; 2001); Ainslie and Monterosso (2004); Bickel and Marsch (2001); Giordano et al. (2002); Odum et al. (2002).
[i]Bickel et al. (2007); Everitt et al. (2001); Everitt and Wolf (2002); Nelson and Killcross (2006); Robbins & Everitt (1999).
[j]Goldman et al. (1987; 1999); Jones et al. (2001); Oei and Baldwin (2002).

to arise from developing allostatic changes (Ahmed & Koob 2005; Koob & Le Moal 2006).

Pharmacologically, chronic nicotine use changes levels of cholinergic receptors in the brain (Flores et al. 1997; Marks et al. 1992). Chronic alcohol use changes function and expression of gamma-aminobutyric acid ($GABA_A$) and N-methyl-D-aspartate (NMDA) receptors (Hunt 1998; Littleton 1998; Valenzuela & Harris 1997). Repeated cocaine (Hurd & Herkenham 1993; Steiner & Gerfen 1998), alcohol (Ciraulo et al. 2003), and opiate (Cappendijk et al. 1999; Weissman & Zamir 1987) treatment all produce changes in endogenous opioid release and in opiate receptor expression. Many smokers titrate the number of cigarettes smoked throughout the day, ensuring a relatively constant blood-plasma level of nicotine (Schmitz et al. 1997).

These neurobiological changes change the identified needs of the agent, and thus imply changes in the evaluation of expected outcomes of drug-taking (or abstinence), which will change action-selection in the planning system.[12] This vulnerability is identifiable by changes in long-term set-points of physiological variables.

4.3. Vulnerability 3: Overvaluation of the expected value of a predicted outcome — mimicking reward

The planning system requires a signal that directly evaluates the successful achievement of a perceived need (thus leading to the qualia of pleasure). A number of authors have suggested that this may reside within the opiate system (Berridge & Robinson 2003; Redish & Johnson 2007). μ-Opiate agonists (such as heroin, morphine, etc.) are generally highly euphorigenic (Jaffe et al. 1997; Mark et al. 2001; Meyer & Mirin 1979). Even though exogenously delivered μ-opiate agonists (such as heroin or morphine) are not a true reward that the system evolved to recognize, they can mimic the reward system and trick the system into believing that it just received a strong reward, which it will learn to return to. Drugs accessing this vulnerability are likely to be highly euphorigenic, particularly with initial use. Heroin and morphine produce profound euphoria very quickly after injection (Koob & Le Moal 2006). This reward signal will be stored in memories associated with the planning system, which would lead to the recall of highly euphoric signals when the planning system recognizes a path to achieve these reward-mimicking drugs. This vulnerability is recognizable by strong craving when agents recall those euphoric events.

4.4. Vulnerability 4: Overvaluation in the planning system

As reviewed earlier, the planning system consists of recognition (memory), search through, and evaluation of

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$S \xrightarrow{(a)} O$ relationships. A fundamental vulnerability of this relationship is in the valuation of the outcome, which is calculated from the level of "need" and the "value" of the outcome satisfying that perceived need, presumably learned through dopaminergic signals (Robinson & Berridge 1993; 2001; 2003; 2004) projecting to the ventral striatum and orbitofrontal cortex. Dopamine firing patterns in the ventral tegmental area (projecting to the ventral striatum and orbitofrontal cortex) indicate changes in the amount of expected or just-received reward (Pan et al. 2005; Roesch et al. 2007; Schultz 2002; Schultz et al. 1997), analogous to the δ signal required for the Q-learning algorithm described in the habit system. Although no computational theories are as yet available describing how these dopaminergic signals translate into changes in evaluation in the planning system, voltammetry recordings from the ventral striatum have shown dopamine signals occurring before both cued and self-initiated actions leading to drug receipt (Phillips et al. 2003; Roitman et al. 2004; Stuber et al. 2004; 2005). These changes presumably modulate the cortico- and hippocampo-ventral-striatal synapses, both during learning (Thomas et al. 2001) and during performance (Goto & Grace 2005a; 2005b; Lisman & Grace 2005; Yun et al. 2004).

Other researchers have suggested that this evaluation process may arise in the orbitofrontal cortex (Padoa-Schioppa & Assad 2006; Plassmann et al. 2007; Schoenbaum et al. 2006a) and that overvaluation in the orbitofrontal cortex can lead to overvaluation of expected rewards (Kalivas & Volkow 2005; Volkow et al. 2003). In rats with a past history of cocaine intake, the orbitofrontal cortex becomes less capable of predicting adverse outcomes than in normal rats (Stalnaker et al. 2006), implying a potential difficulty in identifying negative consequences. Nevertheless, an overvaluation of expected drug outcomes would produce craving (Redish & Johnson 2007) and an increased likelihood of taking actions leading to those expected drug outcomes (German & Fields 2007a).

4.5. Vulnerability 5: Incorrect search of $S \xrightarrow{(a)} O$ relationships

As noted earlier, the prediction component of the planning system is also a memory process, requiring the exploration of multiple consequences from a given situation S. This prediction process has been suggested to require the hippocampus (Jensen & Lisman 1998; 2005; Johnson & Redish 2007) and the prefrontal cortex (Daw et al. 2005), but the specific mechanism is still unknown.

Although the specific mechanisms of storage and access of $S \xrightarrow{(a)} O$ relationships are unknown within the hippocampus and prefrontal cortex, *Vulnerability 5* can occur due to maladaptive and often subtle modifications of system storage and access functions rather than system failure. These systemic modifications may occur as a result of changes in the cell morphology within these areas and plasticity mechanisms within the hippocampus and prefrontal cortex. A number of addictive substances produce such changes. Both hippocampus and prefrontal cortex receive dopaminergic inputs, which are known to change the sensitivity to synaptic plasticity (Huang et al. 1995; Seamans & Yang 2004) and to modulate representations (Kentros et al. 2004; Seamans & Yang 2004) and performance (Arnsten et al. 1994; Murphy et al. 1996). Similarly, morphine and other opiate agonists increase synaptic spine formation in cell culture (Liao et al. 2005) and development (Hauser et al. 1987; 1989). Long-term drug exposure also increases the spine formation in the hippocampus and prefrontal cortex in vivo (Robinson & Kolb 1999; Robinson et al. 2001; 2002). These changes may affect the prediction process, possibly driving it to preferentially search the drug-related potential choices, which would appear clinically as an over-sensitivity to drug-related cues and obsessive consideration of choices leading to drug receipt.

4.6. Vulnerability 6: The illusion of control

When faced with reward distributions that change over time, agents can react in one of two ways: The agent can identify itself as being in a new situation with a different reward distribution, or the agent can identify itself as being in the same situation, but change the expectation of the likelihood of receiving reward. If the agent incorrectly classifies the same situation as different or different situations as the same, the agent may find itself making incorrect decisions.

Misclassification of situations has been primarily identified as a potential cause for problem gambling, in which agents incorrectly identify a statistically unlikely sequence of wins as a separate situation from more-commonly experienced losses (Custer 1984; Langer & Roth 1975; Redish et al. 2007; Wagenaar 1988). This provides the agent with the illusion that certain cues can identify winning situations while other cues identify losing situations (referred to as the "illusion of control"; Langer & Roth 1975; Redish et al. 2007; Sylvain et al. 1997; Wagenaar 1988). Problem gamblers tend to have experienced a statistically unlikely sequence of wins followed by devastating losses (Custer 1984; Wagenaar 1988). This misclassification may arise from excessive recognition of cue changes between the winning and losing experiences (Redish et al. 2007). Problem gamblers are often observed to "explain away" losses by post hoc identification of differences in cues between the losses and memories of wins (also referred to as "hindsight bias"; Custer 1984; Dickerson & O'Connor 2006; Wagenaar 1988). Similarly, near misses, in which gamblers lose but come close to the winning situation, encourage continued play (Parke & Griffiths 2004). These near misses may provide illusory support for the hypothesis that certain noisy cues have a relationship to the predictability of the reward.

4.7. Vulnerability 7: Overvaluation in the habit system

In the habit ($S \xrightarrow{a}$) system, phasic (bursting) dopamine signals are correlated with the value-prediction error signal δ, needed by the temporal difference reinforcement learning algorithm to learn situation-action sequences (Barto 1995; Daw 2003; Montague et al. 1995; 1996). With natural rewards, as the value-prediction system learns to predict those rewards correctly, the value-prediction compensates for the reward, and dopamine at the time of correctly predicted reward decreases to zero with learning (Schultz 1998). Drugs that produce dopamine neuropharmacologically (like cocaine or amphetamine) will bypass that value-compensation system,

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providing a constant "better-than-expected" δ signal. This non-compensable dopamine signal leads to overvaluation in the $S \xrightarrow{a}$ system (Bernheim & Rangel 2004; Redish 2004). Cocaine and many other abused drugs produce large increases of dopamine pharmacologically throughout the striatum (Ito et al. 2002; Kuhar et al. 1988; Roitman et al. 2004; Stuber et al. 2005). This mechanism can lead to the formation of habits, which have been suggested as a key process in late stages of drug addiction (Altman et al. 1996; Di Chiara 1999; Everitt & Robbins 2005; Robbins & Everitt 1999; Tiffany 1990). Clinically, such users would be unlikely to show strong craving and would manifest a robotic drug use, without conscious planning or statements of drug-seeking. Habit-based drug use could well be uncorrelated to the qualia of pleasure.

4.8. Vulnerability 8: Selective inhibition of the planning system

Exposure to drugs can shift the normal balance between systems, emphasizing one system over the other. For example, pretreatment with amphetamine shifts rats to preferentially use systems that do not show devaluation (i.e., habit-based over planning-based systems) (Nelson & Killcross 2006). Alcohol, as another example, has been hypothesized to preferentially impair hippocampal (Hunt 1998; White 2003) and prefrontal (Oscar-Berman & Marinkovic 2003) function, which would shift the normal balance from the planning to the habit systems. Dickinson et al. (2002) found that alcohol-seeking in rats is driven primarily by $S \xrightarrow{a}$ mechanisms and does not show devaluation. Similarly, Miles et al. (2003) found that including cocaine in a sucrose solution prevents devaluation. Such distinctions would appear as a fast increase in habitual responses over planning-based responses.

Following from the hypothesis that prefrontal (executive) systems are involved in the shift from habit back to planning systems (Baddeley 1986; Barkley 2001; Barkley et al. 2001; Dalley et al. 2004; Isoda & Hikosaka 2007), deficits in this executive system would lead to a difficulty in breaking habits (Bechara et al. 2001; Jentsch & Taylor 1999; Lubman et al. 2004). Following from the hypothesis that extinction follows from a reinterpretation of situations (Bouton 2002; Capaldi 1957; Quirk et al. 2006; Redish et al. 2007), this would suggest a difficulty in extinguishing drug-taking. It is certainly possible to extinguish drug-taking in animals (Kalivas et al. 2006; Olmstead et al. 2001), but those extinguished behaviors are particularly susceptible to relapse and reinstatement (McFarland & Kalivas 2001; Shalev et al. 2002). Whether it is more difficult to extinguish some drug-taking behavior in certain agents due to selective inhibition of the planning system or excitation of the habit system is still unknown. Agents falling victim to this vulnerability would show a particularly strong, uncontrolled relapse, likely cue-dependent, and possibly independent of explicitly identified cravings.

4.9. Vulnerability 9: Overfast discounting

As reviewed earlier, there is strong evidence that addicts discount faster than non-addicts (Bickel & Marsch 2001; Reynolds 2006). An important question that is still unresolved is whether these faster discounting factors exist as preconditions or develop with experience. Impulsivity shows a strong heritability that has been hypothesized to underlie a pre-existing factor in addiction (Kreek et al. 2005). Impulsivity has been identified with changes in neuromodulators, particularly serotonin[13] (Chamberlain et al. 2006); changing serotonin levels can lead to online changes in discounting rates (Schweighofer et al. 2004; Tanaka et al. 2004b). (Computationally, serotonin has been explicitly modeled as controlling the discounting factor in temporal-difference learning; Doya 2000a; 2002.) Many drugs of abuse, such as cocaine, directly affect serotonin levels (Paine et al. 2003; Ritz et al. 1987), while in other substances, such as alcohol, self-administration levels reflect serotonin levels (Chastain 2006; Valenzuela & Harris 1997). It is currently unknown whether the excess discounting seen in addicts is a pre-existing condition or a consequence of the addictive process itself (Reynolds 2006). As with many of these vulnerabilities, it is possible to have a positive feedback, in which pre-existing conditions support the entrance to addiction (Kreek et al. 2005; Perry et al. 2005; Poulos et al. 1995), and then post-addictive consequences arising from pharmacology or experience exacerbate it (Paine et al. 2003).

4.10. Vulnerability 10: Changes in learning rates

The decision-making system reviewed earlier depends on learning associations among situations, outcomes, and actions. These systems depend on specific learning rates. Neuromodulators such as acetylcholine and dopamine have been hypothesized to control learning rate parameters (Doya 2000a; 2002; Gutkin et al. 2006; Hasselmo 1993; Hasselmo & Bower 1993; Yu & Dayan 2005). Pharmacological substances that manipulate these learning rates can produce enhanced associations, leading to overdeveloped expectations or habits. For example, nicotine enhances the presence of already available phasic dopaminergic signals in vitro (Rice & Cragg 2004). Following from a hypothesized role of phasic dopamine signals in identifying high-value associations to be stored (Montague et al. 1996; Schultz et al. 1997), this would predict that nicotine would enhance small learning signals, further increasing the likelihood of making cue-related associations. Although there is as yet no direct evidence for a general role of nicotine in learning, if nicotine did generally enhance learning signals, this would make smokers particularly susceptible to cue-driven associations (Chiamulera 2005). Multiple drugs taken simultaneously may interact with each other, and drugs may interact with natural rewards as well.

5. Drugs and the taxonomy of vulnerabilities

The 10 vulnerabilities listed here provide a taxonomy of potential problems with decision processes.[14] Because neuromodulators (such as acetylcholine, serotonin, norepinephrine, and dopamine) are involved throughout the decision-making system (learning $S \xrightarrow{a}$ relations, storing and evaluating $S \xrightarrow{(a)} O$ relations, recognition of situations S, etc.), drugs of abuse are unlikely to access only one subsystem. Because there are differences in these vulnerabilities, any specific drug is also unlikely to access all 10 vulnerabilities. Because behavioral control involves the entire decision-making systems, behavioral

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problems such as gambling are likely to arise from an interaction of vulnerabilities. Although each vulnerability can drive an agent to return to the addictive choice, each vulnerability also produces a characteristic symptomology and can thus be separately identifiable within an agent.

Different drugs are likely to access different vulnerabilities. For example, whereas opiates are generally euphorigenic on initial use (Koob & Le Moal 2006; *Vulnerability 3*), nicotine is often dysphoric on initial use (Heishman & Henningfield 2000; Perkins 2001; Perkins et al. 1996; making *Vulnerability 3* unlikely). However, continued use of nicotine can produce strong allostatic changes (Benowitz 1996; Koob & Le Moal 2006; *Vulnerability 2*), which produce a very strong need to return levels to normal (Fiore 2000). Nicotine also produces increases in the firing of dopaminergic neurons (Balfour et al. 2000; Dani & Heinemann 1996; Pidoplichko et al. 1997), which suggests that it can also accesses the $S \xrightarrow{a}$ overvaluation vulnerability (*Vulnerability 7*). Cocaine use automates particularly quickly (Miles et al. 2003) and produces a very strong cued relapse (Altman et al. 1996; Childress et al. 1992; 1993; O'Brien et al. 1992), suggesting that it also accesses the $S \xrightarrow{a}$ overvaluation vulnerability (Redish 2004; *Vulnerability 7*), presumably through its direct effects on dopamine (Kuhar et al. 1988; Ritz et al. 1987; Stuber et al. 2004; 2005). However, chronic cocaine use can also produce long-term changes in μ- and κ-opiate receptor levels (Shippenberg et al. 2001), suggesting it can also access the allostatic vulnerability (*Vulnerability 2*). The appendix provides more details on drugs and the potential vulnerabilities involved with each.

5.1. Individual vulnerabilities

One of the main thrusts of addiction research right now is the question of why some people become addicted and some do not (Deroche-Gamonet et al. 2004; Koob & Le Moal 2006; Tarter et al. 1998; Volkow & Li 2005b). These individual differences arise from an interaction between the genetics of the individual, the development environment (social and physical), the developmental stage of the individual, and the behavioral experience with the addictive substance (Koob & Le Moal 2006; Kreek et al. 2005; Volkow & Li 2005a; 2005b). Laying out the complete details of individual vulnerabilities are beyond the scope of this article (and are in large part still unknown), but the multiple-vulnerabilities hypothesis put forward here suggests a plan of attack to the problem. Addiction research has been historically aimed at problems with a single drug (e.g., nicotine, heroin, alcohol, etc.) or at unifying parameters across drugs (e.g., the role of dopamine). The multiple-vulnerabilities hypothesis suggests that we should look, instead, at the potential vulnerabilities within the natural learning system.

These vulnerabilities are likely to depend on a number of specific individual parameters. For example, imagine an individual who was particularly sensitive to rewards and punishments. That individual would be more susceptible to *Vulnerability 3* in which a drug of abuse produced a euphorigenic signal. Imagine an individual who was more likely to treat a slightly new situation as new. Such an individual would be more susceptible to *Vulnerability 6* in which wins and losses are not matched. Or imagine an individual in which the effect of nicotine on dopamine was increased. Such an individual would receive a strong dopamine kick with each puff of a cigarette and become particularly vulnerable to *Vulnerability 7*. Perhaps, in some individuals, nicotine produces excessive dopamine release (*Vulnerability 7*), leading to a habit-like addiction, whereas in others, nicotine produces allostatic changes (*Vulnerability 2*), leading to a maintenance-of-levels addiction. Other individuals may have neither of these vulnerabilities, leaving them more resistant to becoming addicted to nicotine.

5.2. Interactions among vulnerabilities

The failure points identified here are not mutually exclusive; they can co-occur. For example, excess dopamine delivered simultaneously to the ventral striatal regions (hypothesized to be involved in the planning system), to the dorsal striatal regions (hypothesized to be involved in the habit system), and to the frontal cortices and hippocampus (hypothesized to be involved in situation-categorization mechanisms) could drive an individual into a host of vulnerabilities. Increased dopamine in the planning system has been hypothesized to lead to increased motivational salience (Robinson & Berridge 2001; 2003; 2004; *Vulnerability 4*). Increased dopamine to the habit system has been hypothesized to lead to overvaluation of $S \xrightarrow{a}$ associations (Bernheim & Rangel 2004; Redish 2004; *Vulnerability 7*). Increased dopamine to the situation-categorization system has been hypothesized to change the stability of categorization systems (Redish et al. 2007; Seamans & Yang, 2004; *Vulnerability 6*). Thus, a single effect of a single drug can access multiple failure points.

Drugs can also produce multiple effects, which can lead to multiple vulnerabilities all leading to maladaptive decisions. For example, cocaine, amphetamine, and methamphetamine pharmacologically block the dopamine transporter (Kuhar et al. 1988; Ritz et al. 1987) leading to increases in dopamine in the ventral striatum (Stuber et al. 2005), but long-term exposure also leads to changes in dopamine receptor levels (Letchworth et al. 2001; Porrino et al. 2004a; 2004b), to a decrease in dopamine release caused by other mechanisms (Martinez et al. 2007), and to changes in long-term depression (LTD) and long-term potentiation (LTP) in ventral (Thomas et al. 2001) and dorsal (Nishioku et al. 1999) striatum. But long-term exposure to cocaine also produces changes in opioid-receptor distributions (Shippenberg et al. 2001). Each of these effects can lead to an agent falling victim to a different vulnerability, which can lead to separate mechanisms driving maladaptive decisions.

Similarly, nicotine has multiple access points throughout the brain (Ikemoto et al. 2006). Repeated nicotine use can lead to allostatic changes in response to the flooding of the system with cholinergic agonists (Benowitz 1996; Koob & Le Moal 2006), but it also leads directly to dopamine release (Pidoplichko et al. 1997), increases the effect of glutamatergic inputs to the ventral tegmental area (Mansvelder & McGehee 2000), and strengthens the effect of already present phasic dopaminergic signals (Rice & Cragg 2004). This combination of vulnerabilities could lead to the subject falling victim to *Vulnerability 2* (allostasis), to *Vulnerability 7* (overvaluation in the habit

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system), and to *Vulnerability 10* (increased learning rates of drug-related cues) simultaneously. Treatment of only the allostatic component (such as through nicotine replacement therapy, Hanson et al. 2003; Rose et al. 1985) would not treat the simultaneous problem arising from the other vulnerabilities.

The fact that these vulnerabilities can interact implies interactions between drugs which can lead to polydrug abuse. Drugs may be synergistic in their effects on a single vulnerability or they may involve multiple vulnerabilities simultaneously. Cocaine and heroin both affect the opiate system, and allostatic changes made in response to one drug may affect the neurobiological response to another (Leri et al. 2003). Nicotine enhances already present dopaminergic signals (Rice & Cragg 2004), thus the presence of nicotine (potentially changing learning rates, *Vulnerability 10*) may enhance the ability of other drugs to drive dopamine-produced overvaluation in the planning (*Vulnerability 4*) or habit systems (*Vulnerability 7*). Similarly, amphetamine can sensitize cue-driven motivational signals (Wyvell & Berridge 2000), which may explain some of the interaction between cocaine and methamphetamine addiction and sexual behavior (Schneider & Irons 2001). Our theory suggests that polydrug abuse arises from the same causes as drug abuse: Interactions between the agent's environment (drugs, cues, and experience) and the agent's internal decision-making system (genetics, planning, and habit systems) lead to the agent falling victim to vulnerabilities in the decision-making system, leading to the continued use of problematic drugs and behaviors.

We are not the first to suggest that decisions to take drugs or to gamble can arise as a consequence of multiple processes. These multiple-process theories are generally discussed in terms of a transition sequence from more cognitive, "planned" processes to less cognitive, more "automatic" processes. For example, Everitt and Robbins (2005) suggest a transition sequence of "actions to habits to compulsion." Oei and Baldwin (2002) suggest a transition in alcohol consumption from a controlled process to a more automatic habit-based process.

In contrast, it is our contention that there are many paths through these vulnerabilities. It is not always a transition from flexible planning strategies to automated habitual strategies.

Animal experiments have found numerous methods through which animals can appear to lose control over drug-taking, including escalation due to extended exposure to drug availability (Ahmed & Koob 1998; 1999; 2004; 2005; Vanderschuren & Everitt 2004), incubation by separation after exposure to drugs (Bossert et al. 2005; Grimm et al. 2001), relapse due to stress (Shaham et al. 2000; Shalev et al. 2000), relapse due to reinstatement (de Wit & Stewart 1981; McFarland & Kalivas 2001), and even that susceptibility time-courses can change between individuals due to unknown (potentially genetic) factors (Deroche-Gamonet et al. 2004; Goldman et al. 2005; Hiroi & Agatsuma 2005; Ranaldi et al. 2001).

Agents can show addictive decisions through vulnerabilities in planning systems or through vulnerabilities in habit systems or through vulnerabilities in the interaction between them. Our suggestion is that there are many vulnerabilities in the decision-making system and thus many ways for an agent to become addicted. This means that there are many transition sequences as well.

5.3. Transitions

Clinically, the transition to addiction is usually described in terms of three stages: initial exploratory or trial use, subsequent maintenance of drug use associated with the beginning of strong desires (craving), followed in some users by a strong, habitual use in which the user loses control of the drug use (Altman et al. 1996; Everitt & Robbins 2005; Kalivas & Volkow 2005; Lowinson et al. 1997; Oei & Baldwin 2002; Robbins & Everitt 1999). This sequence can be described as a path through the vulnerabilities of the decision systems: once the drug or behavior has been sampled, it will be repeated due to euphorigenic, pharmacological, or socially positive effects. Euphorigenic effects will drive repeated use due to associated reward signals (*Vulnerability 3*). Pharmacological effects will drive repeated use due to fast homeostatic changes (*Vulnerability 1*). It is also possible for drugs that are not euphorigenic to be driven by associated socially positive associations, such as has been hypothesized for tobacco (Bobo & Husten 2001; Cummings 2002), alcohol (Bobo & Husten, 2001; Goldman et al. 1987; 1999), and caffeine (Greden & Walters 1997), which we might categorize under *Vulnerability 3*. However, repeated use will lead to potentiation of the $S \xrightarrow{(a)} O$ relationship in the planning system (*Vulnerability 4*) and to the development of allostatic changes (*Vulnerability 2*), which will lead to strong desires and craving. With sufficient habitual use, actions leading to drug use can become over-valued in the habit system through increased value associated with an $S \xrightarrow{a}$ relationship (*Vulnerability 7*). This sequence parallels many examples of normal learning, proceeding from ventral to dorsal striatal systems (Balleine & Dickinson 1998; Everitt et al. 2001; Haber et al. 2000; Letchworth et al. 2001; Packard & McGaugh 1996).

This sequence will not be followed by all individuals or via all drugs of abuse. The timeline with which individuals make these transitions from vulnerability to vulnerability likely depends on a complex interaction between the genetics, development, and drug experience of the individual. We do not expect all addicts to take the same path through this maze of vulnerabilities.

Just as different tasks entail different interactions between planning and habit systems (some tasks entail transitions from planning to habit, other tasks always require the planning system, other tasks require the habit system, and other tasks can entail transitions from habit to more flexible planning systems), we expect different agents (with different genetics, different experiences, etc.) to take different paths through these vulnerabilities. In addition, just as some tasks entail an overlaying of automated habit-like strategies on top of planning-based strategies (e.g., Packard & McGaugh 1996), treating the habit-based vulnerability of a patient may uncover earlier planning-based vulnerabilities. Other agents can show addictive decisions through vulnerabilities in habit or interactive systems without ever passing through planning systems. It is also possible that habit-based addictive decisions may shift to planning-based addictive decisions (e.g., when obstacles are put into place). We argue that,

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in order to understand and treat the issue of addiction, we need to know not only where the patient is in his or her trajectory through these vulnerabilities, but also which vulnerability (vulnerabilities) the patient has fallen victim to.

5.4. Relapse

The fundamental issue with addiction is that of *relapse*, which can be defined as drug-seeking or the making of the addictive choice, even after a period of abstinence.

Relapse has been studied both clinically by measuring populations remaining abstinent from drug use and in animals identifying the return to responding for drug after forced removal (extinction, forced abstinence). In humans, relapse can occur after re-exposure to the drug, to cues associated with drug-taking and drug-seeking, and to stress (Self & Nestler 1998; Shalev et al. 2002). Relapse to behavioral addictions (such as gambling) has not been studied in the same detail, but we have suggested that gambling addiction may be related to the reinstatement of responding seen after extinction of normal rewards (Redish et al. 2007, see also Bouton 2002; 2004). In animals, a return to responding can occur due to acute re-exposure to the drug, to cues associated with drug-taking and drug-seeking, and to stress (Bossert et al. 2005; Kalivas et al. 2006; Shaham et al. 2003). The validity of the reinstatement paradigm as a model of abstinence and relapse is still controversial (Kalivas et al. 2006; Katz & Higgins 2003); nevertheless, the reinstatement paradigm can provide an understanding of mechanisms by which relapse could occur (Epstein & Preston 2003).

All of the vulnerabilities noted earlier can potentially drive relapse to the addictive behavior, but the path to relapse will differ depending on the vulnerabilities involved.

For example, relapse driven via homeostatic needs (*Vulnerability 1*) should occur through the natural time-course of the homeostatic change. Relapse driven through allostatic needs (*Vulnerability 2*) can be driven by changes in physiological set-points, driven in part by cues or by circadian or other rhythmic changes. The natural time-course of these changes can be seen in some smokers who show a circadian time-course of craving (Benowitz 1996; Perkins 2001; Schmitz et al. 1997). Allostatic set-points driving expectation can also be cue-driven (Ehrman et al. 1992; Hunt 1998; Meyer & Mirin 1979; Siegel 1988). Experienced users can show preparation tolerance with cues associated with heroin (Meyer & Mirin 1979; O'Brien et al. 1977; Siegel 1988). Similarly, alcohol users show fewer coordination deficits under the influence of alcohol in alcohol-associated environments (such as bars) than in non-alcohol-associated environments (such as offices) (Hunt 1998). A number of authors have suggested that relapse under stress may be due to cue-driven deviations from homeostatic set-points (Ahmed & Koob 1997; Shaham et al. 2000; Shalev et al. 2000; Weiss et al. 2001).

Relapse caused by expectation (overvaluation in the planning system, *Vulnerabilities 3* and *4*) can be identified by "craving." Such relapse can be triggered by a recall of an $S \xrightarrow{(a)} O$ association, in which the agent recognizes an action-sequence that can get the agent from the situation the agent is currently in (S) to an over-valued outcome (O). The recognition can be cue-driven or may arise spontaneously, but in either case will entail an expectancy of the outcome. As noted earlier, correct decision-making within the planning component requires a search of multiple possibilities. It is likely that once a pathway to a highly valued outcome is recognized, the search will keep returning to that possibility, producing *cognitive blinding* and *obsession* (*Vulnerability 5*). Both craving and obsession are common to pre-relapse conditions in some (but not all) patients (Altman et al. 1996; Childress et al. 1988; Grant et al. 2006; MacKillop & Monti 2007; O'Brien 2005; Sayette et al. 2000).

Note that our theory predicts that craving should be clinically separable from relapse: Because the planning system is flexible, recognition of a path to an outcome (in our theory, craving is recognition of a path to a high-valued outcome) does not necessarily lead to taking that path. Thus, craving can occur without relapse. Because the habit system does not include recognition of an outcome, in our theory, it does not produce craving. Thus, relapse caused by overvaluation in the habit system (*Vulnerability 7*) may be robotic, without craving, perhaps without even conscious recognition (Everitt & Robbins 2005; Robbins & Everitt 1999). (Retrospectively, the addict may believe he or she craved the drug, whether or not any actual craving occurred prospectively; Sayette et al. 2000.)

Multiple vulnerabilities can cause a relapse to the addictive choice, but the pathway to that relapse may be different, depending on the vulnerability involved. Therefore, prevention of relapse will also depend on treating the vulnerabilities involved.

5.5. Treatment

Each vulnerability drives the decision-making process towards the addictive choice and provides a potential access-point for the addiction to relapse, but each vulnerability is a different failure-point of the decision process and leads decision-making to error through a different mechanism. Thus, each vulnerability is likely to require a different treatment regimen. This concept (of different treatments for different vulnerabilities) has enjoyed some recent success and been used to explain historical treatment failures. For example, in a recent study (Grant et al. 2006), significant success was found in treating a subset of pathological gamblers that showed strong urges (craving). Irvin and colleagues (Irvin & Brandon 2000; Irvin et al. 2003) suggest that the well-documented decreasing success of smoking cessation in tobacco studies is due to the presence of available over-the-counter cessation-aid products and thus a changing distribution of smokers participating in the studies.

