Towards a Translational Model of Decision-Making:

Findings from the Web-Surf Task

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Samantha Valerie Abram

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Advisor: Angus W. MacDonald, III, PhD

Co-advisor: A. David Redish, PhD

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Dedication

I dedicate this dissertation to my grandfather, Sherman Fenster (or as I

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Abstract

Interventions targeting cognitive disorders often hinge on assumptions that humans and nonhuman animals recruit equivalent cognitive mechanisms during decision-making. Identifying parallel decision systems across species could help bridge gaps between clinical and non-clinical research, and in turn, improve intervention efficacy. The goal of this dissertation is to assess for similar behavioral and neural markers of decision-making across humans and rodents using a sequential foraging paradigm ("The Web-Surf Task") that was adapted from a rodent spatial neuroeconomic task ("Restaurant Row"). The included studies highlight a functional translational approach that aims to access similar functional constructs via parallel tasks and methodological approaches. The results provide evidence of cross-species behavioral equivalents, such as the ability to detect revealed preferences. Findings from a neuroimaging study suggest that different neural systems track past and forward representations, indicative of human prospection during deliberation (i.e., episodic future thinking). Moreover, neural activation related to difficult decisions is similar to many of the structures that underlie rodent deliberation. Lastly, a risk-variant of the task suggests that regret-instances provide a bridge between our liking and pursuit of rewards. This final study also finds that impulsive individuals may fail to learn from regret. Collectively, this dissertation demonstrates the utility of this novel task for elucidating human deliberative mechanisms and identifying cross-species decision system compatibilities.

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CHAPTER 1: GENERAL INTRODUCTION

In his seminal review, George Ainslie (1975) described the cross-disciplinary study of *impulsive choice*, synthesizing findings from economics, sociology, and behavioral psychology. He opened with a question that continues to motivate researchers: "Why [do] organisms, particularly human beings, often freely choose the poorer, smaller, or more disastrous of two alternative rewards even when they seem to be entirely familiar with the alternatives?" Ainslie posited that, although this question spawned immense research within a variety of disciplines, there was a general disregard among researchers for "their neighbors' work." The need for cross-discipline communication remains a core issue even some 40 years later, particularly for the human and nonhuman animal branches of decision-making research.

Animal models of impulsivity and addiction are considered among the most well-regarded representations of human psychopathology, despite fissures that exist between model validity and the efficacy of human treatments based on these animal models (Hall, De Serrano, Rodd, & Tropepe, 2014; Kalivas, Peters, & Knackstedt, 2006). Coordinating clinical and pre-clinical research to model equivalent behaviors is necessary to understand the mechanisms that underlie impulsivity (Belzung & Lemoine, 2011; Potenza, 2009). Functional translational research is a promising approach in this regard, as it aims to access similar functional constructs via parallel tasks. The success of this approach hinges on the careful coordination of construct definitions, paradigm development, and analytic streams. Although demanding, this type of parallel processing between clinical and pre-clinical science could have an immense impact on our ability to treat psychologically and financially devastating disorders, such as substance abuse and

ADHD (Naqvi & Bechara, 2010). But to achieve this ideal synergy, we must first establish behavioral models that capture fundamental decision processes in human and nonhuman animals.

The purpose of this introduction is to provide a systematic review of the decision-making literature, with a specific focus on behavioral and neurobiological findings from human and rodent studies. I synthesize research across a variety of disciplines that include behavioral neuroscience, ecology, clinical psychology, and personality. This introduction is broadly organized into three main sections: the first section provides a review and critique of the traditional approaches for modeling impulsive choice (i.e., binary intertemporal choice models). The second section highlights foraging models as a promising approach for modeling naturalistic intertemporal decision behaviors. These first two sections are further subdivided into (1) theoretical and mathematical descriptions, (2) human and rodent task designs, (3) relevance to psychopathology, and (4) the underlying neural biological correlates. The third section provides recommendations aimed to improve our investigation of cross-species behavioral parallels and reduce gaps between animal decision model validity and corresponding treatment efficacy.

1.1 Traditional Binary Choice Models

Impulsivity is a multi-dimensional construct that includes a broad range of potentially unrelated maladaptive behaviors (de Wit, 2009b). These behaviors include an impaired ability to withhold responses, the incapacity to wait, or insensitivity to delayed or negative outcomes. The *delay-discounting* phenomenon is arguably the most highly

studied aspect of impulsivity (MacKillop et al., 2012). In particular, delay-discounting

models quantify how quickly reward value declines as a function of temporal delay

(alternatively called *temporal discounting* or *intertemporal choice*; Mazur, 1987). These

models emerged from economics, stemming from the field's emphasis on understanding

choice behaviors within a constrained system (Bickel, Green, & Vuchinich, 1995).

Within this framework, impulsive choice is considered the selection of a smaller,

immediate reward over a larger, delayed reward (Ainslie, 1975). Delay-discounting

models are a common index for measuring impulsivity in addiction and other

neuropsychiatric illnesses (Heerey, Robinson, McMahon, & Gold, 2007; Mackillop et al.,

2011; Marsch & Bickel, 2001; Odum, 2011).

In the following section, I begin with an overview of the mathematical functions

and behavioral techniques often used to measure impulsive choice in human and rodents.

I next review the literature relating impulsive choice with severe psychopathology in

humans and rodents, as well as a discussion of individual differences findings in humans.

Lastly, I discuss the neural circuitry that underlies healthy and aberrant decision-making

behaviors. I conclude this section by describing cross-species parallels and divergences in

the impulsive choice literature, with an emphasis on areas for advancing translational

synergy.

Mathematical Models of Delay Discounting

Two major mathematical models have been proposed to describe temporal

discounting behavior. Economists and decision analysis researchers have traditionally

favored an exponential model (Bickel, Jarmolowicz, Mueller, Koffarnus, & Gatchalian,

2012; Green, Fristoe, & Myerson, 1994; Green & Myerson, 2004; Reynolds, 2006a). The exponential model takes the following form:

$$V = Ae^{-kD},$$ (1)

where V is the subjective (or discounted) reward value of amount A that is available after a delay in D units of time. The k parameter reflects the discounting rate, or the rate at which value decreases with delay, with larger k values reflecting steeper discounting. This parameter has become a fundamental metric for assessing both within-subject (e.g., between offers) and between-group variability (e.g., controls versus drug users; Bickel et al., 2012). The exponential function assumes that value is discounting by a fixed proportion (Bickel et al., 2012; Kirby, 1997). Although this function may explain certain impulsive behaviors (e.g., temporal myopia, which assumes a large discounting rate), empirical research better supports alternative models (Marsch & Bickel, 2001).

One pivotal alternative from the behavioral economic literature is the hyperbolic discounting function (Mazur, 1987). This function takes the following form:

$$V = \frac{A}{1 + kD}.$$ (2)

where V, A, and D are defined in equation (1). Comparable to the exponential function (1), a larger k parameter reflects steeper discounting. However, the hyperbolic function does not assume that discounting occurs at a fixed rate. Instead, reward devaluation is proportional to delay magnitude (Ainslie & Haslam, 1992), where small delay rewards are devalued more rapidly than more delayed rewards.

Many researchers argue that temporal discounting is better captured by the hyperbolic than exponential function in humans across an array of species (Green &

Myerson, 2004; Mazur & Biondi, 2009; Mazur, 2007). However, the optimal discounting

function may hinge on the type of decision at hand (Wikenheiser, Stephens, & Redish,

2013), where the precise nature of the decision is modulated by task specificities (e.g.,

different cost types). Researchers can empirically determine the optimal discounting

model by computing *indifference points*, which is the point at which the immediate and

delayed options are equivalent in value (Green et al., 1994). When indifference points are

calculated over a series of possible delays, researchers can plot an *indifference curve* to

visualize the shape of the discounting function (Marsch & Bickel, 2001). The next

section describes possible procedures for obtaining indifference points.

Methods to Derive Indifference Points

The most common delay procedures used to derive indifference points are the

adjusting-delay (Mazur, 1987) and *adjusting-amount* methods (Rachlin, Raineri, &

Cross, 1991). Mazur (1987) first proposed the adjusting-delay procedure to examine the

influence of delay and uncertainty on reward value. In this method, the shorter delay is

lengthened each time a subject chooses the immediate reward, and reduced each time a

subject chooses the delayed reward. Rachlin and colleagues (1991) proposed the

complementary adjusting-amount procedure, which adjusts the magnitude of the

immediate reward as a function of choice, while holding the larger reward and delay

length constant.

Numerous studies have assumed that both delay procedures tap into the same

behavioral processes (Christensen, Parker, Silbergeld, & Hursh, 1998; Green et al., 1994;

Jimura, Myerson, Hilgard, Braver, & Green, 2009; Raineri & Rachlin, 1993; Rodriguez

& Logue, 1988). Only two studies directly compared these procedures, the first including pigeons (Green, Myerson, Shah, Estle, & Holt, 2007) and the second using humans (Holt, Green, & Myerson, 2012). Green and colleagues (2007) did not observe any systematic differences in the discounting rates produced using the adjusting-amount or adjusting-delay procedures. Holt et al. (2012) used three discounting procedures to assess this claim: adjusting-delay, adjusting-immediate-amount, and adjusting-delayed-amount. The authors found robust magnitude effects for all three discounting methods, whereby smaller rewards were discounted more steeply than larger rewards. Thus, these delay procedures may tap into common underlying decision processes.

Alternatively, one can calculate discounting without indifference points. For instance, Evenden and Ryan (1996) developed a procedure where animals cycle through a fixed list of options. Specifically, the delay to the larger reward increases over the session to improve task efficiency and ensure that subjects remain sensitive to the delay (Odum, 2011). Choice behavior is then quantified as the percentage of times a subject chooses the larger delayed reward. For more extensive descriptions of the procedures used to derive discounting functions in human and nonhuman animals, I refer the reader to Madden and Johnson (2010). Importantly, indifference points are computed from impulsive choice tasks that vary according to several structural dimensions, which are discussed in the following section.

Laboratory Models of Impulsive Choice

Impulsive choice tasks vary along at least three structural dimensions: (1) reward type (i.e., abstract to concrete), (2) cost type (e.g., delay, effort), and (3) the availability

of a reward following a decision (i.e., commitment- versus sustained-choice). The majority of human and nonhuman animal paradigms can be described within this framework. The following section explores these dimensions and the corresponding task designs in more detail, with an emphasis on cross-species comparisons.

Reward Types: From Abstract to Concrete

The rewards used in human paradigms exist along a continuum that ranges from more abstract offers (e.g., hypothetical monetary gains) to concrete gains (e.g., primary reinforcers, such as juice). These reward types are then incorporated into various discounting paradigms, which are further categorized as: (1) *hypothetical*, (2) *real-reward*, and (3) *real-time* paradigms (Reynolds, 2006a). These tasks all entail scenarios in which a subject selects between immediate and delayed outcomes of different magnitudes; however, the precise nature of the reward and delay components differs across paradigms.

Hypothetical paradigms are the most common discounting measure (Green & Myerson, 2004; Odum, 2011), and typically ask subjects to make abstract choices about future monetary gains (Madden & Bickel, 2010), such as:

"Which would you prefer: $10 now or $50 in two weeks?"

Hypothetical discounting paradigms are often used in psychology and neuroscience experiments because they are relatively inexpensive and time efficient to employ. Hypothetical choices are also favorable in situations in which real offers are impractical

or unethical (Kang, Rangel, Camus, & Camerer, 2011). However, researchers have questioned the validity of hypothetical paradigms in modeling real-world decisions (Green & Myerson, 2004; Kirby, 1997; Marsch & Bickel, 2001; Odum, 2011) and other researchers have questioned whether hypothetical and real choices tap into the same underlying systems (Navarick, 2004).

Real-reward discounting paradigms were developed to improve the face validity of hypothetical discounting tasks (Reynolds, 2006a). In real-reward paradigms, one or a few of the choices made by the subject during the task are randomly selected and paid to the subject at the end of the testing session. When compared directly, the majority of studies did not detect differences between discounting rates derived from real versus hypothetical tasks (e.g., Johnson & Bickel, 2002; Lawyer, Schoepflin, Green, & Jenks, 2011; Madden et al., 2004; Matusiewicz, Carter, Landes, & Yi, 2013). Nonetheless, Lagorio and Madden (2005) argued that real-world paradigms may only capture *potentially* real-rewards. Potentially real-reward paradigms should theoretically yield similar results to real-reward paradigms, as subjects do not know which outcome they will receive, assuming that subjects treat all choices as possibly real.

Motivated by this concern, *real-time* (or experiential) paradigms were designed such that subjects could experience the consequences of their choices (e.g., delay, reward) on a trial-by-trial basis (Reynolds, 2006). A few real-time studies used primary reinforcers (Jimura et al., 2009; Kirk & Logue, 1997; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007), although many used monetary rewards of smaller reward magnitude available at shorter delays (Reynolds, 2006; Shiels et al., 2009). Real-time paradigms may be especially valuable for populations that struggle with abstract

decision-making (e.g., children, people with severe mental illness; Reynolds, 2006), as trial-by-trial consummatory responses are perhaps more salient than hypothetical monetary gains available weeks or months away. However, two methodological concerns are worth noting. First, the trial-by-trial structure could confound discounting behaviors with learning effects. For instance, it may be challenging to parse whether an individual is more impulsive or has difficulty adapting behavior based on prior experiences. Second, the frequent use of monetary rewards ultimately detracts from the experiential aim of these tasks. Even though subjects physically receive money (via coin dispenser) on each trial, this does not equate to spending or *consuming* a monetary reward on each trial.

In contrast to human tasks, rodent discounting paradigms are always experiential, given that rodent subjects encounter real-time delays and consume rewards as the consequence of each choice. **In this vein, rewards are frequently in the form of primary reinforcement such as food pellets, saccharin, or a drug.** Rodent discounting paradigms can take on *non-spatial* and *spatial* designs.

Non-spatial paradigms typically require rodents to make a series of lever-presses or nose-pokes to receive reward. For instance, rodents may be placed in operant chambers that contain several nose-poke holes. In such a task, nose-pokes to one hole may deliver a small, immediate reward, whereas nose-pokes to another hole may deliver a delayed but larger reward (Pattij, Schetters, Janssen, Wiskerke, & Schoffelmeer, 2009). Lever-press paradigms are comparable in design, where different levers presses produce rewards of disparate delay and magnitude.

Spatial paradigms frequently require rodents to navigate mazes while making choices. Numerous researchers have adopted maze designs to probe rodent cognitions,

given their inclination towards narrow, winding passages (Dudchenko, 2004). The T-maze is the simplest spatial maze design (Tolman, 1925). In the context of delay-discounting, rats choose between smaller, immediate rewards at one maze arm and larger, delayed rewards from the other maze arm. This design is advantageous in several respects: First, rats tend to alternate arms even in the absence of forced-choice trials. This behavior has been called *exploration* or *investigation* (Dudchenko, 2004; Papale, Stott, Powell, Regier, & Redish, 2012), and may reflect the process by which the rat learns which side of the maze represents which delay type. Second, the T-maze design does not require complex lever-press or nose-poke pre-trainings (Papale et al., 2012). Given these positive attributes, T-mazes are often employed in rodent discounting studies.

Cost Types: Delay, Probability, and Effort Discounting

Comparable to the reward type dimension, **human and rodent discounting models can differ in the *type* of cost involved --- temporal delay, probability of receipt, or effort requirements.** Although delay is most often used, researchers also use *probability* and *effort discounting* tasks that similarly include discrete binary offers (Bari & Robbins, 2013). Distinctions between cost types are important as different response costs may recruit separable neural substrates (Prévost, Pessiglione, Météreau, Cléry-Melin, & Dreher, 2010).

Probability discounting (alternatively called *uncertainty* or *odds discounting*) captures subjective reward value as a function of the *probability* of receipt, given a choice between a smaller certain reward and a larger uncertain reward (Bidwell et al., 2013). For humans, subjective reward value is expected to decrease as the odds of receipt

increase, according to a hyperbolic function (Cardinal, 2006). There is debate as to whether delay and probability discounting reflect the same or dissociable processes, though recent evidence supports the latter assertion. Several studies found that delay- and probability-discounting rates were not highly correlated in humans (Andrade & Petry, 2012; Holt, Green, & Myerson, 2003; Madden, Petry, & Johnson, 2009) or rats (Wilhelm & Mitchell, 2008), and may differentially relate to addiction (Bidwell et al., 2013; Madden et al., 2009).

Effort discounting models describe subjective reward value as inversely related to the effort required to obtain it (Botvinick, Huffstetler, & McGuire, 2009). Consideration of effort costs are important for developing ecologically valid decision-making models, as animals in the wild (and laboratory) must weigh the metabolic costs needed to obtain sustenance or reward (Croxson, Walton, O'Reilly, Behrens, & Rushworth, 2009). Despite this ecological utility, relations between physical effort and choice have been examined far less than alternative decision costs (Klein-Flügge, Kennerley, Saraiva, Penny, & Bestmann, 2015). Most studies suggest that effort costs are discounted linearly (Burke, Brünger, Kahnt, Park, & Tobler, 2013; Phillips, Walton, & Jhou, 2007) or hyperbolically (Grossbard & Mazur, 1986; Prévost et al., 2010; Sugiwaka & Okouchi, 2004). Effort and delay discounting may be functionally similar despite separable neural substrates (Prévost et al., 2010; Reed, Kaplan, & Brewer, 2012); although others challenged this notion by identifying dissociable underlying functions that yielded uncorrelated choice parameters (Klein-Flügge et al., 2015). The extent to which effort and delay-based discounting tap into dissociable systems is further discussed in a later section (see *How Specific Are These Associations?*).

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Room to Deflect: Commitment- versus Sustained-Choice

Choice impulsivity is typically assessed using the kinds of paradigms described in the previous section, where subjects choose between rewards of differing magnitudes available at different costs. These tasks are considered "commitment-choice" procedures, because a subject commits to one option over the other (Reynolds & Schiffbauer, 2005; Shamosh & Gray, 2008). **Alternatively, "sustained-choice" procedures (often called** *delay of gratification* **paradigms) measure choice impulsivity when the smaller immediate reward is continuously available.** This means that even if an individual selects the delayed option, he can deflect to the alternative until the trial ends.

Walter Mischel's Stanford marshmallow experiments during the 1960s to 70s are perhaps the most well-known studies of delayed gratification (Mischel, Ebbesen, & Zeiss, 1972). In one variant, a child was presented a food reward and delay (Mischel & Mischel, 1983). If the child waited through the delay, the experimenter returned and the child received two food rewards, although at any point during the delay the child could ring a bell and the experimenter would return. The failure to wait through the entire delay resulted in only a single food reward. In effect, delayed gratification depends on *cognitive control*, or the capacity to suppress contesting thoughts or action (Casey et al., 2011). Delayed gratification abilities in children have been positively correlated with academic and social competency, SAT scores, and self-regulation abilities in adulthood (Mischel, Shoda, & Peake, 1988; Shoda, Mischel, & Peake, 1990).

Few studies have directly compared delay discounting and delay of gratification paradigms, which have yielded conflicting results regarding their discriminant validity

(Reynolds, De Wit, & Richards, 2002; Reynolds & Schiffbauer, 2005; Rachlin, Brown, & Cross, 2000). A lack of consistent operational definitions has contributed to difficulties in determining whether these paradigms capture distinct impulsivity facets (de Wit, 2009b). For instance, different studies use the terms delay discounting and delay of gratification to reflect either commitment- or sustained-choice tasks (Shamosh & Gray, 2008). Similarly, some researchers ascribe delay of gratification to impulsive behaviors exhibited during *response inhibition* tasks (e.g., Casey et al., 2011), which are believed to reflect *impulsive action* (Bari & Robbins, 2013). These tasks typically require subjects to postpone action until a go-signal appears, restrain action when an unexpected no-go signal appears, or cancel action when a stop-signal appears after the response has begun. Bari and Robbins (2013) distinguish these paradigms from impulsive choice tasks, as one tries to *inhibit* the urge to select an immediate, smaller reward over the larger, delayed reward. Although impulsive choice and action paradigms both fall under the umbrella of "impulsivity", the current review focuses primarily on the former. Nonetheless, rectifying this lack of consistent terminology is of utmost importance for elucidating the extent to which various tasks map onto unique impulsivity branches.

More broadly, it appears that researchers can sufficiently conceptualize human and rodent impulsive choice paradigms according to three parameters (i.e., reward type, cost type, and the ability to deflect). However, clear methodological differences emerge when directly comparing human and rodent task designs. Regardless, established associations between impulsive choice and psychopathologies have encouraged the continued use of discounting tasks in human and nonhuman animal research. The next section examines the literature on discounting and psychopathology, with a particular

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focus on addiction, obesity, schizophrenia, and ADHD. This discussion considers the relevance of task design to specific disorders, as well as knowledge into potential causal mechanisms gained from the rodent literature.

Correlates with Psychopathology

Impulsive Choice and Severe Psychopathology: Findings from Human and Rat Studies
"Loss of Control" Disorders: Drug Addiction, Excessive Gambling, and Obesity

Impulsive choice paradigms are frequently used to investigate aberrant decision-making in **substance addiction**. Numerous reviews have substantiated greater impulsivity in addicts given robust relations with delay discounting parameters (Bickel et al., 2012; de Wit, 2009; Marsch & Bickel, 2001; Reynolds, 2006a). Hyperbolic discounting functions, in particular, capture the *preference reversals* characteristic of addiction, that are related to loss of control and relapse (Bickel et al., 2012). For example, someone with alcohol addiction may prefer the delayed alternative when both options are delayed (e.g., long-term fitness benefits), whereas preference may shift to the immediate alternative as delays decrease (e.g., the clock approaches happy hour). In other words, individuals may wish to abstain when substances are not immediately available, but reverse their preference when substances become readily available. Despite compelling links between discounting and addiction, research remains uncertain as to whether impulsive choice precedes drug use, or if repeated drug use fosters impulsive choice (Bickel et al., 2012).

Animal models are particularly advantageous for elucidating causal relations between drug use and impulsive behaviors (Jupp & Dalley, 2014), as researchers can

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ensure subjects are drug-naïve at the outset (de Wit & Mitchell, 2010). Preclinical models can provide insight as to whether impulsivity is a *determinant* or *consequence* of drug use (Potenza, 2009). Supporting impulsivity as a determinant, rodent research suggests steeper discounting rates may precede various indices of drug use, particularly for amphetamines (Weafer, Mitchell, & de Wit, 2014). Several longitudinal studies have demonstrated similar prospective associations in humans (Audrain-McGovern et al., 2009; Brody et al., 2014; Fernie et al., 2013; Janssen, Larsen, Vollebergh, & Wiers, 2015), although methodological challenges make it difficult to determine the shared causal mechanisms across human and nonhuman animals (Weafer et al., 2014). Nonetheless, discounting rates may represent a risk factor for developing addiction and a promising target for intervention development.

In contrast to the convergent results above, the human and animal literatures diverge as to whether impulsive choice is a consequence of drug use (Weafer et al., 2014). The majority of animal studies note discounting rate changes following acute drug administration, though these effects may depend somewhat on rat strain and drug dosage. Far fewer studies have examined these associations in human subjects (de Wit & Mitchell, 2010), yielding inconsistent results and cross-species discrepancies (Bickel et al., 2012). For instance, acute alcohol administration to humans has been linked with both increased (Reynolds et al., 2006) and decreased discounting rates (Ortner, MacDonald, & Olmstead, 2003), as well as null effects (Richards, Zhang, Mitchell, & de Wit, 1999).

Impulsive choice paradigms are similarly used to examine **excessive gambling** (Bickel et al., 2012), which is conceptualized as a *behavioral addiction*. Comparable to substance use disorders, a plethora of findings reveal increased impulsive choice among

individuals with pathological gambling (Koffarnus, Jarmolowicz, Mueller, & Bickel, 2013); however, some evidence indicates that impulsive action is a better predictor of gambling severity (Brevers et al., 2012). Many studies also posit that comorbidity with substance abuse may yield the highest discounting rates. Andrade and Petry (2012) aimed to elucidate relations between response cost types (i.e., delay versus probability discounting) and specific impulse-related psychopathology (i.e., pathological gamblers with and without substance use), finding that substance use influenced delay but not probability discounting. Accordingly, different response costs may tap into different impulsivity facets, and/or delay discounting may be more sensitive to drug addictions. Regardless, there are considerable similarities across substance use and gambling pathology with respect to behavior and neural substrates (Leeman & Potenza, 2012). Differences between these disorders may be partly attributed to the effects of chronic drug exposure on the brain. If this latter point is indeed true, investigations into behavioral addictions could become a key avenue for investigating the relevant brain circuitry *sans* drug impact.

Potential utility notwithstanding, certain procedural limitations influence the ecological validity of gambling studies in humans (Madden, Ewan, & Lagorio, 2007). Limitations include regulations on the extent to which risks and consequences are real. Animal models can address this issue, though this requires that animal gambling paradigms equivalently capture *loss* (Clark et al., 2013). This notion has led some researchers to adopt rat variations of the Iowa Gambling Task (which involves subjects deducing between several options to maximize gains), rather than employing probability discounting paradigms as done previously (Zeeb, Robbins, & Winstanley, 2009).

Probability discounting paradigms arguably capture the failure to gain an additional reward rather than the loss of resources that occurs from gambling. Consequently, traditional impulsive choice tasks may be ill suited for investigating cross-species parallels in gambling addiction. That said, probability-discounting paradigms are an especially powerful control for delay-discounting tasks, as they allow researchers to discern the specific effects of delay on behavior when rewards are equivalent.

The strong overlap between over-eating and substance use disorders supports addiction models of obesity (Barry, Clarke, & Petry, 2009). For instance, sugar-bingeing in rats can yield behavior equivalent to that observed in drug-dependent rats (Avena, Rada, & Hoebel, 2009). It is therefore unsurprising that obesity and drug addiction produce similar impulsive tendencies and share common neurobiological substrates (Volkow & Baler, 2015; Volkow, Wang, Tomasi, & Baler, 2013). Recent endeavors have linked discounting with **obesity** and body mass, particularly for females (Jarmolowicz et al., 2014). Weller and colleagues (2008) found that obese women discounted monetary rewards more steeply than healthy-weight women. Thus, discounting metrics can capture behavioral tendencies that cut across diagnostically separate, but related disorders.

Other Goal-Directed Disorders: Schizophrenia and ADHD

Schizophrenia is a heterogeneous disorder characterized by a range of symptoms (i.e., positive, negative, disorganized), as well as cognitive, social, and functional impairments. Moreover, motivational and goal-directed deficits are a core issue for treating schizophrenia (Barch & Dowd, 2010). Such concerns have led researchers to investigate how decision-making systems go awry in schizophrenia. Still in its nascent

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stages, the impulsive choice literature for schizophrenia indicates both heightened (Ahn et al., 2011; Heerey, Matveeva, & Gold, 2011; Heerey et al., 2007; Weller et al., 2014) and normative discounting rates (Docx et al., 2015; MacKillop & Tidey, 2011; Wing, Moss, Rabin, & George, 2012) when compared with healthy controls. It is possible that differences observed between groups and/or across studies could be related to smoking covariates (Bickel et al., 2012), given the links between substance use and discounting behaviors.

An alternative theory suggests psychiatric-control differences emerge from disrupted dynamics between working memory capacity, value/cost representations, and motivational processes. Through a series of experiments, Gold et al. (2008) explored the interplay between hedonic experience and cognition in schizophrenia. Interestingly, individuals with schizophrenia exhibited relatively normative experiences of positive emotion when shown evocative stimuli. However, deficits were apparent when patients had to incorporate or weigh multiple factors during decision-making (Heerey, Bell-Warren, & Gold, 2008), which may be explained in part by working memory capacity (see Ahn et al., 2011 and Heerey et al., 2011 for examples); this deficiency may be linked to one or more of the memory systems that are critical to learning and planning (Johnson, van der Meer, & Redish, 2007; Poldrack & Packard, 2003). Individuals with schizophrenia also have difficulties in representing the value (or cost) of different offers (Gold et al., 2008), especially temporally distant rewards (Heerey et al., 2011). Such abnormal cost estimations may underlie disconnects between intact hedonic experiences and goal-directed pursuits (Gold et al., 2013). Taken together, it is possible that aberrant discounting in schizophrenia reflects failures in memory, perceptual, and/or deliberative

decision systems (for a review of these systems see Redish, 2013).

As suggested earlier, real-time paradigms may be a promising alternative for examining decision-making processes in schizophrenia. Such tasks could reduce the abstraction needed to represent temporally distant hypothetical rewards, and thus reduce strains on working memory. If real costs and consummatory rewards were more salient, patients might have less difficulty using immediate experiences to guide subsequent decisions (or less difficultly in mentally representing potential outcomes). In turn, experiential models could enable a more focused investigation into the specific mechanisms impaired in schizophrenia by reducing certain cognitive demands. These endeavors could also foster parallels with animal discounting models of schizophrenia, an area in need of development (Barnes, Der-Avakian, & Markou, 2014).

The perception of time can also influence intertemporal choices (Wittmann & Paulus, 2008). For example, people are more patient when distal rewards are perceived as closer (Lempert & Phelps, 2016). This idea relates to the Construal-Level Theory that describes psychological distance with respect to abstract versus concrete thinking, whereby more distal objects are represented more abstractly (Trope & Liberman, 2010); it is also possible that more distal rewards are harder to 'find' and thus evaluate, from the perspective that deliberation is a mental search process that identifies rewards available in the future (Kurth-Nelson, Bickel, & Redish, 2012). Of note, temporal perception is sometimes altered among individuals with severe mental illness (Dale et al., 2010; Mcdowell, Clementz, & Wixted, 1996; Papageorgiou et al., 2013), and can be influenced by certain drugs (Fowler, Pinkston, & Vorontsova, 2009). Temporal perception is therefore an important consideration for clinical research.

Attention deficit hyperactivity disorder (or ADHD) is a developmental disorder characterized by inattention, hyperactivity, and disinhibition. Steeper discounting rates have been observed for children, adolescents, and adults with ADHD (Bickel et al., 2012). Similar to the schizophrenia literature, group differences were associated with working memory. This common cognitive-behavioral association may provide a novel avenue for modifying impulsivity, and subsequently treating a range of disorders, including substance abuse (e.g., Shamosh et al., 2008). For instance, preliminary findings indicated reduced discounting in stimulant addicts following working memory training (Bickel, Yi, Landes, Hill, & Baxter, 2011). Future schizophrenia and ADHD treatment studies could extend this work to elucidate the importance of working memory, and other cognitive abilities, to impulsive choice and psychopathology. But how does individual variation influence impulsivity? Similarly, are discounting rates only useful for clinical case-control studies?

Individual Differences: Relations with Personality-Based Impulsivity Indices in Humans

The prior section highlights the effectiveness of impulsive choice paradigms for distinguishing psychiatric groups from healthy subjects. Given this wide applicability, excessive temporal discounting has been conceptualized as a core mental health (McClure & Bickel, 2014) or *trans-disease* process that underlies a range of disorders (Bickel et al., 2012). The idea of discounting as a shared behavioral marker speaks to *dimensional* models of psychopathology, in which individuals are characterized according to various symptom continuums as opposed to distinct categories (Cuthbert, 2014; Krueger & Markon, 2006). Rather than emphasizing between-group differences,

a dimensional approach stresses within-group investigations that capture individual variation in traits or behaviors. This approach has critical implications for animal models, as high comorbidity encourages animal researchers to model specific symptom dimensions rather than entire disorders (Fernando & Robbins, 2011).

Historically, personality and individual differences researchers have used self-report questionnaires to evaluate impulsivity dimensions in clinical and non-clinical populations (Cyders & Coskunpinar, 2011; Marsch & Bickel, 2001). Self-report measures are beneficial in several respects (e.g., easy to administer, inexpensive), but are limited by factors like subject response-bias. Reynolds et al. (2006) were the first to directly compare behavioral and self-report impulsivity measures in a non-clinical sample and found no significant overlap. Alternatively, work by Mobini et al. (2007) reported positive associations between discounting rates and self-reported impulsivity. Given discrepancies in the literature, Cyders and Coskumnipar (2011) conducted a meta-analysis to better elucidate relations between these methods. The authors found evidence for a significant association but the effect size was small. Thus, while some lab tasks corresponded with self-reported impulsivity facets, by and large these approaches shared a small amount of variance. Hence, these divergent approaches should not be conceptualized under the same broad impulsivity header. Instead, researchers should classify measures according to the specific one-dimensional concept they were designed to capture, like sensation seeking or impulsive choice. The lack of overlap between self-report and behavioral measures might also motivate researchers to use these measures in *conjunction* to obtain a more comprehensive picture.

An important component of impulsivity research is identifying the biological

systems that support decision-making across species. A detailed account of these systems is necessary for understanding how they break down and in turn, developing effective pharmacological treatments. The next section discusses the neural systems involved in decision-making, with attention to cross-species parallels and psychopathology.

Neurobiological Correlates of Decision-Making: Implications for Psychopathology

Seminal work by McClure and colleagues (2004) first described the brain areas involved in delay discounting, noting dissociable neural systems: limbic areas rich with dopaminergic projections (e.g., ventral striatum [VStr], medial prefrontal cortex [mPFC], orbitofrontal cortex [OFC]) activated for decisions involving immediate rewards, whereas lateral frontal areas (e.g., dorsolateral prefrontal cortex [dlPFC]) activated in response to all choices (immediate and delayed). The authors framed these results as a two-component model of discounting, where the *beta system* weighed immediate rewards and the *delta system* weighed rewards at all delays (Ballard & Knutson, 2009). The two-component model can also be conceptualized as competing impulsive (i.e., limbic areas) and executive control (i.e., frontal and parietal areas) systems. This competing framework then proposes that addiction emerges from the imbalance between two interacting but distinct neural systems (Bechara, 2005). For instance, excessive discounting among individuals with addiction may result from chronic use that decreases function in the executive system (Meier et al., 2012), which in turn, reduces preference for delayed rewards (McClure et al., 2004). Similarly, an underdeveloped or weakened executive system could explain heightened discounting in ADHD or antisocial personality disorder (Bickel et al., 2007).

Findings by Kable and Glimcher (2007) challenged the two-component model offering a one-component model instead. The authors found that many of the impulsive or beta areas (e.g., VStr, mPFC, and posterior cingulate cortex [PCC]) tracked the subjective value of delayed rewards, thus contradicting the claim that these regions form an impulsive system that *primarily* values immediate rewards (although cross-study methodological differences prevented a direct comparison of these findings; Peters & Büchel, 2011). Despite cumulative evidence that supports the dual-system model (McClure & Bickel, 2014), decision-making systems are likely more complex than initially proposed.

Current theories suggest that decision-making is driven by multiple interacting systems (Daw, Niv, & Dayan, 2005; Redish, Jensen, & Johnson, 2008; van der Meer, Kurth-Nelson, & Redish, 2012): The first is the *reflex* system, which is hardwired into the central nervous system and responds immediately to direct dangers and events; it is simple and follows basic rule-based reactions (e.g., pulling your hand away from a hot stove; Redish, 2013). Next is the *Pavlovian* action-selection system, which reacts to expected outcomes in a genetically prewired manner (i.e., species-specific actions that are acquired via associative learning processes; Bouton, 2007). This system is computationally fast. In comparison, the *deliberative* action-selection system is flexible but much slower. This system is responsible for planning actions and maximizing expected rewards (van der Meer et al., 2012), and likely entails searching through a series of mentally simulated future possibilities, i.e., 'episodic future thinking' (Redish, 2016). Finally, the *habit* action-selection system learns the best action to implement for a given situation; importantly, stored actions are fast but inflexible. There are also various

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motor, perceptual, and motivational support systems. These systems are also equipped

with unique but overlapping systems. For instance, the Pavlovian system includes the

periaqueductal gray, ventral tegmental area, amygdala, VStr, and OFC (Ledoux, 2002;

McDannald, Lucantonio, Burke, Niv, & Schoenbaum, 2011), whereas the deliberative

system includes the hippocampus, prefrontal cortex, VStr, ventral tegmental area, and

dorsomedial striatum (Johnson & Redish, 2007; Schacter & Addis, 2011; van der Meer,

2009). Importantly, failure nodes or vulnerabilities within each of these decision systems

may lead to addiction (see Redish, 2013 for review).

