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Critical Review

The Behavioral Economics and Neuroeconomics of Alcohol Use Disorders

James MacKillop

Background: Behavioral economics and neuroeconomics bring together perspectives and methods from psychology, economics, and cognitive neuroscience to understand decision making and choice behavior. Extending an operant behavioral theoretical framework, these perspectives have increasingly been applied to understand the alcohol use disorders (AUDs), and this review surveys the theory, methods, and findings from this approach. The focus is on 3 key behavioral economic concepts: delay discounting (i.e., preferences for smaller immediate rewards relative to larger delayed rewards), alcohol demand (i.e., alcohol's reinforcing value), and proportionate alcohol-related reinforcement (i.e., relative amount of psychosocial reinforcement associated with alcohol use).

Findings: Delay discounting has been linked to AUDs in both cross-sectional and longitudinal studies and has been investigated cross-sectionally using neuroimaging. Alcohol demand and proportionate alcohol-related reinforcement have both been robustly associated with drinking and alcohol misuse cross-sectionally, but not over time. Both have also been found to predict treatment response to brief interventions. Alcohol demand has also been used to enhance the measurement of acute motivation for alcohol in laboratory studies. Interventions that focus on reducing the value of alcohol by increasing alternative reinforcement and response cost have been found to be efficacious, albeit in relatively small numbers of randomized controlled trials (RCTs). Mediators and moderators of response to these interventions have not been extensively investigated.

Future directions: The application of behavioral economics and neuroeconomics to AUDs has given rise to an extensive body of empirical work, although significant gaps in knowledge remain. In particular, there is a need for more longitudinal investigations to clarify the etiological roles of these behavioral economic processes, especially alcohol demand and proportionate alcohol reinforcement. Additional RCTs are needed to extend and generalize the findings for reinforcement-based interventions and to investigate mediators and moderators of treatment success for optimization. Applying neuroeconomics to AUDs remains at an early stage and has been primarily descriptive to date, but has high potential for important translational insights into the future. The same is true for using these behavioral economic indicators to understand genetic influences on AUDs.

Key Words: Behavioral Economics, Neuroeconomics, Alcohol, Delay Discounting, Alcohol Demand, Proportionate Alcohol-Related Reinforcement.

THE fields of behavioral economics and neuroeconomics are increasingly being applied to the study of alcohol use disorders (AUDs), and the goal of this review is to provide an introduction to these perspectives. Most broadly, behavioral economics refers to the hybridization of concepts and methods from psychology and economics to

understand the choices that people make (Bickel and Vuchnich, 2000; Camerer, 1999), and neuroeconomics refers to the further integration of behavioral economics and cognitive neuroscience to understand the neural foundations of those choices (Glimcher et al., 2009; Zak, 2004). For heuristic purposes, these perspectives can be understood in the context of the conventional branches of economics, with a shifting focus from the largest units of analysis to the smallest. Macroeconomics focuses on aggregated indicators of economic activity for large catchment areas (e.g., countries, regions), characterizing the transactions within and between large-scale economic actors. Microeconomics focuses on the allocation of financial resources by businesses, families, or individuals within their economic niches, examining transactions between smaller scale economic actors. One level of deeper, behavioral economics analysis focuses on how individual people allocate their behavioral resources, broadly defined to include money, time, and physical efforts, and investigates the psychological processes and environmental

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contingencies that systematically influence these transactions. Finally, neuroeconomics focuses on identifying the underlying aspects of brain structure and function that underlie the choices people make in their transactions with the world.