Treatment of the homeostatic deviations and allostatic changes in nicotine through nicotine replacement therapy has been extremely successful (Balfour & Fagerström 1996; Benowitz 1996; Hanson et al. 2003; O'Brien 2005; Rose et al. 1985). However, long-term relapse after these treatments is notoriously high (Balfour & Fagerström 1996; Hanson et al. 2003; Monti & MacKillop 2007). This is likely a consequence of the fact that nicotine replacement therapy does not address the other vulnerabilities involved in nicotine addiction (e.g., *Vulnerability 7*).

Treatment of the planning vulnerabilities (*Vulnerabilities 3, 4*, and *5*), which lead to excess expectation of

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positive outcomes (see above) and may be identifiable through craving and obsession (Redish & Johnson 2007), may depend on blocking the misevaluation process. Opiate antagonists have been used to reduce craving in alcohol addictions (Kiefer & Mann 2005; O'Brien et al. 1996) and in gambling (Grant et al. 2006). Many heroin abusers on naltrexone report no craving (Meyer & Mirin 1979; O'Brien 2005, but see Halikas 1997 for another view). Whether this is due to controlling allostatic effects (Koob & Le Moal 2006) or to the blocking of craving and the recognition of future rewards (O'Brien 2005) is still unresolved. Naltrexone treatment of cocaine addicts failed to find a significant effect on craving (Schmitz et al. 2001). It is clear that there is still work to be done to completely elucidate the specific relationship among clinically tested treatments, the qualia identified as craving, and the potential vulnerabilities identified in this article.

Treatment of each vulnerability requires a regimen specifically designed to address that vulnerability. For example, the homeostatic and allostatic vulnerabilities (*Vulnerabilities 1* and *2*) likely require pharmacological treatment to rebalance the system. Overvaluation in the planning system (*Vulnerabilities 3*, *4*, and *5*) likely requires treatment to change the recall and re-evaluation processes, either through pharmacological means or through cognitive behavioral re-training, or some combination of the two. Overvaluation and over-strengthening in the habit system (*Vulnerabilities 7* and *8*) likely require mechanisms with which to strengthen alternative choices available in the planning system. Miscategorization of situations (*Vulnerability 6*) likely requires treatments aimed at executive function and its role in re-categorizing situations. Although we have not proposed specific treatments for any of these vulnerabilities, it is our contention that these failure modes are treatable and that treatments aimed at these specific modes are more likely to be successful than general treatments aimed at the general addicted population.

In general, we propose that the clinical treatment of addiction should not be addressed to the general addicted population, or to specific drugs of abuse. Instead, we propose that treatment should first entail the identification of which vulnerabilities have been triggered within the individual, and then treatment should be addressed to the specific constellation of vulnerabilities into which the addicted patient has fallen.

6. Future work is still needed

The thesis of this review is that addiction arises from vulnerabilities inherent in the decision-making system within the brain. Susceptibility to these vulnerabilities arises through an interaction among the genetics of the individual, the development environment, the social milieu, and the behavioral experience of the individual. We have outlined several vulnerabilities that arise from current theories of the mammalian decision-making system. However, it is important to note that the understanding of that decision-making system is still incomplete.

Exactly what differentiates the planning and habit systems is still being debated (e.g., Daw et al. 2005; Dayan & Balleine 2002; Redish & Johnson 2007). Detailed computational models of the habit system have been developed (Montague et al. 1996; Samejima et al. 2005; Suri & Schultz 1999, but see Berridge 2007, for an alternate view), including how those systems could produce addiction-like behavior (Bernheim & Rangel 2004; Redish 2004). But computational models of the planning system are still in their earliest stages (Daw et al. 2005; Johnson & Redish 2005; Zilli & Hasselmo, 2008). How these systems interact to produce behavior is still unknown.

A number of open questions still remain. For example, the decision-making theories discussed in this article are primarily about reinforcement (delivery of unexpected reward) and disappointment (non-delivery of expected reward). The role of aversion (delivery of punishment) and relief (non-delivery of expected punishment) in these decision-making systems is still unresolved. Negative symptoms clearly play important roles in addiction (Gawin 1991; Jaffe 1992; Koob & Le Moal 2001; 2005; 2006; O'Brien et al. 1992). How to incorporate those negative symptoms beyond homeostatic (*Vulnerability 1*) and allostatic (*Vulnerability 2*) effects is still unclear. Detailed decision-making models in the face of aversion and relief may help elucidate these issues. The fear-conditioning and extinction literature (Domjan 1998; Myers & Davis 2002; 2007) and the roles of the amygdala (Paré et al. 2004; Phelps & LeDoux 2005; Rodrigues et al. 2004) and prefrontal cortex (Milad & Quirk 2002; Quirk et al. 2006) therein are likely to be important starting points for these models.

Similarly, the key parameters that underlie individual differences are still unknown, including whether those key parameters are genetic, environmental, or some combination thereof (Kreek et al. 2005; Volkow & Li 2005b). Models of decision-making can provide candidate variables that may vary across the population, which may change susceptibilities to specific vulnerabilities and would lead to individual reactions to drugs of abuse or potentially addictive behaviors.

The key social definition of a problem addiction relates to the cost to the individual and to society of the addiction. Whereas methamphetamine addiction is a terrible burden on society and thus leads to extreme measures taken to prevent it, caffeine addiction leads to a minor inconvenience to an individual and little or no burden on society. In part, we believe that these differences arise from the different vulnerabilities impacted by these drugs. Problem gambling is often classified as an addiction due in large part to the extreme costs paid by "addicted" individuals. Whether other behaviors, such as shopping or Internet use, should be counted as addictions is an open question (Holden 2001). In this article, we have proposed a new framework for understanding addiction. This new framework provides a new definition of addiction itself as decisions made due to failure modes in the decision-making system. How serious each failure mode is, whether it should be treated, and how it should be treated, are clinical and policy issues that need to be addressed in the future.

The list of vulnerabilities laid out in this target article are certainly incomplete. There are likely to be other processes beyond decision-making that can drive errors, including errors in probability recognition (Kahneman et al. 1982), different responses to gains and losses (Kahneman & Tversky 2000), and errors in memory itself (Schacter 2001). We have not fully explored the potential interactions between the decision-making vulnerabilities, nor have we

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fully explored the interaction between decision-making vulnerabilities and other memory-based errors.

Clinically, we cannot yet relate these potential vulnerabilities to other action-selection and decision-making disorders such as obsessive-compulsive disorder, Tourette's syndrome, depression, mania disorders, anxiety disorders, impulsivity disorders, and so on. However, we believe that the paradigm laid out in this article (taking a basic-science understanding of action-selection and decision-making and identifying failure modes) is likely to be fruitful for understanding many other psychiatric disorders beyond addiction.

More importantly, however, we do not yet have specific clinical instruments with which to identify the presence or absence of each vulnerability within an individual, nor do we have specific clinical treatments (pharmacological, behavioral, or otherwise) to suggest. Our hope, however, is that the framework laid out in this article and the identification of these vulnerabilities can lead to research aimed at identification and treatment.

More work elucidating an understanding of the mammalian decision-making system is clearly needed, but we believe that the current understanding of this system can already illuminate addictive processes. It is our belief that an interaction between basic science research on decision-making, basic science research on the neurophysiological effects of addictive substances and behaviors, and the clinical consequences of addiction will illuminate both processes and will provide new avenues for the treatment of addiction.

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APPENDIX

The vulnerabilities hypothesis laid out in this target article provides a taxonomy of addictive processes. This means that it should be possible to characterize the effects of drugs of abuse (and problematic behaviors) in terms of these vulnerabilities in the decision-making system. In this appendix, we address the clinical and neurophysiological effects of known drugs of abuse in the light of the vulnerabilities identified in the text: cocaine and psychostimulants (A), opiates (B), nicotine (C), alcohol (D), and caffeine (E). Finally, we discuss problem gambling (F).

A. Cocaine and the psychostimulants

The primary neurobiological effect of cocaine and the psychostimulants is to produce large increases of dopamine pharmacologically, by blocking dopamine reuptake (cocaine, Chen et al. 2006; Kuhar et al. 1988; Ritz et al. 1987)[15] or releasing dopamine-containing vesicles (amphetamine, Sulzer et al. 2005). These can be measured quantitatively throughout the dorsal and ventral striatum, and continue to appear, even after cocaine is well predicted (Ito et al. 2002; Roitman et al. 2004; Stuber et al. 2005). This dopamine release bypasses the brain's computational systems, which direct when and how dopamine should be released (Schultz 1998; 2002). This non-compensable dopamine release (Di Chiara 1999) has been hypothesized to lead to an overvaluation within the habit system (Bernheim & Rangel 2004; Redish 2004; *Vulnerability 7*). However, cocaine also leads to dopamine release in the ventral striatum (Ito et al. 2000; Roitman et al. 2004; Stuber et al. 2005), which can lead to development of overvaluation in the planning system as well (*Vulnerability 4*).

Cocaine intake also produces transient euphoric highs (Balster 1973; Gold 1997; Volkow et al. 2003), which implies a component that can mimic reward (*Vulnerability 3*), followed by a very strong post-high crash (Gawin 1991; Koob & Le Moal 2006), which may imply a role of homeostatic mechanisms (*Vulnerability 1*). One potential issue is that psychostimulants can enhance performance of simple tasks and are sometimes used in reaction to fatigue and boredom (Koob & Le Moal 2006), again implying a potential vulnerability in the relief of homeostatic deviations (*Vulnerability 1*). With repeated use, users become tolerant to dosages and the subjective high becomes harder to reach with a given dose (suggesting a role for allostasis, Koob & Le Moal 2006; *Vulnerability* 2).

Cocaine craving is extremely cue-sensitive, in that cues associated with cocaine use lead to strong cravings (Childress et al. 1988; 1992; O'Brien et al. 1992), involving memory circuits including the hippocampus, ventral striatum, and orbitofrontal cortex (Childress et al. 1999; Garavan et al. 2000; Grant et al. 1996; Volkow et al. 2003). These circuits are key components of the planning system and suggest an involvement of excess $S \xrightarrow{(a)} O$ associations, possibly driven by dopamine in the limbic structures (implying a role for *Vulnerabilities 4* and *5*). However, cocaine craving can be separated from drug-seeking behavior (Dudish-Poulsen & Hatsukami 1997), suggesting that, for some patients, drug-seeking depends on the non-craving-producing vulnerabilities. Anecdotal descriptions suggest the presence of cue-induced "robotic" relapse in the absence of identified craving (Altman et al. 1996, implying a role for *Vulnerability 7*).

Some researchers have found that cocaine-seeking is goal-directed (Olmstead et al. 2001), implying an involvement of the planning system (*Vulnerabilties 1* to *5*). However, cocaine and amphetamine have long been associated with motor stereotypies associated with habit-system structures such as the dorsal striatum (Johanson & Fischman 1989; Koob & Le Moal 2006), implying an involvement of *Vulnerability 7*. Other researchers have found that prior treatment with amphetamine can lead to a faster development of automated behaviors, even during navigation and food-seeking (Nelson & Killcross 2006; O'Tuatheigh et al. 2003), implying an involvement of *Vulnerability 8*. That many vulnerabilities are accessed by cocaine may be one of the reasons why successful treatment has been so elusive.

B. Opiates

Opiates have been noted as a drug of choice since ancient times (Koob & Le Moal 2006). Modern opiates include the processed forms of the opium poppy, including opium, morphine, heroin, meperidine (Demerol), oxycodone (OxyContin), and codeine. Abused opiate drugs are all strong agonists of the μ-opioid receptor (Jaffe et al. 1997; Negus et al. 1993; van Ree et al. 1999), in contrast to drugs that have strong κ-agonist properties (Jaffe et al. 1997).

Five components of the reaction to opioid intake have been identified (Koob & Le Moal 2006): a euphoric rush of intense pleasure, often characterized by analogy to sexual orgasm, followed by a general feeling of well-being, followed then by a detached, separated state which can include virtual unconsciousness, and finally, a fade back to an appearance of normality. This is then followed by a fifth, highly dysphoric withdrawal state (Jaffe et al. 1997; Koob & Le Moal 2006).

The presence of the intense euphorigenia suggests a relationship to *Vulnerability 3*. The development of tolerance and the presence of a withdrawal state suggest a potential implication of *Vulnerability 2*. The fact that the withdrawal can occur after only a single use (Azolosa et al. 1994; Harris & Gewirtz 2005; Koob & Le Moal 2006) suggests the presence of homeostatic

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changes (*Vulnerability 1*) as well as long-term allostatic changes (*Vulnerability 2*). However, relapse can also occur well after all identified withdrawal symptoms have subsided (Shalev et al. 2002).

One potential explanation for relapse long after obvious withdrawal symptoms have faded is changes in expectations arising from associations with environmental stimuli (Meyer & Mirin 1979). Homeostatic expectation can also be cue-driven (Ehrman et al. 1992; Meyer & Mirin 1979; Siegel 1988). Experienced users can show preparation tolerance with cues associated with heroin (Meyer & Mirin 1979; O'Brien et al. 1977; Siegel 1988). However, opiate addicts are not generally described as "robotic" (Altman et al. 1996), and opiate addiction generally involves a strong craving component (Meyer & Mirin 1979). These data suggest that the environmental stimuli are more related to $S \xrightarrow{a} O$ associations, rather than $S \xrightarrow{a}$ associations, implying a stronger involvement of the planning system (*Vulnerabilities 4* and *5*) than of the habit system (*Vulnerability 7*).

Many studies have reported that heroin delivery leads to dopamine activity in vitro (Johnson & North 1992) and dopamine release in the accumbens shell in vivo (Caillé & Parsons 2003; Hemby et al. 1995; Kiyatkin 1994; Kiyatkin & Rebec 1997; Tanda et al. 1997; Wise et al. 1995; Xi et al. 1998). Although cocaine and psychostimulants always increase dopamine levels in the nucleus accumbens and striatum, no matter how well predicted (Stuber et al. 2005), Hemby et al. (1995) have reported that heroin only increases dopamine in unpredicted conditions. This finding, however, has not been replicated by other labs (Caillé & Parsons 2003; Wise et al. 1995; Xi et al. 1998) which have found that heroin self-administration does increase dopamine levels in the nucleus accumbens. Kiyatkin and Rebec (1997; 2001) report an increase in dopamine in the nucleus accumbens on initiation of self-administration, in preparation for self-administration, and in response to presentation of a heroin-associated cue, but a sudden drop in response to the actual delivery of heroin during self-administration maintenance. This sequence is very similar to that seen in the lever-press for food (Kiyatkin & Gratton 1994; Schultz 1998; 2002), but very different from cocaine (Roitman et al. 2004; Stuber et al. 2005). Kiyatkin (1994) also reports that passive delivery of heroin led to long-term increases in dopamine similar to that reported by Hemby et al. (1995). Recently Georges et al. (2006) found no effect of morphine on dopamine cells in vivo in morphine-dependent rats. We suggest that re-examining these data in light of the hypothesized roles of the dopamine and opiate systems (Berridge & Robinson, 1998; 2003; Montague et al. 1996; Redish, 2004; Redish & Johnson 2007; Schultz 1998; 2002; and see target article earlier) may be fruitful, and we believe that these data suggest that opiate addiction is not likely to involve *Vulnerability 7*.

C. Nicotine

Nicotine is the primary addictive substance in tobacco products, including cigarettes, as well as smokeless tobacco products (Schmitz et al. 1997). Nicotine is extremely addictive, with a very large proportion of teenagers who sample cigarettes eventually succumbing to long-term regular use (Russell 1990). The neurobiological effects of nicotine are well reviewed elsewhere (Benowitz 1996; Koob & Le Moal 2006) and therefore not reviewed here. Nicotine treatment has primarily been through prevention education (Fiore 2000; Schmitz et al. 1997) and nicotine replacement therapy (Balfour & Fagerström 1996; Benowitz 1996; Hanson et al. 2003; O'Brien 2005; Rose et al. 1985). However, replacement therapy is susceptible to relapse (Balfour & Fagerström 1996; Fiore 2000; Hanson et al. 2003), and current treatments are becoming less successful over time, possibly due to differences in the population still smoking (Irvin & Brandon 2000; Irvin et al. 2003).

Nicotine is, however, dysphoric on initial use (Heishman & Henningfield 2000; Perkins 2001; Perkins et al. 1996). Thus, it is unlikely to access *Vulnerability 1* or *Vulnerability 3*. However, attitudes towards nicotine products can drive positive views of use, which may lead to social pressures that can support initial usage (Cummings 2002).

Nicotine also leads to very large changes in allostatic levels of acetylcholine, dopamine, and other neuromodulators (Flores et al. 1997; Koob & Le Moal 2006; Marks et al. 1992), which would access *Vulnerability 2*. These allostatic effects may be due to changes in levels of cholinergic receptors in the brain (Flores et al. 1997; Koob & Le Moal 2006; Marks et al. 1992). Deviations from allostatic levels lead to very powerful withdrawal effects (Schmitz et al. 1997), which presumably reflect changes in the perceived needs of an agent, which would lead to strong cravings aimed at restoring those deviations. These deviations can be seen in a daily cycle in the reaction to the initial cigarette of the day (Perkins et al. 1996). It is likely that nicotine replacement therapy can affect these allostatic levels, which may suggest that replacement therapy is treating *Vulnerability 2*.

However, nicotine increases the activity of dopamine neurons through the activity of nicotinic acetylcholine receptors on dopamine neurons (Mansvelder & McGehee 2002; Pidoplichko et al. 1997). In addition, nicotine increases the effectiveness of associated dopaminergic signals (Rice & Cragg 2004). These effects could lead to non-compensable value-prediction-error signals (Redish 2004), which would suggest that nicotine use is likely to access *Vulnerability 7*. This vulnerability would lead to excess cue-related triggers. Nicotine shows a particularly high cue-related susceptibility to relapse (Chiamulera 2005; Kenny & Markou 2005; LeSage et al. 2004). Extinction and behavioral treatments potentially aimed at *Vulnerability 7* have had limited success so far (Monti & MacKillop 2007; Schmitz et al. 1997). Providing valuable alternatives has had some success (Higgins et al. 2002).

D. Alcohol

Alcohol has long been identified as a drug of abuse, and it may be one of the first drugs to have been regularly abused by humans (Goodwin & Gabrielli 1997). The neurobiological effects of alcohol are well reviewed elsewhere (Hunt 1998; Koob & Le Moal 2006; Valenzuela & Harris 1997) and hence not reviewed here. Alcohol has extensive neurobiological effects, both in terms of acute effects on membrane lipids and on ion channels as well as long-term changes in expression of $GABA_A$ and NMDA receptors (Hunt 1998; Littleton 1998; Valenzuela & Harris 1997). This may be indicative of allostatic changes (*Vulnerability 2*). Supporting these hypotheses, alcohol intake leads to very strong withdrawal symptoms (Goodwin & Gabrielli 1997; Hunt 1998), both in terms of acute intake (e.g., a hangover, Swift & Davidson 1998, suggesting an involvement of *Vulnerability 1*) and after chronic, long-term intake (Saitz 1998, suggesting involvement of *Vulnerability 2*).

Much of the theoretical drive behind an understanding of alcohol addiction has arisen from the relationship between cognitive expectancies and alcohol consumption ("alcohol expectancy theory"; Goldman et al. 1987; 1999; Jones et al. 2001). These expectancies can be related to the "if-then" cognitive component of the planning system. Thus, early consumption can be due to positive expectations in the planning system (*Vulnerability 3*). There is a strong interaction between alcohol and the endogenous opioid systems (Herz 1997). Some success has been found from pharmacological treatment with opioid antagonists such as naltrexone in alcoholic subjects, particularly in reducing craving (O'Brien et al. 1996; Sinha & O'Malley 1999). Alcohol addiction shows a strong cue-driven craving and desire (Childress et al. 1993; Hunt 1998; MacKillop & Monti 2007; Sinha & O'Malley 1999), suggesting involvement of the planning system. Alcohol users show fewer coordination deficits under the influence of alcohol in alcohol-associated environments (such as bars) than in non-alcohol-associated environments (such as offices), suggesting a cue-driven preparation due to

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expectation of alcohol intake (Hunt 1998). However, Dickinson et al. (2002) found that alcohol intake did not show devaluation even when a comparably trained food-reward did, suggesting a developing involvement of the habit system. Some theories of alcohol consumption have been explicitly tied to the transition from cognitive to automatic learning (Oei & Baldwin 2002). Neurobiologically, the effects of heavy drinking are concentrated on hippocampal and prefrontal cortical function (Devenport et al. 1981a; Hunt 1998; Oscar-Berman & Marinkovic 2003; White 2003), which may lead to an imbalance between the planning and habit systems (*Vulnerability 8*).

Genetic effects on alcoholism have been well studied (Dick et al. 2006; Herz 1997; Stewart & Li 1997), in particular, in the relationship between genes involved in negative consequences of drinking alcohol (Nurnberger & Bierut 2007). Not surprisingly, people who experience more negative consequences during early drinking experiences are less likely to become addicted to alcohol (Goldman et al. 1999).

Alcohol addiction is clearly a spectrum disorder, with a wide variety of paths to dependence (Nurnberger & Bierut 2007). Alcohol intake stimulates dopaminergic neurons in the ventral tegmental area (VTA) and substantia nigra; however, these effects are dependent on the intermediate release of opioid peptides (Di Chiara 1997). It is an interesting (and open) question whether the dopamine release due to alcohol intake is more akin to the non-compensable effect of cocaine (Stuber et al. 2005, suggesting influence of *Vulnerability 7*; Redish 2004) or to the compensable effect of food (Schultz 1998, suggesting influence of *Vulnerability 3*; Redish & Johnson 2007).

E. Caffeine

Although caffeine is often not treated as a typical drug of abuse (Koob & Le Moal 2006), and is not regulated legally at this time, it does have strong psychopharmacological effects and has been identified as leading to a measurable drug-dependence (Daly & Fredholm 1998; Evans 1998; Greden & Walters 1997). The most noticeable affect of caffeine related to abuse is the well-identified caffeine withdrawal syndrome (Evans 1998; Nehlig 1999), which can last for several days once caffeine intake has been stopped. However, after that, there is a very low level of subsequent relapse, and neither craving for caffeine nor robotic automatic caffeine-ingestion behaviors appear. Subjects showing strong withdrawal symptoms are significantly more likely to self-administer caffeine than subjects not showing strong withdrawal symptoms, suggesting that the re-establishment of homeostasis underlies much of the caffeine addiction. This suggests that the primary effect of caffeine is due to easily reversible homeostatic (*Vulnerability 1*) or allostatic (*Vulnerability 2*) effects. Evidence suggests that large doses of caffeine can lead to dopamine release in both accumbens and caudate nucleus, but only in doses much higher than typically seen in human consumption (Nehlig 1999; Nehlig & Boyet 2000). This suggests that caffeine is unlikely to access the other vulnerabilities, which may explain the ease with which caffeine intake can often be stopped.

F. Gambling

Although gambling does not entail direct pharmacological manipulation of the decision-making system, it has been suggested to share many properties with the pharmacological addictions (Dickerson & O'Connor 2006; Potenza et al. 2001), in large part because it entails obvious (and often explicitly acknowledged) problematic decision-making (Dickerson & O'Connor 2006; Potenza 2006; Raylu & Oei 2002; Toneatto et al. 1997; Walker 1992a). Because the primary argument of our unified framework is that addiction entails vulnerabilities in decision-making, we argue that pathological gambling can also be explained within this framework.

The key to pathological gambling has been suggested to lie in distortions in estimates of the value of certain decisions. Agents in general show deficits and distortions in probability estimates, particularly in the difference between probabilities of wins and losses in the face of noisy variables (Dickerson & O'Connor 2006; Griffiths 1994). These deficits may lead to the process known as the "illusion of control" in which agents believe they can control probabilistic situations due to a miscalculation of predictability relationships between cues and outcomes (Langer & Roth 1975; Sylvain et al. 1997). This can lead to "hindsight bias," in which gamblers explain away losses through the back identification of differential cues (Custer 1984; Wagenaar 1988). A number of researchers have argued that these may be the key to the process of "chasing" in which gamblers try to recapture losses by risking larger and larger gambles (Dickerson & O'Connor 2006; Lesieur 1977; Wagenaar 1988). These descriptions suggest that a large part of the gambling addictive process is due to *Vulnerability 6* (Redish et al. 2007).

As noted by Parke and Griffiths (2004), an effective way to create a near miss in a gambling context is to manipulate the "trail" by which the gambler completes the process (Dickerson & O'Connor 2006). This can provide the user with additional cues to identify the situations categorized, providing the user with (incorrect) support for the hypothesis that there is a controllable sequence of situations, which, if the gambler could only control correctly, would lead to the win. Over the last several decades, manufacturers have changed lottery cards, video poker, and slot machines to add additional complexity, providing additional variables and additional cues (Dickerson & O'Connor 2006; Parke & Griffiths 2004), which would increase the likelihood of misclassification of situations (Redish et al. 2007).

This classification component plays a role in both the planning and the habit components, and therefore, we can expect gamblers to potentially show key aspects of the planning or the habit systems or both. Gamblers with problems associated with inputs to the planning system may show the signs of planning system deficits, including explicit expectations, craving, and complex, planned behaviors. Gamblers with problems associated with inputs to the habit system may show a more robotic, less self-recognized gambling behavior. Whether these differences translate to differences in preferred games is unknown but may be a testable avenue for future research.

The opiate antagonists naltrexone (Potenza et al. 2001) and nalmefene (Grant et al. 2006) are effective in the short-term treatment of gambling addiction, but only in subjects with strong gambling urges (i.e., craving, thus suggesting an involvement of the planning system over the habit system). No effective treatment has yet been found for pathological gamblers who do not show strong urges (i.e., suggesting a primary involvement of the habit system over the planning system).

Whether other vulnerabilities (such as an over-release of dopamine with monetary wins) can also lead to pathological gambling is still unknown, but a number of researchers have suggested that there are multiple pathways to pathological gambling (Dickerson & O'Connor 2006).

NOTES

1. Some literatures have suggested that the value used is subjective value or subjective expected utility, in which the expected value is modified by (usually concave) functions (Glimcher & Rustichini 2004; Kahneman & Tversky 2000; Kahneman et al. 1982). Although this can explain changes in risk-seeking and risk-aversion, it does not have a major effect on the failure-points proposed in this article. Other literatures have suggested an importance of additional parameters such as risk and uncertainty (Hastie 2001; Preuschoff et al. 2006; Rapoport & Wallsten 1972).

2. The farther an event is in the future, the more likely it is that unexpected events can disrupt the predicted event (Sozou 1998; Stephens & Krebs 1987). Thus, the farther an event is in

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the future, the more potential there is for error and the less value one should assign to the event. The reward value of future events should therefore be discounted as a function of the time before reward is expected to be received. Additionally, the more quickly one receives a reward, the more one can invest it, presumably providing a positive return (whether in terms of money, energy, or offspring) – again, providing for the necessity of a discounting function (Frederick et al. 2002; Stephens & Krebs 1987). See Madden et al. (in press) for review.

3. The route system has also been termed the *taxon* system (O'Keefe & Nadel 1978; Schöne 1984) or the *response* system (Packard & McGaugh 1992; Poldrack & Packard 2003).

4. The S-A system has been termed the S-R (stimulus-response) system (Dickinson 1985; Domjan 1998; Hull 1943; 1952), but we prefer to use the term $S \xrightarrow{a}$, which prevents confusion with R as indicating reward. In addition, much of the psychology literature is phrased in terms of "stimulus" rather than "situation," but we prefer the term *situation* because that indicates the recognition of context, cue, and interactions between cues, all of which are critical for appropriate behavior. In the machine learning literature, "situation" is referred to as "state" (Daw et al. 2006; Sutton & Barto 1998), but we prefer the term *situation* because in other literatures, "state" refers to internal parameters of the agent (e.g., "motivation states"; Domjan 1998). The categorization of situation includes both internal and external parameters.

5. Because actions selected via $\xrightarrow{a} O$ associations only occur within a context, they too contain situation *S* components and should probably also be identified as $S \xrightarrow{a} O$. Contexts can be differentiated from cueing stimuli in that contextual information changes slowly relative to the time-course of action-selection, whereas conditioning stimuli change quickly. Thus, contextual stimuli cannot be seen as driving actions, but actions are still only taken from within identified situations. We do not explore this issue further here, but note that our concept of situations includes categorizations derived from both contextual and driving stimuli.

6. The role of δ-opiate receptors is more controversial (Broom et al. 2002; Herz 1997; Matthes et al. 1996).

7. German and Fields (2007a; 2007b) have shown that conditioned place preference (Tzschentke 1998) is in fact due to repeated transitions into the drug-associated location, implying that conditioned place preference is evidence of drug-seeking.

8. This inability to recategorize situations' vulnerability will also relate to the interaction-between-systems vulnerability (*Vulnerability 8*), below.

9. It is possible for internal states (e.g., hunger) to be incorporated into the situation *S* term, but this would require separate learning under the different internal-state conditions (e.g., under hungry and thirsty conditions) without generalization.

10. This inability is seen in rats with fimbria-fornix lesions (Hirsh 1974).

11. This version in which value is a function of both situation and the subsequent action is called Q-learning (Sutton & Barto 1998). Other instantiations have been proposed as well. However, the differences are subtle and not critical to our needs in this paper. We therefore only describe the very basics of Q-learning.

12. Although the habit system does not directly take the immediate needs of the agent into account, it is possible that continued positive evaluation of drug-taking (or negative evaluation of abstinence) due to the changed-needs vulnerability could slowly train up the habit system, leading to a shift in drug use from the compulsive, needs-based vulnerability to a more robotic, habit-based vulnerability, independent of changes in homeostatic or allostatic set-points.

13. Other neuromodulators may be involved as well.

14. There are certainly going to be other problems that have not yet been identified, but these 10 can provide a starting point for this discussion.

15. Note that cocaine similarly blocks reuptake of norepinephrine and serotonin through blockage of their respective transporters (Ritz et al. 1987); however, the behavioral/addictive consequences of these effects are not known.

Open Peer Commentary

The origin of addictions by means of unnatural decision

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Abstract: The unified framework for addiction (UFA) formulated by Redish et al. is a tour de force. It uniquely predicts that there should be multiple addiction syndromes and pathways – a diversity that would reflect the complexity of the mammalian brain decision system. Here I explore some of the evolutionary and developmental ramifications of UFA and derive several new avenues for research.