Meta-analytic research indicates the OFC and VStr, specifically the nucleus

accumbens or *NAcc*, are key players in human reward processing (Liu, Hairston, Schrier,

& Fan, 2011). More specifically, the OFC (including medial OFC and ventromedial PFC)

plays a pivotal role in *reward value representation* (Jan Peters & Büchel, 2011),

particularly during reward receipt or consumption (Diekhof, Kaps, Falkai, & Gruber,

2012; Liu et al., 2011). The OFC processes a wide array of reward types, from primary

rewards (e.g., juice, water, pleasant smells), to abstract secondary rewards (e.g., money,

positive feedback, and social stimuli), to conditioned arbitrary stimuli (e.g., light flashes;

Peters & Büchel, 2011). Subdivisions within the OFC have different hedonic coding

functionalities (Berridge & Kringelbach, 2015): while the mid OFC codes the subjective

experience of pleasure (e.g., sex, food), the medial OFC tracks valence and learning of

reward values but *not* pleasure per se. In addition, the lateral OFC subdivision is often

recruited during punishment. Considering OFC functionality more broadly, several delay-

discounting studies noted that OFC lesions in rats yielded an increased preference for

immediate rewards (Kheramin et al., 2002, 2005; Mobini et al., 2002), although an

increased preference for delayed rewards has also been observed (Winstanley, Theobald, Cardinal, & Robbins, 2004).

Compared to the OFC, the striatum is often evoked during reward anticipation and consumption (Diekhof et al., 2012; Liu et al., 2011). Although fMRI studies suggest that these areas share strong functional overlap, findings from the rodent literature indicate that the VStr may be involved in action selection *before* a decision, whereas the OFC may process *post-decision* information (Stott & Redish, 2014). Moreover, dopamine-projection striatal areas like the NAcc may signal prediction errors, or differences between received and expected rewards, that in turn, contribute to learning and motivation (Sescousse, Caldú, Segura, & Dreher, 2013). The NAcc-error association is further corroborated by evidence that midbrain dopamine neurons signal reward prediction error in rodents (Doya, 2008). With respect to discounting behaviors, lesions to the NAcc core (but not shell) may also produce heightened impulsivity in rats (Cardinal, Pennicott, Sugathapala, Robbins, & Everitt, 2001; Pothuizen, Jongen-Rêlo, Feldon, & Yee, 2005). Thus, the OFC and NAcc are pertinent to the study of impulsivity in human and non-human animals.

Other core decision areas include the ventromedial PFC (or *vmPFC*), anterior cingulate cortex (or *ACC*), anterior insula, and amygdala (Liu et al., 2011). Similar to the OFC, the vmPFC is likely responsible for reward value computations and comparisons (Padoa-Schioppa, 2011; Sescousse et al., 2013). In contrast to the OFC, the ACC and anterior insula may be more responsive during the anticipation phase (Liu et al., 2011); this functionality is consistent with reports that the insula processes risk and uncertainty (Kuhnen & Knutson, 2005; Liu et al., 2011; Sescousse et al., 2013). Converging

evidence suggests that the amygdala signals emotional valence (Bickel et al., 2007), rather than intrinsic value (Sescousse et al., 2013). This area may also encode loss-related expected values in humans, which contrasts the VStr, which may solely reflect gain-related expected value (Yacubian et al., 2006). Complementary findings from rodents implicate the amygdala's role in biasing choice when losses (but not gains) are emphasized (Tremblay et al., 2014). Taken together, the amygdala is a key target for assessing gambling-specific neural substrates.

How Specific Are These Associations?

As noted previously, delay and effort-based discounting paradigms may evoke somewhat separable neural substrates. Such distinctions are critical in delineating the specific mechanisms associated with various costs, as separate valuation systems may have evolved in response to different types of environmental costs (Prévost et al., 2010). Moreover, different valuation systems may be differentially weighted across species. For instance, certain primate species show less inclination towards exerting effort but more tolerance towards delay, whereas other species exhibit opposing patterns (Stevens, Rosati, Ross, & Hauser, 2005). A firm grasp on the neural representation of cost among different species can inform the extent to which specific impulsive choice models measure the same constructs *and* translate across species.

Dissociable substrates were first observed in rodent lesion studies: while ACC lesions impacted effort-based decisions in rats (Walton, Bannerman, Alterescu, & Rushworth, 2003), they did not yield impulsive delay-based decisions (Rudebeck, Walton, Smyth, Bannerman, & Rushworth, 2006). Rather, OFC lesions produced more

impulsivity, but did not alter effort-based decision processes. Researchers also found that introducing lesions to the NAcc core *or* disconnecting the ACC and NAcc core similarly impacted effort-based decisions by reducing the preference for high-effort rewards (Hauber & Sommer, 2009). Thus, transfer between these regions may be pertinent to effort-based decision-making.

Human neuroimaging studies similarly highlight the ACC and NAcc in effort discounting. Botvinick and colleagues (2009) first examined the neural correlates of effort discounting in humans, finding that NAcc activation fluctuated with reward outcome and the amount of mental effort needed to obtain reward. Moreover, NAcc activation was correlated with preceding dACC activation, again suggesting that effort-demand information is shared between these areas. Additional human studies further highlight the ACC in effort-based decision-making (Croxson et al., 2009; Hernandez Lallement et al., 2014; Massar, Libedinsky, Weiyan, Huettel, & Chee, 2015; Prévost et al., 2010). Many studies also link VStr activity with effort valuation (Croxson et al., 2009; Hernandez Lallement et al., 2014; Treadway et al., 2012), although the VStr has also been shown to represent delayed reward value but not effort cost (Prévost et al., 2010). Lastly, the insula may also be implicated (Burke et al., 2013; Hernandez Lallement et al., 2014; Prévost et al., 2010; Treadway et al., 2012), perhaps through functional coupling with the prefrontal cortex (Burke et al., 2013) or ACC (e.g., salience network; Prévost et al., 2010).

Effort-based paradigms have become a recent focus for measuring motivational deficits in schizophrenia (Green, Horan, Barch, & Gold, 2015), as these symptoms are linked with daily functioning impairments and represent a novel treatment target

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(Green, Hellemann, Horan, Lee, & Wynn, 2012; Rassovsky, Horan, Lee, Sergi, & Green, 2011). Emerging evidence suggests that individuals with schizophrenia may opt for lower effort options, although there are discrepancies across task designs (e.g., button-pressing versus grip tasks). Moreover, several studies identified relations between willingness to expend effort and motivational deficits, such as apathy and anhedonia (Barch, Treadway, & Schoen, 2014; Hartmann et al., 2014; Wolf et al., 2014).

No studies to date have directly examined the neural activity associated with effort computation in schizophrenia. However, VStr activation has been linked with negative symptom severity (Juckel et al., 2006; Simon et al., 2010; Waltz et al., 2010). Functional and structural abnormalities of the ACC have also been observed in schizophrenia samples (Fervaha, Foussias, Agid, & Remington, 2013). For instance, a recent meta-analysis found that individuals with schizophrenia had reduced ACC activity during an executive task that required effortful responses (Minzenberg, Laird, Thelen, Carter, & Glahn, 2009). Thus it is plausible that dysfunction within (or between) the VStr and ACC could negatively impact effort valuation and motivational processes in schizophrenia. The empirical assessment of these neural associations, and their cross-species parallels, is pertinent as researchers push forth efforts to translate animal effort-based paradigms for use in schizophrenia clinical trials (for recent work in this domain see Reddy et al., 2015).

Summary of the Impulsive Choice Literature: A Within- and Cross-Species Assessment

This section covered behavioral and neurobiological findings from traditional intertemporal choice studies. More broadly, human and rodent impulsive choice tasks

solicit a forced-choice between two discrete options of different values that are available at different time delays. The two research domains converge in the mathematical functions shown to best characterize discounting behavior (e.g., hyperbolic functions), as well as the procedures used to produce those functions (e.g., adjusting delay procedures to derive indifferences points). Furthermore, a common set of neural structures appears to broadly support human and rodent decision-making. Despite these overlapping features, certain methodological differences may challenge cross-species compatibility.

Rodents often experience the consequences of their actions (e.g., delay) and consume primary rewards during each trial, whereas humans typically do not. It follows that delay-discounting tasks likely require animals to use reward experience to guide subsequent responses (Chudasama and Robbins, 2006). With the exception of real-time discounting measures that also include primary rewards, human tasks rarely entail an analogous experiential design. In other words, few human paradigms include real-time delays *and* primary rewards for immediate consumption. This discrepancy raises at least two issues: (1) different stimuli (e.g., primary versus secondary rewards) may evoke separable brain systems in humans, and (2) hypothetical versus real choices may *not* evoke equivalent valuation systems in humans.

With respect to the first issue, rodent tasks typically include primary rewards, whereas human tasks typically include money (Mitchel and Potenza, 2014). This methodological distinction has implications for elucidating the shared neurobiological correlates. A recent meta-analysis examined the extent to which primary (e.g., erotica, food) and secondary (e.g., money) reinforcing rewards showed overlapping neural representations (Sescousse et al., 2013). The results revealed a "core reward system"

that included the vmPFC, VStr, amygdala, insula, and thalamus, as well as reward-dependent activation patterns. In particular, the VStr and right anterior OFC were more likely to be activated by monetary rewards than food or erotic stimuli. The authors posited that, in comparison to primary rewards, secondary reinforcers might be coded in evolutionary recent brain areas, such as the anterior OFC. In contrast to monetary rewards, food stimuli more strongly recruited the dorsal anterior insula and somatosensory cortex, and erotic stimuli more strongly recruited the ventral anterior insula and the extrastriate body area. When collapsed together, primary rewards recruited the middle insula more so than secondary rewards. These results are consistent with theories that the insula coordinates various interoceptive, homeostatic, emotional, and cognitive signals (Augustine, 1996; Cauda et al., 2011; Liang, Zou, He, & Yang, 2013; Mesulam & Mufson, 1982a, 1982b), whereby the insula's integrative nature may be pertinent to processing sensory and emotionally evocative stimuli. Thus, although primary and secondary rewards exhibit several neurobiological parallels (Haber and Knutson, 2010), the observed differences may be critical to successful human-rodent translational. Furthermore, given the insula's prominent role in impulse-related disorders in humans and rodents (e.g., addiction; Abram et al., 2015; Contreras, Ceric, & Torrealba, 2007; Goodkind et al., 2015; Abram et al., 2015; Contreras et al., 2007; Goodkind et al., 2015), a shift towards primary reward paradigms might influence the extent to which impulsive choice tasks effectively capture psychopathology.

In regards to the second issue, the "hypothetical bias" theory indicates that hypothetical valuations are greater than real valuations (Cummings, Harrison, & Rutström, 2013; Johannesson, Liljas, & Johansson, 1998; List & Gallet, 2001). This

theory led researchers to question whether real and hypothetical recruits recruit separable valuation systems in the brain. Two studies by Kang and colleagues (2011; 2013) explored this question using tasks where subjects decided whether to purchase consumer goods. In the first study, the authors found evidence for a common valuation circuit, as both real and hypothetical decisions recruited the medial OFC and VStr. However, the authors did note that certain valuation and cognitive control areas (e.g., OFC, ACC, caudate) were more active for real choices. This latter finding could indicate that real-choice neural activation reflects more careful or deliberate decision-making. The second study extended this work to assess neural differences when choices were made to avoid *aversive* outcomes. Contrary to the hypothetical bias, subjects were willing to pay more to avoid bad choices under real conditions. Similar to Kang et al. (2011), real decisions more strongly activated the OFC and VStr. Real decisions also evoked unique neural activity in the insula and amygdala (areas implicated in negative emotions). This additional insula finding complements the association between the insula and primary rewards described above. Moreover, these studies suggest that, despite a set of core valuation regions, there are detectable neural differences for real decisions; these divergences may be relevant for psychopathology research, e.g., relations between the insula and impulsivity. However, these studies did not directly address neural differences using impulsive choice tasks, and future work is needed in this regard.

Hypothetical discounting measures may capture state and/or trait-level impulsivity in humans. Both state and trait-level factors are posited to affect decision-making behaviors (Bickel et al., 2007). Work by Dixon et al. (2006) provides evidence for this dual process model in a sample of pathological gamblers. The authors observed

stable discounting functions over multiple sessions (trait component), but also context-dependent shifts when subjects were tested in a gambling context (state component). To some degree, these results indicate that hypothetical measures can capture state *and* trait dimensions by modulating environmental features. However, there are inconsistent results regarding how acute drug administration impacts hypothetical discounting rates (Bickel et al., 2013). It is thus important to clarify the specificity of this dual-process model in terms of psychopathological disorders (e.g., behavioral versus substance addiction) and drugs and abuse (e.g., alcohol versus opiates), as this can inform the direction of cross-species translational endeavors.

   Rodents often undergo repeated sessions and/or extensive pre-training. Testing is often repeated daily with upwards of a month or more of training time (Foscue, Wood, & Schramm-Sapyta, 2012). This approach sharply contrasts human research, where subjects typically complete a single session with same-day training. This discrepancy has prompted researchers to develop and test more efficient methods of acquiring rodent decision-making data (Foscue et al., 2012), including a single-session variant of the rodent Iowa Gambling Task that measures stable individual differences (de Visser et al., 2011; Rivalan, Ahmed, & Dellu-Hagedorn, 2009; Rivalan, Coutureau, Fitoussi, & Dellu-Hagedorn, 2011). With respect to human studies, researchers have demonstrated strong test-retest reliability for discounting rates derived from hypothetical tasks among healthy (Matusiewicz et al., 2013; Simpson & Vuchinich, 2000; Weafer, Baggott, & de Wit, 2013) and disordered populations (Baker, Johnson, & Bickel, 2003). However, comparable reports for an experiential discounting measure (i.e., the Experiential Discounting Task; Reynolds & Schiffbauer, 2004) showed poorer test-retest reliability

(Smits, Stein, Johnson, Odum, & Madden, 2013). This psychometric divergence may support hypothetical tasks as measures of stable trait-like features when compared to experiential tasks. That said, a more nuanced understanding of the underlying mechanisms these tasks measure and their corresponding psychometric properties is necessary. For instance, an ideal experiential task would produce stable parameter estimates under constant conditions (e.g., same testing room, same time of day), and varying estimates when influential variables were introduced (e.g., acute drug administration). A thorough account of these psychometric properties could enhance cross-species translation, and convey the optimal amount of pre-training and sessions needed to produce equivalently stable estimates in humans and rodents.

In addition to these cross-species methodological limitations, intertemporal choice models rely primarily on economic theories and techniques, such as the binary delay-discounting tasks described previously. Alternative decision-making models grounded in evolutionary theories may be an important counterpart to binary decision paradigms. The next section will focus on one alternative decision-making model that may be particularly useful in facilitating cross-species translation.

1.2 Serial-Choice Foraging Models

Serial-choice paradigms, specifically foraging tasks, are a naturalistic complement to traditional binary choice investigations (Wikenheiser et al., 2013). In particular, foraging models can provide a computational account of how individuals allocate scare resources (e.g., time) when searching for valuable goods like food, money or drugs (Stephens, 2008). Foraging tasks fall within an alternative class of decision problems,

where options are considered sequentially rather than simultaneously and choices are interdependent (Constantino & Daw, 2015). Essentially, individuals decide whether to accept a current offer (i.e., *foreground option*) or go in search of a superior alternative (i.e., the *background*).

Many of the problems framed within the traditional binary system (i.e., choice between sooner-smaller versus larger-later) can be adequately described within a serial stay/leave framework (Carter, Pedersen, & McCullough, 2015). Take, for example, the scenario where an alcoholic must decide whether to order a drink or abstain. In the binary choice framework, imbibing alcohol entails an immediate payoff, whereas not imbibing yields larger long-term gains (e.g., abstinence). Within the serial framework, the choice to drink represents a *stay* decision, whereas to not drink would represent a *leave* strategy (e.g., individual searches for preferred alternatives elsewhere). This structure may potentially capture the extent to which certain choices are mutually exclusive more realistically than binary models: An individual cannot drink alcohol and abstain at the same moment as suggested by a binary choice model, whereas a drink in the current moment does not preclude future abstinence as indicated by a stay/leave framework.

In the following section, I begin with an overview of traditional foraging theories. I next review the predominant foraging paradigms that have been used with rats and humans to date. Next, I discuss the literature that links foraging models with psychopathology that includes evolutionary support for addictive behaviors. Lastly, I discuss the neural circuitry that underlies foraging decisions. I conclude this section by commenting on the relative value of foraging paradigms, as well as target areas for advancing cross-species foraging models.

While economics typically emphasizes problems faced by humans (e.g., weighing costs of consumer goods), foraging theories emerged to conceptualize non-human animal problems. It is therefore unsurprising that stay/leave paradigms are often preferable to binary choice tasks for modeling naturalistic animal decisions (Hayden, 2015; Kacelnik, Vasconcelos, Monteiro, & Aw, 2011; D. W. Stephens & Anderson, 2001), where is it unlikely that animals encounter concurrent food sources when foraging in the wild (Wikenheiser et al., 2013). Rather, foraging is better described as the choice to exploit or explore: when an animal encounters a potential food source, the animal must elect whether to exploit the source at hand or search for alternatives (Watson & Platt, 2008).

Two of the major issues identified in the foraging literature include: (1) the *patch-leave problem*, where an animal decides when to stay or leave a prey-rich patch for another one, and (2) the *diet selection problem* (also referred to as the *prey selection problem*), where an animal decides whether to accept or reject a prey item (Hayden & Walton, 2014). In the classical patch-leave problem, an animal seeks to optimize behavior in a patchy environment, where food is dispersed in clumps or "patches." The animal exerts a cost when traveling between patches to obtain food. The animal also depletes the available resources at a given patch the longer it remains in that location. Different patches also provide different food types (e.g., small versus large prey). Charnov's (1976) *Marginal Value Theorem* (MVT) indicates that the animal seeks to maximize energy intake as a function of patch type and energy costs (e.g., travel or search time). More specifically, an animal should leave a patch when the rate of return

from the current patch drops below the average rate of return for that environment. The MVT has been shown to apply across an impressive range of species, including worms, insects, fish, birds, primates, rodents, and humans (Stephens, Brown, & Ydenberg, 2007).

In the classical diet selection problem, an animal forages for randomly distributed food items that are encountered in a serial fashion (Mitchell, 1990). The animal elects whether to allocate handling time to the encountered prey, or spend time searching for a preferred alternative. Here, choices are associated with different energetic investments and different rates of energetic return (Watson & Platt, 2008). MacArthur and Pianka (1966) proposed an early prey model function:

$$R = \frac{E}{T_h + T_s},$$
(3)

where R is the net benefit gained by consuming a particular prey, E is the energy gained, T_h is the handling time, and T_s is the search time. Maximizing R derives the diet offering that yields the largest energetic return, and in turn, maximizes evolutionary success. Contrary to the patch-leave problem, optimal diet theory assumes that resource depletion does not occur; thus, the emphasis is on the frequency and type of prey the animal selects. While this model has been used to describe behavior across a variety of species, it may not perfectly characterize real-world decisions (Watson & Platt, 2008); the model predicts that rate-maximizing behavior is to always prefer one prey to the alternatives, although many studies found that subjects showed partial preferences for other prey. The next section will explore the experimental paradigms that researchers have used to investigate the patch-leave and diet-selection problems.

Laboratory Models of Foraging

Patch-Exploitation Paradigms: Evidence of Excessive Exploitation

Charnov's MVT was initially tested in a series of patch-use experiments where birds foraged between groups of pinecones (Krebs, Ryan, & Charnov, 1974). More recently, researchers outside of the ecology field have begun to employ computerized patch-foraging tasks (Blanchard & Hayden, 2014; Calhoun & Hayden, 2015; Constantino & Daw, 2015; Hayden, Pearson, & Platt, 2011). Hayden and colleagues (2011) first used a patch-foraging task with rhesus monkeys, where two monkeys made stay/leave choices by shifting eye gaze towards one of two targets. One target reflected a *stay* choice, where the monkey remained in the current patch and received a juice reward, and the juice reward declined in magnitude each time it was selected. The other target reflected a *leave* choice. If this option was selected, the monkey encountered a delay (to simulate travel time between patches) and the patch was replenished. Consistent with the MVT: (1) monkeys remained in the current patch longer as travel times between patches increased, and (2) patch residence time decreased as handling time increased (i.e., delay before reward delivery). The authors also noted that the MVT model better fit the sequential choice data than a traditional discounting model (i.e., hyperbolic function), even when stay/leave choices were conceptualized as smaller-sooner/larger-later decisions. This suggests that the stay/leave foraging structure may capture a dissociable aspect of intertemporal choice.

Patch-exploitation paradigms have been far less utilized in human research (Bixter & Luhmann, 2013). Hutchinson and colleagues (2008) employed one of the first computerized patch-exploitation studies in humans, where subjects caught

(computerized) fish in ponds and ponds were depleted as subjects caught more fish. The ponds were not replenished, but subjects could switch ponds at any time. Subjects earned monetary rewards for each caught fish (although payment was not delivered until the end). Contrary to predictions, humans delayed patch switching for longer than optimal. Similar "over-staying" tendencies have been observed in other patch-exploitation paradigms with humans (Carter et al., 2015; Constantino & Daw, 2015). Likewise, these findings are akin to foraging animals that over-stay in patches (Nonacs, 1991), or wait through longer-than-necessary delays (Wikenheiser et al., 2013; Carter & Redish, 2016).

The multi-armed bandit task is an alternative patch-exploitation paradigm, where a forager explores a new environment to uncover hidden values at various locations and then exploits the option that yields the greatest value (Addicott, Pearson, Kaiser, Platt, & McClernon, 2015). In an uncertain environment the reward values and locations can fluctuate, thus, the forager's challenge is to maximize long-term gains by adjusting his exploit/explore strategy accordingly. An example of the multi-armed bandit problem is a computerized task that presents four slot machines, where the number of points obtained from each machine shifts gradually across the trials (Addicott et al., 2015; Addicott, Pearson, Wilson, Platt, & McClernon, 2013; Daw, O'Doherty, Dayan, Seymour, & Dolan, 2006). Thus, the subject will obtain the maximum payoff by exploiting the current machine with the greatest yield, and then exploring when that yield declines.

Alternative Foraging Paradigms: Forced Exploration

In contrast to the patch-exploitation paradigms described previously, alternative foraging paradigms may require a subject to explore his environment without the option

to continuously exploit any single reward site. Forced exploration paradigms allow for the assessment of individual preferences and emotional constructs (e.g., regret), which are important features of dynamic decision-making. The "Restaurant Row" task is a spatial foraging paradigm that forces subjects to explore each reward site in sequence (Steiner & Redish, 2014). In this task, rats foraged for food around a circular track that had four feeders (or "restaurants"). Each feeder provided a different flavor of pellet after a variable delay. Upon arrival at a feeder, a tone indicated the delay length before the rat would receive the food pellets. The rat then made a stay/leave choice, i.e., whether to stay and wait through the delay and receive the reward, or travel to the next feeder. Importantly, the rat could not stay at any feeder and receive a second offer. Rather, the rat had to continue to the next feeder to receive a subsequent offer (i.e., forced exploration). The rat could only return to the same reward site after completing a full cycle around the maze. Individual preferences were *revealed* by the rat's willingness to wait out a certain delay length for a particular pellet flavor; these preferences differed across rats but were consistent within-subject and across-session (Abram et al., 2016). Using this paradigm, the authors highlighted the value of serial choice designs, as pairs of consecutive trials tracked distinct emotional events (Steiner & Redish, 2014). In particular, the results revealed specific behavioral and neural signatures for regretful situations (as compared to disappointing situations), where the rat deviated from its behavioral strategy in error.

I designed the "Web-Surf Task" as a human analogue to the Restaurant Row paradigm, drawing from human ethology and information foraging (Abram et al., 2016). Information foraging theory suggests that humans make stay/leave foraging choices when surfing the Internet, e.g., deciding when to begin a new search or follow links within

the current page (Pirolli, 2005). In the Web-Surf Task, humans had 30 minutes to "forage" for rewards in the form of photos or video clips. Comparable to Restaurant Row, there were four galleries (each of which included a different category of stimuli, e.g., kitten clips). The subject was informed of the random delay time upon arrival at the gallery and could then choose to stay and wait through the delay, or continue on to the next offer. Similar to rats, humans showed evidence of revealed preferences that were consistent within subject (i.e., revealed preferences correlated with other preference metrics) but differed across subjects. This study was seminal in that we directly compared cross-species behaviors using analogous tasks *and* operational definitions. In the same vein as traditional discounting tasks, foraging tasks can include different types of costs.

Cost Types: Delay versus Physical Expenditures

The *types* of costs an individual encounters may influence the measurement of foraging behaviors. In the virtual reality patch-exploitation paradigm described by Hayden et al. (2011), monkeys did not physically travel between patches or exert an action to advance; even though the delay created an *opportunity* cost by delaying reward, there was no *physical* cost. Work by Wikenheiser and colleagues (2013) incorporated physical cost via a spatial foraging paradigm that was akin to the diet selection problem. Rats foraged for food around a circular track that included three feeders, where each feeder was associated with a particular delay length. Within the foraging framework, delay reflected handling time. Rats made stay/leave decisions at each feeder: for stay decisions, the rat waited through a delay to receive food pellets as reward; for leave decisions, the rat physically traveled to the next feeder to encounter an alternative offer.

Consistent with prior criticisms of the prey selection model (Watson & Platt, 2008), the rats did not display rate-maximizing behaviors where one prey type was always preferred (nor was rat behavior consistent with a matching strategy or discounting function). That is, rats did not always accept the short delays and reject the medium and large delays as expected by the prey selection model. In response, the authors proposed a modified model that included a parameter for the cost of rejecting potential offers. This parameter enhanced model fit, perhaps suggesting that rejection-aversion is key for capturing complex foraging choices. However, these results depart from earlier studies in which animal foraging behavior did approximate the optimal solution (Stephens, 2008). This divergence may be due to task design differences, as physical and non-physical expenditures may not be equivalent. For example, willingness to wait may not be comparable to physical travel or greater exertion; this was not directly tested but is a critical point for future efforts that seek to reliably model cross-species foraging behaviors.

In comparison to traditional intertemporal choice tasks, there is a dearth of research utilizing foraging paradigms to study psychopathology. However, from an evolutionary perspective, foraging models may be particularly valuable to addiction research. I highlight relevant findings from this literature in the following section.

Foraging and Addiction

The balance between exploitation and exploration is vital to healthy outcomes like food foraging and job hunting (Addicott et al., 2013); however, an inclination *towards* exploitation may foster negative outcomes. Excessive exploitation may lead an

individual to develop and maintain extreme (maladaptive) habits, such as those observed in substance addiction (Graybiel, 2008). For instance, one study found that cigarette smokers exhibited less exploratory behavior than non-smokers on a multi-armed bandit task and exploratory behavior was negatively correlated with impulsivity (Addicott et al., 2013). Dopamine models of addiction support these findings, as chronic abuse may actually decrease dopamine function and reward sensitivity (Volkow, Fowler, Wang, Baler, & Telang, 2009), which in turn, may yield greater exploitation and energy conservation (Beeler, Frazier, & Zhuang, 2012). In comparison, work by the same group did not observe heightened exploitation in pathological gamblers (Addicott et al., 2015). It is therefore possible that foraging behaviors differentially manifest across substance and behavioral addictions, or chronic substance exposure differentially influences the underlying reward pathways that support foraging.

Substance addiction may also be analogous to natural motivation states, such as food deprivation (Nestler & Landsman, 2001). Stemming from this notion, risk-sensitive foraging (RSF) theory suggests that under deprivation conditions, animals will select riskier food sources. For instance, if a deprived animal is faced with two food sources, one that provides a constant amount of food (e.g., 3 pellets) and one that provides a variable amount of food that produces the same average amount over time (e.g., 2-7 pellets, 3 pellets on average), the animal will select the variable option. This model suggests that risky choices are made to increase the chances of immediate survival (Kacelnik & Bateson, 1996); however, this pattern deviates from the optimal behavior one would expect given economic theory. Work by Bickel and colleagues (2004) were the first to demonstrate the RSF model in humans, using a sample of opioid-addicted

individuals. As anticipated, subjects purchased more hypothetical heroin from a variable source when exposed to a deprivation script (i.e., one that described withdrawal symptoms) versus a satiated script (i.e., one that described opioid agonist symptoms). These findings ground opiate seeking in evolutionarily based survival behaviors, yet it remains unknown whether this model extends to other substances or forms of addiction.

To what extent are foraging behaviors supported by comparable neural substrates as compared to traditional decision tasks? And if these neural systems are largely the same, what else can we learn from foraging studies? The next section discusses relevant neural structures, with attention to the unique functionalities captured via sequential foraging paradigms.

The Neural Correlates of Foraging

Foraging paradigms evoke many of the same brain regions as traditional value-based binary tasks (e.g., vmPFC, dorsal ACC [dACC]). Recent work has sought to parse neural activation that distinguishes foraging decisions from other choice behaviors in humans and non-human animals. The dACC is a key focus, which is unsurprising given its pertinence in reward-based decision-making (Bush et al., 2002), behavioral adaptation (Boorman, Rushworth, & Behrens, 2013), effort-based valuation processes (Croxson et al., 2009), and response conflict (Botvinick, 2007). Researchers first investigated the neural basis of patch-leaving decisions in non-human primates (Hayden et al., 2011). This seminal study found that dACC neurons mediated patch-leaving decisions: dACC neurons fired for each choice, and neurons increased in responsiveness the longer the macaque remained in the current patch; once the neurons reached a particular threshold,

the macaque abandoned the patch. Thus, dACC neuronal firing represented a decision variable that indicated the relative value of leaving a patch.

Kolling and colleagues (2012) extended this work to human foraging, finding dissociable value-coding roles for the dACC and vmPFC. While the dACC encoded the average search value of the environment with respect to known alternatives and search costs, the vmPFC encoded value between two well-defined options. dACC activity was positively associated with the value to forage (i.e., searching for a better offer) and negatively associated with the value of engaging the current offer (i.e., the *default* option). Previous reports document the ACC's role in representing choice value (Rushworth & Behrens, 2008); however, Kolling et al.'s (2012) conclusion that the dACC specifically encodes *foraging* value was novel. Furthermore, although several high-profile studies bolstered the dACC-foraging association (Boorman et al., 2013; Kolling, Wittmann, & Rushworth, 2014; Mobbs et al., 2013), this interpretation has not gone without criticism.

Work by Shenhav et al. (2014) challenged the dACC-foraging specificity claim, instead positing that this region responds to *decision difficulty*. The authors' discontent stemmed from notions that the choice to forage is inherently more challenging than resorting to a default option. In two neuroimaging experiments, the authors showed that choice difficulty confounded relations between the dACC and foraging value. Alternatively, the authors suggest, this area may engage more broadly in cognitive control processes that override automated behaviors. Regardless, it is unlikely that the dACC is the sole driver of foraging decisions, as models like the MVT apply to such a extensive array of organisms, including those without brains (Hayden et al., 2011).

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Human neuroimaging studies have also implicated the frontal polar cortex (FPC) in foraging (Rushworth, Kolling, & Mars, 2012). The FPC may represent the value of the best alternative, as opposed to the net average of the alternatives, like the dACC (Boorman, Behrens, Woolrich, & Rushworth, 2009; Boorman, Behrens, & Rushworth, 2011). Specifically, the FPC may be implicated in tracking the advantage of switching to a foregone option (Boorman et al., 2009), or coding the expected value of an untaken or *counterfactual choice* (Boorman et al., 2011).

Although many of the same neural structures track across traditional decision and foraging tasks, sequential foraging paradigms (like Restaurant Row) have the unique advantage of tracking interconnected outcomes. This is because subjects are aware of an overall task structure throughout the session (e.g., "to skip this banana offer means the next offer is cherry."). During Restaurant Row, OFC and VStr recording typically represented the upcoming offer during the choice phase, suggestive of episodic future thinking in rats (i.e., imagining the potential outcome). In comparison, OFC and VStr signals in rats represented the foregone opportunity following regret-instances, in which the animal had deviated from its strategy (Steiner & Redish, 2014). Thus, this task uniquely captured both past and future-oriented thinking in the same neural structures (a topic examined further in Chapter 3).

Implications for Psychopathology Research

As alluded to previously, connections between foraging-specific biological systems and psychopathology are largely under-examined. However, evolutionary theories that link dopaminergic systems with foraging are a promising avenue for

explorations into goal-directed disorders, like Parkinson's disease, schizophrenia, and addiction (Hills, 2006). For example, Parkinson's disease is characterized by dopamine loss that may contribute to impaired feedback-based learning (Shohamy et al., 2004). Researchers tested the effects of dopaminergic drugs on individuals with Parkinson's during a dynamic foraging task, noting that increased dopamine decreased perseverative choices and enhanced learning from positive outcomes (Rutledge et al., 2009). These outcomes may have implications for other goal-related disorders with perseverative behaviors, such as schizophrenia. Although dopamine-foraging-psychosis relations have not been directly tested, prior schizophrenia research connects learning and reward-related impairments with dopamine circuits (Waltz et al., 2013). Moreover, meta-analytic evidence suggests that polymorphisms in genes responsible for dopamine degradation influence prefrontal cognition in schizophrenia (Mier, Kirsch, & Meyer-Lindenberg, 2010). It is then plausible that dopaminergic abnormalities in schizophrenia may contribute to deficits in exploration/exploitation tradeoffs. However, elucidating the precise nature of dopamine-cognitive associations is a challenge, as dopamine manipulations may differentially impact cognitive functions (i.e., cognitive stability versus flexibility), and relations between dopamine and cognition is likely non-linear (Cools & D'Esposito, 2011).

The salience network may also play a role in foraging-psychopathology associations. This network, primarily comprised of the dACC and anterior insula (Seeley et al., 2007), is implicated in a broad range of psychopathologies that includes bipolar disorder, schizophrenia, depression, and addiction (Goodkind et al., 2015). With respect to foraging, one theory suggests that dACC and anterior insula co-activation may signal

errors that encourage behavioral adaptation (Mobbs et al., 2013). Dopamine may underlie this functional chain, as dopamine is fundamental to prediction error signals, as well as various traits and behaviors mediated by the salience network (Palaniyappan & Liddle, 2012). By extension, one might hypothesize that dopaminergic abnormalities, as typical of psychopathologies like schizophrenia, may interact with salience network functionality to impede learning and adaptation, which in turn, could produce suboptimal foraging.

Summary of the Foraging Literature: Implications for Cross-Species Research

Foraging models provide a novel and complementary approach for examining decision-making parallels across humans and non-human animals. Because animals evolved to forage, such tasks may help researchers to reorient focus towards evolutionarily based behavioral and neural systems (Calhoun & Hayden, 2015). However, relatively few studies have assessed foraging in humans, and even fewer have directly compared foraging across species. Nonetheless, this burgeoning literature has already demonstrated several key advancements in our understanding of decision-making and the underlying neural substrates.

The Relative Utility of Foraging Paradigms

Foraging paradigms can capture the interdependent nature of complex intertemporal decisions. As noted previously, real-world intertemporal choices likely occur in dynamic environments where repeated, interdependent decisions are needed to achieve an outcome (Bixter & Luhmann, 2013). Foraging paradigms can account for these integrated dynamics, by employing tasks where choices influence the availability

of future rewards or choices are constrained within a fixed time window. For instance, researchers have used foraging environments to assess trial-by-trial effects, such as the extent to which a subject learns to adjust their behavior across the session (Constantino & Daw, 2015). In a real-world scenario, an animal might need to find food before sunset (or sunrise if it is a nocturnal creature) or before starvation occurs (Doya, 2008; Stephens, 1987). The rate at which the animal learns is then critical to survival. This time-constraint feature is pertinent to psychopathology research, as certain learning deficits may impede optimal foraging strategies; hence, isolating learning processes from other decision parameters could help to distinguish between goal-directed disorders (e.g., *impulsive* decision-making in addiction versus *impaired adaptation* in schizophrenia).

Tasks that entail a fixed time-constraint require that subjects adopt a strategy to maximize earnings (Bixter & Luhmann, 2013; Schweighofer et al., 2006). The need to strategize across trials is more akin to real-world decisions for which cumulative actions are necessary to achieve goals. Time-constrained foraging tasks may be particularly beneficial for cross-species gambling research. Currently, human gambling tasks are limited by design regulations and many animal tasks may fail to capture loss (Clark et al., 2013; Madden et al., 2007). And as noted previously, probability-discounting tasks arguably measure the failure to gain a reward rather than a loss of wagered resources (Zeeb et al., 2009). By introducing a fixed time window, poor decisions can be interpreted as a missed opportunity and loss of resources (i.e., time). This has been demonstrated in rats during the Restaurant Row task (Steiner & Redish, 2014).

Foraging paradigms often take more timing components into account, whereas discounting tasks are primarily concerned with delay until reward receipt. Foraging

models aim to account for every moment spent foraging, including travel time, search time, and risk, whereas discounting tasks ignore many of these components (Mazur, Snyderman, & Coe, 1985). This distinction is not surprising given the frequent use of a fixed time constraint in foraging paradigms, where one seeks to maximize gains within a specific time window (as opposed to one encountering a fixed number of trials or reaching equilibrium to reach task completion). The time constraint again highlights an ecological advantage, assuming that real-world decisions are less likely to entail a fixed number of decisions but may entail a fixed time limit (e.g., animal must find food before sundown). Regardless, parameters derived from typical discounting tasks arguably exclude important contextual factors. For instance, discounting rates are computed solely as a function of reward magnitude and cost, with other relevant decision components unaccounted for. The omission of key parameters could be problematic for mapping specific mechanisms with corresponding biological substrates (e.g., parsing neural activation associated with foraging versus well-defined binary choices).