The postulation of a complex decision system (i.e., with multiple subparts and subprocesses) for explaining addictive and other apparently irrational behaviors has some precedents. In most previous models, however, decision systems were almost invariably modeled by two subsystems in conflict with each other. For instance, Thaler and Shefrin (1981) modeled "the individual as an organization" with two coexisting selves, a "myopic doer" and a "farsighted planner." (For a recent neural instantiation of this two-self model, see McClure et al. 2004.) In these dual decisional models, addiction arose when the myopic doer won the competition against the planner for behavioral control, thereby defining only one single pathway to addiction (i.e., from future-oriented, goal-directed actions to blind habits). What is original in Redish et al.'s unified framework for addiction (UFA) is that there is no winner, no loser. Each decision subsystem has its own specific potential failure points or vulnerabilities, each leading to a specific addiction symptom when accessed by a drug or behavior. Multiple simultaneous or sequential interactions among these vulnerabilities would then generate a wide diversity of possible addiction syndromes and/or transitions. Thus, according to UFA, addiction should be a spectrum disorder whose phenotypic diversity reflects the complexity of the mammalian brain decision system. This new link between brain decision system complexity and addiction diversity has several interesting evolutionary and developmental ramifications. Most of them, however, are almost completely ignored in the target article. In this commentary, I highlight those with special relevance for future research in the field.

First, the divergent evolution of the complexity of mammalian brain decision systems implies that the diversity of possible addictions should vary between different species, in general, and between nonhuman mammals and humans, in particular. Interestingly, the component of the brain decision system with the highest number of potential failure points – the planning subsystem – is also the component that has diverged the most in mammalian evolution. Planning for the far future – which depends on an intact and fully developed prefrontal cortex – has long been, and still is, thought to set humans apart from other animals, including mammals (e.g., Baumeister & Heatherton 1996; Searle 2001; Suddendorf & Corballis 2007). Although more research is needed to better define the planning abilities

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of nonhuman mammals, current evidence nevertheless clearly indicates that they are "stuck in time" (Roberts 2002). For instance, rats or mice – the most frequently used animal models for human addictions – do plan for the immediate future in a goal-directed manner (Dickinson & Balleine 1994), but they are incapable of generating and maintaining long-term goals. The profound divergence in planning between nonhuman mammals and humans should somehow constrain the "addiction space" that the former could explore compared to the latter. To take an extreme example, imagine an agent endowed with a situation-recognition subsystem and a habit subsystem but no planning subsystem (and thus no higher-order subsystem that coordinates the activity of the whole). According to UFA, this myopic agent should be exposed to only three decisional vulnerabilities (i.e., *Vulnerabilities 6*, *7*, and *10*) and, therefore, should be affected by a restricted subset of addictions (i.e., habit-like addiction). Therefore, a critical goal for future research using UFA will be to identify among the actual spectrum of addiction syndromes affecting modern humans the syndromes that are unique to humans and those that are common, *ceteris paribus*, with other animals with less complex decision systems. This research has obvious implications for the current status and future development of animal models of human addictions and, *in fine*, for the neurobiology of addictions, which is still largely based on animal research.

Second, as the brain decision system evolves between species, it also develops within a single individual. In view of its complexity, however, it is highly unlikely that all of the different subparts of the brain decision system will depend on the same developmental programs and thus will develop at the same pace. For instance, the planning subsystem of humans develops more slowly than the habit subsystem (e.g., Blakemore 2008; Ernst et al. 2006). Humans until late in adolescence are shortsighted planners who depend heavily on parental and/or societal foresight. The differential development of each subpart of the brain decision system implies that not all potential decisional failure points will be accessible during the same developmental stage. As a result, the age of onset of drug use is expected to affect the diversity of addiction syndromes and/or transitions that can affect a developing individual. An important challenge for future research will be to determine how the addiction spectrum varies with the age of onset of drug use and how this variation is correlated with the differential development of each subpart of the brain decision system. Alternatively, drug use may also interfere with the proper development of the brain decision system. Thus, drugs of abuse could not only distort or subvert the normal function of a fully developed decision substructure, as conceptualized by UFA, but also retard or even accelerate its development per se. This would change the number of decisional vulnerabilities accessible at each developmental stage and, therefore, the spectrum of addiction pathways. Future research is clearly needed to add developmental dynamics into UFA.

Finally, I would like to stress that although UFA is no doubt an important step toward a unified neurobiological theory of addiction with interesting evolutionary and developmental ramifications, it still falls short of explaining choices between *different kinds* of rewards that are inherent to drug use and addiction. A recent series of controlled choice experiments from our laboratory provides a particularly vivid illustration of this important limitation (Lenoir et al. 2007). Rats with a long history of intravenous cocaine self-administration were allowed to choose between two different actions: one action was rewarded by intravenous cocaine, the other by a brief access to water sweetened with saccharine or sucrose. Previous research has established that prolonged cocaine self-administration accesses most of the decisional vulnerabilities identified in UFA, including vulnerabilities *2* (Ahmed et al. 2002; 2005), *4* (Paterson & Markou 2003), *5* (Ahmed & Cador 2006; Mantsch et al. 2004), and *7* (Ahmed et al. 2003). Thus, according to UFA, with repeated choice, most chronically cocaine-exposed rats should rapidly develop a strong preference for the cocaine-associated action. Contrary to this prediction, however, we consistently found that virtually all rats preferred the sweet sensation over the artificial sensation of cocaine, a preference that was not surmountable by increasing cocaine doses (Lenoir et al. 2007). The discovery that taste sweetness surpasses cocaine reward, even in cocaine-sensitized rats with a long history of cocaine self-administration, represents a serious anomaly, not only for UFA but also for each of the separate neurobiological theories of addiction that it has unified. This anomaly does not necessarily invalidate UFA, however; it may indicate that the decision-making models on which UFA is based are largely incomplete. Specifically, these models were essentially built from data obtained in choice studies involving different dimensions of the *same kind* of reward (e.g., delay, amount, and probability). They are therefore not well adapted for predicting the outcome of choice between rewards as different in kind as a drug reward and a taste reward. Alternatively, this anomaly could also indicate that, as suggested earlier in the context of evolution, rats cannot constitutively develop all the addiction syndromes that may affect humans. More research on choices between drug and non-drug rewards is required here to resolve this anomaly.

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Vulnerabilities to addiction must have their impact through the common currency of discounted reward[1]

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Abstract: The ten vulnerabilities discussed in the target article vary in their likelihood of producing temporary preference for addictive activities – which is the phenomenon that puzzles conventional motivational theory. Direct dopaminergic stimulation, but probably not the other vulnerabilities, may contribute to the necessary concavity of addicts' delay discounting curves, as may factors that the senior author analyzes elsewhere. Whatever their origins, these curves can themselves account for temporary preference, sudden craving, and the "automatic" habits discussed here.

Any or all of the ten vulnerabilities in Redish et al.'s innovative analysis may have a role in addicts' decisions. It is an admirable structure, but this rich menu of potential mechanisms needs to be seen in perspective. Whatever else is true of them, addictive behaviors are goal-directed and usually effective. The final common path of all these vulnerabilities has to be motivation, even modest changes of which can significantly affect addictive choices (Becker et al. 1992; Olmstead et al. 2007). And the best-established property of this motivation is that it is relatively short-term. Each vulnerability needs to be examined as a possible explanation, entire or partial, specifically for the temporary amplification of short-term relative to long-term motivation that induces temporary preference for the addictive activity.

The search for explanations is complicated by the fact that short-term rewards' intermittent dominance of greater long-term rewards extends beyond the identified addictions. Addictions are not a circumscribed set of activities, just the most conspicuous or harmful examples of a broad human tendency to

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develop habits that lure us into continuing them even while we are trying to break them. Some addictions may indeed be due to the physiological properties of a substance, but these must ride on top of whatever general principle makes any rapidly rewarding activity a mixed blessing. Some serious examples do not involve substances – not only gambling (Appendix F) but credit abuse and various kinds of thrill seeking – and some others involve normal substances that we evolved to ingest: Food is a prevalent example. Both kinds of temptation shade over into trivial but unwelcome habits such as drinking too much coffee (Appendix E) or watching a particular kind of TV show. All such choices must have brain mechanisms, of course – there are no disembodied motives – and associated brain processes are being observed in increasing detail; but the brain processes that are observed during addictions are not necessarily different from the processes that govern every choice we make. Even opiates may not "mimick" rewards (*Vulnerability 5*, sect. 3.2.1) but *be* rewards, useless as far as adaptivity goes, but for hedonic purposes only different from other rewards in their power, speed, and (consequent?) long-term failure. Which vulnerabilities can explain preference reversal?

Of the eight that the authors discuss, the most likely candidates for explaining short-term amplifications of motivation are *Vulnerabilities 4* and *7*, those that involve the distortion of error-prediction, in planning and habit systems, respectively, by the direct action of dopaminergic drugs on striatal structures (e.g., Robinson & Berridge 2001). Such action has been observed by several methods, as he reviews. The resulting property of being "wanted but not liked" is clearly an example of temporary preference – "a motivational magnet" (Berridge 2007), but this effect has so far been reported for only short periods of time. It is not known whether this effect changes motivation long enough to affect the value of a weekend coke binge, for instance. And this mechanism would govern only agents that directly elevate dopamine.

Vulnerabilities 1 and *2* describe changes in the value of addictive activities and their alternatives as a result of past or current addictive activity. Evidence for a long-lasting attenuation after taking some agents is strong (Volkow et al. 2002), and addicts often mistake this "grayness" of life for a bleak normality without their drug (my own clinical observation), but this remains a factor both when they are deciding to relapse and when they are deciding not to. By the authors' own account, *Vulnerability 3* seems to involve the genuine (opioid-mediated) pleasurability of some activities, which does not set them apart from motivated activities in general.

Vulnerabilities 5 and *6* involve selective attention to, or interpretation of, contingencies of reward. This selection is motivated. There is no reason to suppose that this kind of "fooling yourself" occurs differently in addictions than, say, in the overly positive belief in others' approval of you or in feelings of efficacy over random events, which all non-depressed subjects seem to develop (e.g., Alloy & Abramson 1979). As a practice that increases current good feeling at the expense of realism, this selective interpretation is itself a relative of the addictions, and itself needs explanation.

As for *Vulnerabilities 8* and, again, *7*, the existence of a habit system distinct from a planning system is certainly well established, but "mindless" would have always been a better term than "automatic" (or "robotic," sect. 3.3.1) for the behaviors it governs. The latter terms imply an ability to override contrary motivation, whereas this selective principle is actually observed to give way to the planning system whenever a choice is subject to conflicting motives. This mechanism seems likely to be limited to those addictions that cause brain damage. Behaviors that persist despite punishment have elicited similar explanations over the years – for example, Freud's "repetition compulsion" (1920/1956) and Watson's "conditioned responses" (1924) – but a motivational explanation is needed.

Vulnerability 10 is basically a space to be developed. Thus, a substantial amount of explanatory work will still have to be done by *Vulnerability 9*. Redish et al. mention only a high rate of discounting (sect. 3.6), but it is the hyperbolic or at least hyperboloid shape of a person's discount curve that predicts she will overvalue rewards only temporarily (Ainslie 1992; 2005). The review the authors cite analyzes possible mechanisms for the hyperboloid shape of people's discount functions (Redish & Kurth-Nelson, in press, in Madden et al., in press), but makes it clear that the hyperboloid shape itself is robust. Whatever its roots, hyperboloid discounting can account for not only overvaluation of imminent rewards but also for two additional phenomena relevant to addictions. First, the sudden cravings that are evoked by mere reminders of past consumptions, which are inadequately explained by linear applications of either hyperbolic discounting theory or conditioning theories, may come from a recursive self-prediction process in which a random increase in a person's subjective probability of relapse increases craving, increased craving increases the probability of relapse, and so on (Ainslie, in press, same volume).

Second, any complex goal-seeking process involves setting up intermediate goals, which become game-like occasions for an emotional reward such as joy, relief, or self-congratulation (Ainslie 1992, pp. 339–43). Then the prospect of a great "score" of a drug will have the same rewarding power as a great score in sports, despite a desire to limit consumption, as will the chance for a restrained eater to neatly finish off a container of food. The rewards for any lifestyle consist of much more than the external rewards that the lifestyle has arisen to obtain. The additional emotional or "game-like" rewards can maintain the activities set up by the lifestyle for long after the ostensible rewards have changed in value – hence the big lottery winners who continue to travel by bus and save grocery coupons. Such a process is more likely than mindless automaticity to underlie consciously unwanted drug-copping habits.

The same potential for game-like reward might be the basic motivating principle of the non-substance addictions, which otherwise have scant rationale in the vulnerabilities discussed here. To the extent that people can anticipate occasions for emotion, they are apt to have the emotion prematurely – the way that familiar scenarios become mere daydreams – and learn to avoid this mainly by making somewhat unpredictable events the occasions for emotional reward, that is, broadly speaking, by gambling (Ainslie 2001, pp. 168–74). This tactic is often adaptive when applied to human relationships and attempts at personal accomplishment, but it can be diverted into short term rewardingness (addictiveness) by finding bets that are won or lost quickly – bets that include but are by no means limited to gambling in the sense of the word that the authors use (Appendix F).

Dopaminergic agents possibly aside, temporary preference comes from the general properties of discounted reward.

NOTE

1. The author of this commentary is employed by a government agency, and as such this commentary is considered a work of the U.S. government and not subject to copyright within the United States.

Addiction, procrastination, and failure points in decision-making systems

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Abstract: Redish et al. suggest that their failures-in-decision-making framework for understanding addiction can also contribute to improving

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our understanding of a variety of psychiatric disorders. In the spirit of reflecting on the significance and scope of their research, I briefly develop the idea that their framework can also contribute to improving our understanding of the pervasive problem of procrastination.

Starting from the idea that addiction involves "the continued making of maladaptive choices, even in the face of the explicitly stated desire to make a different choice" (target article, sect. 1), Redish et al. seek to develop a unified framework for addiction by (1) focusing on research concerning action selection and decision making, and (2) identifying failure points in our decision-making system. As they suggest, this approach may be fruitful for understanding not just addiction, but a variety of psychiatric disorders. I suspect that they are correct, and I want to develop a somewhat different but related suggestion, namely, that their approach can contribute to an improved understanding of the pervasive problem of procrastination.

Although procrastination is more common than addiction, it can figure as a crucial obstacle to realizing intentions to quit engaging in harmful addictive behavior. This fits neatly with the plausible conception of procrastination according to which it involves putting off an action that one should, given one's ends and information, perform promptly.

Even more so than addiction, which is still popularly cast as, at least in part, the product of powerful cravings that disable agents from acting voluntarily and in accordance with their decisions, procrastination is generally assumed to be the product of voluntary choices, and so the failures-in-decision-making approach that Redish et al. employ in their work seems particularly appropriate with respect to understanding procrastination. What better place to look for an understanding of self-defeating but voluntary delays than in research on failure points in our decision-making system?

The most established model of procrastination connects procrastination to problematic discounting processes (O'Donoghue & Rabin 1999a; 1999b; 2001), which is one of the vulnerabilities that Redish et al. discuss in their work. Like other animals, humans seem to discount future utility in a way that sometimes prompts preference reversals (Ainslie 2001; Kirby & Herrnstein 1995; Millar & Navarick 1984; Solnick et al. 1980). This can result in an agent's voluntary acting in a way that he or she planned against and will come to regret. The agent may, for example, keep making exceptions to his or her ongoing plan to cut down on indulgent purchases in order to save money for retirement. Discounting-induced preference reversals can thus foster procrastination.

A recent, complementary model of procrastination focuses on another vulnerability, one that is not directly discussed by Redish et al. but fits very well with their approach, namely, our vulnerability to intransitive preferences (Andreou 2007). Intransitive preferences (where, in particular, one cannot rank a set of options from most preferred to least preferred because there is a circularity in one's preferences) are often prompted by choice situations in which indulgences with individually negligible effects (such as smoking a cigarette) have momentous cumulative effects. Consider an agent who enjoys smoking but also values decent health. Someone in this situation may prefer, for all n, quitting after $n + 1$ cigarettes to quitting after n cigarettes, but also prefer quitting after a relatively low number of cigarettes to quitting after a very high number of cigarettes. This agent has intransitive preferences, and is vulnerable to intransitivity-induced procrastination (Andreou 2005).

Other interesting ideas concerning procrastination might fit comfortably within and be illuminated by Redish et al.'s framework. Consider, for example, the familiar idea that procrastination may be prompted by fear of failure, which may, in different cases, be the product of different vulnerabilities. For example, in some cases, fear of failure may result from the overvaluation of the expected value of stability; while in other cases, it may result from excessively (and perhaps obsessively) focusing on one possible outcome rather than appropriately distributing one's attention over the range of outcomes associated with a situation.

Consider next the idea that procrastination is strongly associated with the pursuit of "ephemeral pleasures" and "ephemeral chores" (Silver & Sabini 1981). Ephemeral pleasures and ephemeral chores are often more immediately gratifying or at least less aversive than the goal-directed actions that are called for by long-term projects. Moreover, ephemeral pleasures and ephemeral chores are often individually compatible with one's long-term projects, though they can accumulate in a way that interferes with these projects. These points suggest a connection between procrastination mediated by the pursuit of ephemeral pleasures and ephemeral chores, on the one hand, and problematic discounting processes or intransitive preferences, on the other.

The vulnerabilities I have been focusing on are vulnerabilities in the planning system, which is only one part of our decision-making system. As Redish et al. stress, problematic decisions can also result from vulnerabilities in the habit system or from vulnerabilities in the interaction of the planning system and the habit system. In the case of procrastination, it seems clear that planning-based vulnerabilities can foster habit-based vulnerabilities as well. If, for example, one's intransitive preferences prompt one to repeat individually negligible but cumulatively destructive actions, a habit-based vulnerability may flourish atop one's planning-based vulnerability. Soon enough, automatic indulgence will replace rationalized indulgence.

Relatedly, coping with procrastination often involves dealing with both planning-based vulnerabilities and habit-based vulnerabilities. Again, consider the agent whose intransitive preferences prompt intransitivity-induced procrastination. Once the agent's problematic indulgences are supported by habit as well, overcoming procrastination will involve (1) dealing with the planning system failure by, for example, adopting a plan that draws some bright lines in order to stop oneself from sliding down the slippery slope along a self-destructive path; and (2) overhauling one's habits so that acting accordingly becomes second nature.

In short, in addition to contributing to our understanding of addiction, Redish et al.'s failures-in-decision-making approach is suggestive with respect to the related, but more pervasive problem of procrastination. Indeed, it is probably less controversial to propose that the approach is well suited to providing a unified framework for procrastination than to propose that it is well suited to providing a unified framework for addiction.

Computing motivation: Incentive salience boosts of drug or appetite states

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Abstract: Current computational models predict reward based solely on learning. Real motivation involves that but also more. Brain reward systems can dynamically generate incentive salience, by integrating prior learned values with even novel physiological states (e.g., natural appetites; drug-induced mesolimbic sensitization) to cause intense

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desires that were themselves never learned. We hope future computational models may capture this too.

Redish et al. provide a valuable and comprehensive analysis of addiction models. They deserve gratitude from the field. Their sophisticated assessment of alternative models and explanatory mechanisms is admirably wide-ranging and thoughtful. In their fine scholarly effort, we would like to highlight what they note remains a significant gap unfilled by any available computational model. As the authors put it, "[C]omputational models of the planning system are insufficiently detailed to lead to specific predictions or explanations of the mechanisms by which outcomes are overvalued" (sect. 3.2.1, para. 4). We think this touches a central problem of dynamic motivation: the *generation of dynamic incentive salience motivation from static learned values*.

Current computational models that Redish et al. elegantly describe are powerful, but they are based purely on associations and memories. They act solely on what they know. In most reinforcement-based models, motivation is encoded as a part of an environmental state associated with the learned value of rewards, based on previous experiences. Motivational states may serve as occasion-setting contexts to modulate the value of rewards that have been previously experienced, and they may also modulate the unconditioned impact of a reward via alliesthesia. But the learned incentive value of the reward is never directly and dynamically modulated by the motivational state of the animal, without an additional learning process to intermediate.

However, evidence indicates the brain does something more when controlling desire. It dynamically generates motivation too, sometimes in surprising ways, by integrating static learned values with changing neurobiological states, some of which may never have before been experienced. Modulation of incentive value by new physiological/pharmacological states can be very potent – even the first time a relevant state occurs (Fudim 1978; Tindell et al. 2005a; 2005b; Zhang et al. 2005).

From the computational point of view, novel integrations of learned cues with new physiological states requires a kind of coupling that has not yet been satisfactorily modeled. Such coupling must connect associative values that have been previously learned and stabilized with current physiological/pharmacological states that can change from moment to moment. This falls into their *Vulnerability 4*, the one that we feel is particularly relevant to drug addiction. In particular, we concur with their assertion that new models are needed to address this point.

Addiction is recognized to usurp natural reward mechanisms, and even natural appetites offer dramatic demonstrations of dynamic generation of motivation (Berridge 2004; Toates 1986). Salt appetite is especially exemplary, because it can be produced as a novel state, as most humans today and most laboratory animals have never experienced a sodium deficiency. Salt appetite transforms the value of an intensely salty taste that normally tastes nasty (such as a NaCl solution that is triple the concentration of seawater). The intense saltiness becomes nice in a sodium-depleted body state, and the same triple-seawater becomes as hedonically positive as a sucrose solution (Tindell et al. 2006).

But what if a rat were not given the newly liked salt taste on its first day in a salt appetite state? What if it were instead given only a Pavlovian conditioned stimulus (CS) that had previously been paired with a salt unconditioned stimulus (UCS) when it was nasty? Cues for the previously nasty salt should have no incentive value according to most models. All the learning models described by Redish et al. make the same prediction here: the CS should elicit only negative reactions on the first trials of sodium deficiency. Any cached value of the stimulus-response (S-R) habit system obtained via a temporal difference mechanism must remain strongly negative, established by the previous pairings with punishing saltiness. Contextual knowledge does not yet exist about the potential goodness of salt in a sodium-deficient state. Even a cognitive-tree search mechanism has no way to infer the new value: its cognitive tree contains only memories of unpleasant saltiness. It lacks a branch for "liked" saltiness, at least until the rat is allowed to taste NaCl in its new physiological state.

Yet data from our lab and others show clearly that the incentive value of relevant cues can be modified on-the-fly based on homeostatic state. Indeed, we find the motivational value of the CS for salt is transformed to positive on the first day in the new state, even before saltiness is experienced: the cue becomes avidly approached and consumed, and it becomes able to fire limbic neurons like a cue for sweetness (Berridge & Schulkin 1989; Fudim 1978; Tindell et al. 2005b; 2006).

Bizarre as this reversal of cue valuation by a natural appetite may seem, nearly the same mechanism is exploited by drugs of abuse to cause addiction (Robinson & Berridge 1993; 2003). For example, other data from our laboratory show that drug-induced sensitization of mesolimbic systems, or acute amphetamine elevation of dopamine levels, causes certain relevant reward cues to dramatically become more "wanted," eliciting more incentive salience (Tindell et al. 2005b; Wyvell & Berridge 2001). The elevation in CS incentive value occurs before the UCS reward has ever been experienced while amphetamine was in the brain, or while the brain was in a sensitized state. In addicts, such sensitized "wanting" is posited to cause intense cue-triggered motivation for drugs that far outstrips their previously learned values (Robinson & Berridge 2003).

The implication of these examples is that desire is not reducible to memory alone. Brain mesocorticolimbic systems are designed to dynamically modulate previously learned incentive values, and they do not necessarily require new learning to do so. As Redish et al. have so admirably shown, current models give a fine account of how previously learned values of reward are recalled and coordinated to predict rewards based solely on previous experiences. We hope future models may also generate new motivation values of the sort we have described in order to more fully capture addiction.

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Addiction science as a hedgehog and as a fox

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Abstract: Redish et al. provide a significant advance in our understanding of addiction by showing that the various addictive processes are in fact all decision-making processes and each may undergird addiction. We propose means for identifying more central addiction processes. This recognition of the complexity of addiction followed by identification of more central processes would help guide the development of prevention and treatment.

In a classic essay, Sir Isaiah Berlin (1953) characterizes how individuals organize their subject matter by referring to the statement attributed to the ancient Greek poet Archilochus: "The fox know many things, but the hedgehog knows one big thing." At one extreme, some scientists may behave as foxes, treating their subject as a pluralistic conjunction of many diverse phenomena. At the other, some may approximate the hedgehog by viewing their subject as a monolith where one or a small number of phenomena play a central role in the subject of interest. The target article by Redish et al. proposes an interesting duality. On the one hand, they suggest that they are unifying the processes of addiction by proposing that the varied and

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numerous phenomena that have been proposed and investigated as potential drivers of addiction are all decision processes. On the other hand, they retain each of the identified processes and do not argue that these heterogeneous processes interact, can be grouped into a smaller number of processes, or differ in their centrality to the phenomenon of addiction. In a very real way, these processes are presented as operating in parallel, and therefore, in our opinion, the preponderance of their theory moves in the direction of the fox. We think there is considerable opportunity, however, within the structure of their theory to move toward the hedgehog and to "know one big thing." Here we offer three ways to a move to greater unity.

Interaction of processes. If these processes all actuate the clinical manifestation of addiction, it would seem that at least some of these processes must interact and mutually drive the process to stability in the addictive state. We consider just two of the processes and illustrate a plausible means by which this interaction may occur. One of the clinically relevant aspects of addiction is the relative insensitivity to price for the addictive commodity. This might result from an interaction between euphoriogenic rewards or reinforcement (*Vulnerability 3*) and temporal discounting (*Vulnerability 9*). Consider that sensitivity to price is affected by the availability of substitutes. For example, a consumer would not buy a commodity for a high price if a nearly identical commodity (a substitute) were available for a substantially lower price. One source of substitution is inter-temporal. For example, a consumer would not buy a commodity for a high price now if a nearly identical commodity (a substitute) were available later at a substantially lower price. However, if the future value of a commodity (say a drug of dependence) is radically discounted, as is often the case (e.g., Bickel & Marsch 2001; Yi et al., in press), then the opportunity for inter-temporal substitution is limited, which, in turn, would result in less sensitivity to price. We think that there is opportunity for some of the other processes illuminated by Redish and colleagues to interact in ways that may plausibly result in known clinical features of addiction.

Co-identity of processes. Some of the processes identified by Redish et al. have had a very limited history of investigation. As such there may be processes that are treated separately for reason of historical contingency of its exploration and naming but are very closely related, if not referring to the same phenomena. Let us again consider two: discounting (*Vulnerability 9*) and balance between the planning and habit system (*Vulnerability 8*). Redish et al. note that drugs may inhibit structures involved with planning over habit systems. These two systems have been variously named (e.g., Bechara 2005), and we have referred to them as "impulsive" and "executive" (Bickel et al. 2007). Importantly, evidence suggests that temporal discounting serves as a summary measure of these two systems. Specifically, McClure et al. (2004) used functional magnetic resonance imaging to scan the brains of normal adults engaged in discounting procedures. Choices favoring the immediately available option were associated with greater relative activation in structures associated with the habit, or "impulsive," system (e.g., limbic region). In contrast, choices favoring the temporally remote option were associated with greater relative activation in structures associated with the planning, or "executive," system (e.g., prefrontal cortex). As such, temporal discounting provides a specific measure of the balance between these competing systems, suggesting that these processes are in fact the same.

Centrality of some processes. To the extent we know how these processes affect and interact with each other, we may come to understand the organization or topology of these processes in addiction. The centrality of these processes may not all be equivalent, and knowing their organization may suggest the most effective means of "treating" the system; that is, some processes may have a greater effect on the system than others. As an example, consider protein synthesis in the yeast. The yeast cell produces approximately 1,870 different proteins (Jeong et al. 2001). However, these proteins are not all equally essential to the yeast cell. Understanding the link among these proteins has shown that highly connected proteins are three times more essential (i.e., deletion results in cell death) than proteins with a small number of links. Suggestions of how to adapt these typological organizations for the study of addiction have been offered (Chambers et al. 2007). Application of such approaches may indicate which component processes are best targeted to ameliorate addiction.

In conclusion, we applaud the work done by Redish et al. It is an important first step, and it puts us on the right footing in our task to understand, prevent, and treat addiction. We may need to know many things to reach our goal, and we hope we will come to know a small number of things that have very big effects.

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Social influence and vulnerability

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Abstract: Redish et al. outline 10 vulnerabilities in the decision-making system that increase the risks of addiction. In this commentary I examine the potential role of social influence in exploiting at least one of these vulnerabilities, and argue that the needs satisfied by social interaction may play a role in decision-making with regard to substance use, increasing the risks of addiction.

The target article by Redish et al. presents a theoretical framework for addiction as arising from an array of vulnerabilities in the way in which individuals make decisions regarding behaviour. In the present commentary, I examine how several aspects of social interaction may exploit the vulnerabilities outlined by the authors.

Redish and colleagues argue that addiction can be viewed as a series of maladaptive choices, and that models of human decision-making can be employed to show how addictions may develop and be maintained. According to Redish et al., these vulnerabilities can lead to incorrect or inappropriate decisions regarding substance use, thereby leading to addiction. To support these positions, Redish and colleagues review a range of studies generally drawn from research on human decision-making, learning theory, and neuropsychology. The authors point out, however, that their theory may have implications for other theories of addiction, including social theories.

There have been numerous social theories of addiction in the literature. For example, social learning theory suggests that addiction may be the result of observation and mimicking of substance use and abuse in role models such as parents (Eiser 1985; Fischer & Smith 2008; Neiss 1993; Raskin & Daley 1991). In addition, a number of theories of addiction suggest that addictive behaviors are developed via affiliation with substance-using peers and others (Bloor 2006; Duncan et al. 1998; Jenkins 1996; Wills et al. 1998). It seems reasonable to assume that social influence, and in particular social influence linked to substance use, may also exploit vulnerabilities in the decision-making system in the ways specified by Redish and colleagues. In particular, it may be argued that social influence may exploit three of the vulnerabilities proposed by Redish et al. – overvaluation of the expected value of a predicted outcome in the planning system (*Vulnerability 4*); incorrect search of situation–outcome relationships (*Vulnerability 5*); and misclassification of situations (*Vulnerability 6*) – in turn increasing the risk of addiction.

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In describing *Vulnerability 4*, Redish and colleagues provide a neurochemical account of how the planning system can lead to an overvaluation of the value of a predicted outcome, via the pairing of a valued outcome (drug use) with some other valued stimulus. It is clear that social interaction might serve as a valued stimulus that, paired with drug use, could lead to an increase in the value of drug use, thereby increasing the risk of addiction. For example, several studies have shown that the initiation of substance use occurs most frequently in social situations (Clark et al. 1999; Galea et al. 2004; Kaplow et al. & Conduct Problems Prevention Research Group 2002). Also, further studies have shown that adolescent substance use patterns are largely influenced by social context (Petraitis et al. 1998; Schuckit et al. 2007; Wilcox 2003). In addition, neuropsychological research has shown that social interaction and relationships may stimulate reward centers in the brain (Caldu & Dreher 2007; Depue & Morrone-Strupinsky 2005; Guroglu et al. 2008; Walter et al. 2005), suggesting that the pairing of social interaction and substance use may lead directly to an overvaluation of substance use, thereby exploiting this particular vulnerability.

Vulnerability 5 involves a memory process by which certain situations may be more likely to lead to certain outcomes (i.e., drug use), because the memory of a valued situation-outcome pairing becomes more salient, blinding the individual to alternatives. Here again, social interaction may play a crucial role in exploiting this particular vulnerability. As mentioned previously, substance use and abuse often occurs in social situations, and individuals who are early (i.e., childhood and early adolescent) initiators of substance use, and thus at increased risk of substance dependence (e.g., Fergusson & Horwood 1997), are more likely to engage in substance use in a social context. Yet another way in which this vulnerability might be exploited is through the salience of social interaction as a cue for memory retrieval. A range of studies have shown that social information is more easily recalled, and that it has more complex and detailed relationships with other information in an individual's associative memory network (Clark & Stephenson 1995; Leone 2006; Reynolds & West 1989; Walker-Andrews & Bahrick 2001). These considerations suggest that the social context in which substance use and abuse occurs may play a key role in exploiting vulnerabilities in the decision-making process related to memory.

Vulnerability 6, situation misclassification, occurs when individuals overgeneralize situations to other situations, despite changes in the nature of the situation. Thus, for example, drug users may be unable to change their drug-taking behavior despite negative consequences arising from their drug use. It could be argued that this vulnerability is exploited when individuals move from the use of one drug to another, more addictive drug, such as the progression of drug use via the gateway mechanism (Fergusson et al. 2006; Kandel et al. 1992; MacCoun 1998). Under this explanation, individuals are more likely to move from drugs that have a lower risk of dependence (i.e., cannabis) to drugs with higher risks of dependence (e.g., cocaine, opiates, methamphetamine; Fergusson et al. 2006; Kandel et al. 1992). Fergusson and colleagues have argued that one of the main drivers of the cannabis gateway is social interaction, and that differential association with individuals who have access to a range of illicit drugs (such as drug dealers) increases the availability of other illicit drugs, thereby increasing the risk that an individual will use these drugs (Fergusson et al. 2006). In this way, generalization from one situation (cannabis use) to another situation (other illicit drug use), arising from social interaction, may lead to an inability to stop using drugs when symptoms of dependence arise from the use of other illicit drugs.

In summary, Redish and colleagues have developed a model that shows how individuals may make maladaptive choices with regard to substance use, leading to increased risk of addiction. It seems clear that social interaction plays an important role in exploiting these vulnerabilities, providing information that may inadvertently increase the risk that individuals will become substance-dependent.

Impulsivity, dual diagnosis, and the structure of motivated behavior in addiction

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Abstract: Defining brain mechanisms that control and adapt motivated behavior will not only advance addiction treatment. It will help society see that addiction is a disease that erodes free will, rather than representing a free will that asks for or deserves consequences of drug-use choices. This science has important implications for understanding addiction's comorbidity in mental illness and reducing associated public health and criminal justice burdens.

As nicely exhibited by Redish et al., we are converging on an understanding that addiction is a disease impacting specific brain systems that control and adapt motivated behavior. Evidence reported here, and continually mounting (Belin & Everitt 2008), paints an increasingly clear picture that addiction is not merely a vague notion of so-called psychological dependence or some unchecked need to feel good all the time. Rather, it is a disease of neurological character, involving brain systems and phenomenological themes reminiscent of Parkinson's or Huntington's disease. Like these diseases, addiction involves progressive changes to the basal ganglia, the primary neural system involved in the ordering and procedural memory of behavioral programming (Everitt & Robbins 2005; Haber 2003; Volkow et al. 2006). Perhaps it has taken us this long to appreciate addiction as a type of progressive cortical-striatal disease because it uniquely seems to involve functions of "free will" that many view as unapproachable as a biomedical topic of exploration. After all, Parkinson's and Huntington's are so obviously *motoric* in nature, and involuntary, whereas any action choice (i.e., to use a drug) appears voluntary, whether in the addict or in the drug-naive.

But now a new picture is emerging: While dorsal cortical-striatal systems govern the relatively inflexible execution of procedural motor programs (i.e., behavior), ventral cortical-striatal systems flexibly and hierarchically govern the ordering, prioritization, and selection of these dorsally represented programs (i.e., motivation) (Gerdeman et al. 2003; Haber et al. 2000; Kelley 2004b; Yin & Knowlton 2006). As facilitated by ever-changing environmental contingencies that provoke rapid changes in striatal dopamine transmission (Bardo et al. 1996; Finlay & Zigmond 1997; Spanagel & Weiss 1999), neuroplastic alterations spanning these striatal regions change the way ventral and dorsal compartments represent information and communicate with one another (Chambers et al. 2007; Graybiel 1998; Hyman & Malenka 2001). Thus, behavioral repertoires are dynamically evolving, highly complex structures, or maps, in which specific motor programs are like destinations interconnected by motivational routes (Chambers et al. 2007). Depending on developmental age, environmental conditions, or inherent individual attributes, cortical-striatal circuits that generate these motivational-behavioral repertoires are themselves physically changing in an unending attempt to provide the most *adaptive* mapping of behavioral organization of the individual to the external world (Chambers et al. 2007).

Equipped with this understanding, there is no need to equate a biomedical understanding of addiction with a hubristic claim that we can absolutely define all the physical mechanisms of "free will." Who knows if we shall ever fully grasp the extreme complexity of human behavioral repertoires? But we can say that if

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this complexity is synonymous with "free will," then addiction is a disease of neural systems that govern free will, in which the adaptive complexity of free will is reduced and compromised. Understanding this process mechanistically may actually be within our grasp.

Redish et al. rightly centralize a general concept of impaired decision-making in the pathophysiology of addiction. Of all contexts in which addiction vulnerability has been identified, two stand out most prominently: adolescent neurodevelopment and mental illness (Chambers et al. 2003; Kessler 2004). Notably, these contexts entail features that are associated with a general theme of impulsivity, whether it be couched in terms of "novelty-seeking," "high risk-taking," "poor judgment" or "decision-making," or "behavioral inhibition deficits." To suggest a succinct, yet inclusive formulation of impulsivity: it is an operational condition in which ventral cortical-striatal circuits consistently fail to produce *adaptive* mapping of behavioral organization onto the external world, despite normative intelligence. Of course, in normal adolescence, such impulsivity is actually quite adaptive, because developing healthy brains have the need and capacity for learning from their mistakes (Chambers & Potenza 2003). But in mental illness, such capacities are episodically or chronically compromised into adulthood, and the mapping of behavioral organization is maladaptively reduced in complexity and/or relatively inflexible to change based on environmental demands.

Across the broad span of mental illnesses in which addiction comorbidity is robustly present (including schizophrenia, bipolar disorder, antisocial and borderline personality, post-traumatic stress disorder [PTSD], various impulse control disorders, and many others) (Kessler 2004), one or more of the following three brain regions are pathologically altered: the prefrontal cortex, the amygdala, and the hippocampus (Charney et al. 1999). *All of these areas normally and robustly send direct glutamatergic projections into the ventral striatum* (Groenewegen et al. 1999; Haber 2003; Swanson 2000). There, these projections not only cooperatively help generate and modulate a rich diversity of firing pattern representations spanning ventral striatal networks (representing motivational information), but they act in concert with, or are acted upon by dopamine, resulting in altered neural connectivity (Goto & Grace 2005a; Hyman & Malenka 2001; O'Donnell et al. 1999; Vanderschuren & Kalivas 2000). Such plasticity likely instantiates the acquisition of new motivational representations contributing to a more complex, highly nuanced, and adaptive motivational repertoire that optimally directs behavioral programming. But, if one or more among the prefrontal cortex, the amygdala, or the hippocampus is compromised due to a pre-existing neurodevelopmental condition (i.e., mental illness), then the complexity and/or adaptive flexibility of the motivational-behavioral repertoire, as generated by striatal networks, is reduced (Chambers 2007). In other words, since limbic inputs to the ventral striatum are relatively impoverished, then the catalogue of motivational representations that may be generated by it are also impoverished in number, complexity, or changeability.

Although some dopamine-mediated neuroplasticity (and adaptive behavioral flexibility) persists that can produce real change in the motivational repertoire, such change may be abnormally limited to conditions or stimuli that produce particularly strong and/or prolonged dopamine (DA) signals (e.g., pharmacological actions of addictive drugs). Without, or before, addictive drug exposure, this situation is clinically perceived as impulsivity, poor decision-making, or other motivational disturbances of mental illness. Upon addictive drug exposure we have a massive epidemic of dual diagnosis (substance disorder comorbidity in mental illness) on our hands to the tune of greater than 50% of all mentally ill or drug-addicted patients seeking treatment (Dixon 1999; RachBeisel et al. 1999). In the de-institutionalization era, no wonder we face such tremendous medical morbidity and mortality from addictions, and homelessness and criminal incarceration of the mentally ill (Lasser et al. 2000; Rosen et al. 2002; Schmetzer 2006).

Consistent with these translational perspectives, animal modeling of dual diagnosis has demonstrated that if certain neurodevelopmental lesion models of mental illness are combined with addictive drug exposure, addiction vulnerability phenotypes are accentuated. For instance, neonatal ventral hippocampal lesions (a comprehensive animal model of schizophrenia) produce a host of biological changes involving prefrontal cortical and ventral striatal circuits (Goto & O'Donnell 2002; Lipska et al. 2003; Tseng et al. 2007). These aspects correspond to increases in acquisition of cocaine self-administration, resistance to extinction, and drug-induced relapse of drug-seeking (Chambers & Self 2002). The lesion also produces elevations of an impulsive approach to natural reward before drug exposure, and synergistic worsening of this trait after cocaine exposure in a manner not seen in control animals (Chambers et al. 2005).

As suggested by Redish et al., identifying differential styles or mechanisms of impulsivity as predictive markers of addiction vulnerability, illness trajectory, or treatment options, is surely a next step for the field. Studying differential forms and patterns of dual diagnosis in both animal models and human populations should represent a major avenue of the exploration. This work will help us elucidate the extent to which the 10 decision-making vulnerabilities suggested by Redish et al. represent truly independent facets of addiction vulnerability or redundant manifestations of the same underlying principle. By determining which of these vulnerabilities carry the most weight of addiction liability in most people, we may arrive at a more parsimonious and "winning" theory of addiction.

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Gambling and decision-making: A dual process perspective

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Abstract: The consideration of gambling as a decision-making disorder may fail to explain why the majority of people gamble, yet only a small percentage of people lose control of their behaviour to the point where their gambling becomes problematic. The application of dual process theories to gambling addiction offers a means of explaining the differences between "normal" and "problem" gambling, augmenting the multiple vulnerabilities proposed by Redish et al.

The explanation of loss of control of gambling behaviour (so-called pathological gambling) presents a considerable challenge for general theories of addiction for two main reasons. First, unlike many other addictions, gambling does not involve the ingestion of substances that alter psychopharmacological states. Second, like many other addictive activities, the majority of the population participates to some degree (Walker 1992b), yet only a small percentage of gamblers develop problems with their gambling behaviour.

The role of decision-making in theories of gambling addiction has not featured as prominently as it should, given the central importance of decision making to gambling (e.g., not only deciding when to initiate a gambling episode and when to cease an episode, but deciding *what* to bet on and *how much* to wager). The identification within a single theoretical framework of

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different types of decision-making vulnerabilities, and their association (to varying degrees) with underlying neurophysiological mechanisms, affords the gambling research community an overarching framework in which to map out decision-making deficits. However, the argument that the explanation of problem gambling is attributed to *Vulnerability 6* (the illusion of control) is, at best, premature. Moreover, the relationship between conscious (explicit) and unconscious (implicit) cognitive processes during gambling needs to be considered in relation to the types of vulnerabilities that Redish et al. outline.

The application of dual processes theories to addiction (see Wiers & Stacy 2006a; 2006b for a recent overview) and the role of two distinct types of decision-making processes in gambling (e.g., Bechara et al. 1997; Evans & Coventry 2006) cuts across a number of the vulnerabilities outlined. It has been argued (Evans & Coventry 2006) that the explanation of gambling behaviour should be seen in the context of two different types of decision making – implicit and explicit systems – mirroring processes with associated neurocorrelates that have been identified in human reasoning research. This opens up three possibilities regarding how decision-making mechanisms might affect gambling behaviour in light of these two systems. First, explicit cognitive processes, in the form of "cognitive distortions," may account for increased gambling behaviour. Second, implicit ("evolutionary older") cognitive processes may account for increased gambling behaviour. Third, the interaction between these two different systems of decision-making may account for the behaviour. Fourth, decision-making involving both or either of these in tandem with additional (non-decision-based) mechanisms may explain gambling behaviour.

The notion that cognitive distortions underlie loss of control of gambling behaviour (Wagenaar 1988) is problematic. First, cognitive distortions when it comes to decision making under conditions of uncertainty are present in the general population as a whole (hence in the gambling population at large), and not just in the relatively small percentage of problem gamblers. So cognitive distortions do not explain the change from so-called normal gambling behavior to the point where someone loses control of their behaviour (see Coventry 2002; Sharpe 2002 for discussion). In tandem with another variable, such as the requirement for a specific high arousal state associated with positive hedonic tone (*Vulnerability 2*), the role of cognitive distortions in gambling is perhaps more appealing. Coulombe et al. (1992) reported an increased incidence of cognitive distortions during gambling for regular as compared to occasional video poker players, together with a significant correlation between arousal increases observed during play and the frequency of (verbalised) erroneous beliefs about gambling. However, Coventry and Norman (1998) found no association between level of gambling behaviour and number of cognitive distortions under more controlled circumstances using a more robust coding scheme for cognitive distortions. So the claim that cognitive distortions underlie loss of control of gambling is controversial at this time.

The importance of implicit (unconscious) processes in relation to human decision-making and reasoning has been demonstrated across a wide range of decision-making and reasoning tasks (Evans 2003). In relation to gambling as a learnt behaviour, people can learn to predict complex patterns through this implicit system, without the necessary acquisition of explicit knowledge. For example, the implicit system is particularly good at pattern recognition and identifying sequential dependencies (so critical for tasks such as language learning). On its own, though, it seems unlikely that loss of control of gambling behaviour can be causally explained by implicit learning. However, the unconscious nature of this system provides a possible key to the role of this system in the explanation of the development of problem gambling behaviour. Evans and Coventry argue that the possible desire for dissociative states and experiences (escaping from the vulnerabilities associated with everyday life; see Kuley & Jacobs 1987) provides a plausible motive to maintain a decision-making system that infers patterns where they do not aid future prediction (e.g., in roulette). Usually the explicit system kicks in when the implicit system does not serve us well, but for gamblers who desire being in an unconscious state, the explicit system may rather act as means of providing post hoc rationalisations (Coventry & Norman 1998) or confabulations that serve to maintain the use of implicit processes. If this view is correct, verbalised cognitive distortions are not causes of continued gambling behaviour, but rather, are a means of maintaining behaviour dominated by a different system of (unconscious) processing.

Consistent with the view that unconscious implicit processes are important for continued gambling, Diskin and Hodgins (1999; 2001) have shown that there is indeed attentional narrowing, an inability to keep track of time, and the experience of dissociative states, in regular gamblers when they gamble.

Decision-making within a dual process framework, in tandem with a cluster of variables associated with positive hedonic tone and escape, illustrate that the explanation of gambling behaviour needs to involve multiple constructs, and multiple vulnerabilities. Detailed process studies of on-line gamblers are desperately needed to identify how the explicit and implicit systems interact over time in the transition from regular to problem gambler.

Different vulnerabilities for addiction may contribute to the same phenomena and some additional interactions

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Abstract: The framework for addiction offered by the target article can perhaps be simplified into fewer, more basic, vulnerabilities. "Impulsivity" covers a number of vulnerabilities, not just enhanced delay discounting. Real-world drug-use decisions involve both delay and probability discounting. The motivational salience of, and attentional bias for, drug cues may be related to a number of vulnerabilities. Interactions among vulnerabilities are of significance and complicate the application of this framework.

The framework outlined by Redish et al. raises some important questions:

1. The ten vulnerabilities described can possibly be collapsed into fewer, more fundamental, vulnerabilities. *Vulnerabilities 1* and *2* both infer that the perceived value of drugs increases in withdrawal (i.e., drug efficacy is enhanced by negative reinforcement). *Vulnerabilities 3* and *4* are, in essence, positive reinforcement models. *Vulnerabilities 4*, *5*, and *10* reflect a hyper-efficient learning process, such that drug-cue associations are learned quickly, are unusually strong, and the conditioned responses to such cues are resistant to extinction. Thus, the framework could be simplified by collapsing these vulnerabilities into fewer underlying processes. We make these observations based on the behavioural consequences of each vulnerability, which is not to say that each vulnerability does not have its own distinct neural substrate.

2. *Vulnerability 9* relates to enhanced delay discounting. The authors refer to this as "impulsivity." However, "impulsivity" has been defined by different authors in many different ways, some of which vary radically from delay discounting, for example, deficits in response inhibition (*Vulnerability 8*), lack

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of perseveration, lack of perseverance, boredom susceptibility, sensation seeking, functional impulsivity, reflection impulsivity, and so on. For example, a recent analysis of behavioural tests of impulsivity (Reynolds et al. 2006) indicated that impulsivity related to disinhibition (*Vulnerability 8*) can be dissociated from impulsive decision making related to delay discounting (*Vulnerability 9*). There is arguably a case for dispensing totally with the potentially misleading umbrella term "impulsivity."

The current framework suggests that delay discounting is a stable characteristic (a trait). However, delay discounting rates are not stable in individuals, as they tend to increase during acute abstinence, as discussed further on (Field et al. 2006; Giordano et al. 2002).

3. The mechanism(s) involved in delay discounting (*Vulnerability 9*) are described as "a source of much controversy." Delay discounting may critically involve the basic cognitive process of time perception (Wittmann & Paulus 2007). Alterations in time perception might affect many vulnerabilities involving the planning system. For example, a slowing down of time perception in "impulsive" individuals might, perhaps counterintuitively, protect individuals from overvaluation of expected rewards (*Vulnerability 3*). This raises the important issue (discussed briefly by Redish et al) of interactions that occur among vulnerabilities. Our own work shows that nicotine withdrawal increases delay discounting (Field et al. 2006), showing that *Vulnerabilities 1* and *2* interact with *Vulnerability 9* (delay discounting). Similarly, Verdejo-Garcia et al. (2007) have reported that, in individuals with substance dependence, the type of "impulsivity" best predictive of lifestyle (legal, employment, family, and social) problems is "urgency," a tendency to respond impulsively when in negative emotional states (Whiteside & Lynam 2001). Such states would clearly be induced by drug withdrawal of various types. This again indicates that *Vulnerabilities 1* and *2* interact with *Vulnerability 9*. Moreover, these findings suggest that such interactions may well be of considerable clinical relevance.

4. Real-world decisions about using drugs involve both delay and probability. The user makes a complex decision about the costs and benefits of using drugs in both the short- and long-term. The immediate gratification of using drugs is a certainty, whereas the benefits of abstinence are not. Focusing on delayed reward alone does not capture the essence of real-world decision-making.

5. The authors interpret attentional bias for drug-related cues in terms of *Vulnerability 5*. However, we suggest that, theoretically, attentional bias might also belong under *Vulnerability 4* (overvaluation in the planning system/sensitization of motivation). For example, Franken (2003) suggested that attentional bias and craving both develop as a consequence of dopaminergic sensitization, and that the two have reciprocal causal effects on each other (craving increases attentional bias, and vice versa). Indeed, our research demonstrates that attentional bias is both associated with (e.g., Field et al. 2005), and caused by (e.g., Field et al. 2004) increases in subjective craving, and that direct manipulations of attentional bias can influence subjective craving (Field & Eastwood 2005). Attentional bias can also be understood in the context of *Vulnerability* 10 (a hyper-efficient learning process) because it develops rapidly as a consequence of pairings between the drug and drug-related cues (for review, see Hogarth & Duka 2006).

6. Recent theoretical views (Goldstein & Volkow 2002; Wiers et al. 2007) suggest potential interactions between the "salience" of conditioned drug-related cues (i.e., attentional bias for those cues; *Vulnerabilities 4*, *5*, and *10*), and deficient inhibitory control (*Vulnerability 8*). According to these models, inhibitory control mediates the impact of conditioned cues, either by directly suppressing responses to those cues, or by acting as a "brake" to prevent powerful responses to cues from influencing drug-seeking behaviour. These models are not inconsistent with the current framework, but they do suggest how *Vulnerability 8* (selective inhibition of the planning system) can influence specific vulnerabilities within the planning system.

7. A radical implication of the theorising outlined in the target article is that individuals develop (relatively) unique paths to addiction, and that treatments based on an individual's specific vulnerabilities are required. Although this is an important idea, we wonder how this would work in practice (even if clinical tools could be designed to assess vulnerabilities), given that vulnerabilities are likely to interact, as outlined earlier. Interactions among vulnerabilities render accurate predictions from the framework difficult to make, particularly as they will change in any individual over time and with drug experience or drug withdrawal. We also wonder how receptive clinicians would be to a framework based on fundamental neuroscience.

In summary, we believe the framework outlined could possibly be both simplified and refined, particularly in terms of emphasising mechanistic interactions among vulnerabilities.

The biopsychosocial and "complex" systems approach as a unified framework for addiction

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Abstract: The "unified framework" for addiction proposed by Redish and colleagues is only unified at a reductionist level of analysis, the biological one relating to decision-making. Theories of addiction may be complementary rather than mutually exclusive, suggesting that limitations of individual theories might be unified through the combination of ideas from different biopsychosocial "complex" systems perspectives.

Conceptualizing addiction has been a matter of great debate for decades. Redish et al. put forth a "unified framework" for addiction, but it is only unified at one reductionist level of analysis (i.e., biological) relating to just one aspect (i.e., decision-making). It is clear that conceptualization of addiction has implications for several groups of people (e.g., addicts, their families, researchers, practitioners, policy-makers, etc.). Obviously, the needs of these groups may not be equally well served by certain models, and in some cases there will be absolute incompatibility. Whether Redish et al.'s "unified framework" will help specific stakeholders (such as policy-makers, practitioners, and the addicts themselves) is highly debatable. Implicit within the claims made by any particular group or individual will be assumptions about what levels and types of risk are acceptable in the pursuit of pleasure, and, more simply, which kinds of pleasure are acceptable and which are not. Any unified framework for the conceptualization of addiction must allow for the bottom-up development and integration of theory by each of these groups – that is, it must be flexible, accountable, integrative, and reflexive.

It is also important to acknowledge that the meanings of *addiction*, as the word is understood in both daily and in academic usage, are contextual and socially constructed (Howitt 1991; Irvine 1995; Truan 1993). Researchers must ask whether the term "addiction" actually identifies a distinct phenomenon – something beyond problematic behaviour – whether socially constructed or physiologically based. There is clearly a case for a complex systems model of addiction. "Complex" for obvious reasons, and "systems" after Davies (1992), who argues that alternative explanations for excessive behaviour require "the development of a 'system' within which drug use is conceived of as an activity carried out for positive reasons, by people who

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make individual decisions about their substance use, and who may take drugs competently as well as incompetently" (p. 163). Gambino and Shaffer (1979) have emphasized the difficulties of re-integrating research and practice in the area of addiction. On the basis of Polkinghorne's (1993) observations on the nature of such divisions, a more flexible theoretical approach, such as the complex systems model, ought to go some way toward bridging the epistemological gap.

The complex systems model corresponds well to the biopsychosocial approach to addiction (e.g., Griffiths 2005; Marlatt et al. 1988; McMurran 1994). It may also be considered to be a descendant of previous multi-factorial approaches to the addiction process (e.g., Wanberg & Horn 1983; Zinberg 1984). Obviously, from the perspective of the complex systems model, it is possible to consider the interaction of both the common and the unique elements of any specific individual's situation. This includes psychological, physiological, social, and cultural factors that may be particular to any individual. It also allows for consideration of the pharmacological properties of specific substances, or the reinforcing properties of certain kinds of behaviour such as gambling. It is important, therefore, to point out that this is not a return to citing the property of "addictiveness" as located within particular substances (or within particular activities). However, it is necessary to be aware of effects that may be common to certain kinds of substances or activities, but not to others.

Neurological and pharmacological work on addiction (despite some discrepancies and disagreements) allows us to remove the emphasis on substance use (and thus lose some of the awkward discourse associated with it) and include behavioural activities, as well as to acknowledge the powerful behavioural dimension of substance addictions (see Sunderwirth & Milkman 1991). For this, Redish and colleagues should be commended because their unified approach allows activities like problem gambling to be considered bona fide addictions. Any activity that is rewarding may thus be seen as potentially addictive, but only those activities with a social disapproval of their attached "risk" are viewed as addictions, rather than habits, in the current climate. This is a strong argument for a greater understanding of the addiction concept.

In a biopsychosocial complex systems model of addiction, the process of addiction is dynamic, in which the addict, while responding to needs for arousal or satiation, and learned patterns of behaviour, as well as reacting to the environment, still has recourse to a decision-making process with regard to the modification of their physiological state. A number of biological, psychological, and socio-cultural factors will determine the nature of this process.

The biological effects of any particular behaviour or drug (i.e., the subjectively experienced intensity, and the stimulating and/or sedating effect of that behaviour or drug) may have a strong relationship with other biological factors (e.g., opponent-process adaptation to that effect), as well as with the psychological factors (e.g., the subjectively experienced craving for that behaviour or drug) and the social factors (e.g., prompting of the craving through peer behaviour), which interact together during the addictive process. The nature of those reinforcing effects will, of course, be essentially similar to, and yet crucially distinct from, those of other activities and substances.

Most of my own research has concentrated on behavioural addiction (i.e., non-chemical addictions), particularly gambling addiction but also addictions to videogame playing, Internet use, exercise, and sex (for summaries of these, see Allegre et al. 2006; Griffiths 2004; 2006; 2008; Widyanto & Griffiths 2006). Redish et al. have a very narrow approach when talking about gambling as an addiction, and their "unified framework" also needs to include these other types of behavioural addictions. Gambling addiction is a multifaceted rather than unitary phenomenon, and the decision-making approach (while useful on some levels) is very limited. Consequently, as with addiction more generally, many factors may come into play in various ways and at different levels of analysis (e.g., biological, social, or psychological). Theories may be complementary rather than mutually exclusive, which suggests that limitations of individual theories might be overcome through the combination of ideas from different perspectives. It is evident that problem gambling (specifically) and addiction (more generally) is a biopsychosocial process (Griffiths 2005; Griffiths & Delfabbro 2001) and that a narrow focus upon one theoretical perspective in the explanation of gambling and addictive behaviour cannot be justified.

Neither necessary nor sufficient for addiction

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Abstract: Although Redish et al. have pulled together a large number of approaches to understanding decision-making and common errors in cognition, they have outlined neither the necessary nor the sufficient attributes of addiction. They are correct in claiming that addiction is multifaceted and probably more akin to a syndrome than a genuine disease. But grasping what that multifaceted syndrome is still eludes us.

Over recent years, about as many frameworks for understanding addiction have been proposed as there are researchers working on the topic. Redish et al. take the ecumenical path and suggest that all frameworks are at least partially right and can be accommodated within a larger theory of decision-making. There are many paths to addiction, as there are many ways this cognitive system can break.

The first difficulty with what the authors propose is that it does not help in predicting, diagnosing, or treating various addictions. They are very clear that a variety of genetic, environmental, social, behavioral, and presumably neural factors lead someone to addiction. Their model does not make any comments on sorting out which factors are relevant under which circumstances. But being able to predict who is likely to become addicted when is probably the biggest lacuna in addiction research today.

In addition, Redish et al.'s proposal offers no clues as to how one should determine which systemic vulnerability or vulnerabilities are tied to which addicted individual. Because different addictive substances and behaviors affect the brain in different ways, we already know that there is much variation in the biochemical specifics of addiction. What we do not know is how to identify the vulnerabilities a particular individual might have, nor do we know whether the vulnerabilities are mutually reinforcing.

Finally, although the authors suggest that one should tailor treatment to the specific breakdowns one finds in the decision-making system, this is *already* what health-care providers do. We already know that addiction has multiple facets, which is one reason treatments are rarely completely successful. We already know that one size does not fit all; indeed, one size does not fit one in most cases. We need multiple interventions at multiple levels to effect changes in most addictive behaviors.

While the authors have cleaned up some of the laundry list of attributes contributing to addiction, they have not shortened the list, nor have they developed a complete list. In other words, their theory of addiction as vulnerabilities in the decision-making process is not sufficient for understanding addiction.

The second difficulty is that the vulnerabilities they identify as contributors to addictive behaviors are not definitive of addiction. Overvaluation in the planning system happens on a regular basis in most people's lives, as does the incorrect

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search of situation-action-outcome relationships, misclassification of situations, and over-fast discounting processes. For example, if people are asked whether they would prefer a fifteen-cent Lindt truffle or a one-cent Hershey's kiss, 73% choose the truffle. But if we ask people whether they prefer a fourteen-cent Lindt truffle or a free Hershey's kiss, only 31% choose the truffle (Ariely 2008). In the normal course of our daily lives, we tend to overvalue free things. These sorts of so-called vulnerabilities in our cognitive processes are well known. They suggest that we are not perfectly rational and that we make errors in our behavioral choices. But these facts are true of all humans, not just those with addictions.

Even the vulnerabilities that intuitively might seem to be tied more closely to addiction – moving away from homeostasis, changing allostatic set points, and euphoric "reward-like" signals – are part of many non-addicted people's daily lives. Patients with depression, schizophrenia, autism, and post-traumatic stress disorder, to name a few conditions, could all be described as having vulnerabilities in their affective reactions. So do people with stressful lives, with new loves, and who are coping with tragedy. The point is that a malfunctioning or oddly functioning decision-processing system is a very normal aspect of everyone's lives. I would argue that it is part of what makes us human. But more importantly, these vulnerabilities are not necessary for addiction.

To summarize my main point again: Although the authors have pulled together a large number of approaches to understanding decision-making and common errors in cognition, they have not really developed anything that helps us predict, treat, control, or understand addiction. They are surely correct in claiming that addiction is multifaceted and probably more akin to a syndrome than a genuine disease. But fully grasping that multifaceted syndrome still eludes us.

Human drug addiction is more than faulty decision-making

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Abstract: We commend Redish et al. for the progress they have made in bringing a measure of theoretical order to the processes that underlie drug addiction. However, incorporating information about situations in which drug users do not exhibit faulty decision-making into the theory would greatly enhance its generality and practical value. This commentary draws attention to the relevant human substance abuse literature.

We commend Redish et al. for attempting to bring a measure of theoretical order to the processes that underlie this important scientific and social problem: drug addiction. However, several aspects of their article warrant further discussion.