Improving Foraging Paradigms for Cross-Species Translation

Many human foraging paradigms lack primary rewards and real-time costs. Although there are exceptions (e.g., Abram et al., 2016; Bixter & Luhmann, 2013), most human tasks lack real consummatory experiences and instead use points or other secondary reinforcers. This discrepancy could impede how individual trials impact subsequent decisions, as immediate trial feedback may be less salient. Similarly, the level of reward abstraction may influence one's ability to imagine potential outcomes when making a choice; that is, abstract rewards may be more difficult to mentally simulate.

Thus, the use of equivalent rewards across human and rodent studies could better parallel investigations of deliberation. Furthermore, differences in reward types may impact neural investigations, as primary and secondary rewards may depend on somewhat dissociable systems (see Summary of the Impulsive Choice Literature: A Within- and Cross-Species Assessment).

The inclusion of risk parameters could further enhance the ecological validity of foraging paradigms. In natural foraging environments, rewards are associated with randomness and uncertainty (Bixter & Luhmann, 2013). The addition of risk parameters to foraging tasks has been shown to impact foraging behaviors in non-human animals. For instance, more variance in the travel time between patches led to decreased exploitation in pigeons (Kacelnik & Bateson, 1996). Among humans, adding uncertainty to the larger-delayed reward in an intertemporal choice task increased preferences for immediate rewards (Keren & Roelofsma, 1995). A more recent study by Kolling and colleagues (2014) showed that human subjects modulated choice behavior as a function of reward uncertainty, available resources, and other opportunities. In particular, increases in risk pressure and risk bonus frequently yielded riskier choices. This work is particularly relevant for pathological gambling, which may be related to baseline fluctuations in risk proneness/aversion. Nonetheless, future work is needed to address how risk parameters influence human decision-making on intertemporal foraging tasks.

1.3 Conclusions

Translational science has the unique opportunity to utilize basic research findings for the development of human treatments. However, the use of analogous tasks is

insufficient for claiming research as *translational* (van den Bos et al., 2013). Rather, the effectiveness of translation depends on continuous cross-talk between human and non-human animal researchers (Abram et al., 2016), and collaborative research programs that ask comparable questions using similar tasks and environments (van den Bos et al., 2013). Assuming this framework, I advocate several areas to further improve translational science:

(1) ***Tight operational definitions*** are critical (de Wit, 2009b), particularly given the heterogeneity that exists within the impulsivity construct, and the immense number of interacting components that underlie decision-making (Ernst & Paulus, 2005). (2) ***Mirroring task complexity*** across species may reduce translational gaps, as many animal studies involve simple procedures that may not capture decision-making intricacies (Rivalan et al., 2009). (3) ***Strong psychometric properties*** of human tasks is pertinent for translating paradigms from healthy to clinical populations (Green et al., 2015). For instance, poor test-retest reliability, scale attenuation, practice effects, or challenging directions can limit or even prohibit the adaptation of a task for clinical trials. (4) ***Emphasizing specific behavioral processes and symptoms*** in task development and analysis could advance treatment initiatives, as dimensional models of psychopathology avoid certain issues that arise from comorbidity.

Limitations

The human foraging literature is still in its nascent stages. Thus, many of the described links between foraging and psychopathology are derived from hypotheses and not empirical evidence (with some exceptions, see Bickel et al., 2004). It follows that

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future research should not only aim to parallel foraging models across species, but also address the extent to which these models capture the continuum from maladaptive traits to severe psychopathology. In turn, such efforts could close gaps between rodent models and human treatment development. As mentioned previously, many of the available foraging paradigms lack a risk or uncertainty parameter that could influence a given task's ecological validity; this is an important area for future task development. Many of the neuroimaging foraging studies are also limited by small sample sizes (e.g., $N < 20$). Future investigations interested in maladaptive trait-foraging associations may require much larger samples, as large samples are needed to capture individual differences with small-to-moderate effect sizes (Abram & DeYoung, 2017).

Closing Thoughts

Experiential foraging paradigms, in particular, provide a promising avenue for translational pursuits. Tasks that incorporate real-time costs and consummatory rewards could foster cross-species parallels and also provide a novel method for investigating decision-making deficits for individuals that struggle with more abstract thinking (e.g., schizophrenia). Moreover, the foraging approach may enhance ecological validity by re-focusing our efforts to understand aberrant decision-making through an evolutionary lens. Lastly, there are a wealth of opportunities and research explorations for effectively adapting pre-clinical foraging paradigms for use with healthy individuals to those with severe psychopathology.

CHAPTER 2: THE WEB-SURF TASK: A TRANSLATIONAL MODEL OF HUMAN DECISION-MAKING

Foreword: This chapter was written in collaboration with Yannick-André Breton, Brandy Schmidt, A. David Redish, and Angus W. MacDonald, who edited versions of the manuscript. The text of this chapter is also published in *Cognitive, Behavioral, and Affective Neuroscience*.

Abstract

    Animal models of decision-making are some of the most highly regarded psychological process models; however, there remains a disconnection between how these models are used for pre-clinical applications and the resulting treatment outcomes. This may be due to untested assumptions that different species recruit the same neural or psychological mechanisms. We propose a novel human foraging paradigm (Web-Surf Task) that we translated from a rat foraging paradigm (Restaurant Row) to evaluate cross-species decision-making similarities. We examined behavioral parallels in human and nonhuman animals using the respective tasks. We also compared two variants of the human task, one using videos and the other using photos as rewards, by correlating revealed and stated preferences. We demonstrate similarities in choice behaviors and decision reaction times in human and rat subjects. Findings also indicate that videos yielded more reliable and valid results. The joint use of the Web-Surf Task and Restaurant Row is therefore a promising approach for functional translational research, aiming to bridge pre-clinical and clinical lines of research using analogous tasks.

2.1. Introduction

Animal models of impulsivity are regarded as being among the most well developed representations of human psychopathology (Kalivas et al., 2006; Madden & Bickel, 2010), and have been key contributors to our understanding of human psychopathologies, such as addiction (Madden & Bickel, 2010; O'Brien & Gardner, 2005). Nonetheless, there remains a gap between model validity and the efficacy of human treatments based on these animal models (Hall et al., 2014; Kalivas et al., 2006). Prior research suggests this gap may stem from untested assumptions that humans and nonhuman animals recruit the same cognitive systems (Demeter, Sarter, & Lustig, 2008). Coordinating human and non-human animal research to model the same behaviors is therefore critical to elucidating the behavioral and neurobiological mechanisms that underlie many psychopathologies (Belzung & Lemoine, 2011; Potenza, 2009). However, this functional approach to translation requires parallel tasks that access similar functional constructs. Here, we present a novel experiential human foraging task translated from a rat food foraging paradigm (Steiner & Redish, 2014). Instead of food, humans foraged for information through an internet-like interface, as a naturalistic analogue to the food rewards used with nonhuman animals (Pirolli, 2005). Our results suggest these tasks captured behavioral parallels in human and rat decision-making.

The Foraging Model of Decision-Making

New theories posit that many psychopathologies are fundamentally problems with decision-making. This notion implies that understanding the causes (and improving treatments) depends on understanding how those decision-making systems work and

break down (Montague, Dolan, Friston, & Dayan, 2012; Rangel, Camerer, & Montague, 2008; Redish, 2013; Redish et al., 2008). Foraging models of decision-making provide a computational account of how humans and nonhuman animals allocate scarce resources (e.g. time) when searching for valuable resources like food, money, or drugs (Stephens, 2008). Sociological observations of drug-users suggest that users are seen as "foraging" for drugs in a "patchy" world of opportunities; for example, smokers looking for the cheapest cigarettes (Feighery, Schleicher, Boley Cruz, & Unger, 2008; Grossman & Chaloupka, 1998), gamblers looking for video poker machines (Schüll, 2012), or heroin addicts looking for narcotics (Hoffer, Bobashev, & Morris, 2009). Thus, foraging paradigms may be a promising approach for examining the complex decision-making systems that underlie addiction or other psychopathological disorders.

Foraging models advance historical intertemporal choice models of decision-making, during which subjects make binary choices between rewards of different value that are available at disparate time delays (often referred to as 'delay-discounting' paradigms). Delay-discounting tasks have been widely used to assess impulsive decision-making among addicted human and nonhuman animals. However, multi-option foraging paradigms may be more akin to real-world scenarios where humans are cognizant of other options or alternatives in the background when making a decision. Moreover, researchers have posited that stay/skip serial foraging choices may better characterize naturalistic decision-making (Stephens, 2008; Wikenheiser et al., 2013). As a result, researchers are using foraging models at an increasing rate in both human and nonhuman animal studies (Benjamin Y Hayden, Pearson, & Platt, 2011; Kolling et al., 2012; Shenhav et al., 2014; Steiner & Redish, 2014; Wikenheiser et al., 2013). A logical next

step is to *develop a foraging model that translates across species; researchers could then use this foraging model to examine cross-species parallels in the maladaptive decision-making behaviors that support psychopathologies like addiction*. This type of translation requires a bridging of research branches, which have typically produced methodologically divergent decision-making paradigms.

Current Challenges in Functional Translation

Decision-making tasks for nonhuman animals are *experiential*, in that they typically entail a rat physically running through a maze or pressing a lever, waiting through real-time delays, and receiving primary reinforcers as reward, like food (Mazur, 1987; Papale et al., 2012). In contrast, efforts to produce comparable human experiential paradigms generally result in one of three approaches for reward stimuli: (1) secondary reinforcers like tallied points that may eventually convert to money (Kolling et al., 2012; Reynolds & Schiffbauer, 2004; Shenhav et al., 2014), (2) secondary reinforcers like coins that are dispensed during the task (Krishnan-sarin et al., 2007; Reynolds, 2006b; Voon et al., 2010), or (3) primary rewards like juice or candy (Kool & Botvinick, 2014; McClure, Ericson, Laibson, Loewenstein, & Cohen, 2007). These methodological differences may impact the underlying reward systems evoked in humans. For example, in scenarios where points/money are summated over the session or the subject randomly receives one or several of their choices at the end (the latter called *real-reward* measures; Reynolds, 2006a), each poor decision may be salient. This is because each choice influences the ultimate gain and/or the subject does not know which final outcome the subject will receive (thus, making each decision important). On the contrary, in *real-time* measures,

the subject consumes rewards at the end of each trial (Reynolds, 2006a). As a result, poor choices may be less salient as individual choices do not influence a post-session outcome. Given these distinctions, it is also possible that *the same reward systems observed in rats are not evoked during human tasks that lack comparable real-time consummatory rewards*.

Researchers have identified and addressed similar methodological gaps with respect to visuospatial paradigms. For example, human studies historically assessed spatial ability via paper and pencil tests, whereas non-human studies assessed spatial navigation via maze-learning tasks (Moffat, Hampson, & Hatzipantelis, 1998). In response, many human studies adopted virtual reality radial mazes and Morris water tasks and successfully identified cross-species behavioral and neural parallels (Bohbot, Lerch, Thorndycraft, Iaria, & Zijdenbos, 2007; Hamilton, Driscoll, & Sutherland, 2002; Hamilton, Kodituwakku, Sutherland, & Savage, 2003; Iaria, Petrides, Dagher, Pike, & Bohbot, 2003). Despite the success of these virtual reality paradigms, these particular tasks did not address the issue of primary versus secondary reinforcement that may be pertinent to decision making (as subjects solely received monetary compensation at the study conclusion). Thus, *experiential human foraging models with primary reinforcement are needed to fill this gap in external validity and provide a link to the animal decision-making literature*.

Primary Reinforcement for Humans

Considering how humans interface with the world on a daily basis while seeking rewards or entertainment may improve insight into the processes underlying decision-

making, which in turn, may guide task development. *Information Foraging Theory* suggests that humans seek and acquire information using the Internet (Pirolli & Card, 1999). More specifically, individuals perform ongoing cost-benefit analyses as they navigate through websites, making stay/skip foraging choices to remain on the current site or move on to the next (Pirolli, 2005). Humans also forage the Internet for rewarding stimuli, frequently presented in the form of video segments or images – each of which we can feasibly incorporate into an experimental paradigm. Such internet-found stimuli may even yield natural reinforcement that is comparable to drugs or food. Recent findings that Internet-addicted individuals exhibited functional and structural brain similarities to drug-addicted individuals bolster this claim (Ding et al., 2013; Kuss & Griffiths, 2012; Weinstein & Lejoyeux, 2013). The combined feasibility and primary reinforcement possible from using videos or photos as reward makes their use a compelling option for human task development.

Study Aims

The current study advances available experiential tasks for humans by developing a foraging paradigm that (1) translates across species, (2) includes primary reinforcement and real-time delays, and (3) integrates natural human ethology into the design. We translated the proposed task directly from a novel stay/skip foraging paradigm, called "Restaurant Row" (Steiner & Redish, 2014), during which a rat had a fixed amount of time to traverse a circular track and collect food rewards from four feeders. Each feeder (or "restaurant") provided a different flavor of food pellet after a random time delay (see Figure 2.1A). We drew from Information Foraging Theory and the burgeoning Internet-

addiction literature to develop the human variant of Restaurant Row, which we call the "Web-Surf Task" (see Figure 2.1B). During this task, humans made a series of stay/skip decisions while traveling between galleries that contain primary rewards (videos or photos), which were presented after real-time delays. In this paper, we illustrate the external and face validity of the Web-Surf Task, as well as cross-species behavioral parallels using the Web-Surf Task and Restaurant Row.

2.2 Methods

Web-Surf Task in Humans

<u>Sample Demographics</u>

The total sample included 64 University of Minnesota undergraduates (72% female, mean age = 20.5), who received extra credit toward a psychology course. The initial round of data collection included both the video (N = 22) and photo versions (N = 15); the second round of data collection included only the video version (N = 27). This resulted in a total of 49 subjects who completed the video version. The University of Minnesota's Institutional Review Board approved the study, and all subjects provided written informed consent.

<u>Web-Surf Task Design</u>

Subjects had 30 minutes to "surf" (or forage) through four galleries (see Figure 2.2 for decision flow-diagram) presented using PsychoPy (Peirce, 2009). In the video variant, each gallery presented a video clip from one of four categories (kittens, dance, bike-accident, landscapes) as a reward. In the photo variant, each gallery presented an

image from one of four categories (kittens, desserts, female faces, or landscapes); we note that we transformed the still images using the Ken Burns panning and zooming effect to parallel the video variant. We selected these particular categories in consideration of future functional neuroimaging data collection and neural decoding analyses. More specifically, we expect these categories will map onto separable neural substrates, as prior evidence indicates unique correlates for faces, bodies, animals, natural scenes, tools/objects, and animals (Doll, Duncan, Simon, Shohamy, & Daw, 2015; Haxby et al., 1999, 2001; Peelen & Downing, 2007; Walther, Caddigan, Fei-Fei, & Beck, 2009). For additional details on the anticipated decoding analyses see Steiner and Redish (2014).

We laid out the task as follows: Upon arrival at a gallery, the subject was informed of the random delay time before video presentation. Delay time was displayed using text and a progress bar similar to those located on an Internet webpage. The subject was given the option to stay and wait for the current reward or skip and continue on to the next gallery. If the subject decided to stay, the subject viewed the stimulus for four seconds and then rated it using a 5-star rating system (1 star = extremely dislike, 5 stars = extremely like). If the subject decided to skip, the subject pushed the "SKIP" button located at the bottom of the screen. After leaving the gallery, the subject "surfed" to the next gallery that presented a new offer (i.e. new video or photo after a new random delay). The subject then completed a series of "NEXT" screens when traveling between galleries, regardless of the decision to stay or skip; this entailed finding and clicking 3 or 5 "NEXT" buttons that were randomly positioned on the screen. We intended the "NEXT" to serve as an analogue to the rats physically running a track to travel between feeders. We designed the buttons to blend into the background to increase the cost for

locating them around the screen. 22 subjects completed the task with 5 "NEXT" screens between galleries; 27 subjects completed the task with 3 "NEXT" screens between galleries.

As preliminary training, subjects completed two forced practice trials, during which we instructed them to push the "SKIP" button for trial one and to stay and wait for trial two. We created this structure to illustrate the two choice options as well as the transition between the galleries. Subjects then completed eight practice trials where they could decide whether to stay or skip.

Restaurant Row in Rats

Sample Characteristics

We used eight adult Brown-Norway rats in this experiment. Our methods were consistent with Steiner and Redish (2014), as we aimed to replicate behavioral findings in a new sample. Our study protocol complied with the National Institute of Health guidelines for animal care, and the Institutional Animal Care and Use Committee at the University of Minnesota approved the protocol.

Restaurant Row Design

Restaurant Row consisted of a circular track with four spokes leading off to food-reward sites (restaurants) as illustrated in Figure 2.1A. Each food-reward site provided a different flavor of food (cherry, chocolate, banana, and unflavored/plain sugar). The rat proceeded around the circle encountering each offer serially. When the rat entered the offer zone, a tone sounded, with pitch indicating the delay (1-30s). The tone counted

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down once per second (change = 250 Hz) until it reached the base tone (1 kHz), at which time the two pellets of the flavor for that restaurant were delivered. If the rat left the offer zone before the delay finished counting down, the tone stopped, the offer was rescinded, and the rat had to proceed to the next restaurant to get food. Because zones were only triggered in a clockwise serial manner, rodents quickly learned to run in one direction. Essentially, the animal made a series of stay/skip decisions, such as – *Is it worth waiting 25 seconds for two banana-flavored food pellets?* In this task, we gave rodents 60 minutes to collect food for the day. The 60-minute time limit means that the encounters were not independent of each other – time spent waiting at one restaurant was time that could not be spent waiting at another. This means that an animal using an economically intelligent strategy should have waited longer for more preferred flavors. Rats' preferences were "revealed" by an increased willingness to wait out a longer delay for a favored flavor of pellet. Each rat completed 9 or 10 sessions in total.

We trained rats in four phases. In the first phase (5-7 days, twice daily), rats completed 30-minute sessions of habituation. The delay at every feeder was 1s and the reward was 2 pellets. During this phase the rat became accustomed to the task, whereby it learned the correct direction of travel and the flavor available at each feeder site. The rat moved on to the next training phase after it reliably ran clockwise around the loop. In the second phase (4 days, twice daily), the 30-minute sessions had increasingly longer delays. The delays began with a range of 1-2 seconds, then 1-3 seconds, and continued to increase by 1 second each day until the rat achieved a maximum of 5 seconds (this trained the rat to wait). In the third phase (10 days, twice daily), the rat completed 30-minute sessions with the full delay set (1-30 seconds). In the fourth phase (5-10 days,

once daily), the rat completed 60-minute sessions with the full delay set (1-30 seconds).

By the end of this final training phase, the rats typically showed delay thresholds (by

visual inspection), skipped high tones, and left the feeder site after reward receipt. From

this evidence, we concluded that the rats understood the task and commenced the

experimental testing portion.

Task-Derived Decision Metrics

To examine behavioral parallels across species we used three decision metrics: (1)

revealed preferences, (2) stated preferences, and (3) decision consistency. We calculated

revealed preferences for each category via a logistic fit function for human and

nonhuman animals (see Figure 2.3). These values reflect the delay time (or delay

threshold) at which a subject reliably began to skip offers for the respective category. In

other words, the inflection point equates to the delay threshold at which a subject had a

50% probability of staying (or skipping). We computed inflection points according to the

following equation (one per category, per subject):

$$\log(\frac{p}{1-p}) = \beta_0 + \beta_1 x \tag{1}$$

where p is the desired probability (50% in this case), β_o is the intercept, β_1 is the slope,

and x is the delay threshold. Notice that the function on the left of equation (1) is the logit

of p, and the function on the right of equation (1) represents a linear regression model

with a single predictor. We then rearranged the equation to solve for x:

$$x = \frac{log(\frac{p}{1-p}) - \beta_0}{\beta_1}. \tag{2}$$

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We considered favored galleries to be those where a subject consistently waited longer for the reward (equating to a higher delay threshold). We acquired *stated preferences* for human subjects only, which included average ratings for each category, as well as post-test category rankings, 1 to 4.

We also measured *decision consistency* in both species, which indicated the extent to which subjects cohered to category-specific strategies (i.e. stayed for trials below threshold, and skipped trials above threshold). Given the economically normative assumption that subjects had a subjective valuation of a particular category and a fixed time constraint, subjects should have stayed when the subjective valuation of a category (reward) was larger than the offered delay (cost). Subjects that deviated from this economically normative model made "economic errors" in that they sacrificed time that could be spent in a preferred location (e.g. time spent waiting for a bike-accident video was time that could not be spent waiting for a [potentially preferred] kitten video). To derive the decision consistency metric we computed the proportion of error trials for each subject (number of error trials divided by the total number of trials).

Analyses

Our first set of analyses assessed behavioral cross-species parallels using the respective tasks. First, we identified evidence of revealed preferences in both species. Next, we evaluated within-subject consistency. For human subjects, we examined the correspondence between a human subjects' revealed and stated preferences; this analysis also provided a measure of the Web-Surf task's external validity. For rats, we evaluated the consistency of the rats' revealed preferences (i.e. delay thresholds) across sessions

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because we could not ask a rat to explicitly state its preference. Third, we investigated whether humans and nonhuman animals exhibited similarities in decision consistency. Fourth, we analyzed decision times to determine whether subjects made quick decisions or waited for cues; we used this measurement to evaluate the face validity of each task. Finally, we examined within-session dynamics to determine whether humans and rats behaved similarly as the session proceeded.

In the second set of analyses, we compared the two variants of the Web-Surf task (video versus photo stimuli). We conducted these analyses to determine which type of stimuli provided the most reliable and valid results, while also considering category homogeneity across stimuli types (rats always received the same reward at a given feeder). We also assessed within-session dynamics and gender differences across the two task variants.

2.3 Results

Humans versus Rats: Revealed Preferences

First, we determined whether human and non-human animal subjects showed evidence of revealed preferences. Figure 2.3 illustrates a side-by-side comparison for a single human and single rat session, where each curve depicts choices for a particular category. In both species, we visually (and statistically) identified a clear inflection point at which the subject had a 50% chance of staying or skipping on to the next offer. The distributions in Figure 2.3 are typical of those we observed from other human and non-human animal subjects (see Steiner and Redish, 2014, for additional rodent examples).

Humans versus Rats: Evaluating Within-Subject Consistency

Next, we evaluated the extent to which both species displayed consistent within-subject preferences. For the human sample (N = 49), we computed two correlations per subject: (1) the correlation between delay thresholds and average category ratings (4 values for each) and (2) the correlation between delay thresholds and post-test category rankings (4 values for each). We found that delay thresholds corresponded with average category ratings, with 69% of correlations above 0.50. Similarly, 73% of correlations between delay thresholds and post-test category rankings were above 0.50. We did not detect significant differences between subjects who completed the 3 versus 5-NEXT versions for rating ($t_{47} = 0.51$, $p = 0.61$) or ranking ($t_{38} = 0.08$, $p = 0.94$) validity correlations.

To determine within-subject consistency for rats, we evaluated delay thresholds across sessions using a repeated-measures analysis of variance (ANOVA). We constructed a model that included delay thresholds as the dependent variable, and zone (i.e. feeder site) and session number as the predictor variables. As shown in Table 2.1, we observed a significant main effect for zone ($F_{3,231} = 4.58$, $p = 0.004$) but not session number ($F_{70,231} = 0.59$, $p = 0.99$), thus indicating that rats had detectable and stable flavor preferences. These results are consistent with across-session rat performance in Steiner and Redish (2014).

Humans versus Rats: Decision Consistency

Third, we examined parallels in decision consistency for humans and nonhuman

animals (see Figure 2.4). In particular, we found that rat subjects exhibited greater

decision instability (mean = 0.12, median = 0.12), compared to human subjects (mean =

0.07, median = 0.08). Several human subjects also had no error trials, which was not the

case for rats. We were also interested in the spread of this decision consistency metric

within each species, as we hope to capture a comparable range of threshold error variance

using the respective tasks. To this end, we used an F-test to investigate differences in

decision consistency *variance* between species and found no significant differences ($F_{49,}$

$_{77}$ = 1.15, p = 0.60). Thus, although humans had less mean decision instability, the spread

of this metric was consistent in humans and rats.

Humans versus Rats: Decision Times

Fourth, we evaluated the association between choice reaction time and delay to

determine whether delay times influenced the speed at which subjects made a decision.

This analysis included a subset of human video subjects (N = 27) for whom the task

recorded skip reactions times. The plots in Figure 2.5 illustrate the relation between

choice reaction time and delay for all human and rat subjects separately. Stay trials are

represented as the full delay time (points along diagonal) and mean times for skip trials

are represented as the points parallel to the x-axis. The blue shaded bands indicate skip

time standard deviations around each possible delay time. Humans and rats made

decisions shortly after arrival at a gallery, with decisions made within 3 seconds or less

for the majority human trials and within 5 seconds or less for the majority of rat trials. In

other words, when presented with a less valuable offer, subjects did not hesitate to skip

and travel towards other potential offers. Instead, both species efficiently decided

whether an offer was preferable or not. This supports the face validity of each task, where neither species waited for a specific cue to decide but made a quick choice and remained engaged in the task. For example, the rats did not appear to wait for a specific tone before deciding to leave.

Humans versus Rats: Within-Session Dynamics

As a final cross-species comparison, we assessed whether human and rat behaviors showed comparable fluctuations throughout the session. To this end, we used repeated measures ANOVAs with choice as the dependent variable, and category/zone and trial number as the predictor variables. We were particularly interested in the trial number term as an indicator of reward satiation, where a significant effect would suggest a change in stay/skip tendencies over the session. Table 2.2A reveals a significant main effect for category ($F_{3,5587} = 110.78$, $p < 0.001$) but not trial number ($F_{1,5587} = 2.03$, $p = 0.16$) for human subjects. Table 2.2B reveals comparable findings for rat subjects, including a significant main effect for zone ($F_{3,13856} = 18.69$, $p < 0.001$) but not trial number ($F_{1,13856} = 1.28$, $p = 0.25$). This suggests that, regardless of species, subjects exhibited differential choice patterns across reward sites but not trial number. In other words, neither species appeared to satiate during the session.

We also assessed the amount of time spent in the reward zone following reward consumption as a function of trial number. In human subjects this equated to the time after viewing a stimulus but before providing a rating (as the subject could not advance to the next gallery before rating the video or photo). In rat subjects this equated to the time after eating but before running to the next zone. A t-test indicated that rats spent

significantly more time lingering in the reward zone than humans, $t_{12207} = 46.23$, $p <$

0.001 (see Figures 2.6A and 2.6B).

<u>Videos versus Photos: Selecting Optimal Stimuli</u>

      To compare the task variants, we first computed correlations between revealed

and stated preferences for the photo (N = 15) and a subset of the video subject (N = 22)

whose data we collected during the same period. For average category ratings, 68% of

video subjects had correlations of 0.50 or above versus 40% of photo subjects. As

depicted in Figure 2.7A, video subject correlations for average category ratings ranged

from -0.31 to 1.00, with a mean of 0.62 and a median of 0.82. The photo subject

correlations spanned a comparable range from -0.76 to 1.00. However, the mean and

median correlations for the photo subjects were lower, with values of 0.27 and 0.35,

respectively. A t-test revealed a significant difference between the groups ($t_{35} = -2.10$, $p =$

0.04).

      A similar pattern emerged for the post-test category rankings, where 72% of video

subjects had correlations 0.50 or above versus 64% of photo subjects (See Figure 2.7B).

Video subject correlations for category rankings ranged -0.40 to 0.99, with a mean of

0.56 and a median of 0.85. The photo subject correlations covered an even larger range,

with bounds of -0.73 and 0.96. As a result, the mean correlation for these subjects was

0.41 and the median 0.55. Although video subjects generally had higher validity

correlations, this difference was not significant ($t_{27} = -0.73$, $p = 0.47$); 8 subjects did not

have ranking data, hence the reduced degrees of freedom.

      We also calculated decision consistency metrics for photo subjects and the same

subset of 22 video subjects. As shown in Figure 2.8, video and photo subjects did not exhibit mean differences in their proportion of error trials (t_{35} = -0.65, p = 0.52). Similar to the human and rat comparison, we also assessed for differences in decision consistency *variance*. Here we did find a significant difference ($F_{21, 14}$ = 0.19, $p < 0.001$), whereby video subjects exhibited a more homogenous pattern of decision instability.

Videos versus Photos: Within-Session Dynamics

Next, we assessed within-session choice behaviors for the two task variants using repeated measures ANOVAs. This entailed two models with choice as the dependent variable, and category and trial number as the predictor variables (i.e. separate models for the initial 22 video subjects and the 15 photo subjects). Table 2.3A reveals a significant main effect for category ($F_{3,2382}$ = 64.35, $p < 0.001$) but not trial number ($F_{1,2382}$ = 0.12, p = 0.73) for video subjects. Table 2.3B reveals similar findings for photo subjects, including a significant main effect for zone ($F_{3,1241}$ = 8.85, $p < 0.001$) but not trial number ($F_{1,1241}$ = 1.72, p = 0.19). Thus, subjects showed significant choice differences as a function of category but not trial duration.

We also investigated whether video and photo subjects differed in the amount of time spent in the reward zone following consumption (after viewing a stimulus but before rating it). As shown in Figures 2.9A and 2.9B, we observed similar patterns using the two task variants (t_{2272} = 0.85, p = 0.39), as human subjects generally rated the videos and exited the reward zone in 5 seconds or less (with comparable variation extending into the 5 – 18 second range).

<u>Videos versus Photos: Gender Differences</u>

Lastly, we built linear mixed models to assess gender differences in category preference; this approach uses restricted maximum likelihood to obtain parameters estimates and can thus accommodate unbalanced designs (i.e. missing data). We constructed two models per task variant (four models total) that included either delay thresholds or average category ratings as the dependent variable, and gender, category, and a gender x category interaction term as the predictor variables. We were particularly interested in the interaction term as an indicator of preference differences across gender. We observed non-significant interactions in all models (see Supplemental Tables 2.1A-2.2B). However, a trend-level gender x category interaction for average category ratings in the video subjects (N = 22) and a subsequent power analysis encouraged us to re-assess for significant interactions using the complete video sample (N = 49). Here, we found significant gender x category interactions for delay thresholds ($F_{3,141} = 2.77$, $p = 0.04$) and average category ratings ($F_{3,138} = 6.12$, $p < 0.001$; see Supplemental Tables 2.3A and 2.3B). Follow-up tests revealed that gender differences were most prominent for the bike-accident and landscape categories. We refer readers to the Supplemental Materials for further details.

2.4 Discussion

The current study proposes a novel experiential foraging paradigm for humans called the Web-Surf Task. We designed this paradigm to assess similarities in decision-making systems in humans and rats. The Web-Surf Task involves individuals making a series of stay/skip foraging decisions as they cycle through four galleries. This task

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builds on available decision-making paradigms in several ways: (1) its experiential design includes primary reinforcement and real-time delays, (2) it entails serial stay/skip offers and is therefore more akin to real-world choices, and (3) it was designed as a direct analogue to a rat foraging task. This last point is particularly salient in the context of psychopathology research, where translational models are critical for developing successful treatments. Our preliminary findings demonstrate both the external and face validity of the Web-Surf task, as well as cross-species behavioral parallels using the analogous tasks. Therefore, the complementary use of the Web-Surf or Restaurant Row tasks could be a step forward for bridging pre-clinical and clinical lines of research.

We first examined cross-species parallels using data from both the Web-Surf Task and Restaurant Row. Our results showed that each task captured individual differences in preference as evidenced by delay thresholds, as well as within-subject consistency in humans and non-human animals. We also found evidence that both species actively made decisions as they traversed through their respective tasks, where each offer (combination of delay length with specific gallery or flavor) represented a certain value that fit within a given subjects' strategic framework. Moreover, we detected cross-species parallels in reward satiation rates, as tendencies to stay versus skip remained relatively stable throughout the session. We did observe cross-species divergences with respect to decision consistency, where rat subjects exhibited more deviations, on average, from the ideal strategy. However, the *spread* of decision instability was similar using the analogous tasks. The tasks also diverged according to post-consumption reward time. In particular, we found that rat subjects spent more time lingering in the reward zone partaking in leisure activities such as grooming.

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We then compared two variants of the Web-Surf Task: one that included video stimuli as reward and a second that included photo stimuli. Our primary intention was to empirically assess which type of internet-available reward stimuli yielded more reliable and valid results. We found that subjects who completed the video version showed greater correspondence between revealed and stated preferences. We also observed a tighter range of decision stability in the video subjects. Hence, although photo categories may appear more homogenous, the data suggest that video rewards yielded more reliable results. These discrepancies may reflect the notion that videos are inherently more rewarding to humans. Comparable findings have been reported in macaques, where animated movies had considerably more reward value than static pictures (Blatter & Schultz, 2006). We also compared within-session dynamics across the two task variants, which indicated similar stay proportions and post-reward consumption times. As a last step, we explored gender differences in category preference. These results suggested that males tended to wait longer for landscape and bike-accident videos, and also rated these categories more highly (although the bike-accident ratings did not attain significance). We were unable to detect gender differences using the photo version, further suggesting an increased sensitivity in the video version.

Previous studies have demonstrated the utility of multi-option foraging models for investigating natural foraging behaviors in human and nonhuman animals; however, ours is the first to compare these processes across species. The Web-Surf Task provides a novel combination of primary reinforcement, real-time delays, and serial stay/skip foraging choices that parallels Restaurant Row.

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<u>Future Directions</u>

Despite the promising overlap of the described tasks, functional translation is a dynamic and evolving process that benefits from ongoing modifications at both the pre-clinical and clinical ends. We therefore suggest several avenues to further reduce cross-species divergences. First, future studies could assess whether decision-making parameters derived from the Web-Surf Task are stable via repeated sessions. This approach would not only foster design parallels with nonhuman animal studies (which typically entail multiple sessions) but also elucidate whether the Web-Surf Task captures state and/or trait-like effects. Some researchers argue that experiential decision-making tasks better capture acute state changes (e.g. drug effects), whereas questionnaire based tasks may tap into stable, trait-like impulsivity (Reynolds, 2006a). Nonetheless, empirical research is needed to assess if the Web-Surf Task, which we consider an experiential measure, can measure state-level fluctuations in a similar fashion to Restaurant Row. Second, researchers could investigate the extent to which various experimental design manipulations (e.g. increasing delay lengths, adjusting distance/effort to travel between feeders or galleries) similarly influence human and rodent behavior. Third, future endeavors could modify the stimuli sets to address specific psychopathology questions (e.g. food pictures or videos for obesity hypotheses, drug paraphernalia for addiction hypotheses, etc.). In effect, such stimuli would serve as a combination of primary *and* conditioned reinforcement. Researchers might then investigate whether satiation rates for these stimuli differ from other primary rewards. Fourth, researchers may examine relations between error trials and psychopathology, particularly the influence errors might have on trial-by-trial behavior. For example, a subject might encounter an unfavorable

scenario where one skips an offer below threshold (where they should have stayed) only to encounter a less favorable offer on the next trial (termed "regret" when seen in rats by Steiner and Redish, 2014). The manner in which a subject uses this experience to guide subsequent decisions may reflect pathological processes. For instance, addicted individuals may continue to deviate from strategy despite negative feelings or repercussions.

Another pertinent avenue for future endeavors is to explore the underlying neural systems evoked during the analogous tasks. Although we restricted the current study to behavioral methods, prior investigations have identified the rodent neural systems recruited during Restaurant Row (Breton, Schmidt, & Redish, 2014; Schmidt, Breton, & Redish, 2014; Steiner & Redish, 2014). Steiner and Redish (2014) found that representations in both orbitofrontal cortex (OFC) and ventral striatum (vStr) reliably tracked choices and preferences (e.g. neuronal signals in these areas differentiated between feeders during reward receipt). Breton et al. (2014) found that compromising OFC with DREADD-driven pyramidal-cell inhibition led to a disruption in flavor preferences, while Schmidt et al. (2014) found that compromising medial prefrontal areas (prelimbic, PL and infralimbic, IL) led to a disruption in hesitation during difficult decisions. Although the homologies between rat and human prefrontal areas remain controversial (Preuss, 1995; Uylings, Groenewegen, & Kolb, 2003), these findings suggest that it would be extremely interesting to compare human neuroimaging findings and rodent neurophysiological findings on these parallel tasks.