First, there are important disparities between the literature cited in the target article and other work in the human substance abuse literature. The article proposes an "explanation for addiction as 'vulnerabilities' in an established decision-making system" (sect. 2.1, para. 1). In essence, the claim is that individuals who engage in maladaptive substance use exhibit deficiencies in decision-making, and that this inability to make correct non-drug-using decisions is a main cause of continued substance use. However, many substance abusers have the capacity to (and do) make rational choices from available options. For example, Hart et al. (2000) compared self-administration of cocaine when either a $5 cash or merchandise voucher was available as an alternative reinforcer, and they found that near-daily cocaine users' choice to self-administer cocaine was significantly lower when cash was the alternative. These results are consistent with other human laboratory data evaluating the influence of alternative reinforcers on cocaine-taking behavior (e.g., Hatsukami et al. 1994; Higgins et al. 1994), and suggest that experienced current cocaine users are capable of making consistent reasonable choices. Similar results have been obtained in opioid abusers. Comer et al. (1997) demonstrated that heroin-dependent individuals' self-administration of the drug was decreased as the alternative money amount increased. Several other investigators have reported similar findings (e.g., Comer et al. 1998; Rosado et al. 2005; Stitzer et al. 1983; Vandrey et al. 2007). A discussion of how these and related findings apply to *Vulnerabilities* 7 and 9 would enhance the proposed theory.

Moreover, research participants in substance abuse studies are required to complete extensive screening procedures prior to study enrollment (see Hart et al. 2008). Typically they undergo psychiatric and medical examinations and several days of training on study procedures, requiring multiple screening visits. Once enrolled in the study – which may consist of alternating inpatient and out-patient phases lasting a couple of months – demanding schedules are imposed, requiring participants to do considerable planning, inhibit behaviors that may be inconsistent with meeting study schedule requirements (e.g., drug use), and delay immediate gratification. All of these have been identified in the target article as potential "failure points." The conclusion that substance abusers are handicapped by compromised decision-making skills that contribute to their addiction is inconsistent with the findings of human laboratory studies of substance abusers.

Second, most of the data supporting the proposed theory come from laboratory animal studies, with limited consideration of the social setting in which the drugs were administered. However, human drug-taking behavior is extremely sensitive to social context. Hart et al. (2005), for example, found that experienced marijuana smokers self-administered significantly more delta-9-tetrahydrocannabinol (Δ^9-THC) capsules (the primary psychopharmacologically active component of smoked marijuana) during social/recreational periods compared with non-social/recreational periods. This and other findings that drug self-administration is influenced by social factors (e.g., Doty and de Wit 1995; Foltin et al. 1989) raises questions about the applicability of the proposed theory to human substance abuse.

Third, the target article defines addiction "as the continued making of maladaptive choices" (sect. 1, para. 1). Appropriately, the definition is derived from the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV-TR) and *International Classification of Diseases* (ICD-10). However, both the DSM-IV-TR and the ICD-10 refer to the phenomenon of interest as substance *dependence* and not *addiction*. It is not clear how the proposed theoretical model deals with individuals who use "addictive" substances, but do not meet criteria for substance dependence. While this omission has implications for several aspects of the model, it is particularly relevant to the discussion of the mediating role of increased dopamine activity on the failure point of the habit system. Overwhelmingly, illicit drug users do not display symptoms associated with dependence (Substance Abuse and Mental Health Services Administration 2007), and many of the substances used by these individuals enhance dopaminergic activity acutely. In our experience with human cocaine and methamphetamine users, for example, many non-dependent individuals report using these drugs several times per week and, in some cases, for many years. In addition, many patients are maintained on daily doses of amphetamines, dopamine agonists, for medical reasons (e.g., to treat attention-deficit/hyperactivity disorder [ADHD]), yet do not meet criteria for a substance use disorder. In fact, some investigators have

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reported that stimulant medication treatment for ADHD is protective against subsequent development of substance abuse (Wilens et al. 2003). Given the widespread licit and illicit use of dopamine-enhancing drugs, the model's failure to address the non-dependent use of so-called drugs of abuse is a serious omission.

Finally, Redish et al. contend that their theory has implications for prevention and treatment. We appreciate that an exhaustive consideration of research on substance abuse would be beyond the scope of the target article. However, we regret the authors' failure to discuss what is arguably the most successful substance abuse treatment strategy: contingency management (for review, see Higgins et al. 2004). This omission might be related to the proposed theory's primary focus on neurobiological explanations of substance dependence, whereas contingency management (consistent with the human laboratory data cited earlier) views such behavior as sensitive to environmental consequences. It is clear that, under certain conditions, drug users can make rational choices that limit their drug intake. A theory that delineates the conditions under which drug users will and will not make maladaptive decisions about their drug use would be of enormous scientific and practical value.

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Are addictions "biases and errors" in the rational decision process?

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Abstract: Redish et al. view addictions as errors arising from the weak access points of the system of decision-making. They do not analytically distinguish between addictions, on the one hand, and errors highlighted by behavioural decision theory, such as over-confidence, representativeness heuristics, conjunction fallacy, and so on, on the other. Redish et al.'s decision-making framework may not be comprehensive enough to capture addictions.

Redish et al. offer a unified framework of decision-making. They use the framework, first, to classify the different kinds of addictions; second, to show how the different theories of addiction are partial descriptions of these kinds; and, third, to prescribe different remedies for each kind. Addictions, they argue, arise from vulnerabilities in the access points of the system of decision-making – vulnerabilities similar to the errors and biases uncovered by behavioral decision research (Kahneman et al. 1982).

Redish et al. propose a decision-making framework based on the distinction among three systems: "cognitive system," which they leave out of the target article, and two action systems, namely, "planning system" and "habit system." The planning system, or, a better term, "deliberation system," involves assessing the values of outcomes (O) of a ray of actions (a), given the situation (S) ($S \xrightarrow{(a)} O$), and then choose the best (optimum) action. The habit system involves specific action in response to a situation, where outcome is absent ($S \xrightarrow{a}$). The outcome is absent because the decision is very inelastic with regard to changes in the situation – which would demand different action if the decision is undertaken by the deliberation system.

It is a step in the right direction to ground addictions in decision-making theory. This commentary, though, finds that Redish et al. have failed to analytically distinguish between addictions, on one hand, and the biases and errors that inflict decision-making as highlighted by behavioral decision research, on the other. Further, this commentary questions whether Redish et al.'s framework is comprehensive enough to explain addictions. To start with, the habit system is not very different than the deliberation system: both are regulated by rational choice.

Redish et al.'s deliberation system resembles the standard notion of rationality. Agents are rational if they obey the transitivity axiom (consistency), completeness axiom (decisiveness), and some other minor axioms (see Kreps 1990, pp. 18–37). Further, agents must also undertake welfare-enhancing acts (see Becker 1976, Ch. 1). But is the deliberation system, and its associated habit system, exhaustive description of behavior? Are organisms motivated only to take the best decision in light of a situation? Humans, for example, have the urge to act creatively and with imagination – that is, beyond what is suggested by the situation – which introduces innovations (Khalil 1997; 2007; Nooteboom 2000, Ch. 9). And such urge, or its frustration in the forms of depression and disorders, might be the basis for accounting for addictions. Although Redish et al. mention depression and disorders at the conclusion of the target article, they fail to incorporate them in their framework.

The main fabric of Redish et al.'s framework is rather the deliberation system, the habit system, and their interconnection. But habits do not lie far from deliberation. As the authors repeatedly state, habits originate from deliberation: When the organism faces repeatedly the same situation, there would be no need to deliberate; the organism would react automatically. This would speed decision-making, economizing on the use of cognitive resources. Such speeding is desirable as long as its benefit exceeds the cost of rigidity.

Despite the fact that habits originate from deliberation, they have different neural substrates. Redish et al., therefore, consider them dichotomous systems. "Because the $S \xrightarrow{a}$ association is a habitual, automatic association, choices driven by $S \xrightarrow{a}$ relationships will be unintentional, robotic, perhaps even unconscious" (sect. 3.3.1, para. 2). But is the habit system unintentional, robotic, or unconscious? The fact that they involve different neural substrates does not mean the two systems are dichotomous. They may involve an efficient division of labor. The same homogeneous structure differentiates itself into substructures, each specializing in a different function. So, the two systems might be underpinned by a common structure, rational choice.

In fact, the habit system does not lie far from rational choice. Let us use Redish et al.'s example of how driving to a new job becomes, after repetition, a habit (sect. 3.1). They recognize that such a habit never escapes the intervention of deliberation – as in the case when road construction closes a route. Nonetheless, aside from such interventions, they consider the habit system as autonomous. Let us assume that one's job moves to a nearby location, where halfway to work, the agent has to take another route. The agent would habitually fail to adjust midway, finding himself driving to the old job. But this repeated mistake does not go uncorrected. The old habit would eventually dissipate, given that the reward is suboptimal. Thus, rationality is, in the final analysis, a regulator of the habit system. We do not have a dichotomy. The habit system is a *subsystem* of deliberation.

If so, Redish et al.'s framework amounts to deliberation and its subsystem. They find that each system and its interaction with the others are full of vulnerabilities that explain a variety of addictions. They recognize that drugs enhance the vulnerabilities, leading to an over-evaluation of outcomes and probabilities. But they also argue that many of the vulnerabilities simply arise from errors in reasoning as uncovered by behavioral decision research (Kahneman et al. 1982; Kahneman & Tversky 2000; Tversky & Kahneman 1981). Therefore, for Redish et al., addictions are analytically similar to errors and biases such as overconfidence, preference reversals, illusion of control, availability heuristic, conjunction fallacy, and so on.

However, there is a major difference between errors of judgment and addictions. Most agents commit the same errors of

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judgment in a *predictable* manner as they commit optical illusions (Ariely 2008). No such predictability exists, as Redish et al. admit, with regard to addictions. For instance, most agents are vulnerable to the switch from the loss frame to the gain frame in the Asian disease experiment (Tversky & Kahneman 1981). Also, most agents fall victim to overconfidence and the conjunction fallacy (Baron 2008, Ch. 6). But, with addictions, individuals vary widely in the manner they may or may not become addicted.

The same decision framework seems unable to explain both biases and addictions. Redish et al.'s framework might not be the proper tool to explain addictions. Addictions, at first examination, are maladaptive actions in the sense that they reduce O. In contrast, the errors that arise from heuristics might be minor nuisances that the organism tolerates because the heuristics, on average, are efficient. In this case, the heuristics are tolerable "bad habits" given that such habits, in comparison to their absence, have positive net effect on O. Addictions, in contrast, totally diminish the ability to produce O. If so, we need another framework, aside from deliberation and habits, to tackle addictions. This framework may have to attend to the urge to be creative, to have a meaningful life, and how it may lead to addiction when the urge is frustrated.

Role of affective associations in the planning and habit systems of decision-making related to addiction

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Abstract: The model proposed by Redish et al. considers vulnerabilities within decision systems based on expectancy-value assumptions. Further understanding of processes leading to addiction can be gained by considering other inputs to decision-making, particularly affective associations with behaviors. This consideration suggests additional decision-making vulnerabilities that might explain addictive behaviors.

Redish et al. show that a fuller understanding of the processes and outcomes of substance use and abuse can be gained by probing the underlying decision-making and self-regulatory mechanisms involved in initiation and maintenance of use. Their analysis of decision-making systems and vulnerabilities in those systems stems from expectancy-value model tenets in the decision-making and behavioral economics literatures, and from conditioning principles and theories in the learning literature. Although the framework put forward by Redish et al. draws nicely on these literatures to propose an integrative model of substance use, there are important processes involved in decision-making and self-regulation which are not well included in this framework.

In particular, affective processes are not well represented in the framework presented in the target article. We know that affective processes are implicated in a variety of issues around substance use and abuse. For example, affective states are reported as antecedents of smoking behavior and of relapses after quitting (Gilbert et al. 2000; Shiffman et al. 1996). In the context of alcohol use, negative affect resulting from acts of discrimination is associated with drinking by members of minority groups (Simons et al. 2006; Terrell et al. 2006). Finally, as Redish et al. point out, intake of some substances directly leads to affective states (e.g., euphoria; Koob & Le Moal 2006). Moreover, research from multiple domains has shown that affective processes are an integral part of "normal" decision-making and both impact and are influenced by the expectancy-value processes discussed in Redish et al.'s analysis. Use of expected-utility rules changes with decision tasks that arouse negative emotion (Darke et al. 2006; Greene et al. 2001). Behavioral choices are influenced by anticipation of experiencing regret, guilt, or other emotions as a result of engaging in a behavior (Richard et al. 1996).

An integrative model of the influence on behavioral choice of cognitively based inputs and affective associations with behaviors has been proposed recently (Kiviniemi et al. 2007). The *behavioral affective associations model* focuses on affective associations with a behavior – feelings and emotions associated with a particular behavioral practice. The model proposes that affective associations with a behavior influence actual behavior; more positive affective associations lead to a greater likelihood of engaging in a behavior. Moreover, according to the model, affective associations mediate influences of cognitive beliefs on behavior. Finally, the model argues that affective associations influence behavioral practices both via mediating cognitive beliefs and through a path that is dissociable from and distinct from the mediation of cognitive beliefs (see Kiviniemi & Bevins 2007 for additional discussion of the model). Affective associations have been documented for alcohol and marijuana use (Simons & Carey 1998) and smoking (Trafimow & Sheeran 1998). Recent data from the Kiviniemi lab shows that affective associations both directly predict use behavior and mediate the influence of expected utility beliefs on use for alcohol, cigarette smoking, and marijuana use.

Thus, there are a variety of reasons to argue that affective associations play a central role in both decision-making about and ongoing self-regulation of substance use. What implications might an affective association analysis have for Redish et al.'s framework for studying addiction? First, consider two components of Kiviniemi et al.'s (2007) behavioral affective associations model: (a) affective associations mediate the influence of expected utility beliefs on behavior, and (b) affective associations influence behavior both in conjunction with (through the mediational pathway) and independent of cognitively based expected utility beliefs. The mediational path suggests that affective associations may serve a self-regulatory role by functioning as an indicator of the expected utility of a behavioral choice or, more broadly, by indicating the overall positivity or negativity of one's cognitively based beliefs (e.g., attitudes, social norms). This would allow decision making to proceed in a faster and more efficient manner than directly accessing cognitive beliefs. Such an analysis is consistent with the work of Damasio and colleagues on the somatic marker hypothesis (e.g., Damasio 1994). The tenet that affective associations can exist and can influence behavior independent of one's cognitive beliefs suggests that the content of one's affective associations with a behavior could conflict with one's cognitive beliefs (e.g., one might perceive a number of negative consequences from alcohol use but still have overall positive affective associations with alcohol and its use).

In the context of substance abuse, this suggests the possibility for an additional vulnerability in the decision-making system. To the extent that affective associations are created relatively independently of one's cognitive beliefs about the behavior (as might be the case for euphoria resulting from use or from associating the drug and its use with other positively valued things), the independent affective associations–behavior pathway might push behavior in different directions than the cognitive beliefs path. Such a conflict between decision-making inputs then raises the important question of which input will "win" and influence behavior. Because cognitively based processes often require some effort by the individual, whereas affective processes are more automatic, it may be the case that affective associations will be more likely to guide behavior. This may be especially

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likely in the context of substance use where impaired cognitive functioning may be a consequence of use (e.g., Hoffman et al. 2006; Kim et al. 2005).

Supporting this point about vulnerability and affective associations are the published examples of unconditioned stimulus revaluation using Pavlovian conditioning with alcohol (Molina et al. 1996; Revusky et al. 1980; Samson et al. 2004). For instance, in a retrospective revaluation design Molina et al. (1996) found that an aversion to a tactile stimulus conditioned with ethanol was abolished if ethanol was later paired with sucrose. More specifically, rat pups first had an aversion conditioned to the tactile stimulus by pairing it with intragastrically administered ethanol. If rat pups then had the ethanol paired with a sucrose solution via intra-oral cannula, the robust tactile aversion was no longer expressed. The previously acquired tactile aversion was *not* lost if ethanol and sucrose were presented in an unpaired fashion (i.e., no temporal contiguity). Molina et al. concluded that the representation of the ethanol unconditioned stimulus (US) was changed by the appetitive conditioning history with sucrose. As such, expression of the earlier conditioned association (memory) was also changed. A similar possibility has been discussed for nicotine (Bevins, in press; Bevins & Palmatier 2004). Applied to the early discussion, here is an example of a choice behavior (avoid aversive stimulus) that was modified not by direct and contrary learning history in that situation. Rather, choice was presumably altered by changing the positive affective qualities of ethanol. Perhaps effortful cognition was involved in this revaluation. However, such an assumption is not necessary to explain the change in choice behavior and, in fact, seems a priori.

In summary, Redish et al. in this target article outline an integrative model of substance use from a decision-making and self-regulation perspective. This model provides much to think about, as well as indicates interesting and likely important paths for future research. However, we suggest that going beyond considering vulnerabilities within an expectancy-value decision system to consider how other inputs to decision-making might inform our understanding of substance use and abuse, can strengthen the framework proposed by Redish et al. In particular, considering the role of affective associations with behavior suggests that an additional decision-making vulnerability influencing substance use might be conflict between affectively based and cognitively based decision systems. Such conflict can explain why behaviors, including substance use and abuse, may depart from expected-utility model predictions.

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Negative affects are parts of the addiction syndrome

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Abstract: Decision-making is a complex activity for which emotions and affects are essential. Maladaptive choices depend on negative affects. Vulnerabilities to drug or non-drug objects depend on previous psychopathological comorbidities. Premorbid individual characteristics allow us to understand why some individuals – and not others – enter into the addiction cycle. Moreover, plasticity of reward neurocircuitry is, at least in past, responsible for these vulnerabilities leading to compulsive drug use.

The field of addiction research is becoming more and more complex, and many hypotheses have been proposed to account for the transition from recreational use to impulsive consumption and to the last stage of this chronic, relapsing disease: compulsive use and addiction. Redish et al. have reviewed some of these theories and have proposed a classification under eight categories in such a way that some researchers will be surprised to find themselves listed under this or that category. The theories cited each stress different aspects, functional or neuropsychological, and different phase of the process, or consider either physiological mechanisms or structural neurobiology. In the target article, Redish et al. propose one more theory, which is more specific and cognitively oriented: the process of decision (decision-making) is hypothesized to be a "unified framework for addiction" and to be operational to provide a classification of potential vulnerabilities. From a Herculean analysis of the literature, but from this restricted point of view, they have identified ten potential different constitutive vulnerabilities.

Scientific analysts alert us about the breaking down and fragmentation of knowledge, a crisis due in part to the reductionism inherent in modern scientific progress. What is needed is to turn toward a more difficult task: to try and propose holistic theories and to conform to the principle of parsimony. Entities should not be multiplied without necessities, according to the principle of Occam's razor. Moreover, most authors now agree about the reality of a common clinical syndrome for all the drug and non-drug addictions (Goodman 1990; 2008) and, underlying it, a common set of neuronal systems, whose dysregulations is supposed to be responsible for the set of symptoms (see Koob & Le Moal 1997; 2001; 2006). The question is to know at which stage the process is examined. It seems that Redish et al. are considering the stage of addiction when maladaptive choices are made in spite of their deleterious consequences, whereas vulnerability is generally studied as an intrinsic factor operating at the beginning of the process, accounting for the huge individual differences in the propensity to move toward impulsive drug-taking or gambling (Anthony et al. 1994; Piazza & Le Moal 1996; Piazza et al. 1989; Substance Abuse and Mental Health Services Administration 2003).

At one moment of the process, there is a passage from impulsive control disorder to compulsive disorder – from a stage where increasing tension and arousal occur before the impulsive act, with pleasure, gratification, or relief during the act, followed by regret or guilt, to a stage of recurrent and persistent thoughts (obsessions) that cause marked anxiety and stress followed by repetitive behaviors (compulsions) that are aimed at preventing or reducing distress. The first stage is most closely associated with positive reinforcement (pleasure, gratification); the compulsive stage is most closely associated with negative reinforcement and relief of anxiety and/or stress (Koob & Le Moal 1997). Addiction involves persistent plasticity in the activity of neuronal circuits mediating a decreased function of the brain reward system and a recruitment of anti-reward systems, now well identified, driving aversive states (Koob & Le Moal 2005; 2008). For the purpose of this commentary, the withdrawal/negative affect stage can be defined as the presence of motivational signs of withdrawal in humans, that is, chronic instability, emotional pain, malaise, dysphoria, and loss of motivation for natural rewards. As dependence and withdrawal develop, brain anti-reward systems are recruited (Koob & Le Moal 2008). Another critical problem is chronic relapse in which addicts return to compulsive drug-taking after acute withdrawal; relapse corresponds to the preoccupation/anticipation stage of the addiction cycle just outlined. A unified framework for addiction cannot avoid the fact, well documented from clinical observations, that affects and emotions are important, if not central, neuropsychological dimensions in this human condition. Needless to say, these dimensions interact with the process of decision-making.

All the neurobiological theories of addiction (we refer to the last stage of the process) agree (see Koob & Le Moal 2006)

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about an interconnected network of regions and neuronal systems including subcortical and cortical structures (Everitt & Wolf 2002; Goldstein & Volkow 2002; Hyman & Malenka 2001; Kalivas & McFarland 2003; Koob & Le Moal 2001; See et al. 2003). All agree also about the fact that the prefrontal region (orbitofrontal, medial-prefrontal, prelimbic/cingulate), associated with the basolateral amygdala, is more and more dysregulated as the addictive process progresses. These two regions are key elements for some of the symptoms and for the dysregulation of the motivational systems described earlier, and finally for the affective negative state from which addicts suffer so much. A pure cognitive approach of the syndrome does not account for what is seen in the real world. Decision-making, impulse control, and loss of willpower to resist drugs (Bechara 2005) are of course very important, and a correlative deactivation of the prefrontal cortex will produce enormous consequences. Drugs, games, and diets are mental objects; they are not addictive by themselves. They will be addictive if they are met by a person vulnerable to their intrinsic properties. If we consider a "healthy mind" making a decision, two groups of specialists in the field have developed the same idea: emotion participates to reasoning-reflective activity and at least in the first stages of decision-making. Kahneman and colleagues (see Kahneman 2003) have described a perception-intuition system – stimulus bound, fast, automatic, effortless, slow-learning and emotional; and a reasoning system – slow, controlled, effortful, not flexible, less emotional with different contents such as conceptual representations and temporal references. The Iowa group (Bechara et al. 1998; 2000, Damasio et al. 2000) refers also to a first emotional stage of the decision, a sort of impulsive system, followed by a reflective one; a peripheral emotional reaction occurs before and orients decision-making. It is possible that these two groups refer to two different parts of the frontal cortex (dorsolateral versus ventromedial).

The subject who enters the impulsive-compulsive spiral is, even before his or her first consumption, not immune to psychopathological disorders. He or she does not have a "healthy mind." Different parts of the brain present some sort of dysfunction. It is well documented that the main source of vulnerability (not to be confounded with polydrug use) is the existence of psychopathologies and behavioral disorders (depression, anxiety disorders, impulsivity, stress, self-dysregulations, etc.), and that holds for more than 80%, if not all, of the subjects who will succumb (Goodman 2008; Le Moal & Koob 2007; Shaffer et al. 2004). These psychopathologies are related to neurobiological dysfunctions in both affective and cognitive systems. It has been proposed with robust arguments (Baumeister et al. 1994; Baumeister & Vohs 2004) that these vulnerable individuals are unable to self-regulate their emotions, desires, motivations, and pleasures. Self-regulation failure is a complex construct; it may lead to impulse control disorders. Here again, the causal mechanisms are not clear and may involve cortical dysfunctions due to subcortical mesolimbic dysfunctions (Piazza & Le Moal 1996), in a negative feedback manner.

In conclusion, there is, I feel, something missing in Redish et al.'s scholarly review: the agency of reward-emotional systems (Koob & Le Moal 2008) and of the stress systems (al'Absi 2007).

Expanding the range of vulnerabilities to pathological gambling: A consideration of over-fast discounting processes

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Abstract: Redish et al. present a compelling, interdisciplinary, unified framework of addiction. The effort to integrate pathological gambling is especially important, but only the vulnerability of misclassifying situations is described in detail as being linked directly to this disorder. This commentary focuses on further developing the comprehensiveness of this framework for pathological gambling using over-fast discounting as an illustrative example.

Redish et al. put forward a framework of addiction that unites competing theories by focusing on key vulnerabilities in the development and maintenance of addictive behaviors and emphasizing their links to the habit and planning systems underlying decision-making. Consideration of pathological gambling within this framework seems particularly valuable as historically this disorder has been conceptualized and categorized separately from substance use disorders (American Psychiatric Association 2000; Hollander & Wong 1995). Based largely on data describing irrational cognitions in pathological gamblers and therapies based on altering these cognitions, Redish et al. argue that vulnerability to pathological gambling falls largely within the domain of misclassifying situations (*Vulnerability 6*). However, many recreational gamblers experience irrational cognitions when gambling, which raises questions regarding the centrality of this feature to pathological gambling (Sharpe 2002). Furthermore, the most thoroughly tested cognitive behavioral therapy for pathological gambling targets more than irrational cognitions, addressing coping with cravings and managing finances (Petry 2005; Petry et al. 2006). Clinical experience suggests that changing erroneous perceptions is not always sufficient in ceasing pathological gambling, as some patients report knowing that they will lose but continue gambling problematically nonetheless.

Consistent with the integrative goals of the target article, we consider *Vulnerability 9* (over-fast discounting) as a failure point with relevance to pathological gambling. While other vulnerabilities (e.g., those related to craving, obsessions, or withdrawal) could be considered, over-fast discounting applies to gambling in important ways and thus was selected for elaboration.

Redish et al. describe the relevance of over-fast discounting of rewards, particularly temporally (i.e., delay discounting; Ainslie 1975; Rachlin & Green 1972), to substance use disorders, citing pre-clinical and clinical data (Kirby et al. 1999; Richards et al. 1999). Delay discounting reflects one aspect of impulsivity (Bornovalova et al. 2005; Moeller et al. 2001). A principal component analysis of self-reported and behavioral measures of impulsivity identified two components, termed "impulsive disinhibition" and "impulsive decision-making," with delay discounting contained in the latter category (Reynolds et al. 2006). Self-reported and behavioral measures of impulsivity, including delay discounting, have not correlated strongly (Krishnan-Sarin et al. 2007). This phenomenon might reflect hypothetical versus real-life differences in risk/reward decision-making, as are often observed, for example, in trying to maintain New Year's dieting resolutions in the setting of chocolate cake being served. Unsurprisingly, preliminary data associate behavioral measures of impulsivity and substance abuse treatment outcome, whereas outcomes were not associated with self-reported measures in the same study (Krishnan-Sarin et al. 2007).

Although several studies of drug abusers have utilized hypothetical drug reinforcers (a small amount of heroin immediately versus a larger amount tomorrow), most work has considered financial choices ($10 immediately versus $12 tomorrow) with the assumption that the drug and money are functionally related. As such, one might hypothesize that the

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typical delay discounting procedure utilizing financial rewards might be even more relevant to gambling than to substance use behaviors. Relatively few studies have directly examined problem or pathological gambling and delay discounting, and existing studies have generated inconsistencies (Reynolds 2006). One study indicated a link between problem gambling and increased discounting of delayed monetary rewards, even when controlling for self-reported impulsivity (Alessi & Petry 2003). A separate study found that pathological gamblers discounted delayed rewards more steeply than non-gamblers (Dixon et al. 2003). However, a third study of young adults found the converse (Holt et al. 2003).

A role for co-occurring substance use disorders is also indicated. One study found that among a sample of substance abusers, probable pathological gamblers discounted rewards more rapidly than did those without gambling problems (Petry & Casarella 1999), although the difference was limited to hypothetical rewards of larger magnitudes. A related study similarly indicated that pathological gamblers discounted delayed rewards at higher rates than did control participants, and gamblers with substance use disorders discounted delayed rewards at higher rates than did non-substance-abusing gamblers (Petry 2001). The only experimental study found that, among pathological gamblers, a classic discounting profile was evident only when conducted in a real-life gambling context (Dixon et al. 2006). It has also been suggested that individuals who engage in different forms of gambling (e.g., slot machine vs. sports) might be discounting rewards differently (Cooper 2007). Thus, although multiple studies indicate that problem and pathological gamblers, like substance abusers, discount rewards more rapidly than do control subjects, the results are not entirely consistent and suggest that specific environmental, developmental, or individual factors influence these processes. This interpretation fits well with the assertion of Redish et al. for addictions in general, that specific vulnerability factors (including over-fast discounting) may be more salient for specific subgroups, even within diagnostic categories.

The scope of *Vulnerability 9* also warrants further consideration. Both positive and negative reinforcement processes have been implicated in addiction (Koob & Le Moal 2001), and considering both with respect to rapid discounting seems important. Although delay discounting has typically been applied to positive reinforcers in comparing smaller immediate and larger delayed rewards, it also may be considered in relation to aversive stimuli in the context of negative reinforcement. In this case, impulsivity involves the selection of a larger, delayed aversive stimulus over a smaller, yet immediate aversive stimulus. Said differently, this describes the tendency to delay experiencing a mildly aversive event, even though this delay likely will result in a more aversive event in the future. Currently, few conceptualizations of delay discounting consider this reciprocal focus on negative reinforcement across substance disorders or pathological gambling. This conceptualization appears particularly relevant to important aspects of pathological gambling such as "chasing" losses, wherein one continues to gamble further, typically leading to greater future gambling losses, instead of accepting the immediate consequences associated with a recent gambling loss.

Redish et al. have advanced the field with this ambitious integrative effort. Further developing this model for pathological gambling as it relates to other vulnerabilities could strengthen the impact of the model and its utility in advancing prevention and treatment strategies for pathological gambling.

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Addiction: More than innate rationality

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Abstract: Redish et al. rely too much on a rational and innate view of decision-making, when their emphasis on variation, their integrative spirit, and their neuroscientific insights point towards a broader view of why addiction is such a tenacious problem. The integration of subjective, sociocultural, and evolutionary factors with cognitive neuroscience advances our understanding of addiction and decision-making.

First, the praise. Redish et al. show us the inherent variability in decision-making. That is a fundamental Darwinian insight, at a remove from the singular focus of the traditional reward paradigm in psychology or prominent evolutionary approaches such as optimality or adaptive modules (Lende 2007; Lende & Smith 2002). Redish et al. accomplish this feat by tying together neurobiological, psychological, and animal research – meaning we no longer face the "black box" of the brain or an over-reaching theory based on one slice of research. Redish et al. build their analysis of addiction on similar strengths – an emphasis on variability in vulnerabilities, comprehensive appraisal rather than a pet theory, and the much-needed linkage of decision-making to different addictive drugs and activities.

Unfortunately, three fundamental problems undermine their overall efforts. First, Redish et al. base their approach on the "rational man" assumption. As they note, the literatures they use "have converged on the concept that decisions are based on the prediction of *value* or *expected utility* of the decision" (sect. 3, para. 1; emphasis theirs). Expected utility lies at a considerable distance from addiction, where excessive involvement in a behavior, social role failure, and the active ignoring of costs are core diagnostic features.

Second, Redish et al. approach decision making as largely innate. Their computational framework works through internal mechanisms, a series of calculations based on expected utility, with the twist thrown in of a fast habit system and a slower planning system. However, both brain research and decision-making research have shown that interactive, environmentally dependent processing are fundamental features of adaptive behavior (Chiel & Bier 1997; Clark 1997; Epstein 2007). This embodied approach stands in direct contrast with a representational (or computational) view of brain function, and it undercuts Redish et al.'s claim that they have presented a unified framework.