For example, these findings are consistent with human neuroimaging findings, whereby studies have shown that medial OFC activation scales proportional to expected

reward value (M. F. Rushworth, Kolling, Sallet, & Mars, 2012), the ventromedial

prefrontal cortex (suggested to parallel rodent OFC; Ongür & Price, 2000; Schoenbaum,

Roesch, & Stalnaker, 2006) reflects rewards and decisions (Balleine & O'Doherty, 2010;

Gläscher, Hampton, & O'Doherty, 2009; Hampton, Bossaerts, & O'Doherty, 2006), and

the dorsolateral prefrontal cortex (suggested to parallel rodent mPFC; Ongür & Price,

2000; Seamans, Lapish, & Durstewitz, 2008) links with deliberative decision processes

(Krawczyk, 2002). One might also anticipate cross-species parallels in recruitment of the

anterior cingulate cortex (ACC; Kolling, Behrens, Mars, & Rushworth, 2012). For

example, evidence suggests that the ACC may monitor performance, such as the yield of

foraging decisions. In particular, the ACC is sensitive to situations where the alternative

value is deemed greater than the current option, thus leading the subject to skip. Lastly,

the anterior insula is an additional target region for tracking reward responsiveness during

the Web-Surf Task, as this area is closely linked to the salience network and has been

shown to activate more strongly in response to primary than secondary rewards in

humans (Sescousse et al., 2013).

Conclusions

Collectively, our findings support the use of the Web-Surf Task as an effective

experiential human foraging paradigm. Many decision-making tasks are concerned with

modeling the motivation (or aversion) to reward and punishment as a means to

characterize impulse-related psychopathology. To effectively model reward requires that

a given task capture the natural ethology of a species – a reason that has led many to

utilize monetary questionnaire or point-based delay-discounting paradigms. However,

money is only symbolically rewarding to humans, and is not a comparable primary reinforcer as the food rewards used in rodent paradigms. Our results demonstrate that video stimuli provide a compelling counterpart to food that can be easily incorporated into an experimental setup. Moreover, the multi-option design enables researchers to evaluate individual differences in preference. This feature may be valuable for researchers interested in mapping various behavioral parameters with other marks of impulsivity (e.g. self-report, neural activation, etc.). Therefore, this research lays the foundation for a stream of functional translational research that seeks to narrow the gap between pre-clinical and clinical research via parallel tasks.

2.5 Figures and Tables

Figure 2.1. Restaurant Row and Web-Surf Task Schematics
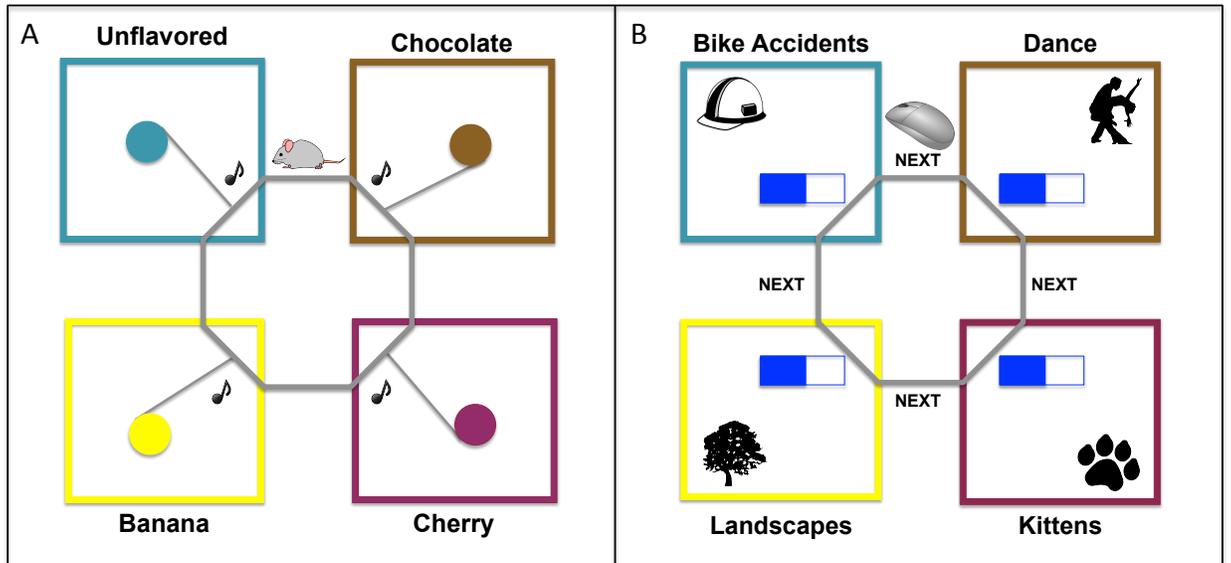
(A) Schematic of Restaurant Row. Rats had 60 minutes to cycle around a circular track and collect food rewards from four feeders ("restaurants"); feeders provided different flavors of pellets after variable delay times. (B) Schematic of the Web-Surf Task. Humans had 30 minutes to cycle through four video or photo galleries; video or photo rewards were represented after variable delay times.

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Figure 2.2. Web-Surf Task Flow-diagram
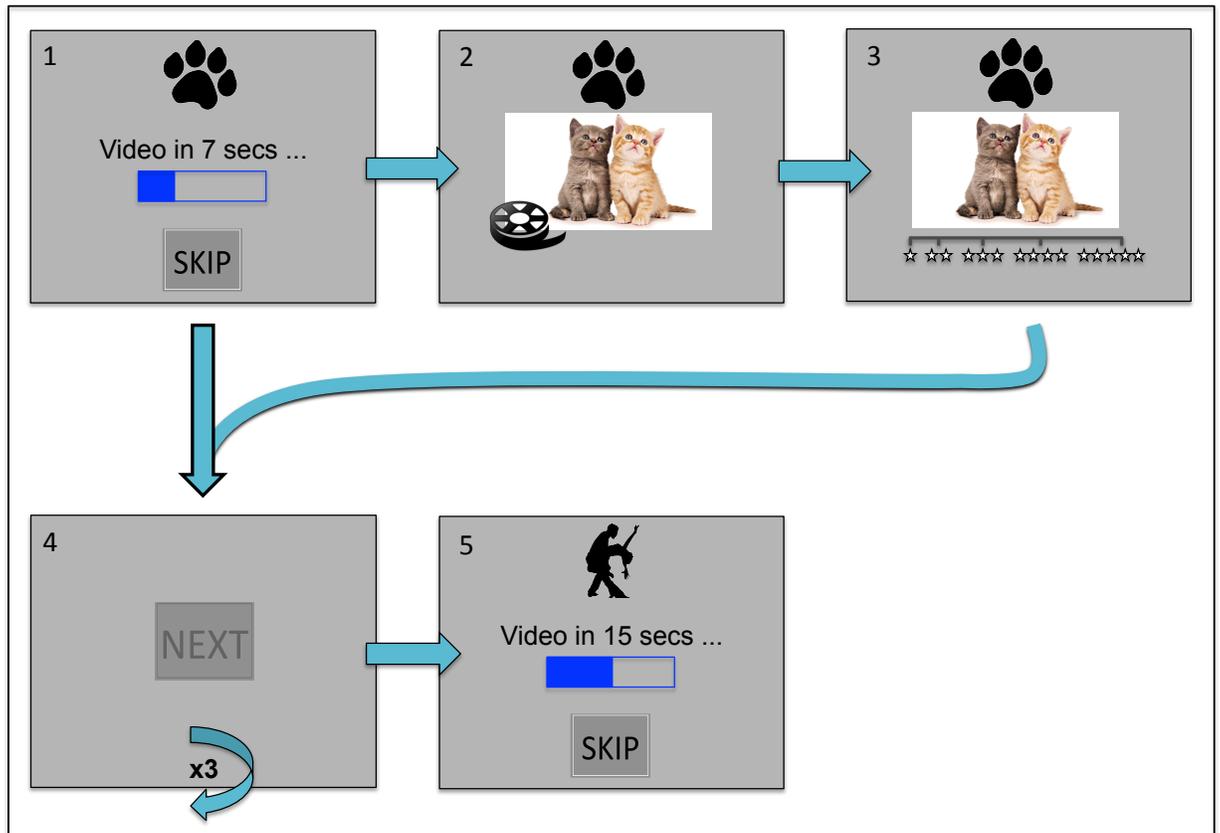
Flow diagram of the Web-Surf Task to illustrate stay/skip decisions. Subject receives an offer (1). If the subject decides to stay: the subject views the video or photo stimulus for 4 seconds (2), rates the stimulus at the end of 4 seconds (3), proceeds through the "NEXT" transition phase (4), and then receives the next offer (5). If the subject decides to skip: the subject moves directly from the initial offer (1) to the "NEXT" transition phase (4), before receiving the next offer (5).

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Figure 2.3. Evidence of Revealed Preferences
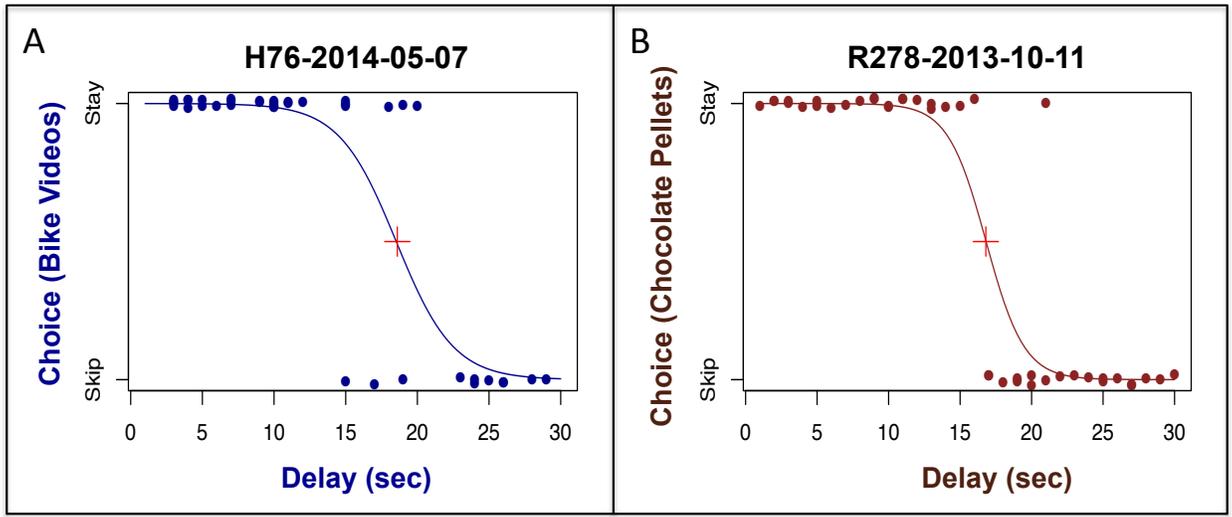
Examples of subject level plots for a single category for the Web-Surf Task (A) and Restaurant Row (B), which show *revealed preferences*. The red plus sign indicates a subject's inflection point, or the delay threshold at which a subject reliably begins to skip offers for a given category (calculated using a logistic fit function). These are typical distributions (see: Steiner and Redish, 2014).

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Figure 2.4. Decision Consistency Distributions
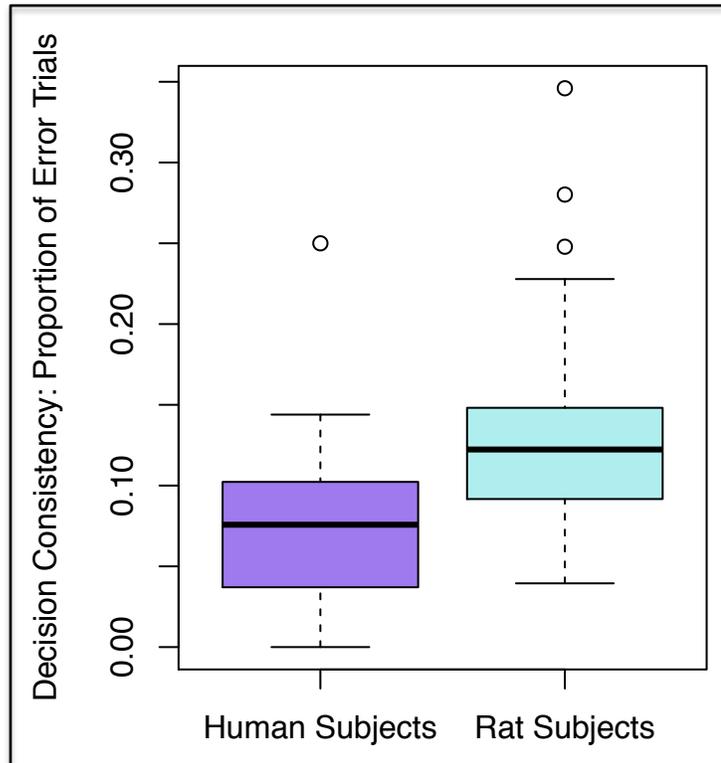
Distributions representing *decision consistency* for the Web-Surf Task (*right*) and Restaurant Row (*left*). Specifically, this metric reflects the proportion of trials for which a subject deviated from his or her strategy (skipped an offer below his delay threshold for the respective category or stayed for an offer above his threshold). Here, the upper and lower bars indicate the range of scores, the shaded area depicts the interquartile range, and the dark horizontal band reflects the median decision consistency score. Circles outside the boxes show outliers.

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Figure 2.5. Choice Reaction Times
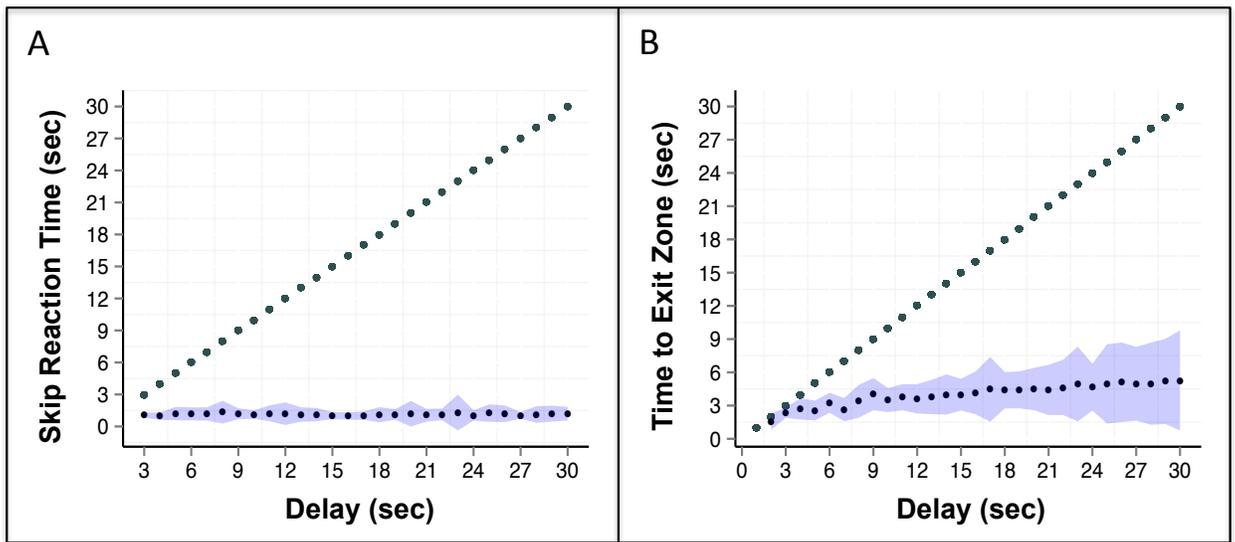
Choice reaction times for the Web-Surf Task (A) and Restaurant Row (B). Stay trials shown as the full delay time (points along the diagonal) and mean times for skip trials shown as the points parallel to the x-axis. Blue shaded bands indicate skip time standard deviations. Decisions were generally made quickly for humans and rats.

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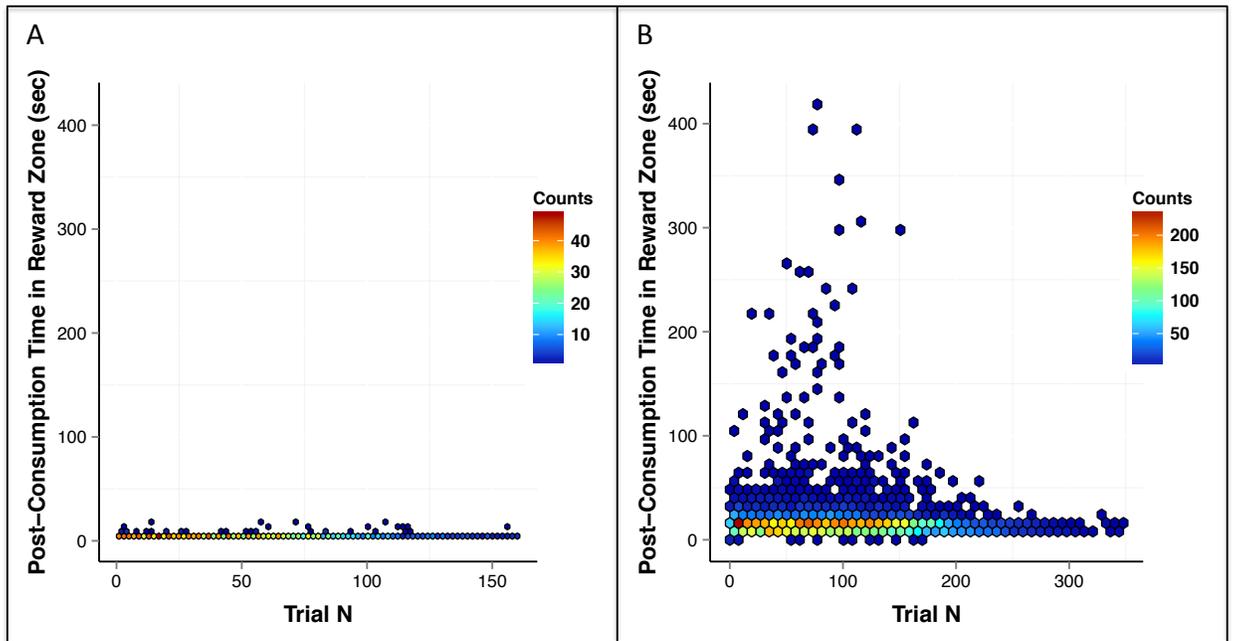
Figure 2.6. Time in Reward Zone (Humans vs. Rats)

Time spent in the reward zone after consumption against trial number (N) for the Web-Surf Task (A) and Restaurant Row (B). In human subjects this equated to the time after viewing a stimulus (video or photo) but before providing a rating. In rat subjects this equated to the time after eating but before running to the next zone. The counts reflect the number of samples included in a given cell.

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Figure 2.7. Correspondence of Revealed and State Preferences
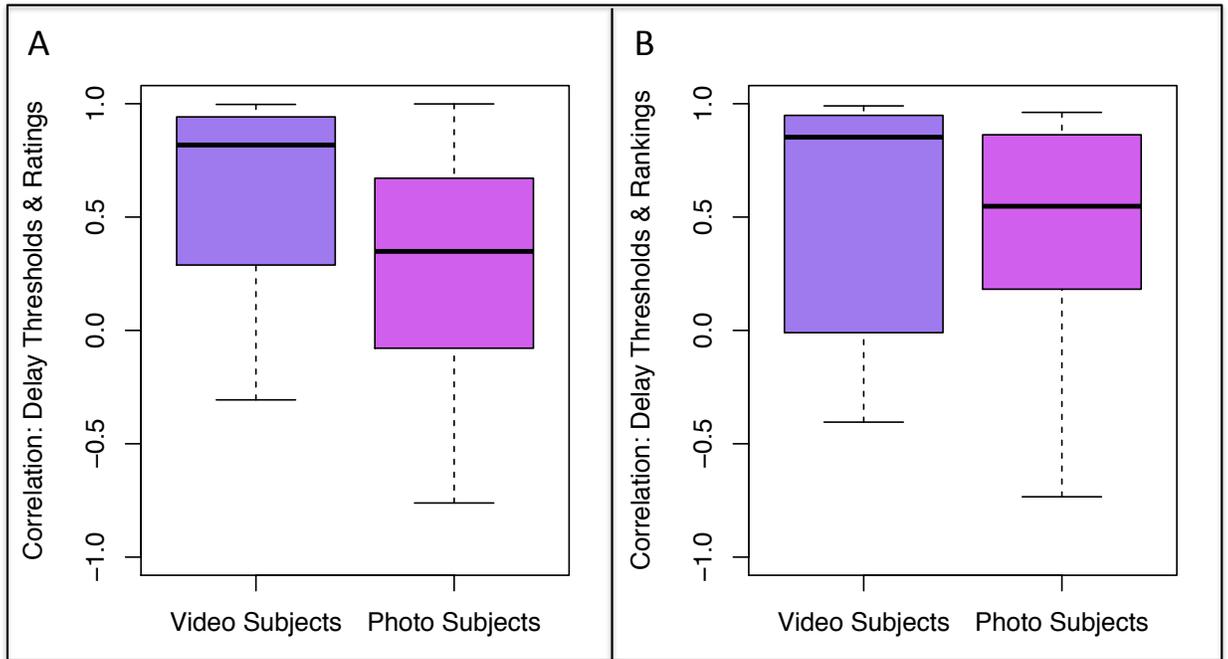
Correspondence between *revealed* and *stated* preferences for both stimuli types. (A) Correlations between delay thresholds (revealed preferences) and average category ratings (stated preferences) for video and photos subjects. (B) Correlations between delay thresholds and post-test category rankings (stated preferences). The upper and lower bars represent the range of correlations. The shaded area represents the interquartile rang, and the dark horizontal band within the shaded area indicates the median correlation.

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Figure 2.8. Decision Consistency (Video vs. Photo)
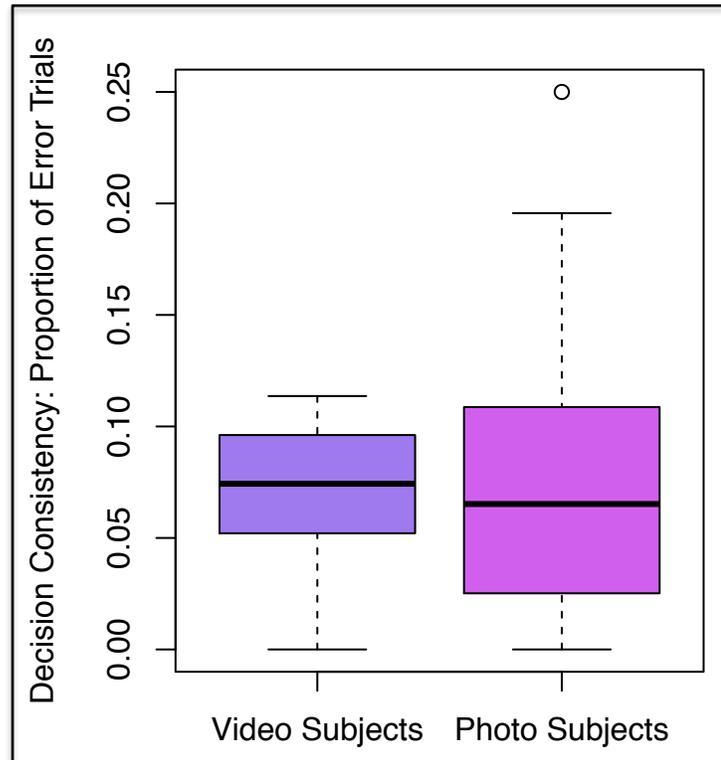
Comparison of video versus photo subjects on measure of *decision consistency*. The upper and lower bars indicate the range of scores, the shaded area depicts the interquartile range, and the dark horizontal band reflects the median decision consistency score. Circles outside the boxes show outliers.

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Figure 2.9. Time in Reward Zone (Video vs. Photo)
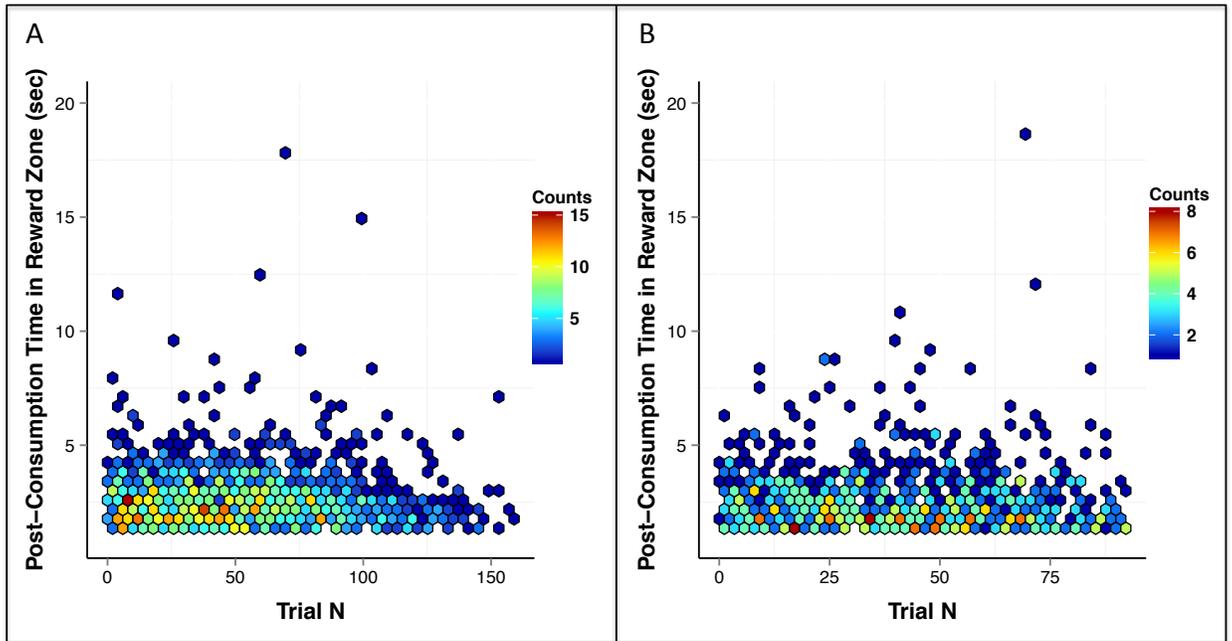
spent in the reward zone after consumption against trial number (N) for the Web-Surf Task, where (A) is the initial 22 video subjects and (B) is the photo subjects. This equated to the time after viewing a stimulus (video or photo) but before providing a rating. The counts reflect the number of samples included in a given cell.

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Table 2.1. Across-Session Threshold Consistency (Rats, N = 8)

Source	df	Sum Sq	Mean Sq	F-Value	*p*-value
Zone	3	523	174.27	4.58	**0.004**
Session Number	70	1581	22.59	0.59	0.99
Residuals	231	8788	38.04		

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Table 2.2A. Choice as a Function of Category and Trial N (Video, N = 49)

Source	df	Sum Sq	Mean Sq	F-Value	*p*-value
Category	3	65.70	21.91	110.78	**<0.001**
Trial Number	1	0.40	0.40	2.03	0.16
Residuals	5587	1104.90	0.20		

Table 2.2B. Choice as a Function of Zone and Trial N (Rats, N = 8)

Source	df	Sum Sq	Mean Sq	F-Value	*p*-value
Zone	3	12.20	4.07	18.69	**<0.001**
Trial Number	1	0.30	0.28	1.28	0.25
Residuals	13856	3015.80	0.22		

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Table 2.3A. Choice as a Function of Category and Trial N (Video, N = 22)

Source	df	Sum Sq	Mean Sq	F-Value	*p*-value
Category	3	37.90	12.63	64.35	**<0.001**
Trial Number	1	0.00	0.02	0.12	0.73
Residuals	2382	467.40	0.20		

Table 2.3B. Choice as a Function of Category and Trial N (Photo, N = 15)

Source	df	Sum Sq	Mean Sq	F-Value	*p*-value
Category	3	4.84	1.61	8.85	**<0.001**
Trial Number	1	0.31	0.31	1.72	0.19
Residuals	1241	226.24	0.18		

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2.6 Supplemental Materials

Videos versus Photos: Gender Differences

Lastly, we built linear mixed models to assess gender differences in category
preference; this approach uses restricted maximum likelihood to obtain parameters
estimates and can thus accommodate unbalanced designs (i.e. missing data). We
constructed two models per task variant (4 models total) that included either delay
thresholds or average category ratings as the dependent variable, and gender, category,
and a gender x category interaction term as the predictor variables. We were particularly
interested in the interaction term as an indicator of preference differences across gender.
Supplemental Tables 1A and 1B summarize the results for the video version (N = 22
subset). Here we found a non-significant gender x category interaction for delay
thresholds ($F_{3,60} = 0.85$, $p = 0.47$) and a trend level interaction for average category
ratings ($F_{3,58} = 2.14$, $p = 0.10$). Supplemental Tables 2A and 2B report comparable
information for the photo version, indicating non-significant interactions for delay
thresholds ($F_{3,39} = 0.73$, $p = 0.54$) and average category ratings ($F_{3,39} = 0.21$, $p = 0.89$).

Given these null findings, we conducted sensitivity analyses to derive the effect
size needed to detect a significant gender x category interaction. For both task versions,
we input the following parameters into the G*Power software (Faul, Erdfelder, Lang, &
Buchner, 2007): alpha = 0.05, power = 0.95, number of groups = 2, number of
measurements = 4, correlation among measurements = 0.5. To achieve a significant
interaction for a sample of 22 (original video subset), we would need an F-statistic of
2.76 and an effect size of 0.32, whereas we would need an F-statistic of 2.85 and an
effect size of 0.40 for a sample of 15 (photo version). Alternatively, a power analyses

revealed that 26 subjects would be necessary to detect an effect size of about 0.30.

We then tested whether utilizing the complete sample of video subjects (N = 49) yielded a significant interaction, given the power analysis above. Supplemental Tables 3A and 3B reveal significant gender x category interactions for delay thresholds ($F_{3,141}$ = 2.77, p = 0.04) and average category ratings ($F_{3,138}$ = 6.12, p < 0.001) for the complete video sample. Based on the significant interactions, we performed follow-up analyses to determine which specific categories drove the gender differences. With respect to delay thresholds, we observed significant gender differences for the bike-accident (t_{47} = 2.65, p = 0.01) and landscape (t_{38} = 3.03, p = 0.004) categories; for the latter we used a Welsh corrected t-test to account for significant gender differences in variance (Levene's test: $F_{1,47}$ = 4.34, p = 0.04), hence the reduced degrees of freedom. We did not detect gender differences for the animal (t_{47} = 0.12, p = 0.91) or dance (t_{47} = 0.38, p = 0.71) delay thresholds. With regards to average category ratings, only the landscape category was significant (t_{47} = 3.55, p < 0.001). Although males generally rated the bike-accident videos higher, this effect did not attain significance (t_{47} = 1.50, p = 0.14). Similar to the delay thresholds, we did not detect gender differences for the animal (t_{47} = -1.04, p = 0.30) or dance (t_{47} = -0.86, p = 0.40) categories.

Supplemental Table 2.1A. Gender Differences in Thresholds (Video, N = 22)

Source	Num df	Den df	F-value	*p*-value
Gender	1	20	0.15	0.70
Category	3	60	7.72	**<0.001**
Gender X Category	3	60	0.85	0.47

Supplemental Table 2.1B. Gender Differences in Ratings (Video, N = 22)

Source	Num df	Den df	F-value	*p*-value
Gender	1	20	12.40	**0.002**
Category	3	58[a]	12.37	**<0.001**
Gender X Category	3	58[a]	2.14	0.10

[a]Two subjects did not have ratings for the bike accidents category, as they skipped every trial, hence the reduced degrees of freedom.

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Supplemental Table 2.2A. Gender Differences in Thresholds (Photo, N = 15)

Source	Num df	Den df	F-value	*p*-value
Gender	1	13	0.54	0.47
Category	3	39	1.47	0.24
Gender X Category	3	39	0.73	0.54

Supplemental Table 2.2B. Gender Differences in Ratings (Photo, N = 15)

Source	Num df	Den df	F-value	*p*-value
Gender	1	13	0.18	0.68
Category	3	39	3.15	**0.04**
Gender X Category	3	39	0.21	0.89

Supplemental Table 2.3A. Gender Differences in Thresholds (Video, N = 49)

Source	Num df	Den df	F-value	*p*-value
Gender	1	47	4.37	**0.04**
Category	3	141	12.21	**<0.001**
Gender X Category	3	141	2.77	**0.04**

Supplemental Table 2.3B. Gender Differences in Ratings (Video, N = 49)

Source	Num df	Den df	F-value	*p*-value
Gender	1	47	1.06	0.31
Category	3	138[a]	28.81	**<0.001**
Gender X Category	3	138[a]	6.12	**<0.001**

[a]Three subjects did not have ratings for the bike accidents category, as they skipped every trial, hence the reduced degrees of freedom.

CHAPTER 3: THE NEURAL BASIS OF HUMAN DELIBERATION

Abstract

The ability to project oneself into the future and pre-experience an event is termed 'prospection' or 'episodic future thinking.' It follows that prospection is critical to deliberation, which is the process of mentally searching through or imagining various possibilities. Internally driven networks may underlie prospection (and in turn, deliberation), given their roles in self-reflection, autobiographical memory, and mental simulation. The imagination literature may also inform our understanding of these decision processes, as the same neural systems are evoked when imagining or perceiving a stimulus. In the current study, we found that humans engaged in episodic future thinking when making decisions, a pattern indicated by comparable neural activation during the consideration of and actual receipt of reward. Further, different brain networks showed representations of past and future outcomes when subjects made decisions, but only tracked current outcomes during reward receipt. We also found that the capacity to imagine outcomes when making a decision predicted more optimal decision-making overall. Lastly, we found that difficult choices recruited similar behavioral and neural responses in humans as previously observed in rats, providing evidence of cross-species parallels in deliberation.

3.1 Introduction

Humans have a remarkable capacity to mentally simulate the future. This ability, often referred to as 'prospection' or 'episodic future thinking', affords individuals cognitive and behavioral flexibility by anticipating potential outcomes in advance (Buckner & Carroll, 2007; Gilbert & Wilson, 2007). Although there is general agreement in psychology regarding the importance of future-oriented thinking to behavior (Fukukura, Helzer, & Ferguson, 2013), recent technological advances provide the tools needed to study prospection and clarify its role in human action.

Prospection is fundamental to *deliberation*, or the process by which one searches through and evaluates various possibilities based on a hypothesized world model (Payne, Bettman, & Johnson, 1993; Redish, 2013). Human deliberative search processes are likely serial, with individual options imagined as concrete future possibilities (Redish, 2016). Further, the ability to search and *find* future prospects may be pivotal to how humans assign value and make decisions (Kurth-Nelson et al., 2012). The current study presents neural evidence of human deliberation; specifically, we find that different brain networks tracked past and future outcomes when subjects made decisions. We also find that the capacity to locate outcomes when making a choice (as indicated by neural representations) predicted more optimal decision-making, demonstrating the role of prospection in deliberation.

Deliberation hinges on several cognitive functions, including episodic future thinking and working memory (Redish, 2016). Autobiographical memory may also play a role in deliberation given evidence that future and past-oriented thinking reflect the same underlying process and neural structures (Addis, Wong, & Schacter, 2007; Hassabis,

Kumaran, Vann, & Maguire, 2007; Spreng, Mar, & Kim, 2009; Szpunar, Watson, & McDermott, 2007). Several neural systems support these cognitive functions: the default mode network (DMN; Raichle et al., 2001), particularly the dorsal medial temporal subsystem, is involved in autobiographical memory, mental simulations, and navigation (Buckner, Andrews-Hanna, & Schacter, 2008; Spreng et al., 2009); the fronto-parietal, or 'central executive,' network is pertinent to active maintenance and manipulating information in working memory (Koechlin & Summerfield, 2007; Müller & Knight, 2006; Sauseng, Klimesch, Schabus, & Doppelmayr, 2005); and the salience network may coordinate the DMN and the fronto-parietal network to guide attention and working memory to salient stimuli (Menon & Uddin, 2010).

Findings from the human fMRI literature on imagination may also inform our understanding of prospection, as the same neural circuits are evoked during both the imagination and perception of a stimulus (Pearson, Naselaris, Holmes, & Kosslyn, 2015). For example, both mental and perceptual images are encoded in the primary visual cortex (e.g., Kay, Naselaris, Prenger, & Gallant, 2008; Naselaris, Olman, Stansbury, Ugurbil, & Gallant, 2015), and memories about past experiences reactivate representations of those prior encounters (Gelbard-Sagiv, Mukamel, Harel, Malach, & Fried, 2008; Miller et al., 2013). Moreover, decisions that require imagination of future possibilities activate the sensory cortical representations of those future outcomes (Doll et al., 2015). Doll's experiment, however, was based on binary choices between discrete offers, which precludes the assessment of prospection beyond the current offer.

Contrary to traditional binary decision tasks, multi-option foraging paradigms entail sequential stay/leave choices (Stephens, 2008; Wikenheiser et al., 2013). For

instance, during a spatial neuroeconomic task called Restaurant Row (Steiner & Redish, 2014), rats had a fixed amount of time to cycle between four feeders and collect different flavored food pellets available after a variable delay. Importantly, the flavor order was held constant, while the delays were random. The rat thus knew the location of the flavors but not the specific delays it would encounter, e.g., to decline the current cherry offer meant a chocolate offer available after an unknown delay would follow.

The difficultly of a choice may also impact deliberative decision-making. 'Vicarious trial and error' (VTE) reflects the tendency for a rat to sometimes pause at a choice point and look back and forth as if imagining the future possibilities (Muenzinger & Gentry, 1931; Tolman, 1939, 1948). Given that VTE is specifically implicated in difficult decisions, it is theorized to capture the indecision that underlies deliberation (Redish, 2016). During VTE, hippocampal place cells show forward-sweeping representations that alternate between options, supporting the idea that a rat is mentally simulating the possible outcomes (Johnson & Redish, 2007). The hippocampus may serve an analogous role in humans, as evidenced by its function in episodic future thinking (Addis et al., 2007; Hassabis, Kumaran, Vann, & Maguire, 2007; Lebreton et al., 2013; Peters & Büchel, 2010a; Szpunar et al., 2007), although this theory has not been tested directly.

The current study identified a set of human deliberative mechanisms using a sequential foraging paradigm, i.e., the Web-Surf Task, and functional neuroimaging methods (Abram et al., 2016). Humans made sequential skip/stay decisions as they cycled between four galleries, each of which offered fun video clips available after some delay. Comparable to Restaurant Row, galleries were presented in a fixed order and

subjects encountered real-time costs and received immediately consumable rewards. We hypothesized that deliberation and consumption would engage similar neural systems exemplifying episodic future thinking in humans. We also hypothesized that humans would exhibit analogous behavioral and neural signatures of VTE; in particular, we expected some overlap between prospective and VTE activation, following notions that VTE involves mental simulation of future trajectories.

3.2 Methods

Subjects

Twenty-five healthy volunteers participated in the current study (52% male, mean age of 28 years, all right-handed). Subjects were recruited via the Craigslist website and reported no prior history of neurological disease or severe mental illness, nor did they have a first-degree relative with a severe mental illness. Subjects completed a urine drug screen prior to participation and only those with a negative screening continued. Four subjects were excluded due to excessive head motion, claustrophobia, or invalid behavioral data. All subjects provided written informed consent and the study procedures were approved by the Institutional Review Board at the University of Minnesota.

Web-Surf Task Layout

Subjects had 35 minutes to cycle between four video galleries (i.e., kittens, dance, landscapes, bike accidents) presented using PsychoPy (Peirce, 2009). Galleries were indicated by the symbol at the top of the screen (see Supplemental Figure 3.1). At the

arrival of the gallery, subjects were presented with an offer that indicated how long they would have to wait for a given reward (i.e., 4-second video clip). If they elected to stay, the delay counted down, the subject watched the video clip, and then rated it on a 1-4 scale. If the subject chose to skip, they proceeded to the next gallery and received a new offer. When traveling between galleries, subjects had to click the numbers 1-4 as they randomly appeared around the screen; this represented a travel cost. Numbers were presented in dark grey against a grey screen to increase the difficulty. Trials were presented in 9 minute blocks, with 45 seconds of a fixation cross-hair shown in between blocks. All subjects completed both in- and outside of scanner practice.

Web-Surf Preview Task

Before the main task, subjects completed a preview task that presented a fixed set of ten 4-second video clips from each category, shown in a random order. A fixation cross-hair appeared between videos for 3-6 seconds. Total task time was approximately 7 minutes. Importantly, this task provided baseline estimates of preference and neural activation for each category, in the chance that a subject skipped all offers from a particular category during the main task.

Value Computations

Value was computed as the category-specific threshold minus delay, where thresholds indicated the delay time at which a subject reliably began to skip offers for a particular category. Delay thresholds were computed separately for each trial, per

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category, using a leave-one-out approach: to obtain the threshold for $trial_i$, we fit a

Heaviside step function to all trials in $category_x$ excluding $trial_i$. This produced a vector

of thresholds with length equal to the number of trials in $category_x$. We used a Heaviside

step function as an alternative to the logistic fit function described in Abram et al. (2016),

as the Heaviside step function can better handle extreme cases (i.e., when a subject stays

or skips all offers in a category). In such instances, the Heaviside step function produces

a reasonable value (e.g., 0 or 30), whereas the logistic fit function is likely to produce a

value approaching infinity. Values ranged -30 to 30, and a value of 0 was equal to

threshold.

fMRI Data Acquisition and Preprocessing

Neuroimaging data were collected using a 3-Tesla Siemens MAGNETOM Prisma

at the University of Minnesota's Center for Magnetic Resonance Imaging. A high-

resolution T1-weighted scan was collected for registration [repetition time (TR) = 2.5 ms;

echo time (TE) = 3.65 ms; flip = 7°; voxel = 1 x 1 x 1 mm]. The main task was collected

using a single echo planar imaging (EPI) run, with the following sequence parameters:

TR = 720 ms, TE = 37 ms, flip angle = 52°, voxel size = 2 x 2 x 2 mm; these same

parameters were used for the preview task EPI sequence.

We carried out standard preprocessing using FMRIB Software Library (FSL

version 5.0.8; Jenkinson, Beckmann, Behrens, Woolrich, & Smith, 2012), which included

brain extraction, motion correction[1], prewhitening, high-pass temporal filtering with

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[1] Average absolute (mean = 0.57 mm) and relative (mean = 0.09 mm) head
displacement.

sigma of 50s, spatial smoothing with a 6 mm FWHM Gaussian kernel, and spatial

normalization and linear registration to the Montreal Neurological Institute (MNI) 152

standard brain. We also employed FSL's topup functionality to correct susceptibility

induced distortions. This entailed collecting additional reverse phase-encoded EPI

sequences to yield two pairs of images with distortions going in opposite directions (one

pair for the main task and one for the Preview Task). The susceptibility-induced off-

resonance field was estimated from these pairs using a method similar to that described in

Andersson et al. (2003). The images were then combined into a single corrected one.

Deliberation and Consumption General Linear Models

Functional data from both tasks were first analyzed using a general linear model

(GLM) approach using the fMRI Expert Analysis Tool (FEAT) within FSL. We modeled

the main task data using five events: skip choice, stay choice, delay, video

viewing/rating, and travel time (i.e., cost phase); we did not separate the viewing and

rating components of the trial, as rating typically occurred quickly (~ 1 second) and we

intended to capture evaluative processes that occurred post-consumption. The model also

included the six standard motion parameters as confound regressors. Our analyses

focused on the two choice events (i.e., *deliberation*) and the video viewing/rating event

(i.e., *consumption*). The events were convolved using a double-gamma hemodynamic

response function (HRF).

We carried out group-level whole-brain analyses using the voxelwise general

linear model (GLM) analysis in FEAT. In terms of main effects, we examined activation

related to making a skip choice (skip choice > 0), making a stay choice (stay choice > 0), and consuming a video (video viewing/rating > 0). We then assessed the extent to which deliberation and consumption evoked comparable neural substrates, given our hypothesis that the imagination of future rewards at the choice point would yield a similar activation pattern as compared to actual reward consumption. Lastly, we evaluated differences between choices and video viewing (i.e., choice > video viewing and choice < video viewing); we only included stay choices, as videos were not consumed on skip trials and we aimed to compare activation during future projections of and receipt of that reward.

For the preview task, we modeled the video viewing and rating for each category as separate events (yielding four regressors of interest), as well as the 6 standard motion parameters as confound regressors. The events were again convolved using a double-gamma HRF. A threshold of $z > 3.09$ and whole-brain corrected cluster extent threshold of $p < 0.01$ were used for all group-level analyses.

Decoding Methods

We used a multi-voxel pattern analysis (MVPA) decoding method, as MVPA methods offer a unique approach for probing episodic memory in humans (Chadwick, Hassabis, Weiskopf, & Maguire, 2010), and are useful for identifying category-specific representations (Norman, Polyn, Detre, & Haxby, 2006). In particular, we employed the Sparse Multinomial Logistic Regression (SMLR; Krishnapuram, Carin, Figueiredo, & Hartemink, 2005) classifier available in the PyMVPA machine-learning package (Multivariate Pattern Analysis in Python, http://www.pymvpa.org; Hanke et al., 2009). We selected this classifier given its computational efficiency and good classification

performance (Krishnapuram et al., 2005; Sun et al., 2009). The SMLR classifier utilizes

multiple regression to predict the logarithm of the odds ratio of belonging to a particular

class. This ratio is then transformed into a probability via a nonlinear transfer function

that ensures all classification probabilities summate to one. The sparse component

promotes a more parsimonious and generalizable solution. For the present analyses we

used the default lambda penalty setting ($\lambda = 1$).

Decoding was conducted on a subject-by-subject basis, and included the

previously pre-processed data to parallel the GLM analyses described above. For all

decoding analyses, we trained the classifier on the Preview Task data. We used the this

approach for several reasons: (1) each subject saw the same set of videos during the

Preview Task,[2] (2) the Preview Task contained trials from every category (whereas

subjects could elect to skip all videos from a category during the main task), and (3) we

did not have to create a 'holdout' set from the main task data. The first step in this

process entailed fitting a GLM to obtain linear model activity estimate images (i.e.,

parameter estimates), which were then supplied as examples to the classifier. Each video

category was modeled as a separate event, and we also included a regressor to account for

the fixation periods between the videos; this event was considered the *other* category, and

provided a baseline from which to compare the four video categories. Samples were

'chunked' to create groups of samples, each of which included two video samples from

each category, as well as the fixation periods between those samples. Chunks are

important given that successive fMRI volumes cannot be considered independent samples

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[2] The first three subjects were excluded from this analysis as they completed a
version of the Preview Task with half the number of trials; this resulted in a sample
of N=22.

due to the forward contamination of the hemodynamic response. This meant that all trials in a given loop (or complete pass through all four categories) were included in the same chunk, as well as four trials from a different loop. We averaged two samples per category when forming chunks, as this approach produces less noisy examples (Pereira et al., 2009). After fitting the model, we z-scored the data with respect to the *other* condition, with scaling done separately for each chunk.[3]

As a preliminary step, we determined whether stimuli from the four categories were distinguishable via SMLR decoding, as the subsequent analyses hinged on successful category separation. We performed 60/40 cross-validation, i.e., left two chunks out, on the Preview Task parameter estimate maps.[4] For the main decoding analyses we used the Preview Task maps to classify neural data during deliberation and consumption. Similarly, we averaged two (or three) samples per category to form the testing set examples. For each testing set example, we fit a GLM to acquire a parameter estimate map; this allowed a direct comparison with training data. We then predicted which category the testing example best represented (i.e., kittens, dance, landscape, bike accidents, or other), and extracted the corresponding probability estimates (one per category). The data in these analyses were masked based on the group-level GLM results.

The final step entailed combining the subject-specific data and re-organizing the probabilities according to the subjects' location within loop (i.e., *previous, current, next, opposite,* or *other* zone) as opposed to the specific category; this approach was used to test whether voxel patterns tracked past, current, or future representations as the subject

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[3] This supports the independence of the chunks and prevents a single outlier chunk from dragging down the global mean.

[4] Two chunks constituted 40% of the data, as the Preview Task was separated into five chunks total.

traversed the task. We used mixed-effects linear models to compare probabilities between the zones; specifically, we regressed zone location on the SMLR probabilities, with subject as a random effect. Models were fit using the MCMCglmm package in R, which employs Markov chain Monte Carlo techniques (Hadfield, 2010; RStudio Team, 2016). We then used the lsmeans packages to determine which zones had probabilities above chance, i.e., $1/5 = 0.20$, when accounting for the five zones.

Deliberation and Consumption Decoding Analyses

Two task-derived and three network-based masks were used for decoding: (1) the cumulative Preview Task mask, (2) the deliberation and consumption overlap mask, (3) a DMN mask, (4) a salience network mask, and (5) a right fronto-parietal control network mask. The network masks were derived using Independent Components Analysis (Abram et al., 2015), and selected given their roles in imagination and deliberation. The DMN map included the medial prefrontal cortex (mPFC), posterior cingulate cortex (PCC), precuneus, and bilateral angular gyrus. The salience network map included the anterior cingulate cortex (ACC) and bilateral anterior insula. The fronto-parietal network map included the right middle frontal gyrus (MFG) extending into the frontal pole, right angular gyrus, and paracingulate gyrus. Decoding was carried out during the choice and video phases of the main task using each of the five masks.

Decoding Accuracy versus Validity Correlation Analyses

As a follow-up to the decoding analyses, we asked whether one's neural representation abilities during deliberation related to their overall decision-making capacity. Using robust regression methods, we correlated deliberation decoding

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accuracies with the average rating validity correlations (i.e., correlations between delay thresholds [*revealed* preferences] and average category ratings [*stated* preferences]). This was done separately for accuracies obtained for each of the five masks, with a Bonferonni correction for multiple comparisons (i.e., $p = 0.05/5 = 0.01$).

We used the average rating validity correlations instead of the post-test ranking validity correlations for two reasons: (1) multiple observations comprised each average rating, lending to better psychometric properties, and (2) ratings occurred immediately after reward consumption on a trial-by-trial basis, which was more akin to our computation of the delay threshold metric.

VTE General Linear Model

A final GLM was used to pinpoint activation related to difficult choices. This model included four regressors (choice, delay, video viewing/rating, and travel), as well as the six standard motion parameters. We weighted each decision and video-viewing event by its distance from the respective category threshold, such that events closer to threshold were weighted more heavily. Importantly, decisions in this model were isolated to the last second of the choice phase. This step was taken given our observation that reaction times differed as a function of offer value.[5] Consistent with prior GLMs, events were convolved using a double-gamma HRF, and evaluated with a threshold of $z > 3.09$ and cluster extent threshold of $p < 0.01$.

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[5] Mixed-effects linear models demonstrated a positive association for skip reaction times and value ($\beta = 0.01$, $p < 0.001$), versus a negative association for stay reaction times and value ($\beta = -0.02$, $p < 0.001$).

3.3 Results

<u>Overlapping Activation during Deliberation and Consumption</u>

We first evaluated neural activation related to deliberation versus consumption. Our results revealed that stay and skip choices activated a similar set of regions, including the ACC, bilateral anterior insula, MFG, bilateral hippocampus, and lingual gyrus (Figure 3.1A), while consumption recruited a circuit including the anterior insula, superior temporal gyrus, hippocampus, amygdala, visual cortices, and other areas. But to what degree are regions recruited during reward consumption also involved in deliberating about those rewards? To address this question, we produced an intersection map to detect voxels that were common to skip choices, stay choices, and video viewing. The intersection map captured the majority of voxels recruited during deliberation, and roughly 50% of the voxels activated during consumption (Figure 3.1A).

Further, a contrast revealed that stay choices activated the ACC, anterior insula, lingual gyrus, MFG, and mPFC (Figure 3.1B) more than video viewing. These regions increased in activation during deliberation, versus a more nuanced pattern for consumption; in particular, consumption led to more activation in the insula and lingual gyrus, decreased activation in the MFG and mPFC, and no changes in the ACC (with large effect sizes for all comparisons). Additionally, video viewing recruited a large cluster in the superior temporal gyrus when contrasted with stay choices (number voxels = 837, $p < 0.001$; *not pictured*).

<u>Distinguishability of Reward Zones</u>

With regards to the Preview Task, we observed similar activation patterns

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across the video categories (Figure 3.2A); regions included the anterior insula,

hippocampus, ACC, lateral occipital cortex, and lingual gyrus. Further, comparing signal

changes across the categories revealed only trend-level differences ($F_{3,96} = 2.73$, $p = 0.05$;

Figure 3.2B).[6] Given the large overlap in activation across the categories during the

Preview Task, we created a cumulative mask for decoding that entailed merging the four

main effect maps. Decoding of the Preview Task data using the cumulative mask

revealed dissociable categories (Figure 3.2C): category-specific probabilities ranged from

about 60 to 85%, and the overall accuracy was 72%. Thus, reward stimuli were

distinguishable via decoding producing similar activation maps.

Evidence of Current and Future Representations during Deliberation

The first set of decoding analyses examined the extent to which task-related

activation patterns tracked a subject's location, i.e., reward zone, during deliberation and

consumption. Essentially, we asked whether the same voxels evoked during consumption

also represented our prediction of future rewards when making a choice. Decoding using

the cumulative Preview Task mask revealed representations of the *current* zone during

consumption (mean = 0.57, SE = 0.01; Figure 3.3A; Table 3.1A). In contrast, decoding

during deliberation revealed future representations of the *next* zone (mean = 0.25, SE =

0.01; Table 3.1B). We then restricted the decoding to voxels contained in the deliberation

and consumption overlap mask, as this included a subset of the cumulative Preview Task

mask (Figure 3.3B). Here we found that activation patterns during deliberation best

reflected the *current* (mean = 0.23, SE = 0.01; Table 3.1B) followed by the *next* zone

[6] Post-hoc Tukey HSD analyses revealed trend-level differences for bike accidents >
dance ($p = 0.08$) and bike accidents > landscapes ($p = 0.08$)

(mean = 0.21, SE = 0.01), while decoding during consumption again represented the *current* zone (mean = 0.52, SE = 0.01; Table 3.1A).

Large-Scale Brain Networks Track Past and Current Representations during Deliberation

While all three networks predicted the current zone during consumption (Figure 3.4A, Table 3.2A), decoding during deliberation provided evidence of past and current representations (Figure 3.4B; Table 3.2B). More specifically, voxels within the DMN best represented the *current* zone (mean = 0.24, SE = 0.013), whereas salience network representations best captured the *previous* and *current* zones (previous mean = 0.24, SE = 0.01; current mean = 0.24, SE = 0.01). In comparison, the right fronto-parietal network tracked all four zones similarly (previous mean = 0.22, SE = 0.01; current mean = 0.23, SE = 0.01; next mean = 0.23, SE = 0.01; opposite mean = 0.22, SE = 0.01).

Decoding Accuracy during Deliberation Predicts Optimized Decision-Making Behaviors

We found that greater decoding accuracy during deliberation predicted higher validity correlations, specifically for voxels within the deliberation and consumption overlap mask (Figure 3.5, $\beta = 0.47$, $p = 0.006$). Decoding accuracies using the other four masks did not predict the rating validity correlations (all $p > 0.10$; Supplemental Table 3.2A). We then tested whether this association was specific to deliberation-related representations, and found that decoding accuracy during consumption was unrelated to validity correlations for all five masks (all $p > 0.10$; Supplemental Table 3.2B).

Difficult Choices Parallel 'Vicarious Trial and Error' Behaviors in Rodents

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In the Restaurant Row task, VTE was observed when a rat received an offer at its threshold, and decreased substantially for offers above or below its threshold (measured as change in head position; Steiner and Redish, 2014). Behavioral analysis revealed an analogous pattern in humans: subjects took longer to make choices for offers that approached threshold, and were fastest for those significantly above or below threshold (Figure 3.6A); this suggests that offers around threshold were especially challenging.

Given these behavioral findings, we next investigated which brain areas were associated with difficult choices. As illustrated in Figure 3.6B, deliberation recruited the ACC, MFG, bilateral hippocampus, posterior cingulate cortex (PCC), and lingual gyrus. Similarly, video viewing evoked voxels within the ACC, hippocampus, and visuospatial areas, as well as bilateral portions of the orbitofrontal cortex, nucleus accumbens, amygdala, insula, and thalamus. An intersection mask revealed that difficult choices recruited the ACC, bilateral hippocampus, and visuospatial areas during both deliberation and consumption (Supplemental Figure 3.2).

As a last step, we contrasted choice and video viewing to determine the extent to which challenging decisions are associated with different brain structures at different points in the decision process. Here, we observed increased ACC and MFG activation during deliberation, versus increased OFC and posterior insula activation during consumption (Figure 3.6C).

3.4 Discussion

Recent theories posit that humans engage in episodic future thinking during deliberation (Buckner & Carroll, 2007; Gilbert & Wilson, 2007; Kurth-Nelson et al.,

2012; Schacter & Addis, 2011). This entails imagining rich and concrete future

representations (Redish, 2016). Using the Web-Surf Task, a sequential foraging paradigm

that entails real-time costs and rewards, we discovered a set of human deliberation

mechanisms indicative of episodic memory *and* episodic future thinking. The sequential

nature of this task uniquely allowed us to track past outcomes and future possibilities:

humans cycled between four video galleries that appeared in a constant order, but varied

trial-to-trial with regards to the specific delay. Subjects developed a schema of the task

that guided deliberation, e.g., "if I skip this kitten video, the upcoming dance video might

have a shorter wait time." We used multi-voxel pattern analysis decoding methods to

uncover categorical representations within large-scale brain networks. Our results

revealed that during deliberation, subjects imagined past and future possibilities within

different parts of the brain; moreover, those who were better at imagining future

prospects performed better on the task. We also assessed for evidence of 'vicarious trial

and error' (VTE) in humans, as this behavior is linked to deliberation via future thinking

in rats (Johnson & Redish, 2007). Humans exhibited behavioral and neural similarities to

rats during challenging decisions, suggesting a common mechanism across species.

Consistent with the fMRI literature on human imagination, our data indicated that

overlapping systems were activated for imagined and experienced outcomes. That is, we

observed similar activation during deliberation and reward consumption. This

deliberation and consumption circuit mapped onto the 'dorsal attention network' that

includes the frontal eye fields, supplementary motor area, superior parietal lobule, and

intra-parietal sulcus (Corbetta & Shulman, 2002; Fox et al., 2005). This network is

implicated in externally direct cognition like visuospatial planning and attention

(Spreng, Stevens, Chamberlain, Gilmore, & Schacter, 2010), and activates in response to visual search and detection tasks (Corbetta & Shulman, 2002; Shulman, 2003). For instance, the dorsal attention network is recruited during the Tower of London task, which involves mentally simulating a series of future actions (Nitschke, Kostering, Finkel, Weiller, & Kaller, 2017). With regards to the current study, this network may underlie the visual construction of future outcomes during deliberation. This notion aligns with our decoding findings that indicated current and future representations were captured using masks containing portions of the dorsal attention network (i.e., Preview Task and deliberation and consumption overlap masks).

Comparable to the neural commonalities detected across real and imagined prospects, simulating future and recalling past events may recruit the same brain areas, particularly the hippocampus and parahippocampal cortex (Schacter & Addis, 2011). The hippocampus and surrounding medial temporal lobe structures are critical to imagining future events (Hassabis et al., 2007; Lebreton et al., 2013; Peters & Büchel, 2010a), and may allow us to evaluate future outcomes via mental simulation (Johnson & Redish, 2007; Johnson et al., 2007). Our decoding analyses using hippocampus-containing networks revealed representations of the upcoming offer and next zone during deliberation. This suggests that the hippocampus, in conjunction with the dorsal attention network, supported the imagination of future possibilities.

We also examined neural decoding patterns within other relevant decision-making networks. The default mode network (DMN) revealed representations of the current zone during deliberation. This network is involved in self-referential and internally driven cognition. Core DMN structures like the medial prefrontal cortex (mPFC), precuneus,

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and posterior cingulate cortex are involved in autobiographical memory and prospection (Spreng et al., 2009). The mPFC, in particular, is found to code subjective value, to integrate multiple factors for complex decisions, and to simulate how a future event might feel (Benoit, Szpunar, & Schacter, 2014; Peters & Büchel, 2010b). With respect to our findings, DMN voxels may simulate the affective qualities of an upcoming event by integrating relevant autobiographical and value information. In comparison, voxels within the salience network represented past outcomes and current options. This network, which includes the anterior cingulate cortex (ACC) and anterior insula, detects behaviorally relevant stimuli to help guide behavior (Menon & Uddin, 2010; Seeley et al., 2007). The anterior insula is also critical to conscious interoceptive monitoring (Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004; Kurth, Zilles, Fox, Laird, & Eickhoff, 2010; Zaki, Davis, & Ochsner, 2012). It is then possible that the salience network coordinates information regarding recent experiences and available options to direct attention to salient stimuli; in turn, this could optimize goal-directed behaviors aimed to increase desirable and decrease undesirable outcomes. Lastly, we found that the right fronto-parietal network, which includes right-lateralized middle frontal gyrus (MFG) and parietal structures, captured representations of all four zones. This network is involved in initiating and adjusting control in response to feedback (Dosenbach et al., 2007; Dosenbach, Fair, Cohen, Schlaggar, & Petersen, 2008), spatial working memory (Ikkai & Curtis, 2011), and maintenance of object- and space-based attention (Scolari, Seidl-Rathkopf, & Kastner, 2015). In the current context, this network may support spatial attention and working memory by maintaining a broad representation of the task's layout.

A key finding revealed that one's ability to accurately imagine options when deliberating predicted how well that subject generally made choices that led to rewards that they liked. A recent theory by Kurth-Nelson et al. (2012) may explain this result: the authors propose that the evaluation of outcomes entails a search process that indicates which rewards are available in the future. The authors posit that expected value hinges on how easily one can find a reward, with more temporally distant rewards being harder to find and thus devalued. Within this framework, subjects with poorer neural representations may fail to project themselves into the future, which is necessary for evaluating potential outcomes. The specific network implicated in this finding included regions engaged in the dorsal attention network, as well as bilateral portions of the anterior insula and hippocampus. As noted previously, these areas may support deliberation given their roles in episodic future thinking, visuospatial planning, and interoceptive monitoring.

We also detected several cross-species parallels: First, reaction-time patterns in humans were analogous to rodent VTE behaviors during Restaurant Row, as indicated by longer reaction times on offers closer to threshold (i.e., more difficult choices; Steiner & Redish, 2014). Second, hippocampal activation scaled with choice difficulty during deliberation and consumption. In rodents, VTE occurs during deliberation and entails forward-hippocampal sequences that alternate between options (Johnson & Redish, 2007). Taken together, VTE may represent a cross-species mechanism that underlies deliberation and prospection (Doll et al., 2015; Redish, 2016). In addition to the hippocampus, difficult choices recruited the ACC and MFG (including the dorsolateral prefrontal cortex [dlPFC]) more strongly during deliberation. These areas are

implicated in cognitive control and conflict monitoring, and might respond to the

uncertainty and error potential of difficult trials (Botvinick, Cohen, & Carter, 2004;

MacDonald, 2000); previous research also implicates the ACC in decision difficultly

during a foraging task (Shenhav et al., 2014). Moreover, the MFG is theorized to initiate

VTE (Redish, 2016). This follows from rodent findings that disrupting hippocampal

representations actually increases VTE, making the hippocampus an unlikely candidate

for initiating the VTE process (Bett, Murdoch, Wood, & Dudchenko, 2015; Robbe et al.,

2006). Instead, the rodent prelimbic cortex, arguably homologous to the human dlPFC,

might initiate this process, given its role in outcome-dependent decisions and influence

on goal-directed activity in the hippocampus (Dalley, Cardinal, & Robbins, 2004; Ito,

Zhang, Witter, Moser, & Moser, 2015; Killcross & Coutureau, 2003; Sharpe & Killcross,

2015; Spellman et al., 2015). Findings from the nonhuman primate literature that the

dlPFC generates action plans prior to action execution further support this theory

(Mushiake, Saito, Sakamoto, Itoyama, & Tanji, 2006; Saito, Mushiake, Sakamoto,

Itoyama, & Tanji, 2005). Compared to deliberation, consumption led to more activation

in the lateral orbitofrontal cortex (OFC) for difficult trials. This is also consistent with the

rodent literature, which notes the OFC's role in post-decisional outcome evaluation

(Steiner & Redish, 2012; Stott & Redish, 2014).

One proposed distinction between real and imagined events is that imagined

events are often *comparative* while actual experiences are not (Gilbert & Wilson, 2009).

For example, students who imagined that they received a low grade predicted that they

would feel worse if they expected a high grade than if they expected a low grade;

however, students felt badly regardless of their expectation (Golub, Gilbert, & Wilson,

2009). This suggests that prospects contain comparative features that do not necessarily impact our reaction to the real experience. Our decoding results tell a similar story. We found that different neural systems represented different zones when making a choice, whereas all neural systems represented the current zone during reward receipt. This suggests that comparative processes were critical to deliberation but not consumption. Perhaps during consumption, the actual experience of the current reward is much more salient than the experience one is not having (in this case the alternative options), thus rendering comparisons less likely (Gilbert & Wilson, 2009).

Conclusions

The current study employed a sequential experiential foraging paradigm to evaluate human deliberation. Our results indicated that different neural systems tracked past and future outcomes during the choice phase, while these systems always represented the current offer during reward receipt. Moreover, the capacity to represent outcomes during deliberation predicted overall decision-making abilities on this task. Lastly, with regards to cross-species parallels, humans demonstrated comparable behavioral and neural signatures of VTE, which could suggest a common mechanism that translates across humans and rodents.

3.5 Figures and Tables

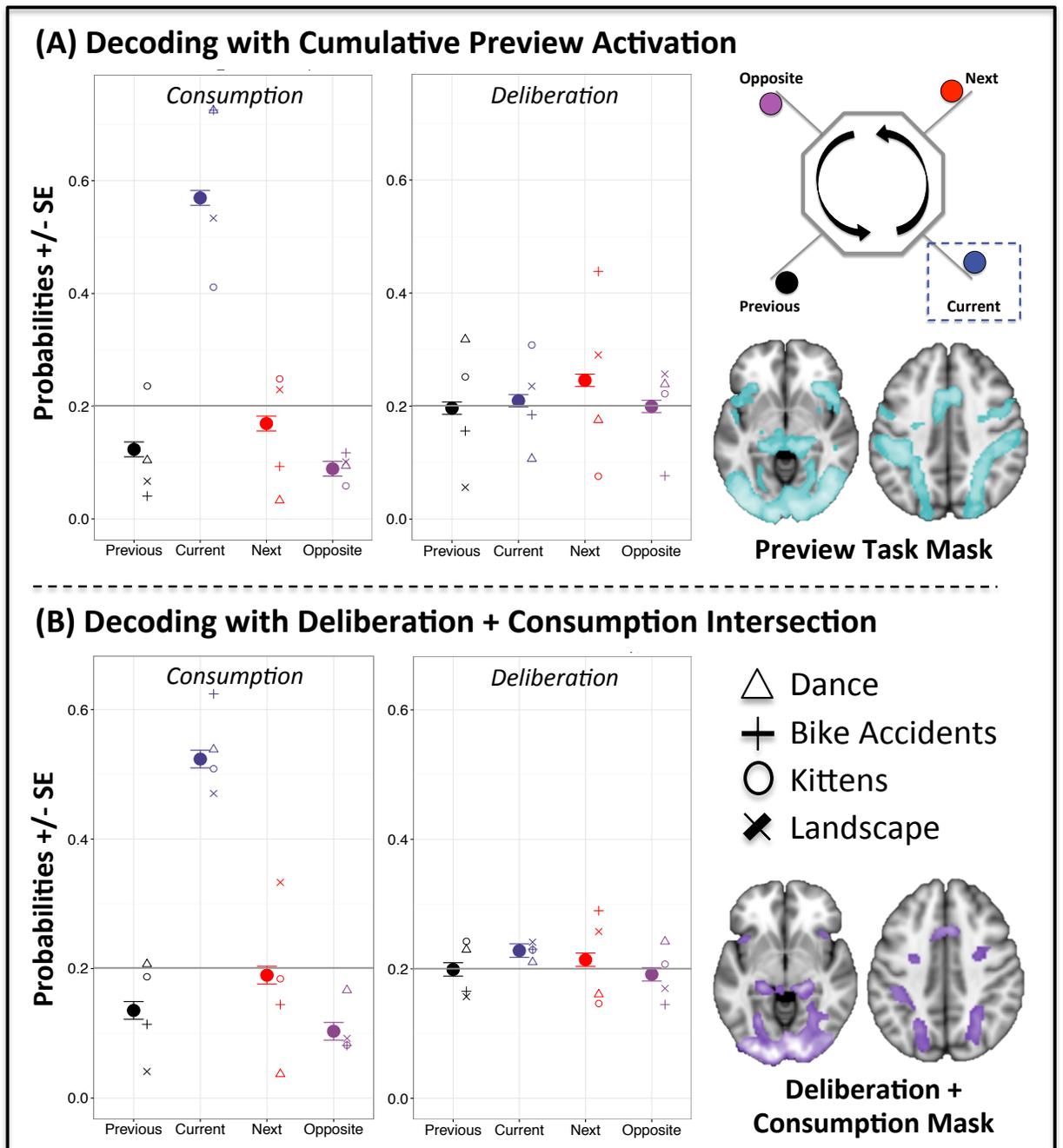**Figure 3.1.** Deliberation versus Consumption Neural Activation
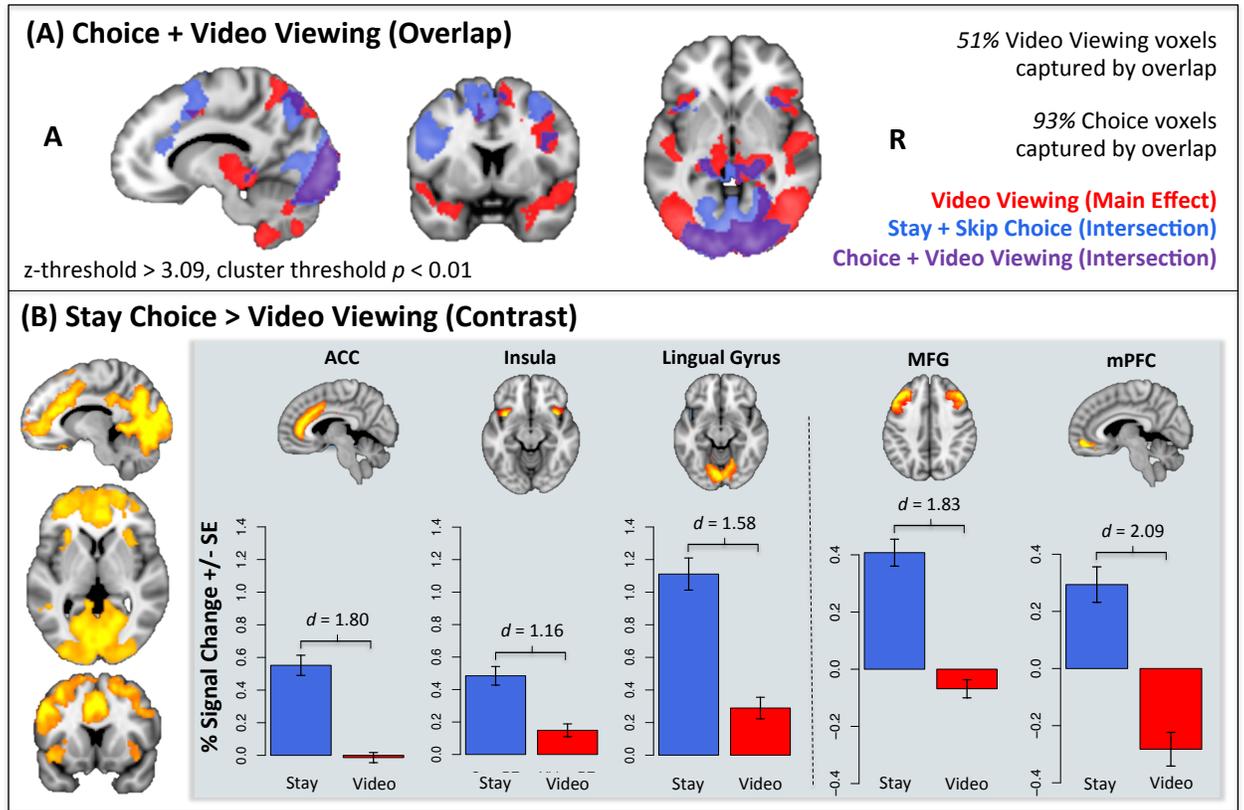
(A) Main effects of deliberation (*light blue*) and consumption (*red*) from the main task. Choices and video viewing events recruit an overlapping set of regions (*purple*). (2) When compared to video viewing, stay choices more strongly activate voxels in several cognitive and sensory areas.