Third, Redish et al. do not draw on either ethnographic or clinical case studies of addiction, which hampers their ability to find creative connections between decision-making research and addictive behavior. This point is especially clear late in the target article, when they write, "the decision-making theories discussed in this article are primarily about reinforcement (delivery of unexpected reward) and disappointment (non-delivery of expected reward)" (sect. 6, para. 3). Unexpected rewards and non-delivery do not add up to addiction.

For example, with gambling, Redish et al. emphasize *Vulnerability 6* (the misclassification of situations and the illusion of control). Using situations (rather than stimuli), neural plasticity, and the cognitive dynamics of "control," the authors bring a novel interpretation for why addicts get in such a rut about recognizing the costs of their behavior. However, this interpretation builds from their ability to get away from a rational innatist position, precisely through situations, plasticity, and illusion.

Thus, implicit assumptions of rationality and innate computation hamper the development of a unified approach to how decision-making plays into addiction. Addiction involves subjective, sociocultural, and evolutionary elements, and these elements help us get at the "why" of addiction (Lende 2005a; 2007). Rather

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than assuming that rationality explains why, more fruitful approaches can be achieved by combining anthropology and other social sciences with the biological and behavioral sciences (Hruschka et al. 2005).

Why do people use and abuse drugs? Environmental inequality makes a direct impact on decision-making (Bourgois 2002; Singer et al. 1992), for example, in social position, dopamine function, and cocaine use (Morgan et al. 2002), or in the quality of the environment and the reinforcement of cocaine and heroin (Alexander 1987; Alexander et al. 1981). Similarly, moving beyond the individual misclassification of situations, sociocultural context can directly shape heavy drinking, particularly the effect alcohol has and the amount that people drink (Heath 2000; MacAndrew & Edgerton 1969; Marlatt 1999).

Moreover, the understanding of relapse is enhanced through incorporating elements of self-efficacy, cognitive dissonance, and personal attribution (Brownell et al. 1986). Rather than blaming the situation, the person blames "personal weakness," heightening the chance of further relapse due to continued "loss of control" (after all, already lost control once . . .). In other words, relapse is more than a decision-making vulnerability based on the computation of benefits or costs in any particular situation.

Finally, drug users seek things from substance use – intentions, subjective experience, and meaning all matter in what users want. For example, heavy methamphetamine users often engage in "functional use," seeking to enhance a skill or to be in an altered state while still engaging in socially acceptable behavior (Lende et al. 2007). Craving, long seen as psychobiological, is often defined by users in reference to personal control, rather than being separable into a cue-, drug-, and withdrawal-driven typology (Bruehl et al. 2006).

Instead of reducing the habitual and compulsive aspects of addiction to computational decision-making, these behaviors and experiences can drive addiction. A renewed focus on the psychology of interest (Silvia 2008) and the use of wheel running as a behavioral model for compulsive involvement (Rhodes et al. 2003; 2005; Sherman 1998) show us an important insight often lost in experimental models: neurobiology and decision-making serve behavior, not the other way around.

A core part of any behavioral involvement, including addiction, is subjective experience. To take one example, Robinson and Berridge's (2001) incentive salience (discussed in Redish et al.'s *Vulnerability 4*, overvaluation in the planning system) depends as much on the meaning of drug use as it does on the action of the mesolimbic dopamine system (Lende 2005b). Heightened salience is a measurable trait, using a psychometrically valid scale (Lende 2005b). At the same time, both cultural symbols and an individual's sense of self impact what users desire and seek out. In my ethnographic research, one girl who smoked marijuana nearly every day explained what she wanted: "estar en un video" ("to be in a video"), where attention was shifted away from how she felt in her traumatic yet culturally valued family environment. This type of compulsive involvement, both in itself and as a step away from a traumatic everyday life just waiting to return, is central to why some people use drugs to such excess.

Bridging the gap between science and drug policy: From "what" and "how" to "whom" and "when"

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Abstract: For all its problems, the microeconomic "rational addiction" theory had the appeal of making clear predictions about the effects of various drug policies. The emerging picture of the "what" and "how" of addiction is far more complex. Addiction scientists might help bridge the science–policy gap by devoting more attention to the "whom" and "when" of addiction.

Redish et al. document tremendous progress in the scientific understanding of the "what" and "how" of drug addiction. Strangely, as our understanding of addiction advances, its implications for rational drug policy seem to recede – at least relative to the now discredited "rational addiction" account of microeconomists Gary Becker and his colleagues (e.g., Becker et al. 2004).

There are various ways in which the science of addiction might produce a more reasoned, less ideological approach to drug abuse policy (see MacCoun 2003). The influence could be technological, in the form of more powerful treatments, diagnostic tools, or even safer psychoactive drugs. The influence could be behavioral, in the form of advice about the design of optimal prevention, deterrence, and harm reduction tactics. Or the influence could be rhetorical and conceptual, changing the very way we think about the problem.

Advances have been steady but incremental on the technological front, and I leave it to other commentators to address that topic. On the rhetorical front, one couldn't ask for a more potent reframing than the mid-1990s claim that addiction is a chronic relapsing disorder (O'Brien & McLellan 1996). This view arguably helped facilitate the growth of the drug court movement, but it still wasn't enough to curtail the steep growth in the federal drug prisoner population in the decade that followed. The public's flexible image of the addict as enslaved and yet still blameworthy allows ready assimilation of most new facts about addiction (see MacCoun & Reuter 2001). At least in the United States, citizens seem less interested in how someone becomes addicted than they are in the question "could the actor have done otherwise?" But addiction scientists have been more reticent at addressing the middle ground between philosophy and technology – behavioral questions about how to do prevention, deterrence, and harm reduction.

Redish et al. are admirably circumspect about offering prescriptions for policy makers. Still, it is worth highlighting some ways in which an improved neuroscience complicates, rather than simplifying, drug policy analysis. As our understanding of addiction has grown in sophistication, it has also grown in complexity. Where earlier models implicated a small handful of core mechanisms (e.g., tolerance, withdrawal, and craving), Redish and colleagues implicate eight distinct vulnerabilities. If one wanted to design an addiction machine robust enough to withstand random environmental shocks or hostile tinkering by saboteurs, eight overlapping mechanisms would seem to offer more than enough redundancy.

If, as some contend (e.g., Becker et al. 2004), drug addicts behave like rational microeconomic consumers, then we could deduce fairly clear policy predictions about the perils of prohibition and the promise of sin taxes and optimal regulatory enforcement. And in one way, the rational choice analysis fares better than some might expect; estimates of the elasticity of demand suggest that even heavy drug users are price sensitive (see Manski et al. 2001). But ultimately the rational addiction model fails on both empirical and theoretical grounds (Auld & Grootendorst 2004; Gruber & Koszegi 2001; Skog & Melberg 2006).

Behavioral economic models of addiction (see Vuchinich & Heather 2003) are more realistic and better supported, though perhaps still too simplistic. At first glance, a mechanism like hyperbolic discounting is appealing because it offers a fairly modest modification to the economic choice equation. But because hyperbolic discounting produces preference reversals (unlike the standard exponential account), it makes less determinate predictions. Still, the behavioral economic approach teaches us that heavy users may respond to fairly modest carrots (Bickel et al. 1995) and sticks (Kleiman 2001) if we deploy them promptly and saliently.

Redish et al. offer an even richer framework for thinking about the "what" and "how" of addiction. But I would urge addiction

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scientists to take up the "whom" and "when" questions as well. Drug policy has a broad set of tools, including the legal status of a drug; criminal sanctions against users and dealers; interdiction and source country controls; drug prevention, education, and rhetoric from the bully pulpit; drug treatment; taxes, advertising controls, and other regulatory mechanisms; drug testing; and bans on employment, welfare, and other benefits. If we want to deploy those tools more effectively, efficiently, and humanely, we need to better understand how these eight decision vulnerabilities play out in real-world behavior. For example, which people are at greatest risk of each vulnerability? Can we identify them early, and if so, how should we help them? When is the most effective time to intervene, and should timing trump concerns about paternalism or stigma? How does each vulnerability influence the choice among drugs (substitution and complementarity), as well the likelihood of any "gateway" progression across drugs? Do differences in vulnerabilities across drugs imply that there should be differences in our policies across drugs? And are there better ways to design secondary prevention and deterrence strategies to overcome impairments in the decision process?

Linking addictions to everyday habits and plans

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Abstract: Redish et al. trace vulnerabilities in habit and planning systems almost exclusively to pharmacological effects of addictive substances on underlying brain systems. As we discuss, however, these systems also can be disrupted by purely psychological factors inherent in normal decision-making and everyday behavior. A truly unified model must integrate the contribution of both sets of factors in driving addiction.

Redish et al. treat addictions as maladaptive, repeated responses that arise through vulnerabilities in the interaction between a slow-learning, goal-independent habit system and a fast-learning, goal-oriented planning system. Although we applaud Redish et al.'s attempt to locate addiction within a "unified theory of decision making in the mammalian brain" (target article, Abstract), their approach ultimately traces vulnerabilities in the habit and planning systems to the direct pharmacological effects of addictive substances. In doing so, they neglect substantial evidence that the interplay between these behavioral control systems also is affected by a range of psychological and environmental factors that are commonplace elements of daily life and normal decision making (e.g., Reason 1990; Wood & Neal 2007). We argue that a unified theory of addiction must integrate these normal (i.e., non-pharmacologically induced) psychological processes. In support, we (1) review data showing that the role of habit- and planning-based behavioral control varies dynamically in everyday life and not simply in instances in which pharmacological agents have disrupted normal control, and (2) discuss specific implications for a subset of the vulnerabilities advanced in the target article.

As we have elaborated elsewhere, the distinction between habit-based and planning/goal-based behavioral control is studied across a range of subdisciplines within psychology and neuroscience (Neal et al. 2006; Wood & Neal 2007). In laboratory settings, the two systems can be operationalized by relatively direct tests (e.g., presence versus absence of reinforcer devaluation effects in animals; Dickinson et al. 1995) or by manipulating the procedures of behavioral training (e.g., observational versus feedback-based learning in humans; Poldrack et al. 2001). In real-world settings, the strength of the planning component is quantified by self-reported intentions to engage in the behavior in the future, whereas strength of the habit component is quantified by the frequency and context stability of past performance (see Neal & Wood, in press). The relative contribution of planning versus habit-based control can then be determined by regressing future behavior on each of these measures to determine which predictor is the strongest, and hence, which system primarily is controlling the behavior.

Real-world behavior prediction studies using this method typically yield statistical interactions in which strong habits trump strong intentions (i.e., intentions cease to predict behavior when habits are strong). This interaction has emerged in models predicting purchasing fast food, watching TV, driving the car, taking the bus, recycling, donating blood, exercising, and reading the newspaper (Danner et al., in press; Ferguson & Bibby 2002; Ji & Wood 2007; Ouellette & Wood 1998, Study 2; Verplanken et al. 1998; Wood et al. 2005). Supporting the extrapolation from everyday habits to addictions, similar patterns have emerged in studies of smoking cessation. For example, in Baldwin et al.'s (2006) study, participants' initial success at quitting was predicted by planning-related constructs, whereas over the long term, only the number of months that participants had been quit predicted whether they continued not to smoke.

The behavior prediction data have important implications for Redish et al.'s model because they suggest the habit-based component of behavioral control often dominates actual behavior even in the absence of any dysfunction associated with a pharmacological agent. In such cases, we presumably must look to normal psychological processes for an explanation. A key question then becomes, to what extent do such normal psychological processes also contribute to addictions, for which pharmacologically induced dysfunction likely is a factor? In the remainder of this commentary, we consider this question by exploring several purely psychological factors that may contribute to *Vulnerabilities 4*, 5, 7, and 8, which Redish and colleagues trace instead to pharmacologically induced dysfunction.

Vulnerabilities 4 and 5 involve, respectively, overvaluation in the planning system and incorrect search in stimulus-action-outcome evaluation. These biases are attributed to the direct effects of addictive substances on neural systems underlying the valuation and search of action outcomes. However, there is an additional, pervasive information processing mechanism that may also contribute to this vulnerability. That is, people often rely on their past behavior to infer their preferences (Ouellette & Wood 1998). Repeated actions lead to especially strong preference inferences (e.g., "I smoke a lot so I must really like it"). People tend to make such inferences when they are uncertain about the actual causes of their behavior (Bem 1972), as is often the case with habits. Thus, *Vulnerabilities 4* and 5 plausibly may be induced or enhanced by a pervasive tendency to infer preferences from past behavior, leading to overvaluation or incorrect search for previously experienced outcomes.

Vulnerability 7, involving overvaluation in the habit system, also is traced in Redish et al.'s model to bottom-up effects of drugs on neurotransmitter systems. However, evidence from everyday habits indicates that higher-level decision-making processes involving switching costs also can lock people into repeating past actions and choices. That is, the familiarity of an action decreases decision costs and thus increases the relative cognitive switching costs for alternative actions (e.g., Murray & Häubl 2007). Of course, switching costs may well be encoded as overvaluation of habits in the dopaminergic system that Redish et al. describe in relation to *Vulnerability 7* (see Niv et al. 2007). Our point is simply that overvaluation in the habit system need not solely be the product of drug-induced dysfunction but also may be the product of normal decision-making processes involving switching costs.

Vulnerability 8 addresses factors that disrupt the planning system and thereby reduce its scope to correct a misguided habit system. Although Redish et al. trace such disruptions to the pharmacological effects of drugs such as amphetamines and alcohol, our own model of habits predicts that the effortful inhibition of habits in

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favor of planned behavior is impaired by reductions in psychological self-control that are commonplace in daily life (Wood & Neal 2007). This prediction builds on substantial evidence that effortful self-control draws on a single domain-general psychological resource that is temporarily depleted with use (Muraven & Baumeister 2000). Using field experiments, we have shown that reduced self-control impairs people's capacity to implement planned behavior and perpetuates habits in the real world (Neal et al. 2008). Thus, the balance between habit and planning systems is dynamically responsive not solely to pharmacological agents but also to the many factors that deplete self-control in daily life (e.g., emotion regulation, complex decision making).

In summary, studies of everyday behavior repetition largely align with Redish et al.'s core premise regarding interacting behavioral decision systems corresponding to habit- and planning-based control. However, such studies also show that the relative influence of each system depends on a range of everyday psychological processes, including normal inferences, switching costs of decisions, and self-control capacity (Wood & Neal 2007). A truly unified model of addiction must consider the contribution of these processes alongside pharmacologically induced dysfunction.

The disunity of Pavlovian and instrumental values

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Abstract: A central theme of the unified framework for addiction advanced by Redish et al. is that there exists a common value or incentive process controlling Pavlovian and instrumental conditioning. Here we briefly review evidence from a variety of sources demonstrating that these incentive processes are in fact independent. Clearly the influence of Pavlovian predictors and goal values on choice offer distinct potential targets for pathologies of decision-making.

Redish et al. advance a unified framework of decision making in which they explicitly conflate Pavlovian (stimulus-outcome) and instrumental (action-outcome) learning processes into a single "planning component." They justify this by arguing that both processes "entail an expectancy of the outcome that must be evaluated to produce an expectancy of a value" (sect. 3, para. 8). However, it becomes clear that situational cues are assumed to be ultimately responsible for initiating action selection in the planning system; based on these cues, the agent "calculates the consequences of potential actions" and then "calculates the value of those consequences" (sect. 3.2, para. 2). This simplified view, although parsimonious, is at odds with a number of things we know about the role played by environmental cues in action selection.

First, the "unified framework" assumes that the evaluative processes that govern the performance of instrumental actions – for example, lever pressing for food – also control the performance of conditioned responses – for example, anticipatory approach to the location of food during a signal previously paired with food delivery. The authors are encouraged in this view by the fact that both instrumental actions and conditioned responses are sensitive to post-training manipulations of outcome (or unconditioned stimulus [US]) value. However, there is in fact considerable evidence that changes in outcome value affect these two categories of behavior through fundamentally different incentive processes (Balleine 2001; 2004). One particularly effective way to reduce the value of a food is by pairing it with illness, which can be readily induced with an injection of lithium chloride. Rats given just one such pairing tend to immediately suppress their conditioned approach responses, but continue to lever press for the devalued food, at least when tested in extinction (Balleine & Dickinson 1991). However, giving rats the opportunity to actually consume the devalued outcome (either between training and testing or during the actual test session) is sufficient to reduce their lever press performance, suggesting that direct contact with the outcome is needed to learn that it is no longer an instrumental goal. The incentive processes controlling conditioned approach performance apparently do not require such explicit feedback. This is not just true of taste aversion learning but also of shifts in food deprivation (Balleine 1992), water deprivation (Lopez et al. 1992), sexual motivation (Everitt & Stacey 1987), thermoregulation (Hendersen & Graham 1979), and drug-related states (Balleine et al. 1994), among other motivationally based shifts in incentive value. There is also evidence that the evaluative processes guiding Pavlovian and instrumental learning are neurally dissociable. Although orbitofrontal cortex (OFC) lesions have been shown to disrupt the effect of outcome devaluation on conditioned approach performance (Gallagher et al. 1999; Pickens et al. 2003; 2005), we have reported that OFC lesions do not impair the sensitivity of instrumental lever pressing to outcome devaluation (Ostlund & Balleine 2007).

Second, the "unified framework" fails to distinguish between the roles played by instrumental discriminative stimuli and Pavlovian conditioned stimuli in action selection. Discriminative cues can act to signal particular action-outcome relationships; for example, in biconditional discrimination experiments rats learn that two discriminative stimuli signal different and opposite action-outcome relationships; that is, S1 signals R1 → O1 and R2 → O2, whereas S2 signals R1 → O2 and R2 → O1. In this situation, discriminative cues play a critical role in guiding devaluation performance, such that rats will tend to suppress their performance of an action when the prevailing stimulus signals that the devalued outcome is going to be earned (Rescorla 1991). However, Redish et al. assign conditioned stimuli the same capacity to guide goal-directed action selection. It is true that conditioned stimuli can *influence* instrumental action selection. For instance, rats will tend to increase their performance of an action previously rewarded with a particular outcome when presented with a cue that has been independently paired with the same outcome relative to a cue paired with a different outcome (Kruse et al. 1983). However, it has more recently been shown that this Pavlovian-instrumental transfer effect is insensitive to manipulations of outcome value; that is, conditioned stimuli continue to selectively retrieve actions with which they share a common outcome even after that outcome has been devalued (Holland 2004; Rescorla 1994). Such findings suggest that conditioned stimuli do not play a significant role in guiding the evaluation of instrumental goals and instead appear to bias action selection through a separate associative priming process. This latter process likely reflects the information provided by these cues; Delamater (1995) has shown that degrading the Pavlovian CS-US contingency is sufficient to abolish the selective influence of Pavlovian cues on instrumental performance.

Furthermore, we have found evidence that instrumental outcome devaluation and Pavlovian-instrumental transfer effects are neurally dissociable at the level of the prefrontal cortex. In rats, OFC lesions have no effect on the sensitivity of instrumental performance to outcome devaluation, as mentioned earlier, but they are effective in disrupting Pavlovian-instrumental transfer, at least when they are made after training (Ostlund & Balleine 2007). In contrast, lesions of the prelimbic region of the medial prefrontal cortex have been shown to disrupt instrumental outcome devaluation performance but leave Pavlovian-instrumental transfer intact (Corbit & Balleine 2003).

This evidence that Pavlovian and instrumental conditioning are controlled by distinct incentive processes has implications for Redish et al.'s ultimate aim, which is to identify aspects of decision-making that are vulnerable to drug abuse. They describe *Vulnerability 4* as the tendency for repeated drug exposure to

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produce "overvaluation in the planning system" (sect. 4, para. 8), and argue that "sensitization of motivational signals drives excess motivation for certain events" (Table 5). Although it has been shown that post-training amphetamine sensitization enhances the sensitivity of instrumental performance to Pavlovian-instrumental transfer (Wyvell & Berridge 2000), as we have argued, this effect is not likely to be due to an overvaluation of the instrumental reward. In fact, it has more recently been shown that rats sensitized to amphetamine *after* instrumental training are unimpaired in their ability to use outcome value to select between actions even though rats sensitized to amphetamine *before* training showed impaired outcome devaluation performance (Nelson & Killcross 2006), consistent with the view that drug exposure resulted in excessive habit formation, something Redish et al. identify as *Vulnerability 7*.

We support the authors' attempt to apply concepts developed in associative learning to the study of addiction, but we believe that, rather than trying to blur the lines between Pavlovian and instrumental learning, it would accord better with the evidence to recognize that these two fundamentally different forms of learning provide unique potential determinants of the pathological drug seeking induced by drug addiction and, therefore, unique targets for its treatment.

Timing models of reward learning and core addictive processes in the brain

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Abstract: People become addicted in different ways, and they respond differently to different interventions. There may nevertheless be a core neural pathology responsible for all distinctively addictive suboptimal behavioral habits. In particular, timing models of reward learning suggest a hypothesis according to which all addiction involves neuroadaptation that attenuates serotonergic inhibition of a mesolimbic dopamine system that has learned that cues for consumption of the addictive target are signals of a high-reward-rate environment.

Redish et al. superbly organize current knowledge of addiction into an elegant system of conceptual folders. Their claims that different people succumb to addiction under different pressures, and that we should expect variability in the way clinical populations respond to various interventions, are persuasive. However, their remark that "treatments aimed at these specific modes are more likely to be successful than general treatments aimed at the general addicted population" (sect. 5.5, para. 4), while presently true, invites an overly strong reading to the effect that we should not expect to find any core neural process that is *always* crucial to the distinctively *addictive* properties of some but not most suboptimal behavioral habits, and which neuropharmacological interventions could target. Certainly, we do not now know there is such a core process. However, the evidence that Redish et al. so ably review remains compatible with this hypothesis. What might lead them to underestimate its probability is their treating *Vulnerabilities 2*, *4*, *6*, *7* and *9* as separate, bypassing reasons for suspecting they may be faces of one process.

The dopamine circuit from ventral tegmental area and substantia nigra pars compacta (SNpc) to ventral striatum (especially nucleus accumbens [NAcc]) is, as the authors emphasize, a learning system. Its learning function has sometimes been modeled as seamlessly integrating reward prediction, reward valuation, salience maintenance of perceptual targets that cue expectations of reward, and preparation of motor response (McClure et al. 2003). More abstractly, Panksepp (1998) has conceptualized this integrated circuit as a "seeking system." Merely because theorists conceptually distinguish all of these functions doesn't mean that the circuitry of the brain does so.

Another theoretical distinction of importance here that may also lack a clear basis in neural functioning is that between classical and operant conditioning. It is undermined by Gallistel and Gibbon's (2000; 2002) timing models of conditioning phenomena, according to which animals represent the durations of intervals and the rates of events, and conditioned responding occurs as a function of the comparison of rates of reward. On these models, animals are drawn to environments with higher such rates by gradient climbing, rather than by forming explicit associations between stimuli and conditioned responses, or between behaviors and specific expected outcomes. Call such processes "G-learning." In addiction studies there has been a long-running and unresolved debate over the relationship between supposedly classically conditioned cravings and apparently instrumentally conditioned preparations for consumption of addictive targets. Perhaps the debate has been inconclusive because these are one and the same process so far as neural implementation is concerned. Addictions might then be conceptualized as high-reward-rate "environments" that lure organisms' attention and approach, unless the dopamine system is opposed – as it appears to be, successfully in non-addicts, by serotonergic and GABAnergic signals from the prefrontal cortex (PFC).

Daw (2003) computationally models G-learning and temporal-difference (TD) learning, of the kind implicated in Redish et al.'s *Vulnerability 7*, as complementary. Suppose an animal has learned a function that predicts a reward at t, where the function in question decomposes into models of two stages: one applying to the interval between the conditioned and the unconditioned stimulus, and one applying to the interval between the unconditioned stimulus and the next conditioned stimulus. Then imagine that a case occurs in which at t nothing happens. Should the animal infer that its model of the world needs revision, perhaps to a one-stage model, or should it retain the model and regard the omission as noise or error? This is the problem that underlies Redish et al.'s *Vulnerability 6*. In Daw's account, the animal uses G-learning to select a world-model: whichever such model matches behavior that yields the higher reward rate will be preferred to alternatives. Given this model as a constraint, TD learning can then predict the temporal placement of rewards ("when"-learning). This hybrid approach allows Daw to drop unbiological features of the original model of TD learning by the dopamine system: tapped-line delay timing and exogenously fixed trial boundaries.

If this is on the right track, then the mesolimbic dopamine circuit's response to an addictive target does not involve a breakdown: it is functioning just as evolution intended. The casino, for example, *is* a high reward-rate environment. Furthermore, because of its variable reward schedule, the casino continually challenges the system's "when"-learning and prevents the dopamine signaling, as represented by the TD algorithm, from settling down. Addictive drugs may all encourage the same response by interfering with the reliability of neural clocks, a possible vulnerability Redish et al. do not explicitly consider, but which might be expressed as changes in allostasis, their *Vulnerability 2*.

If addicts' dopamine circuits are working just as promised in the Darwinian user's manual, what has gone wrong, at the level of neural functioning, in their case? The answer may be Redish et al.'s *Vulnerability 9*: neuroadaptation in inhibitory (serotonergic and other) circuits resulting from continuous dopamine overload in NAcc. This vulnerability, as caused by the mechanism identified in *Vulnerability 7*, is expressed as *Vulnerability 4*. (*Vulnerability 6* is simply an expression of *Vulnerability 7* given consumption of addictive targets.)

The only evidence that, as far as I can see, Redish et al. provide against a common central role in all addictions for *Vulnerability 7*

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is their claim that cravings must implicate the planning system, whereas the mesolimbic dopamine system is part of the habit system. This claim must be defended against alternative neural accounts of cravings. Seamans and Yang (2004) suggest that dopamine action gives rise to two possible states in the ventromedial prefrontal cortex (VMPFC), depending on which of two groups of receptors, D1 or D2, predominates. Where D2 reception predominates, multiple excitatory inputs promote VMPFC output to NAcc. Where D1 reception predominates, all signals below a high threshold are inhibited. In cocaine withdrawal, protein signaling to D2 receptors is reduced, thus inducing the animal to seek stimuli that can clear the high D1 threshold. Learned cues that such stimuli (e.g., cocaine) are at hand may then arouse the system. Here is a potential dopaminergic model of the mechanism by which habituation gives rise to cravings. A craving might simply be the uncomfortable phenomenology associated with the dopamine system's pulling attention away from motivators, alternative to the addictive target, on which frontal and prefrontal systems are "trying" to focus. That the person can, when probed, name what eliminates the discomfort, and that frontal cognition helps her seek its consumption, does not in itself show that goals set by a planning system are necessary for cravings.

Cue fascination: A new vulnerability in drug addiction

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Abstract: Redish et al. propose a constellation of vulnerabilities inherent in the brain's decision-making system. They allow over-attention to cues a minor role in drug addiction. We think this is inadequate. Using the established links among drug cues, dopamine, and novelty, we propose a fuller account of this key feature of addiction, which we call the phenomenon of cue fascination.

In the target article, Redish et al. characterize drug use in terms of a constellation of vulnerabilities inherent in the brain's decision-making system. Unlike previous approaches to addiction, this characterization is flexible enough to deal with multiple features of addictive drugs and addicted individuals. We maintain, however, that the authors' sharp separation between the appraisal of situational cues and expected outcomes in motivating drug use fails to consider how cues can play more than a signaling role in habit formation or the reward system. The phenomenon of cue fascination suggests that any description of decision-making vulnerabilities in drug addiction must address how an addict's interest in drug cues can influence habit formation or the calculation of expected benefits.[1] We believe that the authors' attempt to incorporate over-attention to drug cues within the tenth vulnerability, where they note that over-attention to drug cues may be related to changes in learning processes, substantially mischaracterizes this phenomenon, especially when paired with their model of robotic drug use. A fuller and more robust account of this key feature of addiction, when incorporated with the rest of the decision-making system, will strengthen the usefulness of this model.

Over-attention to drug cues has often been characterized largely in terms of classical conditioning. The drug cue is a conditioned stimulus that becomes paired with drug use and consequently acquires physiological and behavioral relevance as a precursor to drug ingestion (see, for example, Carter & Tiffany 1999). We suggest that this model is incomplete. In many cases, the addict's interest in drug cues reflects an intrinsic fascination with the circumstances of the drug use itself. A simple example illustrates this point. Smokers attempting to quit often find themselves staring at packages of cigarettes. In some cases, smokers express an urge merely to touch or look at a cigarette. When reminded of their resolve to quit, these smokers might say, "But I don't want to smoke a cigarette, I just want to hold one." While this phenomenon remains understudied, and the typical response to such statements is skepticism, accounts of drug use and addiction in humans and animals reveal similar episodes of intense interest in drug cues, often without corresponding expectations of drug rewards. In these circumstances, drug-addicted individuals experience a persistent absorption in environments or cues associated with past drug use. Rosse et al. (1993) describe compulsive crack cocaine foraging behavior ("chasing" or "geeking") in addicts who have no expectation of finding lost fragments or pieces of the drug. A study of drug-use rituals similarly suggests that drug cues and paraphernalia take on added significance or meaning for drug users even in instances where those rituals delay or obscure the impact of taking the drug itself (see Zinberg 1984). We suggest a model in which drug-related cues have an attraction for addicts that is in important respects independent from both a conscious desire to use drugs and what Redish et al. call a "robotic," automatic, habitual response to cues.

This characterization of over-attention to drug cues corresponds to neurophysiological studies that pair drug cues with increased levels of dopamine in the mesocortical limbic system. The theory of incentive salience (Robinson & Berridge 1993) suggests that the relation between drug cues and drug use is given not merely by their relation to hedonic response, in which cues become associated with the pleasure derived from the drug itself, but rather by their influence on core wanting (Berridge & Robinson 2003). Although folk psychological accounts of motivation have typically paired "liking" with "wanting," Berridge and Robinson (1993) suggest that these processes correspond to distinct neural substrates that are, in fact, dissociable in the laboratory. Increases in dopamine signaling have been traced not only to the ingestion of drugs, but also to the presence of drug cues. In both cases, there is a corresponding increase in incentive salience, or core wanting, even in the absence of increases in hedonic rewards. Although the theory of incentive salience has been enormously influential, exactly what feature of addicts' experience is referred to by "wanting" has been unclear. Robinson and Berridge (2004) have attempted to clarify "wanting" in terms that are useful for our present purposes. "[T]he process of incentive salience attribution . . . transforms the sensory features of ordinary stimuli or, more accurately, the neural and psychological representations of stimuli, so that they become *especially salient stimuli, stimuli that 'grab the attention'*" (p. 352, emphasis added).