Figure 3.2. Preview Task Neural Activation and Decoding
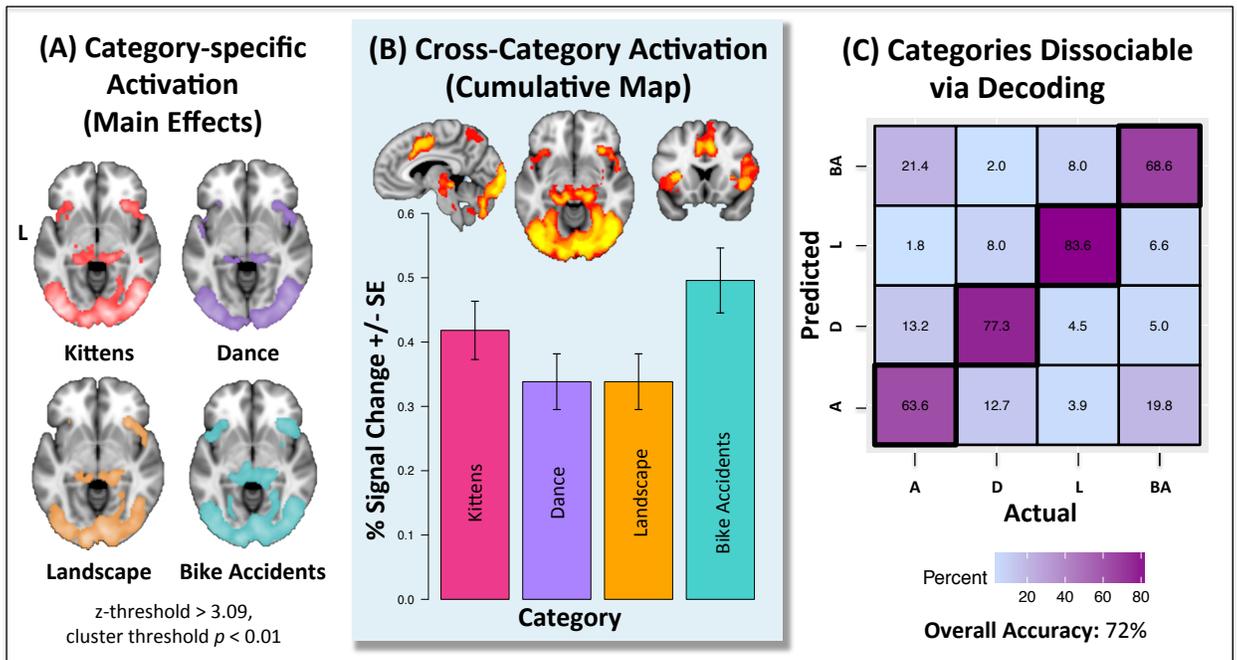

(A) Main effects of each video category during the Preview Task. (B) Minimal activation differences across categories. (C) Despite activation similarities, the four categories were dissociable using decoding methods.

Figure 3.3. Evidence of Current and Future Representations during Deliberation

(A) Decoding using cumulative Preview Task activation mask indicated current representations during consumption versus future (*next*) representations during deliberation. (B) Decoding using the deliberation and consumption intersection mask, indicated current representations for consumption versus current and future representations during deliberation. Error bars reflect within-subject standard errors.

Figure 3.4. Large-scale Brain Networks Track Past and Future Representations
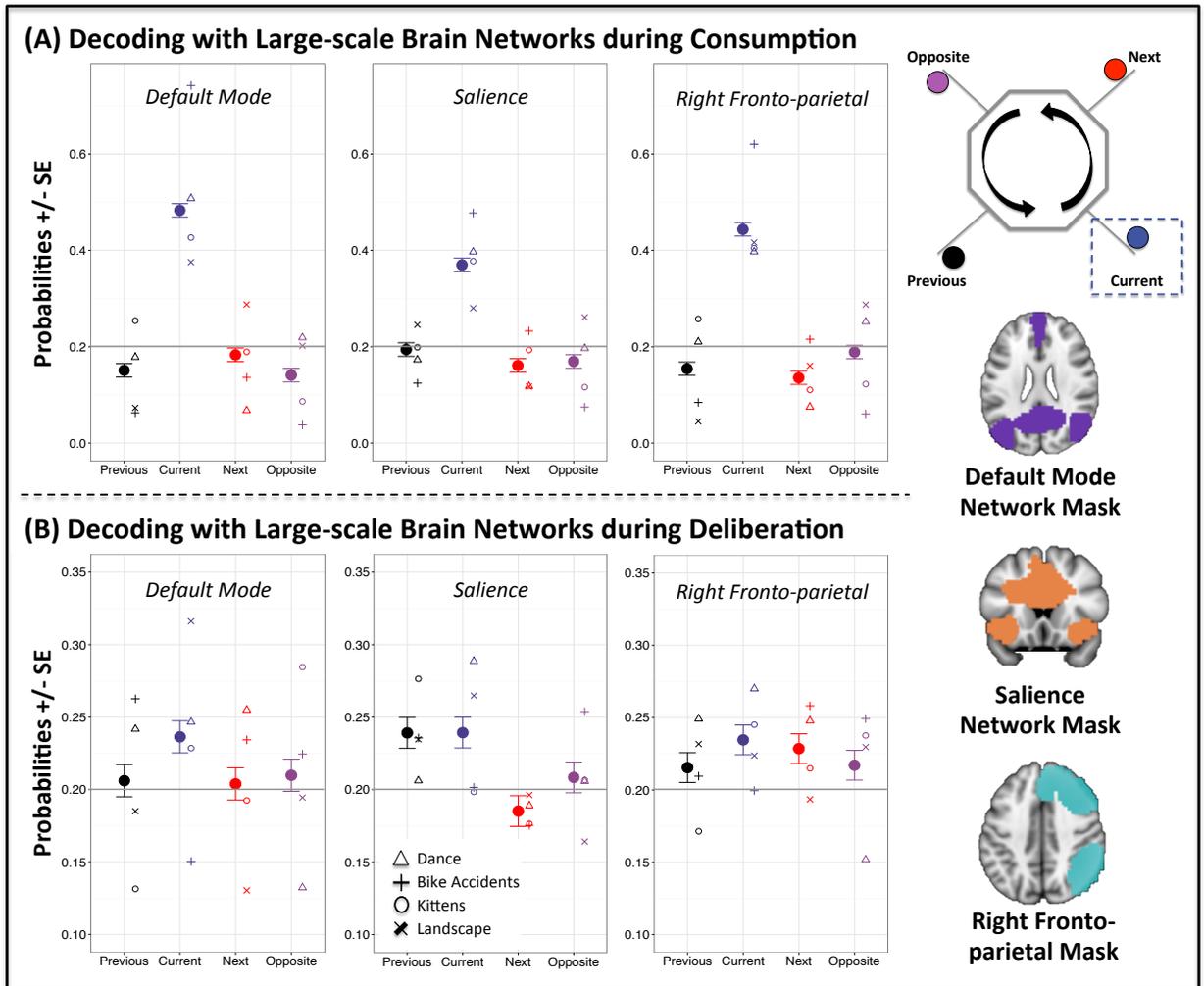
(A) Decoding using three network-based masks (i.e., default mode, salient, and front-parietal networks) represent the current category during consumption. (B) These same networks track different representations during deliberation. Specifically, the default mode network represents the current zone, whereas the salience network tracks the past (*previous*) and current zones, and the right fronto-parietal network represents all zones greater than chance.

Figure 3.5. Decoding Accuracy during Deliberation Predicts Decision-making
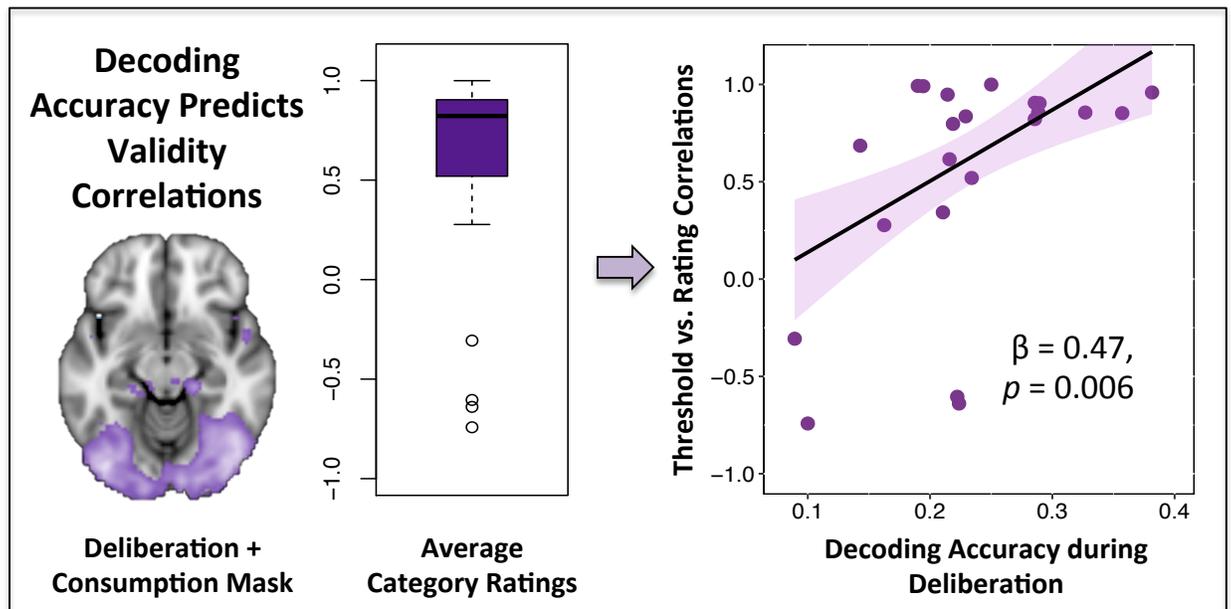
Higher decoding accuracies during deliberation (for the deliberation and consumption mask) positively correlated with rating validity correlations, i.e., correlation between delay thresholds and average category ratings.

Figure 3.6. Neural and Behavioral Evidence of 'Vicarious Trial-and-Error'
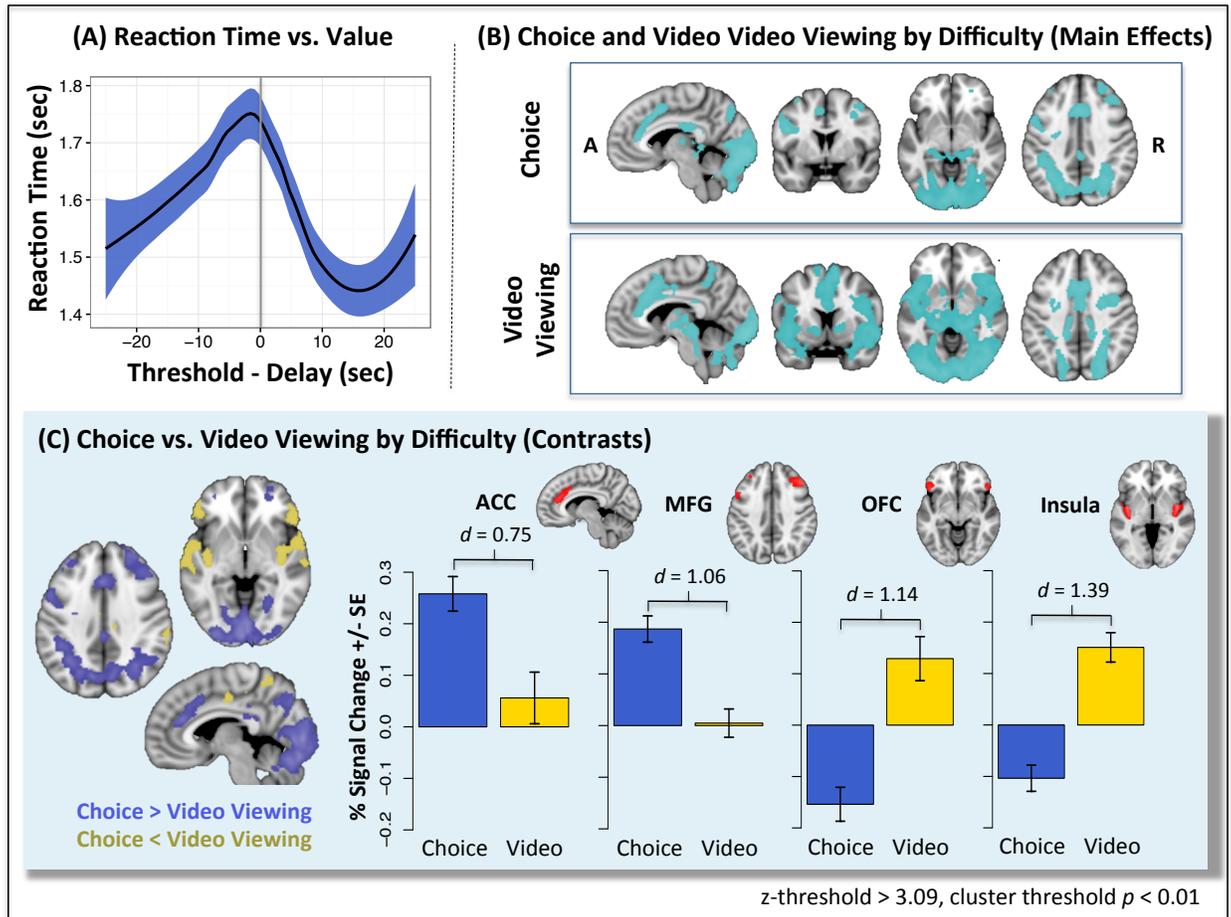
(A) Subjects were slowest to make a decision for offers closer to threshold (indicated by vertical line at 0). (B) Activation related to difficult choices during deliberation (*top*) and consumption (*bottom*). (C) Contrasts reveal which cognitive and sensory areas are associated with difficult choices during deliberation versus consumption.

Table 3.1A. Consumption Decoding using Task-based Masks

Zone Comparisons	B	CI	*P*-value
Preview Task Mask			
Current > Previous	-.45	[-.48, -.41]	**<.001**
Current > Next	-.34	[-.44, -.37]	**<.001**
Current > Opposite	-.48	[-.52, -.45]	**<.001**
Deliberation + Consumption Mask			
Current > Previous	-.39	[-.43, -.35]	**<.001**
Current > Next	-.33	[-.37, -.30]	**<.001**
Current > Opposite	-.42	[-.26, -.38]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Table 3.1B. Deliberation Decoding using Task-based Masks

Zone Comparisons	B	CI	*P*-value
Preview Task Mask			
Next > Previous	-.05	[-.08, -.02]	**.002**
Next > Current	-.04	[-.06, -.01]	**.01**
Next > Opposite	-.05	[-.08, -.02]	**.002**
Deliberation + Consumption Mask			
Current > Previous	-.03	[-.06, .00]	**.03**
Current > Next	-.01	[-.04, .01]	.32
Current > Opposite	-.04	[-.06, -.01]	**.006**

B: unstandardized coefficient; **CI:** confidence interval.

Table 3.2A. Consumption Decoding using Large-scale Network Masks

Zone Comparisons	B	CI	*P*-value
Default Mode Network			
Current > Previous	-.33	[-.37, -.30]	**<.001**
Current > Next	-.30	[-.34, -.26]	**<.001**
Current > Opposite	-.34	[-.38, -.30]	**<.001**
Salience Network			
Current > Previous	-.18	[-.21, -.14]	**<.001**
Current > Next	-.21	[-.25, -.17]	**<.001**
Current > Opposite	-.20	[-.24, -.16]	**<.001**
Right Fronto-parietal Network			
Current > Previous	-.29	[-.33, -.25]	**<.001**
Current > Next	-.31	[-.35, -.27]	**<.001**
Current > Opposite	-.25	[-.30, -.22]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Table 3.2B. Deliberation Decoding using Large-scale Network Masks

Zone Comparisons	B	CI	*P*-value
Default Mode Network			
Current > Previous	-.03	[-.06, .00]	**.04**
Current > Next	-.03	[-.06, -.01]	**.02**
Current > Opposite	-.03	[-.05, .00]	.06
Salience Network			
Current > Previous	.00	[-.03, .03]	.99
Current > Next	-.05	[-.09, -.02]	**<.001**
Current > Opposite	-.03	[-.06, -.01]	**.03**
Right Fronto-parietal Network			
Current > Previous	-.02	[-.05, -.01]	.19
Current > Next	-.01	[-.03, -.02]	.67
Current > Opposite	-.02	[-.05, .01]	.21

B: unstandardized coefficient; **CI:** confidence interval.

3.6 Supplemental Materials

<u>Validity Analyses</u>

Choice behaviors conformed to a sigmoid pattern, where subjects typically accepted offers above threshold (i.e., 0), and declined those below threshold (Supplemental Figure 3.3A). This suggests our threshold metric was a good indicator of decision behaviors. Comparable to the previous studies, we correlated the four category thresholds with average category ratings and post-test category rankings separately. We found that 76% of the average rating correlations were above 0.5 and 88% of the post-test ranking correlations were above 0.5 (Supplemental Figure 3.3B). These values are well within the range of prior reports (Abram et al., 2016).

<u>Decoding using Preview Task Residual Mask</u>

Given the commonalities between the two task-derived decoding masks, we produced an additional Preview Task residual mask that excluded voxels contained in the deliberation and consumption overlap mask (Supplemental Figure 3.4A). Using this mask we most strongly detected future representations of the *next* zone during deliberation (mean = 0.25, SE = 0.01), versus representations of the *current* zone during consumption (mean = 0.53, SE = 0.01; Supplemental Figure 3.4B; Supplemental Tables 3.1A and 3.1B). This suggests the areas unique to activation during reward receipt are particularly pertinent to future projections.

<u>Value General Linear Models</u>

We were also interested in whether similar neural structures were evoked when

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evaluating an offer at the choice point versus reflecting on the experience of that reward after consumption. To this end, we constructed three GLMs to assess activation related to value (i.e., threshold – delay) and likability ratings: the first weighted choice and consumption events by value, the second by average category rating, and the third by the actual rating. The first two models included four regressors (choice, delay, video viewing/rating, and travel), and the six standard motion parameters. For the decision value model, we weighted each choice and video viewing event by the offer value for that trial; this meant that trials with delays further below the threshold were weighted more highly. For the average rating model, we weighted choice and video-viewing events by the average rating for that category. This allowed us to model both stay and skip trials in the decision phase, given that skip trials did not have an associated rating. Both models isolated the last decision for the choice regressor, and the first second of the rating for the video viewing/rating regressor (i.e., each event was approximately 5-sec as the video viewing portion was 4-sec). This approach was taken given correspondence between value and choice reaction times (see Methods, *VTE General Linear Model*), as well as correspondence between ratings and rating reaction times.[7]

Lastly, the actual rating model included five regressors, with skip and stay included as separate regressors, along with the six motion parameter regressors. Only stay choice and video viewing events were weighted by the corresponding rating. We again isolated stay choice events to the last second, and video viewing/rating events to that first second.

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[7] Mixed-effects linear models demonstrated a negative association for ratings and rating reaction times ($\beta = -0.08$, $p < 0.001$), suggesting subjects took longer to make lower ratings.

As shown in Supplemental Figure 3.5, the value systems recruited similar neural structures, such as the ACC, MFG, and lingual gyrus. Contrasts revealed greater activation during deliberation than consumption for trials weighted by value (Supplemental Figure 3.5A) and average rating (Supplemental Figure 3.5B); more specifically, this model demonstrated increased activation in the ACC, mPFC, and MFG (*not pictured*) during deliberation, versus deactivation in these areas during consumption. The average rating-weighted model similarly demonstrated increased activation during choice in the ACC and MFG, although the ACC did not deactivate during consumption as found in the value-weighted model. It is possible that the value metric captures evaluative processes most critical to the decision phase, hence scaling with deactivation in reward valuation areas during consumption. In contrast, the rating metric may hold value during both deliberation (e.g., "how much do I typically like kitten videos?") and consumption (e.g., "how much did I enjoy that kitten video?") phases; this could account for the fact that the valuation neural structures often showed less but not decreasing activation during consumption (most evidence in Supplemental Figure 3.6B, which depicts the actual ratings). We also note that for all three of the value models, only the decision greater than video viewing contrast was significant. This could suggest that, in general, valuation systems are more strongly engaged when making a decision than passively consuming a reward.

Supplemental Figure 3.1. MRI Web-Surf Task Layout and Flow-diagram
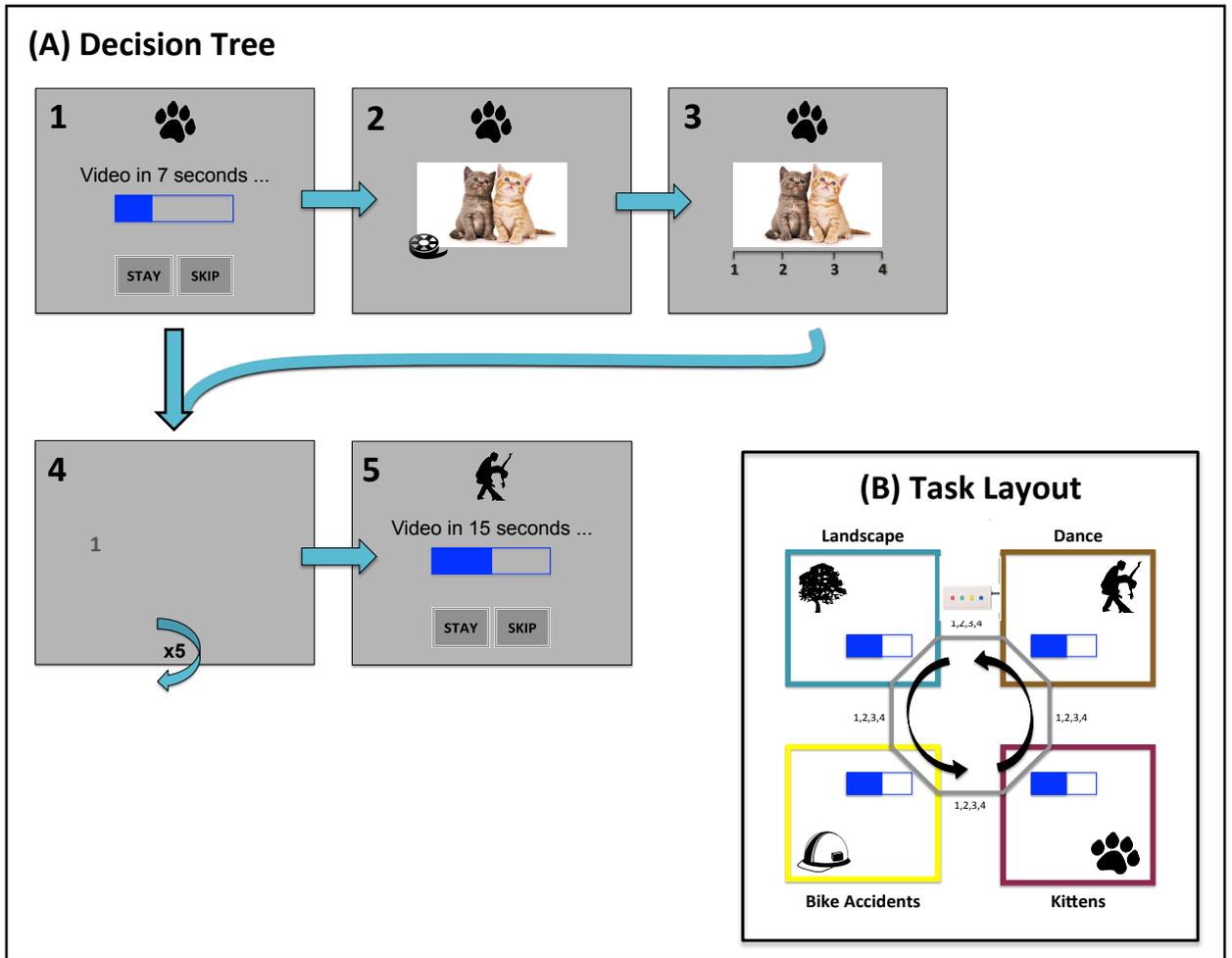
(A) Flow diagram illustrates differences between a stay and skip trial. If the subject stays (1), they wait through the delay, view the 4-sec video clip (2), and rate the video (3). If they instead choose to skip, they proceed through the cost phase (4), and arrive at the next offer (5). (B) Schematic of Web-Surf Task. Subjects had 35 minutes to cycle between the four video galleries in the depicted order.

Supplemental Figure 3.2. Deliberation + Consumption Overlap for Difficult Choices
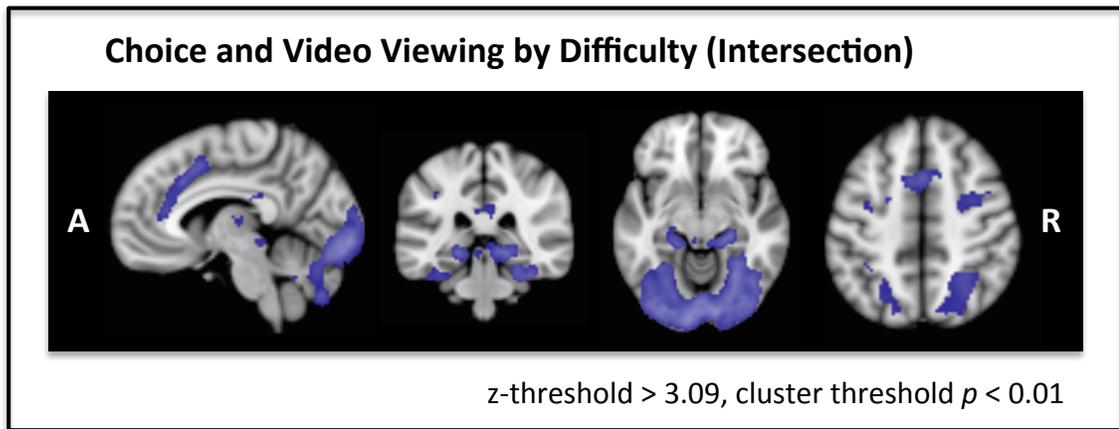
Difficult decisions recruit overlapping areas during the choice and video viewing phases.

Supplemental Figure 3.3. Task Validity
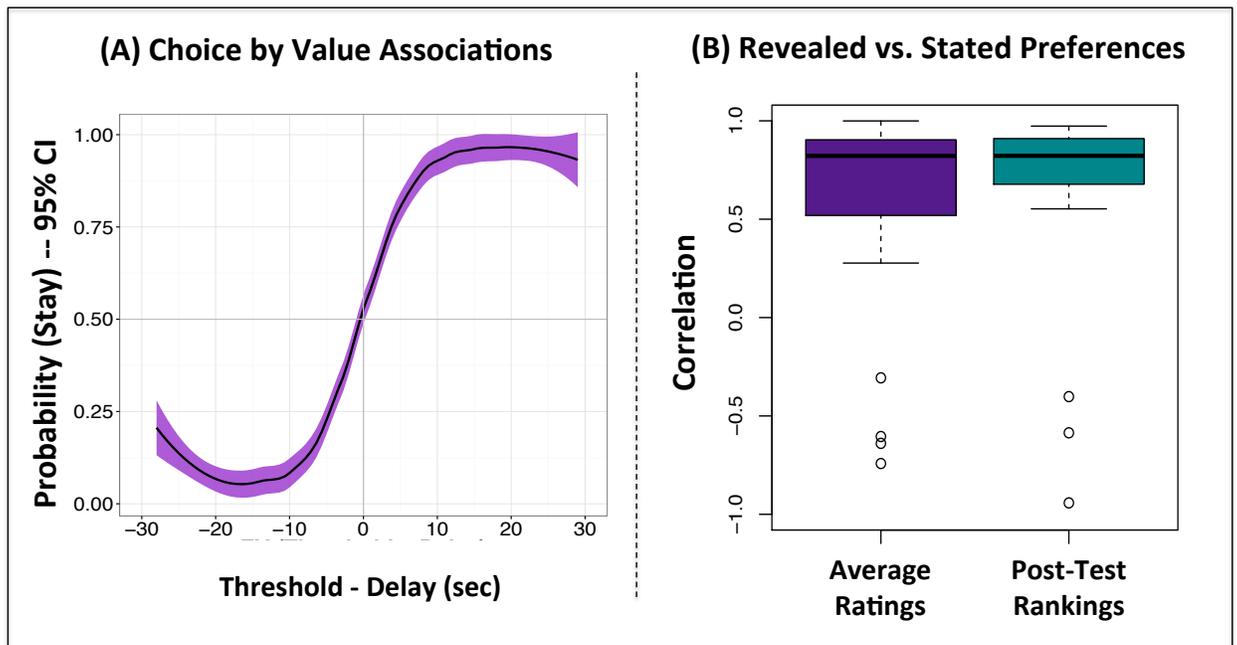
(A) Choice pattern conformed to a sigmoid shape, suggesting that subjects typically declined low-valued offers (i.e., left of the 0) and accepted high-valued offers (i.e., right of the 0). (B) Distribution of validity correlations that relate delay thresholds with average category ratings (*left*) and post-test category rankings (*right*).

Supplemental Figure 3.4. Evidence of Future Representations during Deliberation
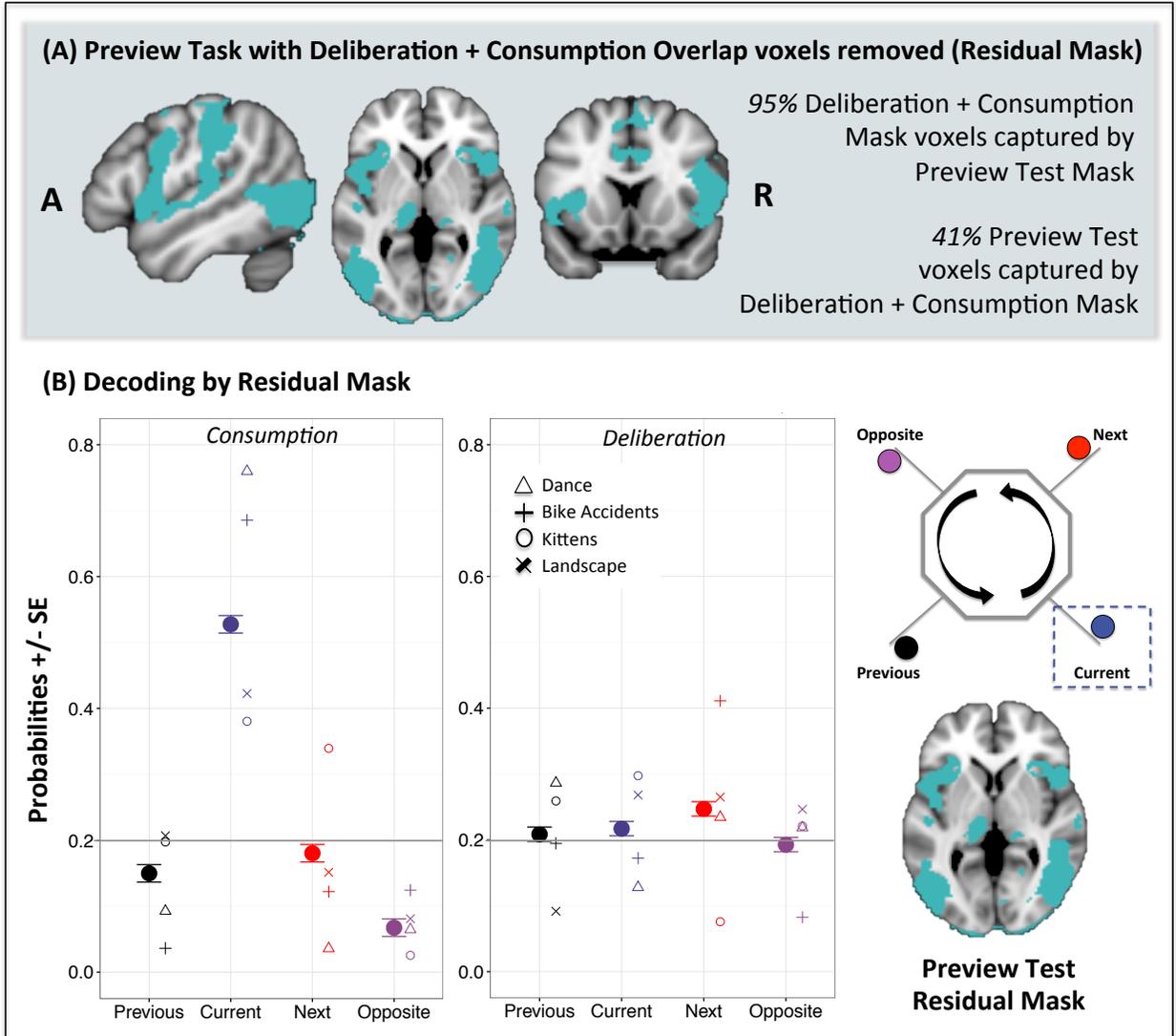
(A) Preview Task residual mask excluded voxels that were also contained in the deliberation and consumption overlap mask. (B) Decoding using the residual mask revealed current representations during consumptions versus the strongest representations of future (*next*) during deliberation.

Supplemental Figure 3.5. Value and Ratings Evoke Similar Neural Activation
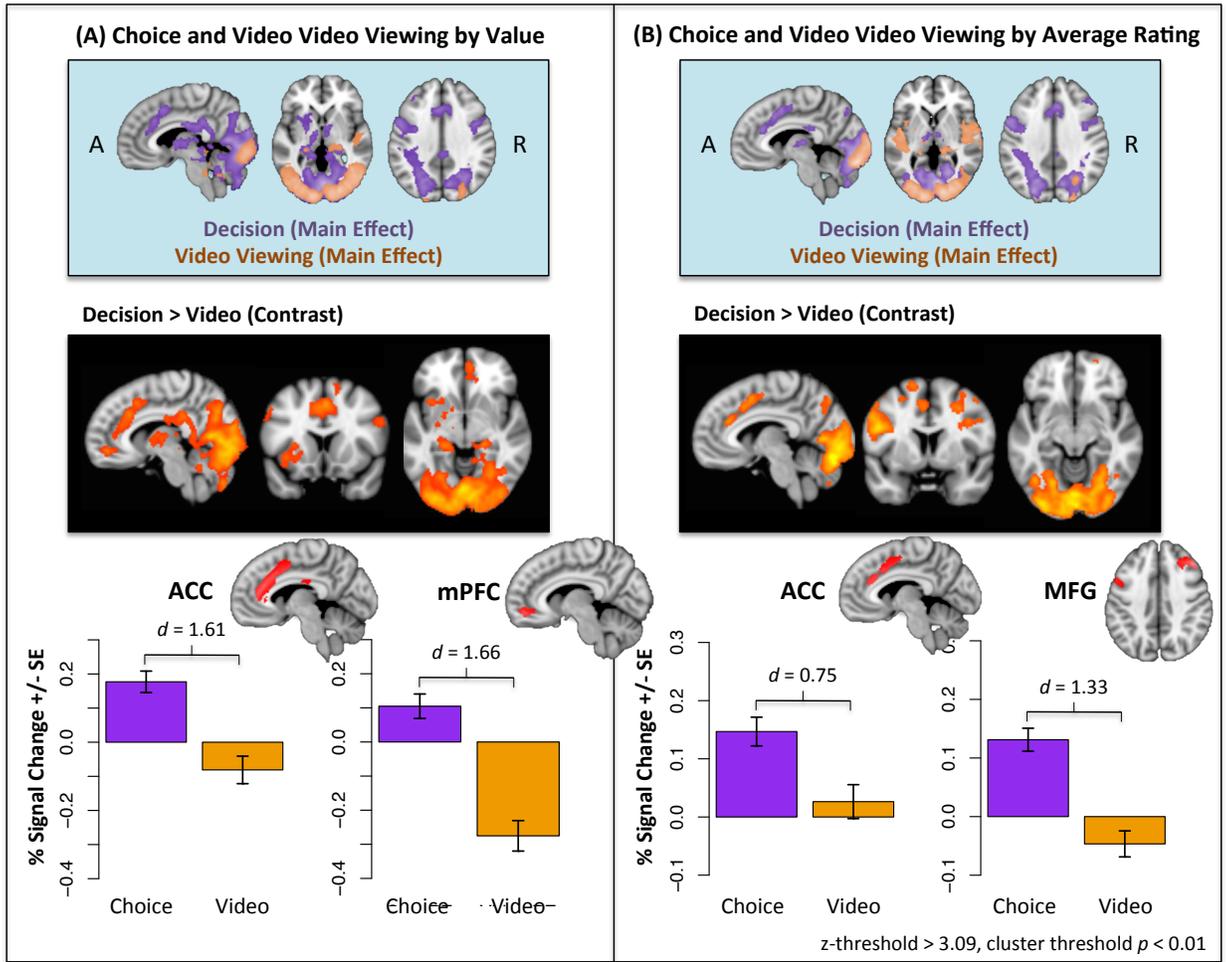
(A) Deliberation and consumption activation associated with higher valued offers. Choices more strongly activate frontal regions than video viewing. (B) Deliberation and consumption activated associated with higher average category ratings. A similar pattern emerged, with stronger activation in frontal regions for the choice phase.

Supplemental Figure 3.6. Neural Activation Driven by Actual Ratings
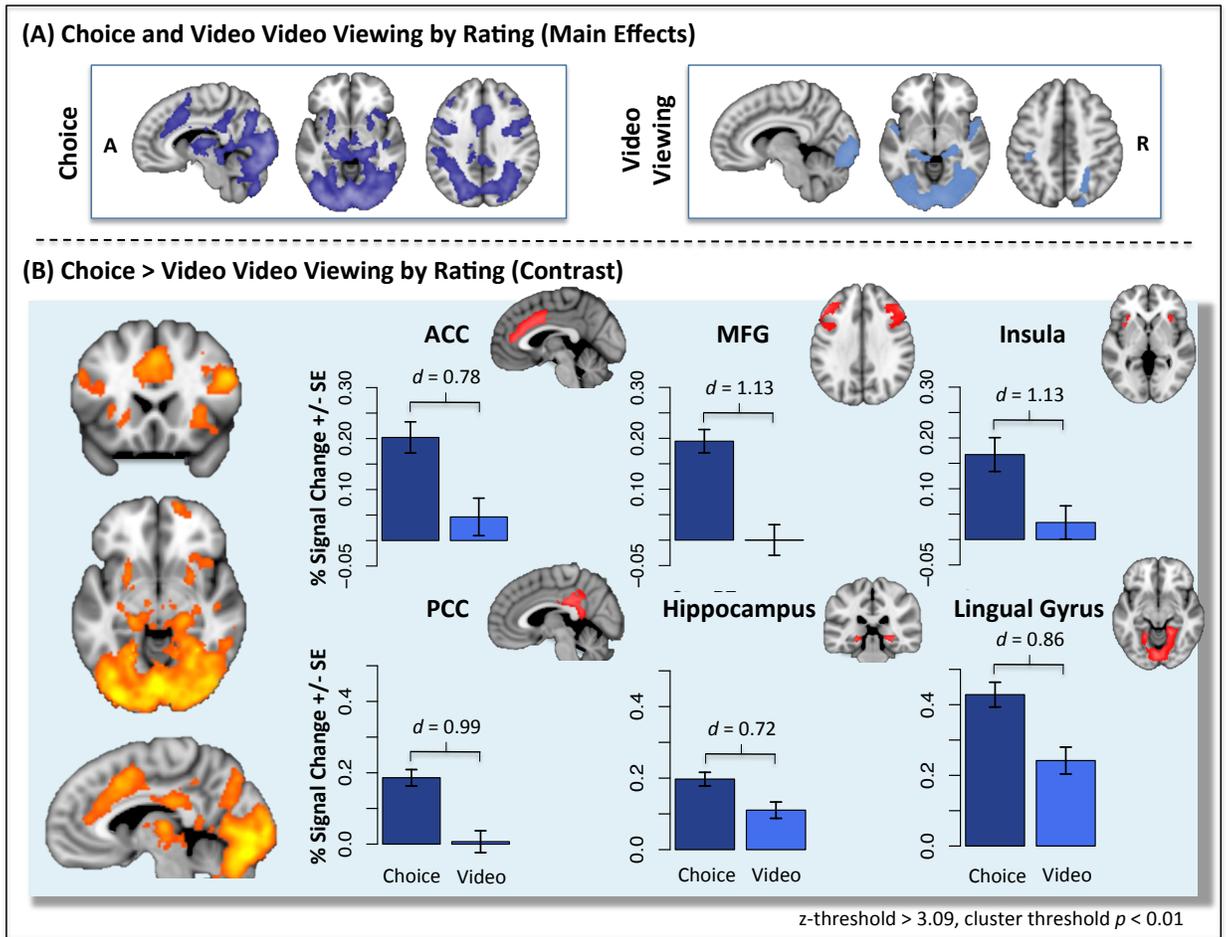
(A) Main effects for stay choice and video-viewing events associated with higher rated rewards. (B) Contrasts for stay choices greater than video viewing revealed stronger activation across a variety of cognitive and sensory areas.

Supplemental Table 3.1A. Consumption Decoding using Residual Mask

Zone Comparisons	B	CI	*P*-value
Current > Previous	-.38	[-.42, -.34]	**<.001**
Current > Next	-.35	[-.39, -.32]	**<.001**
Current > Opposite	-.46	[-.42, -.34]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 3.1B. Deliberation Decoding using Residual Mask

Zone Comparisons	B	CI	*P*-value
Next > Previous	-.04	[-.06, -.01]	**.006**
Next > Current	-.03	[-.06, .00]	**.01**
Next > Opposite	-.05	[-.08, -.03]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 3.2A. Decoding Accuracies during Deliberation

Mask	B	*P*-value
Cumulative Preview Task	.19	.19
Deliberation + Consumption	.47	**.006**
Default Mode Network	.13	.37
Salience Network	.22	.13
Right Fronto-parietal Network	.12	.81

B: unstandardized coefficient

Supplemental Table 3.2B. Decoding Accuracies during Consumption

Mask	B	*P*-value
Cumulative Preview Task	.13	.40
Deliberation + Consumption	.08	.59
Default Mode Network	.07	.66
Salience Network	.17	.22
Right Fronto-parietal Network	.09	.54

B: unstandardized coefficient

CHAPTER 4: LEARNING FROM REGRET: DISSOCIATING LIKING FROM WANTING IN HUMAN NATURALISTIC FORAGING

Foreword: This chapter was written in collaboration with A. David Redish and Angus W. MacDonald, who edited versions of the manuscript.

Abstract

Both emotion and motivation are fundamental, but arguably separable, contributors to human decision-making. Prominent hypotheses suggest that liking of reward is dissociable from the pursuit of reward in the decision-making process. These components have separable neural substrates, and reward enjoyment and pursuit are driven apart in addiction. Using a human foraging paradigm, we report for the first time that these processes are linked within the context of *regret*. More specifically, reward likability (i.e., ratings) following regret-inducing experiences directly predicted the pursuit of future choices. However, reward likability and choice behaviors were dissociated following situations that invoked disappointment or relief. Additionally, highly impulsive individuals showed less risk-aversion after regret-inducing experiences, but no differences in their levels of reward likability under the same conditions. This suggests that impulsivity is specifically related to aberrant pursuit-of-reward learning, particularly when choices that result in bad outcomes lead to regret.

4.1 Introduction

Affective processes have predictable and pervasive influences on human decision-making (Lerner, Li, Valdesolo, & Kassam, 2015); however, the extent to which affect and motivation are separable processes within decision-making remains disputed (Chiew & Braver, 2011; Dolan, 2002). For example, the incentive salience model posits a dissociation between the "liking" (i.e., subjective pleasure) and "wanting" (i.e., motivation towards reward) components of reward, because these processes rely on dissociable neural mechanisms (Berridge & Robinson, 1995, 2003). The construct of regret may bridge these two facets when there is disagreement between liking and wanting, such as the regret that one experiences when a new purchase does not fulfill expectations from its advertisement.

Regret exists at the intersection of value and agency: it occurs when an individual receives an unfavorable outcome for which they are responsible, and entails the realization that an alternative (counterfactual) action would have yielded a preferred result (Bell, 1982). Regret is often contrasted with disappointment, which follows the receipt of a less valuable outcome but is not the result of an individual's mistaken action (Bell, 1985; Loomes & Sugden, 1986). Consequently, agency and counterfactual thinking distinguish regret and disappointment, given that disappointment lacks the sense of personal responsibility and recognition of preferred alternatives that are fundamental to regret (Coricelli et al., 2005). In response to regret, individuals often learn to make choices that minimize future negative outcomes (Coricelli, Dolan, & Sirigu, 2007; Loomes & Sugden, 1982), while the inability to learn from regret may be integral to certain psychopathologies like addiction (Chiu, Lohrenz, & Montague, 2008). These

learning mechanisms arguably manifest as *regret*-aversion but not necessarily *risk*-aversion, as regret-minimizing choices can entail risk-avoidance or risk-seeking behaviors (Zeelenberg, Beattie, van der Plight, & de Vries, 1996; Zeelenberg & Pieters, 2004; Zeelenberg & van Dijk, 1997).

We previously devised a human foraging paradigm, called the "Web-Surf Task" (Abram et al., 2016), based on the rodent neuroeconomic task called Restaurant Row (Steiner & Redish, 2014); we adapted Restaurant Row as it revealed counterfactual thinking in rats through sequential decisions (Steiner & Redish, 2014). These parallel tasks entailed serial stay/skip choices regarding offers of real-time delays and primary rewards (i.e., food in Restaurant Row, video clips in the Web-Surf Task). The inclusion of experiential rewards represents a key difference in our task design as compared to traditional decision tasks, since previous decision tasks have largely relied on abstract secondary rewards (Reynolds, 2006a). We observed comparable decision valuation systems across species, as well as high correspondence between choices and consummatory responses among humans (i.e., delay thresholds related to video ratings). This work bridged cross-species models of decision-making, while also demonstrating the Web-Surf Task's capacity to dissociate wanting and liking in humans. However, because humans had limited experience on the task, they did not show the sequential regret effects seen in rats. We therefore designed a modified version of the Web-Surf Task that introduced counterfactual outcomes using risky offers.

In the risk-variant of the Web-Surf Task (Figure 4.1A), humans encountered serial offers that presented a set of possible delays (Figure 4.1B). The true delay was only revealed if the subject elected to stay. Rewards included 4-second video clips from four

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categories. Using the risk trial example in Figure 4.1B, the *good* outcome is receipt of the 5-second delay, the *bad* outcome receipt of the 15-second delay, and the *mid* outcome receipt of the 10-second delay. In comparison, non-risk trials presented offers with three identical delays. Subjects made stay/skip decisions as to whether to accept an offer or try their luck at the next category. They also rated how much they liked each video clip they saw. As in the original task, humans had a fixed amount of time to forage; this means that subjects should have made economically maximizing decisions and stayed when the subjective value of an offer exceeded its cost.

We used this novel risk task to resolve the question of how post-outcome emotions impacted wanting and liking in a foraging environment. Our results revealed that immediate consummatory responses and pursuit of future rewards were dissociated, except within regret-inducing situations (i.e., bad outcomes resulting from personal agency). Additionally, regret fostered risk-aversion following negative affective experiences and risk seeking following positive affective experiences, suggesting that subjects became regret-averse but not necessarily risk-averse. We then asked whether individual differences in impulsivity differentially tracked these decision systems. Our innovative approach allowed us to see that impulsive individuals may not differ in how they feel regret; rather, they fail to learn from regret-inducing situations.

4.2 Methods

<u>Subjects</u>

A sample of 105 undergraduate students (81% female, average age 20.2 years) from the University of Minnesota completed the current study and received

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compensation in the form of extra credit towards psychology courses. The ethnic breakdown of the sample was as follows: 63% Caucasian, 26% Asian, 4% Black/African American, 3% Hispanic, 1% American Indian/Alaskan Native, 1% Native Hawaiian/Pacific Islander, 2% other. The University of Minnesota Institutional Review Board approved the study, and all subjects provided written informed consent.

Experimental Design

Subjects had 40 minutes to travel between galleries that provided video rewards from the four categories described in Abram et al. (2016): kittens, dance, landscapes, and bike accidents. Comparable to the original task, offers were presented in text and a webpage-like progress bar. Video rewards lasted four seconds and subjects rated each viewed video using a 1-4 system (4 = highest) according to how much they liked that video. Subjects advanced between galleries by clicking on the numbers 1-4 as they randomly appeared around a gray screen, with numbers in a slightly darker shade of gray to increase difficulty. At the end of the session, subjects ranked the categories 1-4. A stay choice was coded 1 and a skip choice coded 0.

Delays ranged 3 to 30 seconds. Risk level was reflected by the width of an offer and was either 0 (non-risk) or greater than 0 (risk). Thus, for a non-risk trial, the lower, mid, and upper values were equivalent, e.g., "Video in 7, 7, or 7 secs…" All other offers were considered risk trials. We did not allow for a risk of one second, as this would have led to a non-integer mid value, e.g., "Video in 5, 5.5, or 6 secs…"

<u>Trait-Level Impulsivity Measure</u>

Subjects completed the 100-item version of the Externalizing Spectrum Inventory (ESI; Krueger, Markon, Patrick, Benning, & Kramer, 2007), which captures general disinhibition processes (e.g., theft, irresponsibility), substance use/abuse, and callous aggression.[8]

<u>Delay and Probability Discounting</u>

A computerized delay- and probability-discounting paradigm was administered.[9] This entailed subjects making a series of binary choices between monetary rewards of different reward magnitudes associated with different temporal delays (e.g., "Would you prefer $5 now or $10 in two weeks") or probabilities (e.g., "Would you prefer $5 for sure or $10 with a 75% chance"). Offers ranged from 50 cents to $10. The task lasted approximately 10 minutes. A discounting rate (or k-value) was computed for the delay and probability trials separately using a hyperbolic function (Ainsle, 1975), yielding two k-values per subject. Higher k-values reflect more rapid discounting of delayed rewards, and have been linked with impulsivity (Bickel et al., 2012).

<u>Delay Threshold Computations</u>

Subject-specific delay thresholds were computed separately for each trial using a leave-one-out approach; this yielded four thresholds, one per category. Thresholds were indicative of revealed preferences, reflecting the delay time at which a subject reliably began to skip offers for a particular category. To obtain the threshold for $trial_i$, we fit a

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[8] Missing self-report data for 1 subject.
[9] Missing delay- and probability-discounting data for 3 subjects.

Heaviside step function to all trials in category$_x$ excluding trial$_i$. This produced a vector of thresholds with length equal to the number of trials in category$_x$. We used a Heaviside step function as an alternative to the logistic fit function described in Abram et al. (2016), as the Heaviside approach is better equipped to handle extreme cases (i.e., when a subject stays or skips all offers in a category). In such instances, the Heaviside step function produces a reasonable value (e.g., 0 or 30), whereas the logistic fit function is likely to produce a value approaching infinity. Importantly, thresholds were computed using the mid value of each offer for risk trials only. Non-risk trials were then assigned a threshold equal to the mean of the threshold vector for the respective category.

Value Computations

Expected value for risk trials was calculated as follows:

$\frac{1}{3} \times [(\text{Threshold}_t - \text{Lower Delay}_t) + (\text{Threshold}_t - \text{Mid Delay}_t) + (\text{Threshold}_t - \text{Upper Delay}_t)]$,

where *t* refers to trial (e.g., Figure 4.1C). Expected value for non-risk trials was computed as the category-specific threshold minus delay, given that all delays in a non-risk offer were equal. Actual value for all trials equated to the category-specific threshold minus the delay received (e.g., Figure 4.1C). Values ranged -30 to 30, and a value of 0 was equal to threshold.

Group-Level Deliberation and Affective Value Models

We evaluated relations between framing (i.e., good/bad outcome), agency (i.e., risk/non-risk), and deliberative choice via linear mixed-effects models. We fit models using the MCMCglmm package in R, which uses Markov chain Monte Carlo

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techniques (Hadfield 2010; R Core Team, 2015); for plotting purposes, we used the lmer and lsmeans packages (Bates, 2007; Lenth 2016).[10] The main model included choice at the current trial as the independent variable, actual value received and outcome type at the previous trial as fixed-effect dependent variables, and subject as a random effect: [Choice$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$ + (1|subject)]. This model included risk trials for which the subject stayed, and the following trial was also a risk trial. This allowed us to evaluate whether the type of outcome on the previous trial influenced subsequent risk seeking or aversion. Note that higher values in Figures 4.2A and 4.2B indicate an increased likelihood of staying.

Follow-up models were used to clarify the influence of framing and agency on choice, using trials matched by actual value received on the previous trial; trials were matched on a subject-by-subject basis and then combined for the group analysis. The first subset included trials for which subjects received the good or bad outcome (i.e., stayed on a risk trial) and encountered risk on the following trial. The second subset included trials for which subjects stayed and received the bad outcome or stayed on a non-risk trial of equivalent value, and encountered risk on the subsequent trial. Because each subject's contributing trials only included a portion of the possible values, we included actual value as a nested variable in the following model: [Choice$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$ + actual value$_{t-1}$:outcome type$_{t-1}$ + (actual value$_{t-1}$|subject)]. We included the interaction term, as we were particularly interested in whether framing effects or agency shaped value-by-choice sequencing effects.

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[10] We note that the parameter estimates obtained using the `MCMCglmm` and `lmer` packages were nearly identical.

We carried out a similar approach to evaluate influences on the liking system. The main rating model included mean-centered rating as the independent variable (i.e., centered to the average of the respective category), actual value and outcome type at the previous trial as fixed-effect dependent variables, and subject as a random effect: [Rating$_t$ ~ actual value$_t$ + outcome type$_t$ + (1|subject)]. This model included risk trials for which the subject stayed. We also produced two follow-up subsamples of trials matched by actual value at the previous trial; this was to compare ratings that followed good versus bad outcomes and ratings that followed bad outcomes versus non-risk offers. We fit the following model using each of the subsets described above: [Rating$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$ + actual value$_{t-1}$:outcome type$_{t-1}$ + (actual value$_{t-1}$|subject)].

Lastly, we produced an integrated mixed-effects model that examined direct relations between deliberative choice and affective value, while considering the effects of framing and agency. In particular, we were interested in whether affective responses interacted with actual value or offer type when predicting subsequent decisions (building off the prior choice model detailed above). This model then regressed choice on the current trial, on actual value, mean-centered rating, and outcome type of the previous trial, two interaction terms, and subject as a random effect: [Choice$_t$ ~ actual value$_{t-1}$ + rating$_{t-1}$ + outcome type$_{t-1}$ + actual value$_{t-1}$:rating$_{t-1}$ + actual value$_{t-1}$:outcome type$_{t-1}$ + (1|subject)]. In this model, outcome type coded good outcomes, bad outcomes, and non-risk offers; this metric then reflected the framing and agency manipulations.

Subject-Specific Deliberative Choice and Reward Likability Models

We fit subject-specific models based on the main choice and rating group-level

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models. We first regressed choice on the actual value and outcome type of the prior trial: [Choice$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$]. We extracted the unstandardized outcome type coefficient that reflected one's likelihood to stay following receipt of the good versus bad outcome, with higher values indicating an increased tendency to stay after receiving the bad outcome. For the rating model, we regressed mean-centered ratings on the actual value and outcome type of the prior trial: [Rating$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$]. We again extracted the unstandardized outcome type coefficient for good versus bad outcomes, with higher coefficients reflecting better ratings following the bad outcome.[11]

Using the extracted coefficients, we assessed the extent to which subjects' behavioral patterns corresponded with trait-level impulsivity (i.e., ESI total scores). We computed two partial correlations that controlled for age, sex, and ethnicity. We included these demographic covariates based on prior research linking these variables with self-report and/or behavioral impulsivity measures (de Wit et al., 2007). Partial correlations were calculated via robust regression methods to reduce the influence of outliers. ESI scores were log-transformed to improve normality.

Binary Choice Comparison Models

To compare parameters derived from the Web-Surf Task versus the discounting paradigm, we computed three robust partial correlations. The first two correlations predicted total ESI scores from the log-transformed delay and probability k-values,[12]

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[11] We excluded 1 subject with a coefficient less than 4 standard deviations below the mean.
[12] We excluded 9 subjects with invalid k-values (discounting rates of 0).

while controlling for age, sex, and ethnicity. The third tested whether the subject-level coefficient from the Web-Surf Task that indicated sequencing responses following receipt of a good versus bad outcome still predicted ESI scores, after controlling for the two k-values and the age, sex, and ethnicity covariates.

4.3 Results

Regret Influences Deliberation and Reward Likability

We first tested how post-outcome emotions impacted deliberative decisions and ratings via framing effects and degree of agency. Here, framing effects were specific to risk trials, where a given delay was framed as good, bad, or in-between (mid) depending on its placement within an offer. We assessed the effects of agency by comparing risk and non-risk trials that were matched by actual value (i.e., value computed using the true delay), where the true delay was only known at the outset of the non-risk trials.

We defined regret-inducing situations as one in which the subject stayed on a risk trial and received the bad outcome; we note that our definition derives from an offer's outcome *type* but not *value*, meaning that a regret trial could have an actual value above 0. In regret-inducing situations, counterfactual thinking represented knowledge of the better alternatives from a given offer, where the alternatives included receipt of the good or mid outcomes from that offer. We contrasted these trials with those expected to provoke disappointment, in which the subject accepted a non-risk offer of equivalent value; however, because the true delay was known during the choice phase, there was no mismatch between the outcome and a known and better alternative within that offer (thus differentiating regret and disappointment). We also compared regret-inducing situations

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to those characterized by <u>relief</u>, where the subject received the good outcome on a risk trial.

Regarding framing and agency, we examined whether the type of outcome on the previous trial influenced subsequent choices. When controlling for actual value, subjects were less likely to accept a successive risky offer if they previously received a bad versus good outcome (Figure 4.2A; Table 4.1); importantly, this effect was not better explained by global risk-aversion trends or trial-specific risk-aversion (see Supplemental Materials, *Global Risk-Aversion Confound Analyses* and *Trial-Specific Risk-Aversion Confound Analyses*). To clarify this result, we produced a subset of data that matched good and bad outcomes by actual value, on a subject-by-subject basis. The top graph in Figure 4.2B illustrates the interaction between outcome type and value for good versus bad outcomes (Supplemental Table 4.1A), showing that the negative framing of a previously bad outcome impacted relations between value of the previous trial and choice on the current trial (B = 0.015, CI = [0.006, 0.023], $p < 0.001$). More specifically, we found that subjects became risk-averse after a bad offer of lower value, and risk-seeking after a bad offer of higher value. These analyses demonstrated the predicted relationship to regret. In contrast, we did not detect an association between the previous trial's value and successive choice after receipt of a good outcome (B = 0.000, CI = [-0.010, 0.009], $p = 0.96$).

Next, we assessed the role of agency on deliberative choice, using a data subset that matched bad outcomes and non-risk trials by actual value, on a subject-by-subject basis. The bottom of Figure 4.2B highlights the impact of agency on subsequent choice (Supplemental Table 4.1B), with a positive association between the previous trial's

value and current choice for bad outcomes (B = 0.012, CI = [0.004, 0.021], p = 0.002), but no relation for equivalently valued non-risk offers (B = -0.001, CI = [-0.009, 0.007], p = 0.83). These findings again show that regret induced risk-seeking and risk-averse behaviors. In contrast, relief and disappointment-inducing situations did not influence relations between value and choice.

But to what extent do post-outcome emotions contribute to our liking of a reward? To address this question, we carried out comparable analyses on the video ratings. When evaluating framing effects on ratings, we observed an opposite pattern, with subjects rating videos that followed a *bad* outcome more highly than those that followed a good outcome (Figure 4.2C; Table 4.2); again, this result was not accounted for by global trends of likability ratings (see Supplemental Materials, *Global Risk-Aversion Confound Analyses*). Follow-up analyses using value-matched trials revealed an interaction between actual value and rating for bad versus good outcomes (Supplemental Table 4.2A; top of Figure 4.2D), with bad outcomes yielding a positive association between value and rating (B = 0.013, CI = [0.004, 0.021], p = 0.002) and good outcomes a negative association (B = -0.011, CI = [-0.019, 0.001], p = 0.03). Although not significant (interaction term in Supplemental Table 4.2B), we saw a similar pattern to the deliberation versus agency model, with agency having a more substantial impact on relations between bad outcomes and ratings as compared to non-risk trials (bad outcomes: B = 0.007, CI = [0.000, 0.013], p = 0.04; non-risk: B = -0.002, CI = [-0.008, 0.004], p = 0.48; bottom of Figure 4.2D).

Generally, experiences we have enjoyed lead us to seek out those experiences again. We therefore tested whether likability ratings directly guided future choices under the different conditions of interest (Figure 4.3; Table 4.3). We found that, following

regret-inducing situations, relatively lower ratings predicted risk-aversion whereas relatively higher ratings yielded risk-seeking behaviors (B = 0.040, CI = [0.004, 0.074], *p* = 0.03). However, we did not detect associations between likability ratings and subsequent choice following good outcomes (B = 0.009, CI = [-0.028, 0.039], *p* = 0.63), or non-risk trials (B = 0.011, CI = [-0.017, 0.043], *p* = 0.51), suggesting a violation of this principle.

Failure to Learn from Regret Predicts Impulsivity

To explore the importance of regret to impulsive traits, we investigated whether trait-level impulsivity modified the relationship between the wanting and liking systems. Specifically, we were interested in whether highly impulsive individuals were less influenced by regret when making choices, a pattern observed among chronic smokers and individuals with psychopathy (Baskin-Sommers, Stuppy-Sullivan, & Buckholtz, 2016; Chiu et al., 2008). We also predicted that impulsive individuals would exhibit comparable consummatory responses (i.e., likability ratings) following regret experiences; although differences in affective responses were not examined in the chronic smoker sample (Chiu et al., 2008), evaluations of the psychopathy sample revealed intact affective regret sensitivity for high psychopathy individuals (Baskin-Sommers et al., 2016).

We obtained subject-specific estimates that reflected associations between the previous outcome and current choice. Informed by the group-level model, we computed a parameter that compared a subject's likelihood of accepting a risky offer after receipt of a good versus bad outcome on the prior trial. Consistent with our expectation, impulsive

individuals showed an inverse pattern to that observed at the group level (partial $r = 0.26$, $p = 0.006$; Figure 4.2E); these individuals were more likely to accept a risky offer after having just received a bad outcome, signifying a potential deficiency in learning to avoid future regret. In contrast, the association between outcome type and ratings was unrelated to impulsivity scores (partial $r = -0.01$, $p = 0.95$; Figure 4.2F). Together, these results indicate that impulsivity tracked individual differences in deliberative choices but not consummatory responses.

Discounting Rates do not Predict Impulsivity

Lastly, given the extensive literature that utilizes traditional binary choice tasks to evaluate impulsivity (de Wit, 2009a; Reynolds, 2006a), we tested whether metrics from a monetary delay- and probability-discounting paradigm better explained individual differences in impulsivity. The median R^2 was 0.85 and 0.90 for the delay and probability discounting rates (i.e., logged k-values), respectively. Distribution qualities of the discounting rates were as follows: delay k-values (median = -5.27, SD = 2.08), and probability k-values (median = 0.26, SD = 0.84); we note that distribution values for the delay k-values are comparable to those reported in a large sample of healthy adults (de Wit, Flory, Acheson, McCloskey, & Manuck, 2007). The partial correlations revealed that discounting rates did not predict trait-level impulsivity (delay k-value: partial $r = 0.13$, $p = 0.23$; probability k-value: partial $r = 0.04$, $p = 0.74$). Moreover, the coefficient that tracked regret-choice relations in the previous section still predicted impulsivity when accounting for the two k-values (partial $r = 0.24$, $p = 0.03$).

4.4 Discussion

For the first time we demonstrate how the experience of regret bridges the affective and motivational processes that are dissociated within other emotional frameworks. In the current study we employed a risk-variant of the Web-Surf Task to assess how post-outcome emotions shaped choice and consummatory responses in humans. To this end, we capitalized on a naturalistic foraging task's capacity to isolate liking from seeking behaviors. Our results showed that regret-inducing situations (i.e., receipt of the bad outcome on a risky gamble) influenced both reward likability and deliberative choice, and provided a connection between these processes. We also found that trait-level impulsivity tracked whether regret influenced future decisions, and this association was not better explained by performance on a traditional delay-discounting task.

Our examination of the deliberation system showed that subjects became more risk-averse following regret-inducing situations, although follow-up analyses revealed a more nuanced picture where subjects exhibited both risk-averse and -seeking tendencies depending on the value of the previous offer. In particular, risk-aversion followed receipt of bad outcomes of lower value, whereas risk seeking followed bad outcomes of higher value. These results are comparable to prior reports (Zeelenberg et al., 1996; Zeelenberg & Pieters, 2004), in which regret drove individuals to minimize future regret in particular (i.e., after bad outcomes of low value).

Compared to the deliberation system, our initial analysis of the liking system revealed an opposite effect, whereby subjects liked videos that followed a negative outcome more than those following a good outcome. This could be described as a sunk-

cost effect, where the perception of more effort or time spent yielded greater investment (Arkes & Blumer, 1985). We clarified this effect by parsing the influences of framing effects and actual costs on ratings. We found that, in the context of regret, more time spent led to a decrease in liking whereas less time spent led to an increase in liking; hence, the perception of more effort on lower cost trials may have escalated personal investment. Conversely, in the context of relief, low-valued trials were rated better than high-valued trials, suggesting that reward likability was driven down by cheaper offers framed as requiring less effort (e.g., "I did not have to work particularly hard for this reward, so it must not be as good"). These cost-related behaviors are akin to the overly patient strategies observed in rats on spatial foraging tasks, such as rats accepting suboptimal offers (i.e., waiting through longer delays) when the perceived behavioral investment was high (Carter & Redish, 2016; Wikenheiser et al., 2013).

We then assessed how recent video ratings guided decisions, to determine whether liking and wanting represented separable processes. In effect, these systems were only linked under regret conditions, in which higher ratings predicted more risk-seeking following regret-inducing situations only (versus no linkage for disappointment or relief). This provides additional evidence that perceived effort was critical to valuation, and in bridging consummatory responses with motivation.

Taken together, our group-level results demonstrate that, contrary to rational choice theory, human choices were not invariant to different representations of the same offer (see Tversky & Kahneman, 1986, for review). Instead, flaws in value and effort perceptions predictably influenced decisions. This is similar to the systematic preference shifts described by Kahneman and Tversky under prospect theory (1979), i.e., evidence

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that "losses loom larger than gains." But do individual differences modulate these valuation and choice mechanisms at the subject level?

Our individual differences analyses revealed that more impulsive subjects became less risk-averse after regret, which could suggest aberrant learning. This explanation stems from the work of Chiu and colleagues (2008) who found that choices made by chronic smokers were not guided by a "fictive" (or counterfactual) learning signal, despite no loss in production of the signal. More broadly, this result fits with the substance use diagnostic criteria that describe tendencies to pursue or consume rewards despite the potential negative consequences (American Psychiatric Association, 2013). Importantly, the current findings demonstrate that this type of impaired learning mechanism may be present in nonclinical samples.

The individual differences analyses also showed that impulsivity did not predict relations between regret and reward likability. Thus, more impulsive individuals did not systematically differ in their affective experiences following regret. This result is similar to a recent report that separately evaluated affective responses and choice in psychopathy; specifically, individuals with psychopathy reported comparable negative affect in response to regret-inducing outcomes, but did not use prospective regret signals to guide future choices (Baskin-Sommers et al., 2016). Taken together, impulsivity discriminated between affective and motivational responses to regret, as impulsivity scores were specifically associated with future choice tendencies.

Conclusions

To summarize, we used a translational foraging paradigm to examine the effects

of regret on human valuation processes. Our results suggest that regret impacted

immediate consummatory responses and future choices, as well as more direct relations

between liking and wanting. We also found that trait-level impulsivity was associated

with impaired regret-induced learning, but not affective responses to regret, thus

supporting notions that wanting and liking can be discriminated via substance use.

4.5 Figures and Tables

Figure 4.1. Risk-Variant Web-Surf Task Layout and Flow-diagram
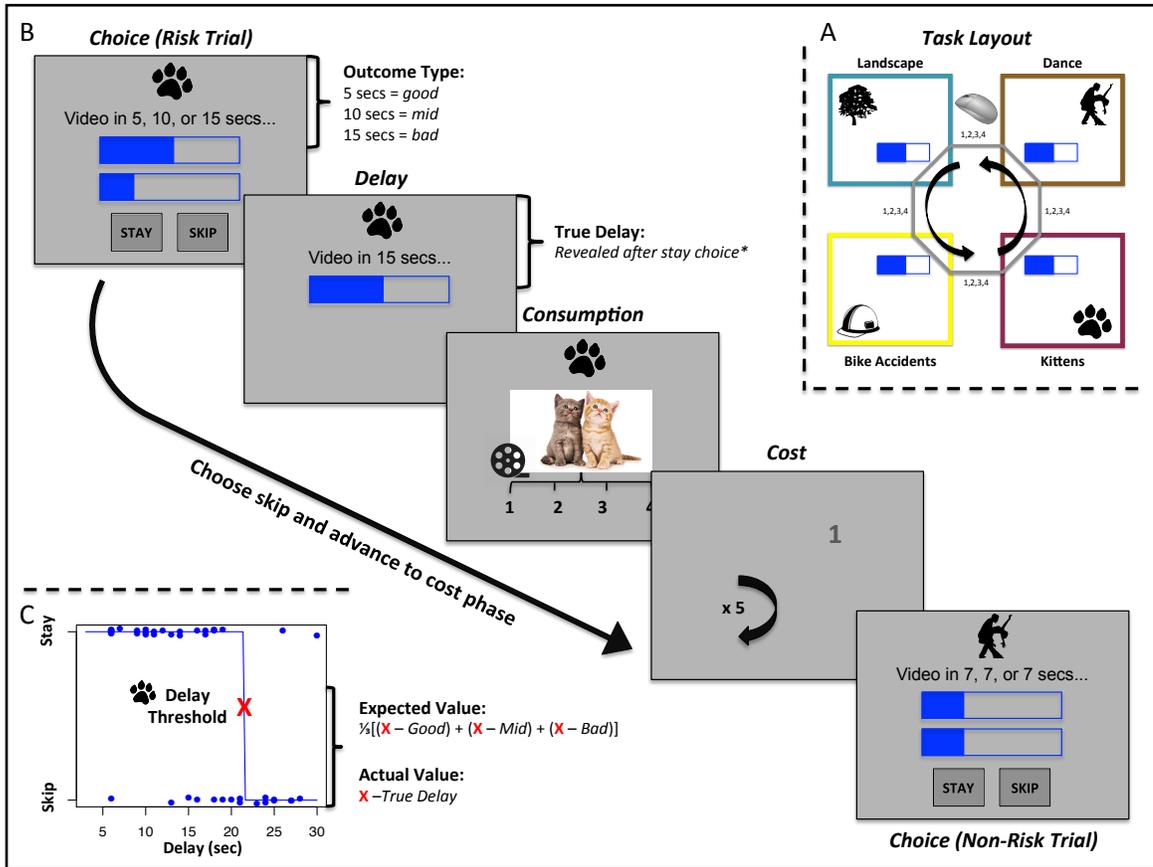
(A) Schematic representation of the risk-variant of the Web-Surf Task. Subjects cycled between four video galleries (kittens, dances, landscape, bike accidents) in a constant order. (B) Flow diagram illustrates sequencing between risk and non-risk trials. For a risk trial, the true delay is only revealed if the subject stays. If they instead skip, they advance directly to the cost phase before encountering the next offer. (C) Description of threshold and value computations. Subject-specific delay thresholds indicated the delay at which a subject reliably began to skip offers for a given category. Expected value was calculated using the initial offer (before the subject has chosen to stay), taking all three delays and the category-specific threshold into account. Actual value was calculated using the true delay (only revealed after a stay choice) and the category specific-threshold.