Drug cues "grab the attention" because they release dopamine. Indeed, Kotler et al. (1997) report that, for cocaine addicts, "cocaine cues *by themselves* increase dopamine release" (p. 251, emphasis added). We believe, however, that another well-documented feature of dopamine release offers insight into the psychological processes that underlie addicts' experience of drug cues. We refer to dopamine's association with the experience of novelty (see Freeman et al. 1985; Garris et al. 1999; Schultz 1998). Studies of paranoid schizophrenic patients note that "the dopamine system which under normal conditions is a mediator of context-driven novelty/salience in the psychotic state becomes a creator of aberrant novelty and salience" (Kapur et al. 2005, p. 61). This inappropriate marking results in patients reporting a subjective state characterized by fascination. This link between dopamine and novelty suggests that the experience of the drug cue for the addict is a very particular kind of experience: the fascination of a novel object. If

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this is true, then the addict is someone for whom a certain class of objects in the world – objects associated with drug cues – never becomes familiar, never becomes dull, never loses the fascination that accrues to what is new.

The link between dopamine release and drug cues is well established, as is the association between dopamine release and novelty. We suggest that putting these pieces together will bring out some important implications of Berridge and Robinson's work on drug cues. In the target article, Redish et al. consign the phenomenon of "over-attention" to cues to the catch-all "tenth vulnerability," where they connect it to increased learning effects (see sect. 3.6). This is inadequate. Over-attention to drug cues, the phenomena that we call cue fascination, offers a new way to characterize susceptibility to drug use as well as new avenues for drug treatment.

NOTE

1. This commentary is an equal collaboration between its authors. The phenomenon was first discussed in Michael Clune's manuscript *The Memory Disease*. However, the term "cue fascination" originates in this work.

E pluribus unum? A new take on addiction by Redish et al.

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Abstract: Neuroscientists and psychologists have proposed a variety of well-supported theories to explain addiction. Many of these theories suggest that addiction results from a single process or dysfunction across all of its forms. The authors of the current review, in contrast, have used a well-defined theoretical account of decision-making to outline the variety of dysfunctions that could account for addictive behavior.

One major theme in studies of the neural basis of addiction has been a search for a final pathway common to the actions of all addictive drugs. For example, it has been proposed that addiction is caused by aberrant associative learning arising from altered dopamine neurotransmission (Di Chiara 1999; Kelley 2004a; Robbins & Everitt 1999). Psychostimulants, as well as opiates, nicotine, ethanol, and cannabinoids, all have effects on dopaminergic neurotransmission through various pathways (Di Chiara & Imperato 1988; Tanda et al. 1997; Wise & Bozarth 1987). Observations such as these have bolstered the hypothesis that addiction is at its root a unitary phenomenon. Indeed, even pathological gambling, an addiction that is not a substance dependence, may be related to changes in dopamine function (Zack & Poulos 2004). Of course the dopamine-learning hypothesis of addiction is only one account; other unified hypotheses have also been advanced to explain addiction. These include proposals that addiction results from disrupted hedonic homeostasis (Koob & Le Moal 1997), from sensitization of incentive motivation (Robinson & Berridge 2000), or from disruptions to prefrontal-mediated executive processes (Schoenbaum et al. 2006a; Volkow & Fowler 2000), among others. What these disparate theories have in common is that they each seem to suggest that addictive behavior arises from one basic dysfunction. But while each of these theories can marshal persuasive evidence in its support, each also has substantial areas of evidence that it cannot explain. For example, dopamine transporter knockout mice will still self-administer cocaine (Rocha 2003), an observation difficult to explain if altered dopamine neurotransmission is the only pathway to cocaine addiction.

In the current review article, Redish et al. have reconceptualized addiction as stemming not from a single unitary dysfunction but rather from a variety of underlying causes, each of which impact decision-making. In so doing, the authors take a position similar to that of others, who have viewed addiction as a disorder characterized by maladaptive decision-making (Bechara 2005; Kalivas & Volkow 2005; Schoenbaum et al. 2006a). In this view, addictive behavior is that which has escaped the normal mechanisms that control decision-making. However the current review is unique in that it uses this idea to explore the many different aspects of decision-making that theoretically could be disrupted in addiction. Because decision-making arises from a collection of interacting processes, each with a distinct neurobiological basis, addiction could arise from a disruption to any one of these processes. After laying out the possible "vulnerabilities" in the decision-making process, the authors go on to show how dysfunction in each of these different vulnerabilities might be best explained by a different theory of addiction that has been advanced by other investigators. As this approach recognizes, the wide variety of theories of addiction that have been advanced over the past decades may not be mutually exclusive. Rather, each one could point to different members of a whole family of addictions.

The great strength of this approach is that it can be used to explain why addictions to different drugs, and even to a single drug in different cases, may have different properties. For example, multiple subtypes of alcoholism, which vary according to the amount and importance of craving, have been recognized by some clinicians (Addolorato et al. 2005; Monterosso et al. 2001). According to the authors' schema, addictions in which craving plays a large role could be explained by a different kind of dysfunction than those in which craving plays less of a role. However, even if certain theoretical distinctions, such as this one, turn out not to be applicable to addiction, the overall idea of distinguishing addictions by the specific aspect of decision-making that they disrupt is surely a good one. Mechanisms that appear to point to a final common pathway of all addiction, such as an increase in dopamine transmission in the ventral striatum, could be epiphenomena in some addictions rather than their root cause.

The ideas of Redish and colleagues also raise some broad questions. One of these, for instance, is how the idea that addiction reflects multiple underlying decision-making dysfunctions could itself be tested. The very strength of the framework advanced by these authors – that it is so powerful and wide-ranging, and can subsume so many theories of addiction – is also a potential weakness. What kind of result could falsify it? Related to this is the question of whether all of the theoretical vulnerabilities in the decision-making process identified by Redish et al. are equal in explanatory power, or whether some of them are more fundamentally involved in addiction than others. One possibility might be that some apparently disparate vulnerabilities in decision-making could reduce to a common neurobiological substrate. For instance, the authors identify the overvaluation of a predicted outcome as one vulnerability that may be associated with dysfunction of the orbitofrontal cortex (OFC) in certain addictions. However, a drug-induced dysfunction of the OFC could also lead to other vulnerabilities separately identified by the authors, such as an abnormally fast discounting function (Roesch et al. 2007). The underlying problem in both of these vulnerabilities might be a disruption in the ability to signal the value of expected outcomes by the OFC. Such a finding would in no way invalidate the approach of Redish et al., but it might modify their framework. Presumably, these are the kinds of questions and hypotheses that this important new approach is designed to stimulate and bring to the forefront.

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A mismatch with dual process models of addiction rooted in psychology

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Abstract: The model of addiction proposed by Redish et al. shows a lack of fit with recent data and models in psychological studies of addiction. In these dual process models, relatively automatic appetitive processes are distinguished from explicit goal-directed expectancies and motives, whereas these are all grouped together in the planning system in the Redish et al. model. Implications are discussed.

We appreciate the attempt in the target article by Redish et al. to provide an integrative framework for addiction from a multiple systems view, and we find many of the suggestions regarding addictive behaviors thought provoking. Our main concern is related to the lack of fit of the theoretical framework with recent data and models from psychological science.

Redish et al. distinguish between two broad processes that jointly explain addictions: an explicit and slow planning system, relying on stimulus/response-outcome (S/R-O) associations, and an implicit and fast habit system relying on stimulus-action/response (S-A/R) associations (Table 3 of the target article). In many recent psychological theories of addiction, a distinction is also made between two broad systems that superficially resemble the proposed systems (e.g., Deutsch & Strack 2006; Evans & Coventry 2006; Stacy & Wiers 2006; Wiers & Stacy 2006a; 2006b; Wiers et al. 2007). These models follow general dual process models in psychology in which the most characteristic difference between the systems concerns the representational format, not the contents of the associations (e.g., Strack & Deutsch 2004). In this model, the reflective system uses the representations in the impulsive system and can perform logical operations on these representations, such as negation or placing the contents in a different time (e.g., the future). Deutsch et al. (2006) have demonstrated the consequence of this difference in representational format. When an association is learned and later participants are told that in fact the association was not true, participants correct this as becomes evident from their explicit expectancies, but when their automatic associations are assessed, they still show the original association. A study by Krank and Swift (1994) shows that this can have serious real-life consequences: adolescents who were told that alcohol does *not* make you sexy (a prevalent alcohol expectancy in adolescents; Goldman et al. 1999), showed *stronger* automatic associations between alcohol and sex a week later. This effect is opposite to what would be predicted if this association was only governed by a propositional planning system (cf. Gawronski et al. 2008).

Relatedly, Redish et al. do not acknowledge a range of automatic associations that are conceptual (multi-modal) in nature, which do not necessarily involve S-A/R associations. These associative processes can be dissociated from explicit memory and operations of the planning systems. Examples include associations processed during semantic priming (e.g., Hutchison 2003; Weingardt et al. 1996), implicit conceptual memory (e.g., Levy et al. 2004), or construct activation tasks (e.g., Arndt et al. 2002). The automatic activation of a variety of different classes of associations (beyond S-A/R) can spontaneously bias processing and judgments in ways that do not appear to involve planning, as revealed in social psychological research (e.g., Bargh & Morsella 2008). Hence, our general point here is that there are many more associative processes that predict behavior than the S-A/R associations of the habit system and that these can be dissociated from explicit memory processes in the planning system.

When we turn to psychological addiction research, recent studies have found that relatively automatic processes such as an attentional bias for a substance, automatic memory associations, and action tendencies to approach alcohol are relatively independent from explicit processes such as motives and expectancies (see Wiers et al. 2007 for a review). Expectancies and substance associations typically show low correlations and predict unique variance in substance use (e.g., Houben & Wiers 2006; Stacy 1997; Wiers et al. 2002). In recent studies, the relative predictive power of automatic substance associations and explicit expectancies to explain substance use was assessed in adolescents who differed in working memory (WM) capacity. For smoking (Grenard et al., in press) and alcohol use (Thush et al. 2008), substance use was better predicted by automatic associations in participants with relatively poor WM capacity. Interestingly, Thush et al. (2008) found the opposite pattern for explicit expectancies, which predicted alcohol use better in participants with high WM capacity. Hence, some individuals' substance use appears to be more driven by their automatic associations, whereas others (with equally strong automatic substance associations but with a stronger WM capacity on top) appear to be more "rational" substance users. In summary, the distinction between relatively automatic or implicit associations and explicit expectancies has been fruitful in psychological research on addiction (see Wiers & Stacy 2006a; 2006b; Wiers et al. 2005; 2007). Although Redish et al. also differentiate between two main systems (planning and habit), many of the processes distinguished in psychological research appear to be inaccurately grouped together and subsumed in their planning system.

A third issue concerns the role of conscious motivation in drug seeking. Redish et al. state that overvaluation of expected drug outcomes leads to craving and that this overvaluation in the planning system might be the result of incentive salience attribution, citing Robinson and Berridge (1993; 2003). These authors, however, differentiate between "wanting," the neural process of incentive salience attribution, and subjective craving, which can, but does not necessarily, result from the unconscious "wanting" process. This distinction may explain, for example, that smokers, after a Pavlovian conditioning procedure, show strong approach tendencies to smoking stimuli, particularly in the presence of cues predicting smoking opportunity, without these cues eliciting increased subjective craving (Thewissen et al. 2007). In line with this distinction, a recent meta-analysis found low correlations between subjective craving and an attentional bias for alcohol (Field et al., in preparation). Redish et al. attribute devaluation and need-dependent evaluations exclusively to the planning system. However, recent studies suggest that automatic evaluations can be need-dependent (e.g., Seibt et al. 2007).

In summary, we believe that there is evidence that relatively automatic appetitive processes in addiction should not be categorized together with subjective craving and explicit expectancies in the planning system. This does not imply that they are part of the habit system either. Perhaps these relatively automatic processes are an intermediate step between explicit processes in the planning system characteristic of drug use initiation and the reward independent associations characteristic of the habit system in late phases of addiction (cf. Everitt & Robbins 2005).

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The elephantine shape of addiction

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Abstract: By summarizing, in a single piece, various current perspectives on addiction, Redish et al. have performed a useful service to the field. Their central message is that addiction comprises many vulnerabilities rather than a single vulnerability. Such a message may not be new, but it is worth repeating.

The various perspectives on addiction, as listed in Table 1 of the target article, remind me of the fabled blind men touching the elephant, and Redish et al. deserve credit for combining the different accounts to give us a sketch of the elephant's shape. But keen sight they have not given us, and in our attempts to understand addiction we are still groping in the dark.

Much of the article is a straightforward summary of various decision systems in the brain, each associated with distinct learning capacities; little of it covers actual work on addiction. But this is no fault of the authors, since little research so far has focused on the effects of addiction on neural systems mediating decision-making. Although recent studies have begun to look at this question (Nelson & Killcross 2006; Schoenbaum & Setlow 2005; Stalnaker et al. 2006), at present we must rest content with the hypothetical nature of the vulnerabilities enumerated.

In their review of the literature on the brain's decision systems, Redish et al. underscore the importance of behavioral analysis in our attempt to understand addiction, because every system they discuss is delineated by behavioral assays developed over many decades. Unfortunately, though such assays have become standard tools among serious students of learning and behavior, they are rarely used in addiction research.

In this age of molecular supremacy, what some researchers want, above all, is the so-called addiction center of the brain, so they can safely disregard the rest in their attempt to nail down the critical molecule(s) for addiction, in the hope that the molecule of their choice will turn out to be the master switch. Such wishful thinking is certainly understandable, but the danger with wishful thinking, in science as in life, is that sooner or later it will be shattered by reality. For decades, the nucleus accumbens served as the center of addiction, but as we learn more and more about the Pavlovian and instrumental learning systems of the brain, it is becoming clear that the accumbens (or the mesolimbic pathway) cannot be the sole substrate of addiction. If Redish et al. tell us anything about the neural mechanisms of addiction, it is that the entire brain (literally the cerebrum) is critical, but that distinct functional systems within it are involved in distinct "vulnerabilities."

To some this is bound to be disappointing news, leaving little room for real science. To those who believe that science gains rigor as it zooms in on the particular, the integrative activity of the brain is no doubt too nebulous an object for any rigorous analysis. For others it may suggest a new approach that focuses on interactions between neural systems in behaving organisms.

How can the entire brain be tackled? Paradoxically, this is not a question to which neuroscientists today devote much thought, but we can hardly afford to ignore it any further, especially when attempting to understand a process like addiction. It is to precise behavioral analysis that we must turn if we wish to dissociate global functional processes at the level of neural circuits. And what is striking about the field of addiction is precisely the lack of any detailed characterization of behavior – of what animals actually do after they become addicted. There is no lack of data, but a lack of meaningful data on the effects of addictive substances on the decision systems in the brain, because the field remains fixated on a few uninformative measures like conditioned place preference. Such procedures are a legacy from the study of learning decades ago, and they do not reflect the critical developments in this field since then. Our knowledge of the decision systems reviewed by Redish et al. are largely the product of modern behavioral work, and they have yet to be examined in any detail in the field of addiction.

That is not to say that what we have learned about the various decision systems will provide an infallible guide for addiction research. Far from it; as this article makes clear, much conceptual confusion still remains regarding how these systems are to be demarcated. To me the categorization of various types of learning without a detailed discussion of specific data is not a fruitful approach. One can always find studies in the literature that happen to support a particular classificatory scheme. One lab showed X, another Y – but the key question is whether they were trying to measure the same thing and whether the experimental results can be replicated by others. In the absence of a general consensus about what is actually done and what the data are, given a defined condition, one can argue ad infinitum about which system is which, and how each should be named, without contributing anything to the debate.

In short, although Redish et al. provide a fine introduction to the study of addiction, and a convenient starting point for future discussions, their article also reveals how far we are from anything approaching genuine understanding. As so often happens in the primitive stage of scientific inquiry, a wild abundance of data masks the lack of fundamental experimental findings, and a great variety of perspectives hides the poverty of theoretical advances. This is due, no doubt, to our ignorance of the detailed mechanisms underlying reward and decision-making, and an article like this will have served its purpose if it can only remind us of the need to go back to the laboratory.

Authors' Response

Addiction as vulnerabilities in the decision process

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Abstract: In our target article, we proposed that addiction could be envisioned as misperformance of a decision-making machinery described by two systems (deliberative and habit systems). Several commentators have argued that Pavlovian learning also produces actions. We agree and note that Pavlovian action-selection will provide several additional vulnerabilities. Several commentators have suggested that addiction arises from sociological parameters. We note in our response how sociological effects can change decision-making variables to provide additional vulnerabilities. Commentators generally have

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agreed that our theory provides a framework within which to site addiction and treatment, but additional work will be needed to determine whether our taxonomy will help identify and treat subpopulations within the addicted community.

Our target article proposed that addiction is a spectrum disorder, with the different aspects arising from misperformance (*vulnerabilities, failure-modes*) of the machinery of decision-making. The 25 commentaries are generally supportive and have provided several different viewpoints on our theory ranging from the molecular to the sociological. In this response, we address those additional viewpoints and show how our theory incorporates them.

We start with a review of the major issues raised in the commentaries (sect. R1) and then proceed with clarifications of several issues that were unclear in the target article (sect. R2). We then discuss revisions to the proposed framework for decision-making (sect. R3), particularly the incorporation of additional components such as Pavlovian action-selection mechanisms, and revisions to the proposed taxonomy of addiction (sect. R4), particularly the role of additional processes such as negative affect. From there, we turn to the question of predictions and falsifiability (sect. R5), to identifying specific additional vulnerabilities (sect. R6), and finally to implications for treatment, clinical assessment, and policy (sects. R7 and R8).

R1. Introduction: The parameter space of addiction

Theories of decision create an interacting parameter space of behavior, decision, and brain function, within which we can place terms such as *addiction*, *compulsion*, *dysfunction*, and *illness*. Our target article identifies addiction as arising from failures in the machinery of decision-making. **Ahmed** suggests that we have created an "addiction space" within which the different observations and theories of addiction can be placed.

The most contentious issue raised is whether our framework of decision-making and thus of addiction is complete and whether we have separated fragments that should have been merged (**Bickel & Yi**; **Goudie, Field, & Cole** [**Goudie et al.**]). We note that there is at least one additional component which needs to be factored into theories of addiction: Pavlovian conditioning and affect (**Kiviniemi & Bevins**, **Ostlund & Balleine**; see also Balleine 2001; 2004; Dayan et al. 2006). However (with the addition of this Pavlovian/affective component), our framework holds up very well to the potential counterexamples raised in the commentaries. (See, for example, our discussion of the effect of expectancies later in response to **Wiers, Havermans, Deutsch, & Stacy** [**Wiers et al.**])

The second contentious issue is the extent to which addiction is explicable as a single phenomenon or whether it is in truth a spectrum of disorders with separably identifiable etiologies. **Le Moal** suggests that our theory is just one more theory to add to a large list of potential theories (which he seems to reject). However, we would argue that our theory is a synthesis of many theories (including Le Moal's) and in doing so unifies a larger space than the other addiction theories. **Hardcastle** points out that our list is neither complete nor shorter than prior lists on addiction, and thus provides neither a necessary nor sufficient definition of addiction. Three important questions arise here: (1) Is it possible to shorten the list? (2) Does our taxonomy more directly reflect separable components? (3) Can our theory provide a framework within which to explain the phenomena within addiction? We would argue that our vulnerabilities reflect a priori failure-modes of the decision system and as such are more likely to reflect separable components. The extent to which our vulnerabilities reflect the actual mechanisms of addiction is going to require additional work in the clinical realm. As noted by several commentators (e.g., **Ahmed**, **Bickel & Yi**, **Yin**), our proposal is only the first step to identifying this process-space within which we can find the dysfunction that is addiction.

One issue raised by several commentators is the question of whether our "unified framework for addiction" is truly unified. **Griffiths** suggests that it is unified only at a biological level. Several commentators (**Boden**, **Goudie et al.**, Griffiths, **Lende**) argue that addiction arises at a more sociological level. The sociological effects on addiction are very interesting, particularly from a policy perspective (**MacCoun**), but we suggest further on that any sociological effects must change the decision-making systems because, in the end, the addictive behavior (taking the drug, playing the game) is fundamentally an individual action. We argue that the theory we have proposed can incorporate social and ethnological levels as well, because it provides a parameter space within which to understand the social and ethnological effects on decision-making.

As we will discuss later, there are many unanswered questions that remain, both within our understanding of the machinery of decision-making itself as well as within the potential dysfunctions. Other decision failures can also be sited within this framework. For example, **Andreou** places the problem of procrastination into the framework of decision failures, identifying this also as a consequence of succumbing to a vulnerability within the system. Similar suggestions have been made that mental illness (such as schizophrenia, obsessive-compulsive disorder, and other problems) can be seen as failure-modes of neural functional machinery (Paulus 2007), which may explain the comorbidity often seen with addiction (**Chambers**).

R2. Clarifications

Several of the commentaries seem to have misunderstood claims made in the target article. Before responding to issues raised within the commentaries, we wish to clarify certain points of our theory.

R2.1. Our theory is looking at all stages of addiction

Several commentators have attempted to place our theory at a specific "stage" of the addiction process. For example, **Le Moal** suggests that we were looking at the "end-stage of addiction." This was not our intention at all. The unified model of decision-making should be able to explain behavior, and thus, it should be able to explain not only all aspects of addictive use, but also non-addictive use. The vulnerabilities hypothesis says that addiction arises when drug use occurs because drug use is

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inappropriately driving decision-making. A similar case can be made for failure-modes arising from non-pharmacological consequences (such as in gambling or other behavioral addictions).

Because much behavior moves from expectancy-based, planning-capable systems ($S \xrightarrow{a} O$) to stimulus-response, sequence-based, habit-like systems ($S \xrightarrow{a}$), drug use will often proceed through the same stages that normal behaviors do (Everitt & Robbins 2005). However, as noted in the target article, not all behaviors proceed through the same sequence. It is possible for some behaviors to remain controlled by flexible $S \xrightarrow{a} O$ systems, and it is possible in some behaviors for the process to return to being controlled by the $S \xrightarrow{a} O$ system after being controlled by the $S \xrightarrow{a}$ system. Our contention is that *all* components of the decision-making system have failure-modes, that these failure-modes will be clinically identifiable, and that successful treatment will require the identification of these failure-modes.

It is important to note that not all subjects will show all failure-modes. Our suggestion that addiction is a spectrum disorder implies that addiction can arise from any of the vulnerabilities (i.e., that it is an *or* process), and that any, some, or all of these failure-modes may be active within any specific subject. As noted by **Ahmed**, most of the previous theories of addiction have assumed that addiction arises from a loss of a cognitive, flexible, planning-capable ability to a habitual, compulsive, automatic system. Several commentators (e.g., **Le Moal**) have incorrectly assigned such a model to us. In fact, our model explicitly posits that both systems have potential failure-modes. Addicts can lose control due to a vulnerability in the planning system, to a vulnerability in the habit system, or to a vulnerability in their interaction. With the addition of a Pavlovian/affective system ($[SO] \xrightarrow{a}$; **Berridge, Zhang, & Aldridge** [**Berridge et al.**]; **Kiviniemi & Bevins**; **Ostlund & Balleine**; see further on in this response), there will be additional vulnerabilities in that system as well as in its interaction with the other systems (Balleine 2001; 2004; Breland & Breland 1961; Dayan et al. 2006).

R2.2. Falling victim to a vulnerability does not imply that all decision making is faulty

Several commentators assume that falling victim to a failure-mode implies that a component is unavailable to decision-making. For example, **Hart & Krauss** suggest that because addicts can actually plan and make decisions, they must not have a problem with decision-making. We explicitly suggest that each decision, and each failure, will be caused by an interaction between drugs, the individual, and the experience. These failure-modes will be both partial and specific. By analogy, a patient with allergies has a failure of his immune system, but still can mount an appropriate immune response to a viral attack. Similarly, a drug addict who overvalues heroin can still plan, both how to get the heroin, and how to get to a clinic. It is in the contrasts of those plans that overvaluation becomes an issue.

R2.3. Drugs are economic objects and users are sensitive to cost

As first predicted by Becker (1976, Becker & Murphy 1988), drugs are economic objects and thus sensitive to price and cost. Although there is strong evidence that changes in drug costs lead to changes in drug use, drug use remains less elastic to cost than a rational theory would predict (**MacCoun**). Nevertheless, they do remain at least somewhat sensitive to cost (Becker et al. 1994; Grossman & Chaloupka 1998; Liu et al. 1999). Similarly, many experiments have shown that drug use in both animals (Carroll 1993; Carroll et al. 1989; Elsmore et al. 1980; Lenoir & Ahmed 2007; Lenoir et al. 2007; Nader & Woolverton, 1990; 1991) and humans (Hart et al. 2000; Hatsukami et al. 1994; Higgins et al. 2002; 2004) is decreased with the provision of alternate options. Several commentaries incorrectly attribute to our theory the prediction that drug use would be entirely inelastic and that any evidence that drug users are sensitive to cost would disprove computational theories of drug addiction (e.g., **Hart & Krauss**).

Most current computational models (and most animal experiments) suggest that drug users should remain sensitive to costs: drug users become willing to pay very high cost for drugs, but if a drug user is given the option between high- and low-cost drugs, they will select the lower cost. For example, Figure 2 of Redish (2004) explicitly shows the modeled drug user (*Vulnerability 7*) being sensitive to cost. Thus, sin taxes remain an important policy issue and a potential means of attacking the drug problem (**MacCoun**). It is important to differentiate a drug user's ability to recognize costs and to select the lesser-cost drug from rationality.

Similarly, it very interesting how small (inconsequential) rewards (like \$5 trinkets; **Hart & Krauss**) can serve as alternate rewards to reduce drug use more than simply increasing the cost of the drugs by \$5. This implies that these vouchers and alternate rewards are accessing other mechanisms beyond cost increases. An important open question is to determine why these voucher systems work, and for whom. As we discuss later (see *Treatments*), our prediction is that these voucher systems are allowing the decision-making system to somehow get around a vulnerability. Which vulnerability is involved and how those trinkets allow a user to circumvent and accommodate that vulnerability remains an open question for future research.

R2.4. Addiction arises from misperformance of the decision-making machinery

We selected the term *vulnerability* (or *failure-mode*) from an analogy to engineering to reflect the concept of a machine doing the wrong thing because of an interaction with conditions that it was not evolved to handle. However, several commentators (e.g., **Le Moal**, **Hart & Krauss**) have taken the term to imply an intrinsic factor preceding any interaction with conditions. Some commentators (e.g., **Neal & Wood**) have taken this term to imply that all effects were due to pharmacological manipulations of the system. Other commentators (e.g., Hart & Krauss; **Wiers et al.**) have taken it to imply that a system misperforming because of a vulnerability entails a complete failure of the system involved. These are all misunderstandings of our terminology.

A "vulnerability" in our terminology is simply any mechanism by which the machine misperforms. This misperformance can be caused by pre-existing conditions, by pharmacological manipulations, by natural experiential

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sequences (e.g., gambling), or through an interaction of these conditions.

Note that a subject can still use a system that is misperforming because of a vulnerability within that system. Thus, a subject with a pre-existing strong planning system (**Wiers et al.**) may be more likely to use that planning system, whether correctly or incorrectly. In fact, the example given by Wiers et al. is exactly what our theory would predict: In users with strong planning systems, drug use is more likely to arise from overvaluation in those planning systems, whereas in users with weak planning systems, drug use is more likely to arise from overvaluation in the non-planning, habit system.

R3. A framework for understanding the machinery of decision-making

Several commentators ask whether this is a reasonable and correct taxonomy of decision-making (**Wiers et al.**), whether we have missed certain components (**Berridge et al.**, **Kiviniemi & Bevins**, **Le Moal**, **Ostlund & Balleine**), and whether our theory depends on assumptions of rationality (**Andreou**, **Hart & Krauss**, **Khalil**, **Lende**, **Neal & Wood**). We address each of these issues in turn.

We wish to start by stating that our fundamental claim that addiction arises because of failures of decision-making and can be best understood and treated by identifying what those failure-modes are, does not actually depend on the specific framework of decision-making that we have identified. As noted by **Yin**, this framework is only the first step. Additional research will be needed to validate, extend, and correct the decision-making framework. The framework laid out in the target article is based on rational neuroeconomics because of its simplicity. We would argue that these other, more complex theories (e.g., prospect theory [Kahneman & Tversky 1979], or multiple memory theories [Schacter 2001, Schacter & Tulving 1994]) would also have additional vulnerabilities (failure-modes) through which behavior could be driven incorrectly. Our theory is that addiction lies within those failure-modes. For example, recent work has suggested the existence of fictive learning signals (e.g., regret) (Bell 1982; Lee 2008; Lohrenz et al. 2007). Chiu et al. (2008) found that smokers' brains reflected those fictive signals correctly, but their behavior did not. This mismatch identifies a potential unidentified vulnerability whose mechanism needs to be understood.

R3.1. A role for affect and Pavlovian conditioning

In addition to the "planning" ($S \xrightarrow{a} O$) and "habit" ($S \xrightarrow{a}$) systems, the framework laid out in the target article identified a further condition ("observation", $S \longrightarrow O$), which we identified as not entailing an action and thus as not part of the decision-making system. As noted by **Ostlund & Balleine**, this system is better described as a Pavlovian association ($[SO]$), which can drive actions through Pavlovian conditioning processes ($[SO] \xrightarrow{a}$). This could be phrased as an "evolutionary pre-wired response" to expected outcomes (Dayan et al. 2006). As noted by Balleine (2001; 2004), this Pavlovian process proceeds through an affect-based system in which the outcome first produces an emotional affect, which then drives a pre-wired response (approach or avoid, fight or flight). The connection to affect suggests that this may be similar to the direct affect-action component posited by **Kiviniemi & Bevins**. Current computational models that examine actions produced through this system are limited (Balleine 2001; 2004; Dayan et al. 2006); nevertheless, several models have identified vulnerabilities in Pavlovian and Pavlovian-instrumental interactions that can lead to incorrect behavior (Balleine & Ostlund 2007; Breland & Breland 1961; Dayan et al. 2006).

R3.2. Dynamic motivational control

The issue of dynamic motivational control as raised by **Berridge et al.** has important implications for how the $S \xrightarrow{a} O$ system evaluates the expectation of value from the expectation of action. As noted by Berridge et al., cached-value or cached-action reinforcement learning systems (our $S \xrightarrow{a}$ system) cannot accommodate changes in value. However, decision-making systems based on expectancies of outcomes derived from searching through models of the world (our $S \xrightarrow{a} O$ system) can theoretically change valuation on fast time-courses. Current planning system models (e.g., Daw et al. 2005; Niv 2006; Niv et al. 2006b; Redish & Johnson 2007), and recent experimental results directly examining search and expectancies (Johnson & Redish 2007; Padoa-Schioppa & Assad 2006; Ramus et al. 2007; Schoenbaum et al. 2006a), provide a first step towards this because these models calculate value on the fly through $S \xrightarrow{a} E(O) \rightarrow E(V)$.