Figure 4.2. Previous Experiences Predict Choices and Likability Ratings
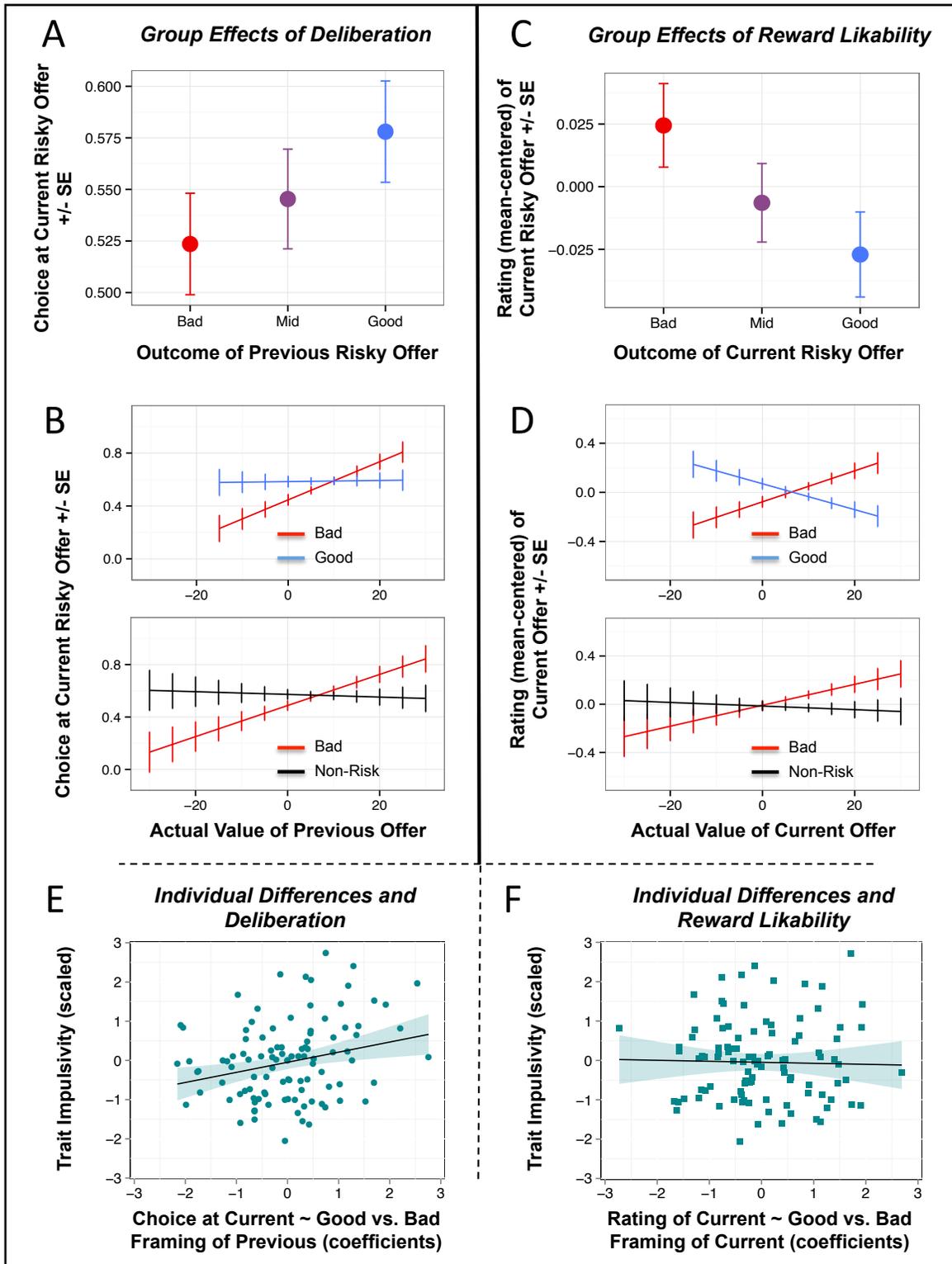
(A) Proportion of stay choices at current risky offers following receipt of the good, bad,

or mid outcome on the previous risk trial. Red represents a regret-inducing situation (bad outcome with personal agency); blue indicates a relief-inducing situation (good outcome with personal agency). Subjects were more risk-averse after regret-inducing experiences. (B) Interactions between previous outcome type and actual value when predicting choices on subsequent risky offers. Black represents a disappointment-inducing situation (lack of personal agency). Subjects became risk-averse following regret instances of low value, versus risk-seeking after regret instances of high value (whereas no associations between value and choice were detected for the relief or disappointment conditions). (C) Likability ratings following the receipt of the good, bad, or mid outcomes on the current risk trial. Subjects rated videos that followed regret-inducing situations more highly than those that followed relief instances. (D) Interactions between previous outcome type and actual value when predicting immediate likability ratings. After a regret-inducing experience, subjects tended to rate videos that followed a low value offer worse than those that followed a high value offer; the inverse pattern was found for video linked to relief instances. A similar pattern emerged when comparing regret and disappointment trials. (E) Relations between trait-level impulsivity and the likelihood of accepting a risk offer after previously receiving the bad outcome. Impulsive subjects showed less risk-aversion in response to regret. (F) Relations between trait-level impulsivity and immediate likability ratings. Impulsive subjects did not differ in their ratings following regret instances. Error bars in a-d indicate within-subject standard errors. Shaded bands in e-f represent 95% confidence intervals.

Figure 4.3 Regret-induced Experiences Bridge Liking and Wanting
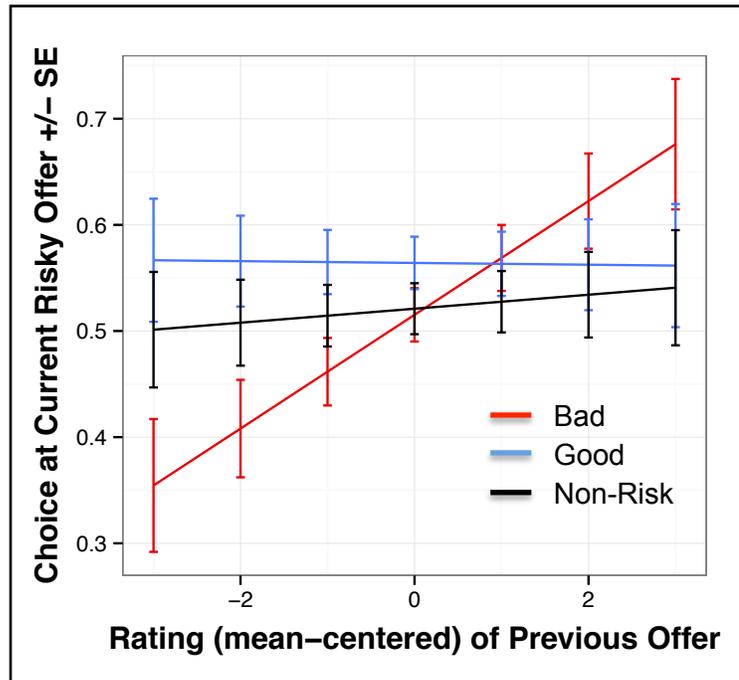
Interaction between previous outcome type and rating when predicting choices on subsequent risky offers. Following receipt of the bad outcome (i.e., regret-inducing situation), subjects were more risk-averse after lower-rated videos and more risk-seeking after higher-rated videos; no association was detected for the other conditions. Error bars represent within-subject standard errors.

Table 4.1. Choice by Previous Framing Main Model

Predictor Variable	B	CI	P-value
Actual Value	-.006	[-.008, -.004]	**<.001**
Outcome Type (Bad vs. Good)	-.054	[-.092, -.015]	**.006**
Outcome Type (Mid vs. Good)	-.033	[-.065, -.001]	**.05**

B: unstandardized coefficient; **CI:** confidence interval.

Table 4.2. Rating by Framing Main Model

Predictor Variable	B	CI	*P*-value
Actual Value	.002	[.000, .004]	.07
Outcome Type (Bad vs. Good)	.051	[.004, .100]	**.04**
Outcome Type (Mid vs. Good)	.021	[-.022, .069]	.37

B: unstandardized coefficient; **CI:** confidence interval.

Table 4.3. Choice by Rating Integrated Model

Predictor Variable	B	CI	*P*-value
Actual Value	-.006	[-.008, -.004]	**<.001**
Rating	.040	[.006, .076]	**.03**
Outcome Type (Good vs. Bad)	.049	[.014, .088]	**.01**
Outcome Type (Non-Risk vs. Bad)	.007	[-.029, .043]	.69
Actual Value × Rating	.002	[.001, .004]	.13
Rating × Outcome Type (Good vs. Bad)	-.055	[-.110, -.006]	**.04**
Rating × Outcome Type (Non-Risk vs. Bad)	-.048	[-.098, .001]	.06

B: unstandardized coefficient; **CI:** confidence interval.

4.6 Supplemental Materials

<u>Validity Analyses</u>

We evaluated the current task's external and face validity using methods described in Abram et al. (2016). For each subject, for each category, we averaged the vector of delay thresholds produced using the leave-one-out method described above; this yielded four thresholds per subject. We measured external validity by correlating revealed preferences (i.e., delay thresholds) with stated preferences (i.e., average category ratings and post-test category rankings), and obtained two validity correlations per subject. Subjects showed similar validity correlation distributions to those presented by Abram et al. (2016; Supplemental Figure 4.1A); threshold and rating correlations had a median of 0.66, while threshold and ranking correlations had a median of 0.60.

To examine face validity, we plotted skip decision times against mid delays, to test if subjects made quick skip decisions regardless of delay length or appeared to wait for cues. Comparable to Abram and colleagues (2016), subjects responded efficiently irrespective of the delay (Supplemental Figure 4.1B).

<u>Global Risk-Aversion Trends</u>

We assessed global trends in choice patterns and affective responses using linear mixed-effects models. The first model included choice as the independent variable; number of videos viewed (i.e., consumed up to trial t), expected value, and a risk/non-risk categorical indicator as the fixed-effect dependent variables; and subject as a random effect. We also included the video consumption by risk/non-risk interaction term to assess differential relations between consumption and choice as a function of risk:

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[Choice$_t$ ~ number videos consumed$_t$ + expected value$_t$ + risk/non-risk$_t$ + number consumed videos$_t$:risk/non-risk$_t$ + (1|subject)]. All trials were included in the choice model.

Our findings revealed that risk level differentially influenced stay/go choices, whereby subjects were even less likely to accept a risk than non-risk offer as they consumed more videos (significant satiation × risk interaction, $p = 0.004$; Supplemental Figure 4.2A); that is, subjects became more risk-averse across the session. This interaction was present if the consumption variable was replaced with the number of good outcomes or bad outcomes, suggesting this effect was not solely driven by accumulated negative experiences (but instead reflected reward satiety). We also note that because stay choices were coded as 1, higher values in Supplemental Figure 4.2A indicate an increased likelihood of staying.

The second model was structurally equivalent to the first, but included mean-centered ratings as the independent variable: [Rating$_t$ ~ number videos consumed$_t$ + expected value$_t$ + risk/non-risk$_t$ + number consumed videos$_t$:risk/non-risk$_t$ + (1|subject)]. Only stay trials were included in the rating model, as subjects only rated videos during stay trials. In contrast to the global decision trends, we did not detect an interaction between satiation and risk on ratings ($p = 0.65$; Supplemental Figure 4.2B). Thus, even as subjects increasingly rejected risk offers over time, their liking of risk and non-risk videos remained similar (Supplemental Tables 4.3A and 4.3B).

Global Risk-Aversion Confound Analyses

Given the results in the prior section, we conducted analyses to determine

whether global risk-aversion tendencies confounded the trial-by-trial effects presented in the *Regret Influences Deliberation and Reward Likability* section. Specifically, we constructed the following mixed-effects models that included the additional consumption parameter: 1) [Choice$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$ + number videos consumed$_t$ + (1|subject)], and 2) [Rating$_t$ ~ actual value$_t$ + outcome type$_t$ + number videos consumed$_t$ + (1|subject)]. The inclusion of the consumption parameter did not undermine the prior results, which remained largely unchanged (Supplemental Tables 4.4A and 4.4B). Thus, global trends did not better account for the choice or affect sequencing effects.

Trial-Specific Risk-Aversion Confound Analyses

As an additional follow-up, we parsed the effects of the categorical (high, low, mid) and continuous (0-30 seconds) risk dimensions on choice. Our intention was to demonstrate that the general tendency to prefer offers with lower risk, i.e., a more narrow offer window, would not better account for the sequential effects in the *Regret Influences Deliberation and Reward Likability* section. We built the following model to address this potential confound: [Choice$_t$ ~ actual value$_{t-1}$ + outcome type$_{t-1}$ + risk$_t$ + (1|subject)]. Supplemental Table 4.5 shows that, although subjects were more likely to accept offers with a narrower risk window (indicated by the negative *Risk* coefficient), the effect of post-decisional regret was unaffected by the addition of this parameter.

Subject-Specific Risk-Aversion Trends

We also fit subject-specific models based on the global risk aversion models to obtain individual risk-aversion estimates. For the choice model, we regressed choice on

the number of consumed videos and expected value: [Choice$_t$ ~ number videos

consumed$_t$ + expected value$_t$]. This analysis was restricted to risk trials given the

significant consumption by risk interaction at the group level. For the rating model, we

regressed mean-centered ratings on the number of consumed videos, expected value, and

the risk/non-risk categorical variable: [Rating$_t$ ~ number videos consumed$_t$ + expected

value$_{t+}$ risk/non-risk$_t$]. This analysis included all stay trials given the non-significant

risk/non-risk interaction at the group level. We extracted the unstandardized consumption

coefficients from both models. Using comparable methods to those described in the prior

section, we obtained partial correlations between the two subject-level coefficients and

total ESI scores.

We observed a trend-level positive association between ESI scores and the choice

~ consumption coefficient (partial r = 0.17, p = 0.06; Supplemental Figure 4.3A).[13] In

effect, more impulsive individuals showed a reverse pattern from the global effect, with

an increasing acceptance of risky offers over time (i.e., more risk-seeking). We did not

detect an association between ESI scores and the rating ~ consumption coefficient (partial

r = 0.10, p = 0.31; Supplemental Figure 4.3B).

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[13] We excluded 1 subject with a coefficient greater than 4 standard deviations
above the mean.

Supplemental Figure 4.1. Task Validity
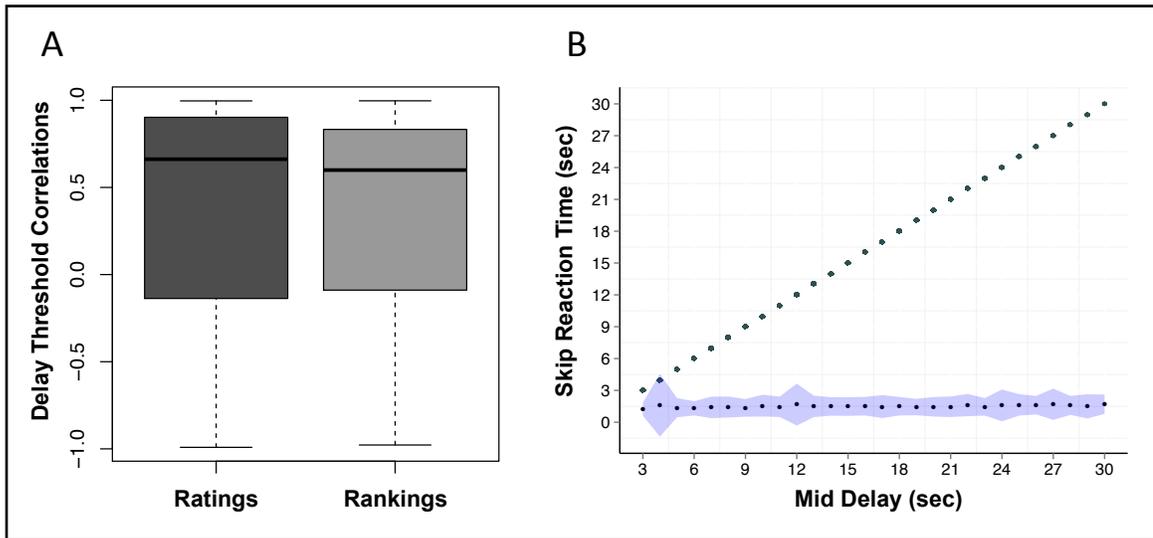
(A) Distribution of validity correlations that relate delay thresholds with average ratings (*left*) and post-test category rankings (*right*). (B) Evidence of face validity, where subjects made quick skip decisions regardless of the delay (i.e., mid delay). Stay trials are represented as the full delay time (points along the diagonal); mean times for skip trials are represented as the points parallel to the x-axis, with the blue shaded bands indicating skip time standard deviations.

Supplemental Figure 4.2. Global Risk-Aversion
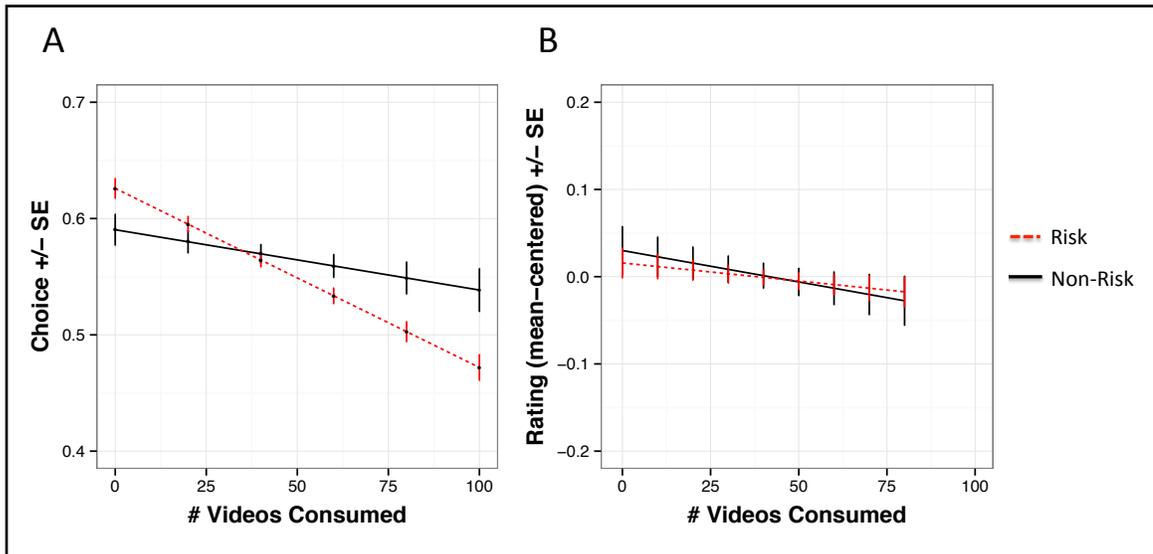
(A) Subjects became more risk-averse as the task progressed. (B) Subjects' likability ratings for risk and non-risk videos did not differ over time.

Supplemental Figure 4.3. Risk-Aversion and Impulsivity
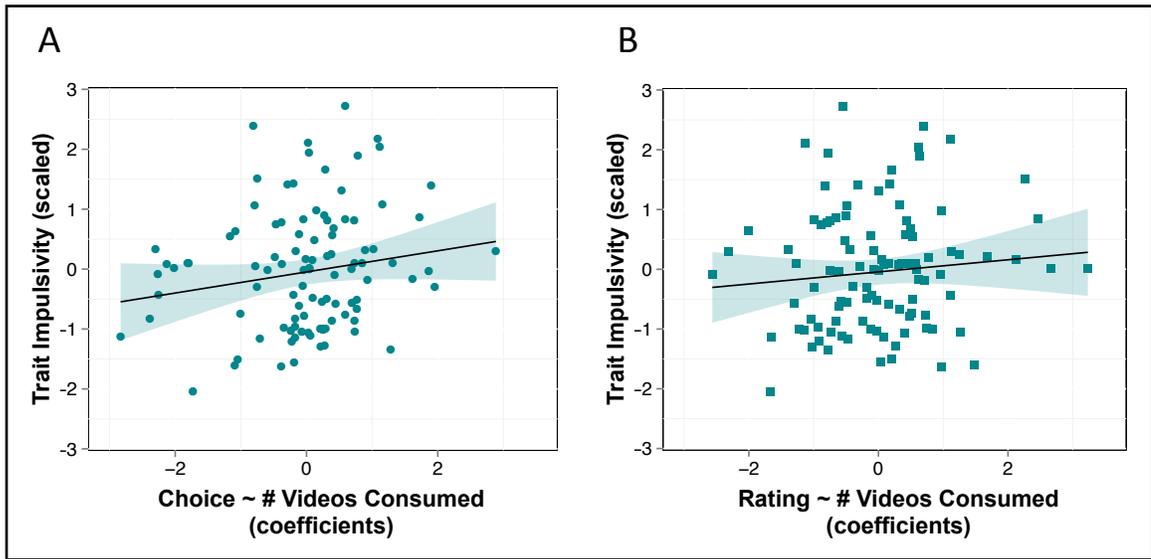
(A) Trend-level association between trait-level impulsivity and global risk-aversion tendencies, with impulsive subjects showing more risk seeking over time. (B) No association between trait-level impulsivity and global rating trends.

Supplemental Table 4.1A. Choice by Bad vs. Good Follow-up Framing Model

Predictor Variable	B	CI	*P*-value
Actual Value	.012	[.002, .021]	**.02**
Outcome Type (Bad vs. Good)	.137	[.020, .240]	**.01**
Actual Value × Outcome Type	-.014	[-.026, -.003]	**.008**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.1B. Choice by Bad vs. Non-Risk Follow-up Agency Model

Predictor Variable	B	CI	*P*-value
Actual Value	.012	[.003, .020]	**.006**
Outcome Type (Bad vs. Non-Risk)	.083	[-.016, .182]	.11
Actual Value × Outcome Type	-.013	[-.023, -.002]	**.03**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.2A. Rating by Bad vs. Good Follow-up Framing Model

Predictor Variable	B	CI	*P*-value
Actual Value	.013	[.003, .021]	**.008**
Outcome Type (Bad vs. Good)	.148	[.004, .261]	**.02**
Actual Value × Outcome Type	-.023	[-.035, -.009]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.2B. Rating by Bad vs. Non-Risk Follow-up Agency Model

Predictor Variable	B	CI	*P*-value
Actual Value	.008	[.000, .017]	.06
Outcome Type (Bad vs. Non-Risk)	-.008	[-.115, .099]	.91
Actual Value × Outcome Type	-.010	[-.022, .002]	.11

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.3A. Choice by Consumption Model

Predictor Variable	B	CI	*P*-value
# Videos Consumed	-.001	[-.001, .000]	.06
Expected Value	.036	[.010, .064]	**.01**
Risk/Non-risk	.032	[.031, .033]	**<.001**
# Videos Consumed × Risk/Non-risk	-.001	[-.002, .000]	**.004**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.3B. Rating by Consumption Model

Predictor Variable	B	CI	*P*-value
# Videos Consumed	-.001	[-.002, .000]	.21
Expected Value	-.014	[-.077, .047]	.68
Risk/Non-risk	.002	[.001, .004]	**.008**
# Videos Consumed × Risk/Non-risk	.000	[-.001, .002]	.65

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.4A. Choice by Consumption Confound Model

Predictor Variable	B	CI	*P*-value
Actual Value	-.006	[-.008, -.004]	**<.001**
Outcome Type (Bad vs. Good)	-.051	[-.087, -.013]	**.01**
Outcome Type (Mid vs. Good)	-.033	[-.065, .001]	.06
# Videos Consumed	-.001	[-.002, -.001]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.4B. Rating by Consumption Confound Model

Predictor Variable	B	CI	*P*-value
Actual Value	.002	[.000, .004]	**.02**
Outcome Type (Bad vs. Good)	.054	[.007, .104]	**.03**
Outcome Type (Mid vs. Good)	.021	[-.022, .065]	.37
# Videos Consumed	.000	[-.001, .000]	.27

B: unstandardized coefficient; **CI:** confidence interval.

Supplemental Table 4.5. Choice by Risk Confound Model

Predictor Variable	B	CI	*P*-value
Actual Value	-.006	[-.008, -.005]	**<.001**
Outcome Type (Bad vs. Good)	-.054	[-.090, -.016]	**.006**
Outcome Type (Mid vs. Good)	-.031	[-.065, .007]	.11
Risk	-.004	[-.006, -.002]	**<.001**

B: unstandardized coefficient; **CI:** confidence interval.

CHAPTER 5: GENERAL DISCUSSION

The current body of work explored human deliberative mechanisms using a translational decision-making task, called the Web-Surf Task. Specifically, these studies aimed to identify cross-species behavioral and neural parallels, as well as mechanistic failures among highly impulsive individuals. The first study presented the Web-Surf Task in parallel to its rodent predecessor, Restaurant Row (Steiner & Redish, 2014). The second study explored the neural correlates of decision-making during the task; the results revealed evidence of prospective thinking during the choice phase, and that the extent to which a subject accurately imagined future outcomes was related to their overall decision-making ability. We also detected cross-species parallels when evaluating behavioral and neural responses to difficult trials. Finally, the third study, which employed a risk-variant of the Web-Surf Task, found a link between the enjoyment and pursuit of rewards under conditions of regret. Further, this study found that impulsive individuals exhibited aberrant learning after regret, suggesting that the failure to use regret may contribute to maladaptive traits related to addiction. Taken together, these studies highlight the utility of the Web-Surf Task for exploring complex cognitive phenomena in humans (within a single-session), and evaluating how specific mechanisms translate across species.

5.1 Study 1 Summary and Conclusions: Introducing the Web-Surf Task

Results from the first study offered an important starting point for those that followed. This study uniquely compared human and rodent data using analogous statistical procedures. The identification of basic behavioral parallels, e.g., cross-

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species evidence of revealed preferences or delay thresholds, laid the foundation for subsequently implementing the task in the MRI scanner. Of note, the Web-Surf Task grew out of a previous translational endeavor for which cross-species behavioral similarities were less established before neuroimaging data collection; thus, these initial results were especially motivating.

A second goal of the first study was to determine which type of stimuli to include in the Web-Surf Task: videos or photos (both of which are immediately consumable). Early debates raised concerns that videos were less consistent than photos, while photos were less rewarding than videos. Our results found that videos provided more reliable and valid results. This was rather unsurprising given the wealth of videos available on the Internet and our youthful demographic. Nonetheless, a direct comparison of these stimuli classes allowed us to draw this conclusion based on data rather than assumption.

Taken together, the Web-Surf Task using video stimuli provided a nice analogue to Restaurant Row. We next investigated the neural systems evoked during the Web-Surf Task, with a continued interest in cross-species similarities and differences.

5.2. Study 2 Summary and Conclusions: The Neural Basis of Human Deliberation

The primary goal of this study was to evaluate deliberation mechanisms in humans using General Linear Models (GLMs) and multi-voxel pattern analysis methods; the latter approach was implemented to parallel the neural ensemble recordings used in Restaurant Row. Several key findings emerged from this study. First, we found neural evidence of imagination. Specifically, the GLMs revealed large swathes of overlapping activation during the choice and video viewing phases of the task; this suggests that the

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same brain areas evoked when experiencing an outcome are also needed to mentally simulate the prospect of that outcome (Pearson et al., 2015). This result fits with emerging evidence that human prospection entails the representation of specific future outcomes (e.g., Doll et al., 2015).

A critical goal of Study 2 was the confirmation that the included video categories were indeed separable using decoding. When initially selecting categories, I reviewed the fMRI decoding literature to determine which objects or scenes map onto unique neural substrates. Despite this process, there still remained the possibility that we would be unable to parse the stimuli, given that the selected videos were complex and there was some element of within-category heterogeneity (as we did not display repeated videos). Fortunately, the decoding was successful: Decoding of the Preview Task data revealed that the categories were highly dissociable, despite the similarity of the category-specific GLM activation maps. This dissociability was further corroborated by the consumption decoding results. In particular, we consistently found the strongest representations of the current category during consumption. Thus, the videos observed during the main task were well matched with those shown during the Preview Task.

These decoding successes allowed us to then explore the deliberation phase. Here we found that different neural networks (e.g., dorsal attention, default mode, salience, etc.) represented different reward zones during deliberation. These results indicate that different systems are involved in imagining past and future outcomes. Comparable to Restaurant Row, the sequential nature of the Web-Surf Task was instrumental to these analyses; that is, we could track not only upcoming outcomes (as done by Doll et al., 2015), but also past experiences. We also found that subject-specific decoding

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accuracies predicted overall decision-making behaviors. One's capacity to imagine future prospects may then be critical to assigning value, and making choices that maximize the intake of more valuable rewards.

A final component of this study focused on the neural circuitry involved in difficult choices. This analysis paralleled 'Vicarious Trial-and-Error' (VTE) findings from rodents. First, we found that subjects' reactions times were slowest for offers that approached threshold, a pattern comparable to findings from Restaurant Row (Steiner & Redish, 2014). The GLM results revealed further cross-specifics parallels. In particular, difficult choices recruited the hippocampus, anterior cingulate cortex (ACC), and dorsal attention network during deliberation or consumption. We also found that deliberation more strongly activated the ACC and middle frontal gyrus (MFG) as compared to consumption, while consumption more strongly activated the orbitofrontal cortex (OFC) and middle/posterior insula.[14] We also note that the main effect for consumption included bilateral portions of the nucleus accumbens (NAcc), although this area did not emerge in the contrast map. These regions map well to those evoked in rats during VTE, particularly the hippocampus and prelimbic cortex (arguably homologous to the primate dorsolateral prefrontal cortex; Redish, 2016). OFC recruitment during consumption also aligns with rodent findings that implicate the OFC in signaling post-decisional information (Steiner & Redish, 2012; Stott & Redish, 2014). With regards to possible cross-species divergences, we did not detect NAcc activity when making difficult choices (Redish, 2016); this contradicts theories that the NAcc is responsible for pre-decisional evaluation. It is possible that the GLM model used to evaluate difficult choices was not

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[14] As noted in the General Introduction, the middle insula has been implicated in processing primary (versus secondary) rewards.

optimized for this purpose, i.e., isolating decisions to the last second aimed to address confounds regarding reaction time and value associations, but perhaps prevented us from capturing early NAcc signals.

Although Study 2 yielded critical insights into human deliberation, we remained troubled by one limitation of the task: its failure to capture regret. A pivotal discovery from the Restaurant Row data was that rats exhibited behavioral and neural markers of regret on sequential trials (Steiner & Redish, 2014). Because humans only completed one testing session, we did not acquire a sufficient number of 'regret' trials in either Study 1 or 2. To overcome this issue, we designed an alternative version of the Web-Surf Task that introduced counterfactuals within a trial via risky offers.

5.3. Study 3 Summary and Conclusions: Regret and Impulsivity

The final study examined relations between the liking and wanting of rewards using a risk-variant of the Web-Surf Task. This version was unique in that subjects did not know the true delay unless they chose to stay and accept the gamble. We defined regret-inducing situations as those in which subjects received the bad deal on a risk trial *and* they were responsible. We compared regret-inducing situations to those expected to provoke disappointment (bad outcomes that lacked personal agency) and relief (good outcomes). Our analyses focused on how subjects differently reacted to these conditions, as evidenced by their choices on subsequent trials and their rating of video rewards.

Our first major finding indicated that both the pursuit of rewards and the enjoyment of rewards were influenced by regret. That is, subjects became risk-averse following regret-inducing situations characterized by low value, but risk-seeking

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following regret-inducing situations of higher value. These results are comparable to findings that regret led individuals to minimize future regret in particular (i.e., after bad outcomes of low value; Zeelenberg et al., 1996; Zeelenberg & Pieters, 2004). Moreover, regret-instances influenced both choices and ratings, while disappointment-instances did not. This suggests that personal agency is a key factor in modulating decision-making.

Second, video ratings following different emotional conditions reflected sunk cost effects. In the context of regret, more time spent led to decreased ratings whereas less time spent led to increased ratings. This could suggest that the perception of more effort on lower cost trials escalated personal investment. We compared this effect to the relief-inducing trials and found the opposite pattern: low-valued trials were rated better than high-valued trials, suggesting that reward likability was driven down by cheaper offers framed as less effortful. These effects are akin to the overly patient foraging strategies of rodents, for which the perception of high behavioral investment led rats to accept high delay offers (Carter & Redish, 2016; Wikenheiser et al., 2013).

We also observed a direct connection between the liking and wanting systems: specifically, video ratings predicted subsequent choices following regret-inducing experiences only, i.e., these decision components remained dissociated following disappointment and relief scenarios. This challenges prior theories that liking and wanting constitute separable systems (Berridge & Robinson, 1995, 2003), by illustrating at least one context in which they are linked.

This study was the first to explore psychopathology using the Web-Surf Task. In a large non-clinical sample, we tested relations between task-derived parameters and trait-level impulsivity scores (measured using the Externalizing Spectrum Inventory, ESI;

Krueger et al., 2007). We found that highly impulsive individuals failed to learn from regret-inducing situations (i.e., they became risk-seeking and not risk-averse), but they did not differ in their immediate emotional reactions to those scenarios (i.e., reward ratings). This finding is consistent with evidence that chronic smokers were not guided by error signals despite exhibiting no loss in production of those signals (Chiu et al., 2008). Our results are also akin to a study on regret in psychopathy that demonstrated failures in regret-learning, but intact affective responsiveness (Baskin-Sommers et al., 2016).

Collectively, these results have broad implications across the areas of decision, emotion, and psychopathology research. Regret is a universal emotion that can have a powerful impact on our choices. Moreover, the failure to use regret may be a transdiagnostic factor present across various psychopathological disorders. This transdiagnostic conceptualization is critical, as our understanding and treatment of mental illness continues to draw from dimensional models of psychopathology, such as the RDoC (Research Domain Criteria) framework (Cuthbert, 2014). The link between regret-learning and impulsivity in a nonclinical sample speaks to these dimensional conceptualizations, in which maladaptive traits are present along a continuum from healthy to disordered individuals (Krueger, Markon, Patrick, & Iacono, 2005).

5.4 Future Directions

This collection of studies sets the stage for a breadth of future research. In this section, I focus on potential applications for cognitive and psychopathology research, as the included studies were limited to non-clinical samples. In particular, I discuss extensions of the Web-Surf Task for elucidating the behavioral and neural mechanisms

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that underlie addiction, psychosis, and psychopathy.

First, the finding for a link between poor decoding and decision-making has critical implications for cognition. Does this association suggest that certain individuals are unable to develop a cognitive map of the task (Tolman, 1948)? Of note, the hippocampus is fundamental to this ability, and one of the regions involved in our observed decoding deficit (O'Keefe & Nadel, 1978). Spatial memory training may enhance hippocampal growth (Lerch et al., 2011). It follows that future extensions could directly train spatial navigation skills and assess whether alterations in hippocampal function/structure impact one's representational abilities.[15] Additionally, one limitation of the current studies is that we did not ask subjects to explicitly state the order of the categories during the debriefing. Future studies could include this step to determine whether these subjects are aware of the task's layout but lack well-defined category representations, i.e., they know dance videos come next but cannot generate concrete future options.

Second, future studies are needed to explore relations between failures of regret-related learning among individuals with addiction. Such studies would benefit from the inclusion of multi-dimensional impulsivity measures, like the ESI, as a means to parse relations between mechanistic failures and specific impulsivity facets. For instance, alcohol consumption is most associated with sensation seeking and positive urgency (the latter being the propensity to engage in maladaptive and impulsive behaviors when in response to positive mood states; Stautz & Cooper, 2013). One might then explore the

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[15] Working memory training could be an alternative approach, given evidence that working memory training decreases discounting in stimulant addicts (Bickel et al., 2011).

extent to which sensation seeking tendencies differentially explain task performance. Is this failed learning mechanism equivalently captured by a heightened pursuit of risk? Or are these dissociable contributors?

Researchers could also investigate the impacts of different mood states on modulating impulsive behaviors. Work by Yuen and Lee (2003) used sad, neutral, and happy video clips to induce the respective moods before subjects completed risk-taking tasks. Their data indicated that individuals in an induced depressive state were more conservative in their risk-taking tendencies. With regards to findings from Chapter 4,[16] it is possible that short-lived regret-inductions are not sufficient for shifting behavior and stronger manipulations are needed (perhaps even ones that activate empathic circuits). In turn, understanding how affective states influence risk-seeking behaviors may be of value to addiction treatment initiatives.

Third, the Web-Surf Task's capacity to parse decision components could help elucidate goal-directed deficits in schizophrenia. Historically, anhedonia, or a diminished capacity to experience pleasure, has been linked to impaired goal-directed activity in schizophrenia (Rado, 1953). However, accumulating data paints a different picture: goal-directed deficits are not the result of an enjoyment deficit, but instead reflect failures to represent reward value or engage in key exploratory behaviors (Barch & Dowd, 2010; Strauss, Waltz, & Gold, 2014). For instance, individuals with schizophrenia exhibit comparable neural activation in response to emotional stimuli (Taylor et al., 2012), but struggle to utilize episodic memory when recreating past emotional experiences (Strauss & Gold, 2012). The Web-Surf Task provides a unique approach for examining relations

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[16] This is a reference to the failed regret-related learning observed among highly impulsive individuals.

between reward representation and hedonic capacity. Future studies could assess relations between neural representation accuracies at the choice point and consummatory pleasure; do representation abilities predict reward enjoyment or are these processes largely separable? Moreover, are there detectable differences in the representation of recent experiences (i.e., episodic memories) versus potential outcomes (i.e., episodic future thinking)? The sequential task design could shed interesting light on how recent experiences shape goal-directed pursuits.

Lastly, I discuss possible extensions of this task for understanding psychopathy. Psychopathy is associated with a lack of remorse and regret, features that have been attributed to low empathy and failures to generate negative affective responses to aversive stimuli (Patrick, 2007). Recent work by Sommers-Baskin and colleagues (2016) found that individuals with psychopathy failed to use prospective regret to guide future choices, despite intact emotional responses to regret. The authors then argued an alternative viewpoint to psychopathy: maladaptive decision-making may arise from a failure to generate forward models rather than a basic emotional deficit. The Web-Surf Task could be used to validate and extend this study: Researchers could first test whether individuals with psychopathy exhibit comparable consummatory responses (i.e., likability ratings) following regret, but are not driven to avoid risky offers on subsequent trials. Researchers could then explore potential representational failures during deliberation to directly test the alternative theory proposed by Baskin-Sommers et al. (2016). In summary, this task has broad utility for evaluating representation failures in psychopathology.

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