The extent to which value can actually be calculated on the fly is an interesting, open question. As noted in the commentary by **Ostlund & Balleine**, devaluation of outcome in instrumental learning (A-O, $S \xrightarrow{a} O$) paradigms requires experience with the outcome before the change in responding (Balleine 2001; 2004). In contrast, Pavlovian paradigms can change immediately, without a prior interaction (Balleine 2001; 2004). The experiments cited by **Berridge et al.** fit well within this distinction. These experiments imply an interaction between the homeostatic/allostatic vulnerabilities and the other vulnerabilities. The dynamic control of motivation will lie in that interaction (Niv et al. 2006b). But exactly how that dynamic control of motivation happens, computationally, is still unknown. Theoretically, the dynamic control of motivation is possible in both the Pavlovian ($[SO] \xrightarrow{a}$) and Instrumental ($S \xrightarrow{a} O$) systems; however, current models have not explored how those expectations of value are calculated from the expectations of outcome. An important question remains whether dynamic controls of motivation are only influencing planning systems (as suggested by these models) or whether they can also influence habit systems as well. Several computational models of motivation in habit systems through changes in latency to action (Niv 2006; 2007; Niv et al. 2006a; 2006b; 2007) have been proposed. Although these models do not dynamically control goals (there is no expectation of outcome in $S \xrightarrow{a}$), changes in latency and reaction time can change distributions across goals under specific experiments (Niv 2006; Niv et al. 2006b).

In a similar analysis, **Sarnecki, Traynor, & Clune** [**Sarnecki et al.**] suggest that dopamine can drive increased attention, and that attention can drive motivational control. We note that the temporal difference

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algorithms imply a shift in dopamine to cues predicting reward (Montague et al. 1996; Schultz 1998; Sutton & Barto 1998) and drugs (Redish 2004). These shifts occur in Pavlovian ($[SO]\xrightarrow{a}$), instrumental ($S\xrightarrow{a}O$), and habit ($S\xrightarrow{a}$) systems.

R3.3. New models of shifting systems

As noted earlier, new computational models based on reinforcement learning concepts (Sutton & Barto 1998) have addressed Pavlovian/affect systems (e.g., Dayan et al. 2006); instrumental learning systems, based on search through models of the world (e.g., Daw et al. 2005; Johnson & Redish 2007; Niv et al. 2006b; Redish & Johnson 2007) or on added memory components (e.g., Zilli & Hasselmo 2008); and habit learning systems (e.g., Daw 2003; Doya 2000b; Montague et al. 1996; Redish 2004; Suri 2002). However, it is important to note that these models do not directly address the question of "What is a unified action?" as asked by **Chambers** (see also Chambers et al. 2007). These questions can be related to early computational models of decision-making at human scales, such as the early models of chunking (Graybiel 1998; Newell 1990).

R3.4. A new framework

Thus, we can re-describe our framework as consisting of three components: Pavlovian (in which actions are evolutionarily driven or "pre-wired" for a given outcome, even when associated with other stimuli: $[SO]\xrightarrow{a}$); instrumental (in which actions are decided upon through a deliberative search through future possibilities and their consequences: $S\xrightarrow{a}O$); and habit (cached-action or cached-value systems, in which actions are associated with specific situations, and continued without consideration of the potential outcomes: $S\xrightarrow{a}$). (See Table R1.) Our theory posits that all three systems have potential failure-modes which can drive addictive behaviors and that interactions between failures in different systems can drive addictive behavior. For example, **Neal & Wood** note that habit failures can arise because of an interaction between normal learning mechanisms and faulty decision-making in the planning system.

R3.5. Faulty decision-making in normals

Several commentators (**Andreou**, **Hart & Krauss**, **Khalil**, **Lende**, **Neal & Wood**) noted that the simple neuroeconomic hypothesis of maximizing expected utility that we began our target article from has been known to be incorrect for many years. We do not deny that even normals show many non-simple (and non-rational) decision-making processes. For simplicity, we started our theorizing from the maximizing-value neuroeconomic model. We believe that these more complex theories will also have failure-modes.

We note, however, that our theory is, in fact, descriptive and not normative. For example, search is, by definition, incomplete, even in normals (see *Vulnerability 5*). Nothing in our model guarantees transitivity. Thus, our model does not actually fit the "rationality" definitions identified by **Khalil**. However, as noted in the target article, other errors exist as well (e.g., judgment errors [Kahneman & Tversky 1979], framing errors [Windmann et al. 2006], and memory errors [Schacter 2001]). Our argument is that the better our understanding of the decision-making machine, the better our understanding of its potential failure-modes will be, which will lead to better abilities to identify and treat addiction.

R4. A taxonomy of addiction

One of the major claims of our article is that addiction is a spectrum disorder, consisting of many interacting subparts. **Hardcastle** suggests that health-care providers already view addiction as a multifaceted disorder. Certainly, the subset methodology within the *DSM-IV-TR* (American Psychiatric Association 2000) and *ICD-10* (World Health Organization 1992) would suggest this. However, this view is not shared by all scientists or clinicians as can be seen in the **Ross** and **Le Moal** commentaries.

In particular, **Hardcastle** takes us to task for neither shortening the list nor being complete. If addiction is in truth a spectrum disorder, it may not be possible to shorten the list. Additionally, as noted by **MacCoun**, which behaviors constitute addictions depend on sociological definitions. Our hope is that by starting from failure-modes of the decision-making machine, we will approach a more parsimonious division of behavior which can improve the ability of clinicians to guide patients to treatment.

R4.1. Is there really one (hidden) unifying principle?

Several commentators suggest that there is really only one unifying principle. However, as noted in the target article, this is belied by the limited success of treatments across the general population (but strong success within subpopulations), by the multifaceted nature of addiction, and by the subset methodologies in the *DSM-IV-TR* (American Psychiatric Association 2000) and *ICD-10* (World Health Organization 1992).

Ross suggests that the underlying principle may arise from timing errors within the dopamine system. However, animals without dopamine will still self-administer drugs (Rocha et al. 1998; Volkow et al. 2002), and timing theories of reinforcement do not fit all of the animal-learning literature. The combination of differences between reinforcement (delivery of unexpected reward) and disappointment (non-delivery of expected reward; see Redish et al. 2007) and timing errors in dopamine is likely to be an important component of some addictions, particularly non-pharmacological addictions, such as gambling, video games, and Internet addictions. However, this combination cannot explain all addictions. It is unlikely to explain addictions with a high predictability of reward-delivery (such as heroin or cocaine). For many pharmacological substances, faster and more reliable delivery methods lead to higher addictive liability (e.g., smoking nicotine vs. nicotine gum vs. the nicotine patch [Henningfield & Keenan 1993], or crack vs. powder cocaine [Balster 1973; 1988; Gold 1997]). Nevertheless, Ross's hypothesized interaction is likely an important vulnerability in decision-making systems.

Le Moal suggests that entities should not be multiplied without necessity and accuses us of proposing "one more theory." However, as noted by **Stalnaker & Schoenbaum**,

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Table R1. *Three components of the decision-making machine*

System	Description	Learning Theory		Reinforcement Learning	Expectation
Affect	$[SO]\xrightarrow{a}$	Pavlovian	S-S	Prewired actions	E(O) → A
Planning	$S\xrightarrow{a}O$	Instrumental	A-O	Model-based RL	E(O) → E(V)
Habit	$S\xrightarrow{a}$	Habit	S-R	Cache-based RL	E(V)

many single-process theories have been suggested, and do not fit the data. We disagree with Le Moal's conclusion that all of the neurobiological theories of addiction agree on the network involved in addiction. While the anatomy itself is not in contention, many theorists disagree about the underlying neurophysiology of addiction (for example, compare the different description of the underlying neurophysiology of addiction in Everitt & Robbins 2005, in Kalivas et al. 2006, and in Koob & Le Moal 2006). Disagreements range through the importance of the role of withdrawal (Koob & Le Moal 2006; Robinson & Berridge 2003), the role of opioid signals (Laviolette et al. 2004), and the role of dorsal striatum (Everitt & Robbins 2005). Even within his commentary, Le Moal notes both ventral striatum and prefrontal cortex as separate dysregulations. Although a strong claim of our theory is that there are many dysregulations, it is certainly possible (and likely!) that some processes are more essential than others. Nevertheless, the fundamental claim of our theory is that addiction is a spectrum disorder with multiple underlying etiologies.

R4.2. Can some of the vulnerabilities be merged or combined?

Just as our framework of the decision-making machine is only a first step, our taxonomy of addiction is also only a first step. Several commentators suggested merging some of the vulnerabilities. A final definition of what constitutes a failure-mode, the extent of those failure-modes, and the variability and interaction between them will require more work from both the basic science and the clinical sides.

Goudie et al. suggest merging *Vulnerabilities 1* and *2* (the *homeostatic* and *allostatic* vulnerabilities). Although both vulnerabilities reflect changes in internal definitions of needs and targets, Koob and Le Moal (2006) make a strong case for separating the concepts of homeostasis and allostasis. Whether a single process can explain (and treat) them or whether they need to be treated separately will depend on future work directly addressing homeostasis and allostasis in the context of decision-making systems. Goudie et al. also suggest that both *Vulnerabilities 3* and *4* are examples of positive reinforcement within the planning system. Yet Berridge and Robinson (2003) have shown differences between hedonic reward delivery and overvaluation, suggesting that they arise from different pharmacological processes, which would imply they will have different vulnerabilities to pharmacological manipulation. Similarly, Goudie et al. note that *Vulnerabilities 4*, *5*, *7*, and *10* are all examples of hyperlearning, but hyperlearning in planning systems will be very different from hyperlearning in habit systems. As an example of the complexity within this taxonomy, **Bickel & Yi** suggest merging *Vulnerabilities 8* (*Interactions between planning] and habit*) and *9* (*Temporal discounting*). These can be seen as two kinds of impulsivity – an inability to inhibit a prepotent response in a go/no-go task (*8*) and over-fast temporal discounting (*9*). Yet, Goudie et al. and **Lejuez & Potenza** note that there are multiple kinds of impulsivity and cite data from Reynolds et al. (2006) that there is no correlation between these two experiments. The real question that needs to be addressed is whether the vulnerabilities are clinically separable and clinically treatable as separate processes.

Several commentators noted that these vulnerabilities interact. **Bickel & Yi** note that sensitivity to price is affected by the availability of substitutes, implying that discounting can interact with homeostatic levels. **Berridge et al.**'s concept of dynamic motivational control implies a necessary interaction between homeostasis/allostasis and planning systems. **Goudie et al.** note that homeostasis and attention to cues interact. And **Neal & Wood** note that the balance between habit and planning is sensitive to normal processes such as stress. Finally, **Coventry** asks what would large errors in situation recognition (*Vulnerability 6*) do to small errors in the other vulnerabilities, such as the learning *Vulnerabilities 3* to *7*? These interactions are only just now beginning to be studied at a computational level (e.g., Daw et al. 2005; Dayan et al. 2006; Niv et al. 2006b; Redish et al. 2007).

R4.3. What about a role for other memory systems in addiction?

Several commentators suggested addiction components not included in the original decision-making taxonomy. In particular, four additional decision-making components were suggested, including negative components (**Le Moal**, **Lende**), affective (emotion) components (**Kiviniemi & Bevins**, **Le Moal**), Pavlovian components (**Ostlund & Balleine**), and semantic and working memory components (**Wiers et al.**).

R4.3.1. Negative components. One of the largest gaps in the theory laid out in our target article is the lack of an explicit role for negative components in the decision-making model. We acknowledge the importance of negative components in decision-making but note a gap in the current computational modeling of decision-making literature. Negative effects (punishments, aversive signals) are treated as negative rewards, and non-delivery of punishments (relief) is treated as positive rewards. Similarly, the non-delivery of positive rewards (disappointment) is treated as negative rewards. Extinction studies demonstrate that aversion is a very

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different process computationally from non-delivery of expected reward (Redish et al. 2007).

Even if one follows the concept of aversion and reinforcement as parallel processes (with relief and disappointment as the non-delivery of expected punishments and rewards) (Daw et al. 2002; Redish et al. 2007), decision-making in the face of aversion is still not parallel (computationally) to reinforcement. With reinforcement, one thing draws an agent to it, other choices can be ignored (except in that they may provide potentially better choices). From a satisficing perspective (Simon 1955), after observing a reward, one has information about a minimally successful choice. The potential for improvement must be balanced with the cost of exploration (Stephens & Krebs 1987; Sutton & Barto 1998). In contrast, after a punishment, one only has information about what *not* to do. The question of what action should be taken still remains unanswered. This has led to a gap in the decision-making literature. We believe that this is an important missing component of the computational literature and that a computational model filling this gap will provide additional vulnerabilities, which will provide important components to our understanding of addiction.

R4.3.2. Emotion and affect – Pavlovian components. Both **Le Moal** and **Kiviniemi & Bevins** argue for an important component of affect in the vulnerabilities of addiction. Le Moal seems to attribute all addiction to errors of affect. But this belies the presence of robotic users (Sayette et al. 2000; Tiffany 1990). It also belies addicts' own descriptions, which differentiate "craving" and "withdrawal" (Robinson & Berridge 2003). We would suggest that affect must have a computational effect on the decision-making process, perhaps through an interaction between homeostatic and allostatic needs and the other vulnerabilities (**Bickel & Yi**, **Berridge et al.**, **Goudie et al.**). Perhaps, emotion and affect are means by which expectancies are evaluated ($E(O) \rightarrow E(V)$, which would influence *Vulnerability 4*), or perhaps emotion and affect change the set of actions considered at any time (which would influence *Vulnerability 5*). Kiviniemi & Bevins suggest the presence of a third action system: $affect \cdots \xrightarrow{a}$. We suspect that this may be related to the difference between Pavlovian and instrumental conditioning (**Ostlund & Balleine**; see also Dayan & Balleine 2002 and Dayan et al. 2006), and to the dynamic control of motivation (Berridge et al.). As discussed earlier, one can fold in a model of Pavlovian action selection based on affective implications of expected outcomes ($[SO]\xrightarrow{a}$). The relation of these issues with homeostatic and allostatic changes has only just begun to be studied computationally (Dayan et al. 2006; Niv et al. 2006b). The implications for addiction are well worth additional study.

R4.3.3. Semantic memory, working memory, episodic memory, and so on. Psychological theories of memory include many components beyond the simple "situation-recognition" component discussed in the target article. Recent computational models (e.g., Daw et al. 2005; Zilli & Hasselmo 2008) have begun to explore how working and episodic memory can enable the mechanisms underlying search and planning systems ($S\xrightarrow{a}O$).

Our theory suggests that these memory systems will interact with the decision-making machinery to provide additional vulnerabilities. Taking the example cited by **Wiers et al.**, subjects with poor working memory capacity are more likely to use automatic associations in drug use. In our interpretation, this would be due to a stronger automatic ($S\xrightarrow{a}$) system. In contrast, Wiers et al. also note that subjects with high working memory capacity are more sensitive to explicit expectancies. Given the likely relationship between working memory, expectancies, and the planning ($S\xrightarrow{a}O$) system (Redish & Johnson 2007; Zilli & Hasselmo 2008; see discussion in target article), users with strong working memory are more likely to fall victim to vulnerabilities in the planning system, whereas users with poor working memory are more likely to fall victim to vulnerabilities in the habit system. This is exactly the major point of our theory: it should be possible to subdivide addictive populations based on neuropsychological tests (strength of working memory) and see differences in the mechanisms underlying their addictions (dependence on expectancies). We predict that these two groups will require different treatment regimens in order to break their addictions.

R5. Predictions and falsifiability

Stalnaker & Schoenbaum ask, *How can this theory be tested? What falsifies it?* Obviously, if a single, underlying cause of addiction is found (such as suggested by **Ainslie**, **Le Moal**, or **Ross**) or if all addicts pass through a single sequence (as suggested by Le Moal), then our multiple-vulnerabilities theory would be wrong. However, such a clear alternative is unlikely to be found. Instead, we need to identify specific predictions and consequences of our theory.

The key prediction of our theory is that addiction should consist of multiple dissociable, but potentially overlapping, syndromes. This implies that there should be multiple subgroups within addiction, and that each subgroup will need different treatment regimens. We suggest, furthermore, that these subgroups can be best defined by *vulnerabilities* or *failure-modes* of decision-making systems. While the specific taxonomy proposed in the target article is certainly incomplete, it can provide a direction with which to proceed in our understanding of addiction. In a sense, as noted by **Ahmed**, our theory suggests theories of decision-making provide a "space" within which addiction can reside. Each individual will have a different parameter subspace based on that individual's decision-making machinery, which will change the individual's susceptibility to potential addictions. As noted by Ahmed, this implies that there should be species, age, and developmental differences in addictions. We would note also that there should be genetic and experiential (sociological) differences as well.

Different species of animals have different cognitive and decision-making abilities. Although the ability of nonhuman animals to encode non-local information, to create expectancies of their future, and to plan based on those expectancies is still controversial (Buckner & Carroll 2007; Johnson & Redish 2007; Johnson et al. 2007; Roberts et al. 2008; Suddendorf & Busby 2003), it is clear that different species have different abilities. In particular, it is clear that different species will show different abilities within planning and habit systems and different balances

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between these systems, as well as different interactions between them. This means that the availability and likelihood of the available vulnerabilities will differ between species. This also means that a cross-species comparison of behavioral liability to addiction subtypes may be a fruitful avenue for future addiction research.

Ahmed notes that a similar distinction can be made across development. Adolescents and adults have very different addiction liabilities (Casey et al. 2008; Chambers et al. 2003; Kelley et al. 2004; **Chambers'** commentary). These changed behavioral and psychological decision-systems should change the addiction space and provide different vulnerabilities.

Similar arguments can be made as to genetic and structural differences. Each individual's addiction subspace is going to be strongly influenced by its genetic variability. For example, Frank et al. (2007) have shown a triple dissociation with learning rates and three different dopamine-related polymorphisms. Our theory predicts that these effects on learning and decision-making should imply different susceptibilities to different addiction vulnerabilities identified in the target article, the commentaries, and this response.

Chambers suggests that mental illnesses known to change both brain function and decision-making systems could provide insights into these differences. These changed decision-making systems should, again, have different liabilities. This may explain the comorbidity seen between addiction and many mental illnesses.

This suggests a fascinating experimental paradigm in which lesions known to affect decision-making systems (e.g., hippocampus [HC], prefrontal cortex [PFC], different components of striatum) can be predicted to shift the addiction space and thus the availability and likelihood of vulnerabilities and the liability of different aspects of the addiction syndrome.

An additional falsifiable aspect of our theory is that each of the identified vulnerabilities entails a set of predictions. For example, the opiate theory of Redish and Johnson (2007) predicts that dopamine will not be released from well-predicted opiate delivery (by analogy to food-reward; Schultz 1998).[1] If this prediction was found to be wrong, then the opiate explanation for *Vulnerability 3* (*mimicking reward*) would be wrong. However, such a result would not demolish the entire theory. *Vulnerability 7*, as laid out in Redish (2004), is dependent on the validity of the temporal difference reinforcement learning theory (TDRL) explanation of dopamine signaling (Montague et al. 1995; 1996; Schultz 1998). If the TDRL explanation for dopamine signaling is wrong (Berridge 2007), then *Vulnerability 7* is wrong. But again, such a result would not demolish the multiple-vulnerabilities theory itself.

R5.1. A framework within which to search for other vulnerabilities

Scientific theories have many purposes beyond providing predictions to disprove. They also provide a framework within which to place and understand questions and answers (Ben-Ari 2005; Mayr 1998). Our theory provides just such a framework for addiction. It says that addiction arises as failure-modes of decision-making. Our theory thus suggests a path for future work to (1) elucidate the decision-making system, and (2) look for failures within it. A recent very exciting example is that of Chiu et al. (2008) who found that smokers' brains reflect fictive learning signals, but do not respond to them. Chiu et al.'s work implies the presence of an as-yet-unspecified vulnerability in this disconnect that can be looked for and identified.

R6. Additional vulnerabilities

In the target article, we argue that there are vulnerabilities in the decision-making machinery of humans and animals, and we identified ten potential vulnerabilities. As explicitly noted in the target article, that list is not complete. Several of the commentators suggested additional vulnerabilities.

Vulnerability 11: Errors in expectations

Boden notes that in addition to errors in valuation, the planning system can also include errors in the actual outcome expectations. In a sense, these are errors in the calculation of the outcome to expect in the $S \cdots \xrightarrow{a} O$ relationship. In the computational language of model-based reinforcement learning paradigms (Daw et al. 2005; Niv et al. 2006b), it entails errors in the calculation of the probability distribution $P(s'|s, a)$. It would have effects similar to *Vulnerabilities 3* (*Mimicking reward*), *4* (*Overvaluation in planning systems*), and *5* (*Errors in the search process*). In particular, social expectations (**Goudie et al., Griffiths**, **Hardcastle**, **Hart & Krauss**, **Kiviniemi & Bevins**, **Lende**) can change expected outcomes and thus lead to incorrect expectations. Examples include alcohol expectancy theory (Goldman et al. 1987; 1999) in which expectations of consequences of drinking lead to increased or decreased drinking, particularly under conditions in which the planning (expectancy) system is more active (**Wiers et al.**). A similar issue can be identified in misapplication of probability of outcome and misunderstandings of statistics (**Ainslie**, **Goudie et al.**, **Ross**).

Vulnerability 12: Errors in construction of past memory

As noted by **Neal & Wood**, errors in construction of past memory of success can change the expectation and evaluation of future consequences (Gilovich et al. 2002; Kahneman & Frederick 2002; Schacter 2001).

Vulnerability 13: Timing errors

Differences between reinforcement and disappointment (Redish et al. 2007) mean that multiple samples of unpredictable reinforcement scattered among unpredictable lack of delivery of expected reward will lead to excess reinforcement. As noted by **Ross**, either timing errors (Daw 2003) or unpredictable timing (such as seen in video games, gambling, and Internet packet delivery) can lead to an inability for predicted δ signals to cancel out appropriately.

Vulnerability 14: Pavlovian and affective errors

As discussed earlier, our two-system theory ($S \xrightarrow{a} O$ vs. $S \xrightarrow{a}$) is incomplete and needs to incorporate a Pavlovian ($[SO] \xrightarrow{a}$) component based on evolutionary precompiled actions taken in response to affective responses to situation-outcome associations (**Kiviniemi & Bevins**, **Ostlund & Balleine**). This system and its interaction with the other systems will provide additional vulnerabilities

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that will need to be incorporated into the theory (Balleine 2001; 2004; Breland & Breland 1961; Dayan et al. 2006).

Sarnecki et al. expand on one aspect of *Vulnerability 10* (*Learning rate modulators*), which they call "cue fascination." The concept is that cues become goals or targets in their own right (**Ainslie**). It should be noted that this is a key concept within many learning theories, including both Pavlovian conditioning (Dickinson 1980; Mackintosh 1974) and temporal difference reinforcement learning theory (Montague et al. 1996; Redish 2004; Sutton & Barto 1998). **Goudie et al.** suggest that attentional biases interact with craving, so that craving can cause and be caused by excess attention to cues. The underlying etiology of craving is an open question that will require additional experiments in the context of decision-making (Niv et al. 2006b; Redish & Johnson 2007).

Vulnerability 15: Interactions with standard behavioral learning mechanisms

Continued use of drugs through one vulnerability can lead to learning through normal behavioral learning mechanisms, even if there is nothing explicitly failing about the other mechanisms. For example, **Neal & Wood** note that habits are generally hard to break – inhibition of a well-trained response is difficult and requires effort (Dickinson 1980; Gray & McNaughton 2000; Husain et al. 2003; Isoda & Hikosaka 2007; Iversen & Mishkin 1970; Sakagami et al. 2006). This means that continued drug use due to a planning vulnerability (e.g., *Vulnerability 3*: *Mimicking reward*, or *Vulnerability 4*: *Overvaluation in the planning system*) can lead to development of a habit through normal mechanisms. Intransitive preferences (Ainslie 1992; 2001; Rachlin 2004), normal procrastination effects (Andreou 2005; O'Donoghue & Rabin 1999a), and switching costs of decision making (Wood & Neal 2007), can lead to continued use once started (perhaps because of one vulnerability, e.g., *Vulnerability 1*: *Homeostatic effects*) despite a lack of additional failures of the decision-making system (**Andreou**, **Neal & Wood**).

Vulnerability 16: Implications of social issues

Some commentators (**Boden**, **Griffiths**, **Lende**) suggested components occurring at other than neurophysiological levels, for example, those arising from social issues. These commentators asked about the implication of levels of analysis, particularly raising social and ethnographic reasons for drug taking, seeking, and continued use. Our claim that addiction arises from errors in decision-making would imply that these social interactions would be reducible (perhaps through a complex mechanism) to changes in expectations, valuations, and action-selection.

Taking the example by **Lende** that some people use amphetamine to increase skills,[2] our argument is that this increased skill use is an expectation of the future ($P(s'|s, a)$). Ignoring the potential downside of continued use can be seen as incorrectly calculating the expectation of the future (an error in $P(s'|s, a)$, see above) or incorrectly evaluating that expectation (*Vulnerability 4*). The examples given by **Hart & Krauss** and **Griffiths** relating peer behavior and other psychosocial factors imply changes in expectations and evaluations. **Boden** explicitly suggests this, noting that social interaction can drive overvaluation (peer pressure, *Vulnerability 4*), that social context can stimulate memory retrieval and can increase recall (changing search parameters, *Vulnerability 5*), and that over-generalization (*Vulnerability 6*) can lead to a lack of appreciation of the dangers of moving from low-risk (gateway) drugs to high-risk drugs.

R7. Treatment and assessment

We end our response with a discussion of the implications of our theory for the clinical and policy realms.

From a clinical perspective, the main implication of our theory is that because each addict's problem will be due to a spectrum of vulnerabilities/failure-modes, each addict will require a treatment regimen guided towards those vulnerabilities. These implications can be contrasted with molecular theories (**Yin**; e.g., Nestler 2005) and other theories of unified causes for addiction (e.g., **Le Moal**), which would imply that there would exist a single magic bullet treatment for all addicts. Our theory suggests that such a magic bullet does not exist.

Several commentators have brought up the question of how the individualized treatment regimen suggested by our theory would work in practice (**Goudie et al.**, **Hardcastle**). Hardcastle notes that many clinicians already individualize treatment. This is certainly true in practice, and we review several examples further on. However, we suggest that because the effects of these treatments on decision-making systems are not known, it has been difficult to steer addicts to appropriate treatments, or to determine how treatments might interact to provide a potential individualized treatment regimen. A similar discussion can be made as to policy, including the effect of taxes, criminal punishments, education, and interdiction (**MacCoun**). There are many treatments currently being used for addiction, including providing alternative rewards and vouchers (Higgins et al. 2002, 2004), behavioral (Carroll et al. 2004), and social treatments (e.g., 12-step programs), as well as various pharmacological treatments (Grant et al. 2006; Hyman 2005; Meyer & Mirin 1979; O'Brien et al. 1996). In general, treatments work very well for subpopulations. Subpopulations within addicted groups have been found in alcoholism (Addolorato et al. 2005; Crabbe 2002; Nurnberger & Bierut 2007; **Stalnaker & Schoenbaum**, **Wiers et al.**), in nicotine addiction (Irvin & Brandon 2000; Irvin et al. 2003), and in gambling (Grant et al. 2006; Sharpe 2002; **Coventry**, **Lejuez & Potenza**, **Griffiths**).

Lejuez & Potenza note that there is more to treatment than correcting errors. This is an important insight and may lead to alternative methods that could enable addicts to behaviorally prevent relapse even without directly eliminating the active vulnerability. For example, there may be treatments that can change the balance between planning and habit systems as a means of decreasing the influence of one or the other (**Bickel & Yi**). Treatments will presumably move patients to new portions of the addiction-space. An important question then is: *What are the trajectories of patients within treatment?* Different treatments will move different subpopulations in different ways. It is even possible that some treatments will

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shift different subpopulations toward other, previously unrealized vulnerabilities.

We suggest that two important next steps in addiction research are:

1. *To develop clinical tests that could differentiate subpopulations*. For example, the differences in working memory noted by **Wiers et al.** could be used to steer different subpopulations of alcoholics to different treatments. As another example, the identification of subjective craving in gamblers allowed Grant et al. (2006) to find significant success with Nalmefene in treating problem gambling. Our hope is that our theory provides a framework within which such clinical tests can be situated.

2. *To identify the effects of known (or novel) treatments on the decision-making system, particularly on vulnerabilities within the decision-making system.* For example, **Hart & Krauss** note the remarkable success of providing small alternate rewards (such as $5 vouchers) for abstinence. Raising drug prices by $5 would not lead to a similar success. So what is it about actually being forced to make a decision with an explicit alternate choice that helps some addicts maintain abstinence? Our hope is that our theory provides a framework within which to explain those treatments.

R8. Policy, framing, philosophical space

As noted by some commentators (**Griffiths; MacCoun**), the key question for addiction is that of framing and policy. Approximately a decade ago, addiction was reframed by Leshner (1997) and others (e.g., O'Brien & McLellan 1996; O'Brien et al. 2006) as a chronically relapsing, remitting disorder or disease. In doing so, these scientists moved addicts from sinners to be reviled to patients to be treated. Unfortunately, as also noted by **MacCoun**, the neuroscience complicates rather than simplifies the drug policy analysis.

But we believe the first question is actually: *What is addiction?* Like many definitions of addiction, we started from a definition of addiction as maladaptive decisions, but this is, of course, insufficient. There are many cases in which we celebrate choices made despite negative consequences. For example, we celebrate Martin Luther King going to jail for his beliefs. Or perhaps, even more specifically, we celebrate the middle-class whites who left their homes and comfort to march with Dr. King. It would be ludicrous to say that they were addicted to marching for civil rights for others. As another example, Osip Mandelstam continued to write poetry after he was thrown in the Soviet gulag. Do we really want to say that he was addicted to poetry?

In order to step away from this controversy, the *DSM-IV-TR* and *ICD-10* do not use the word "addiction" and instead refer to "dependence." This leads to a difficulty in defining non-pharmacological behaviors as addictive (e.g., gambling, shopping, sex, or Internet addictions) (Holden 2001; Potenza 2006; Potenza et al. 2001; **Griffiths**). Even in the context of pharmacological addictions, current clinicians have begun arguing for a return to the term "addiction" (O'Brien et al. 2006, **Hart & Krauss**).

As noted by **Griffiths**, addiction is a contextual and socially constructed term. It is dependent on the policy implications of the behavior and on the social disapproval of said behavior. But again, there are behaviors that are maladaptive, socially disapproved of, but not addictive.

One thing that is clear from the commentaries is that few people seem to agree on the core features of addiction. This is part of what makes addiction such a difficult and controversial issue. We believe that our vulnerabilities view may be able to unify some of the debate by asking how animals (including humans) make decisions and starting to examine the definition of addiction as failures in those decision-making systems.

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NOTES

1. As noted in the target article, this prediction is still unresolved because several labs have found conflicting results (Caillé & Parsons 2003; Hemby et al. 1995; Kiyatkin & Rebec 1997; 2001; Xi et al. 1998; Wise et al. 1995).

2. Caffeine use may be a better example of this, because it is also often used to increase skills but has fewer side effects (Daly & Fredholm 1998; Greden & Walters 1997; see Appendix E in the target article).

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