Beyond heuristics, however, behavioral economics and neuroeconomics are less like singular academic disciplines and more like a federation of scientific lines of inquiry from different intellectual traditions. There are some commonalities, but also surprisingly large differences in the foundational assumptions and phenomena of interest. Considering the multidisciplinary nature of the field, this is not surprising, but a consequence of the heterogeneity of perspectives is the importance of “connecting the dots” from theory to methods to findings in a given area. Achieving that continuity in applying behavioral economics and neuroeconomics to understand the AUDs from one specific perspective is the goal of the current article. Specifically, this review is intended to be a *précis* of the theory, methods, empirical findings, and active research questions in the operant behavioral formulation of behavioral economics. As such, it is not intended to be exhaustive and does not provide all existing economic perspectives on AUDs. In addition, the primary scope of this review is human studies; studies using preclinical animal models will only be included when pertinent. In terms of structure, the first section introduces the theoretical foundations; the second section describes 3 key processes—delay discounting, alcohol demand, and proportionate alcohol-related reinforcement—and provides a concise survey of the behavioral findings for each; the third section reviews clinical interventions that employ behavioral economic principles; the fourth section discusses progress in applying neuroeconomics to AUDs; and the fifth section identifies gaps in knowledge and current research priorities.

THEORETICAL FOUNDATIONS

The theoretical basis for using behavioral economics and neuroeconomics to study AUDs comes from 2 sources, its conceptual fit with the foundations of normative behavioral economics and the extension of an operant learning approach to AUDs. In the first case, common themes in virtually all behavioral economic research are a focus on choice behavior and understanding rational and irrational preferences (Camerer, 1999; Camerer et al., 2003). The focus on choice behavior is because selections among mutually exclusive outcomes are among the smallest units of analysis in economic exchange (broadly defined to include the exchange of one commodity [e.g., money, time, effort] for another [e.g., good, service, or behavioral outcome]). The focus on rationality is to address the general assumption of a rational actor in economics in general (i.e., preferences that are consistent over time and maximize positive outcomes). As a result, a major theme in behavioral economic research is identifying the ways in which individuals systematically deviate from rationality.

Probably, the most famous example of this is prospect theory, which has revealed asymmetric (i.e., irrational) sensitivity for losses compared to gains (Kahneman, 2003), insights for which Daniel Kahneman shared the 2002 Nobel Prize in Economic Sciences. These normative studies on behavioral economics reveal the way that irrational preferences are not simply stochastic, but reflect systematic deviations from rational actor models, what Ariely (2010) refers to as “predictably irrational” behavior. With regard to AUDs, these conceptual perspectives are highly relevant because choice behavior is a similarly critical antecedent of drinking. However internally conflicted or subjectively avolitional a person may feel, the behavior of an individual with an AUD is to reach out, lift a glass or bottle, and drink alcohol, a behavioral act of choice. In addition, at least from a clinical perspective, AUDs present as persistently irrational behaviors: continued drinking despite substantial and escalating negative consequences and strong personal desire to gain control over the behavior.

The second theoretical basis for behavioral economics comes from the tradition of operant learning theory. Using basic behavioral science as first principles, alcohol use (healthy or unhealthy) is theorized to be a prototypic operant behavior that is maintained by the reinforcing properties of the drug (Bigelow, 2001; Higgins et al., 2004). The foundational studies that support an operant perspective on AUDs come from residential laboratory studies in the late 1960s and early 1970s. These early studies demonstrated that alcohol consumption could be examined under controlled experimental conditions and was not unique as a reinforcing commodity (e.g., Mello and Mendelson, 1965; Mendelson and Mello, 1966; Nathan et al., 1970). In addition, residential laboratory studies convincingly demonstrated that alcohol consumption was sensitive to increases in response cost and the presence of alternative reinforcers (e.g., Bigelow et al., 1972; Griffiths et al., 1977; Sanders et al., 1976; for a review, see Bigelow, 2001), key predictions from operant theory. Using self-report measures, it is also clear that alcohol has both positively reinforcing properties that enhance an experience (e.g., stimulation, self-perception, social enhancement, gustatory properties) and negatively reinforcing properties that remove unpleasant experiences (e.g., anxiolysis, alleviation of depression) (Carey and Correia, 1997; Corbin et al., 2011; Darkes et al., 2004; Herschl et al., 2012; Kuntsche et al., 2008). Importantly, these different forms of positive and negative reinforcement are not mutually exclusive and operate concurrently, reflecting an individual’s underlying motivational schemata for alcohol reinforcement. Figure 1 presents an integrative operant/behavioral economic theoretical perspective on AUDs at a conceptual level. Alcohol’s positively and negatively reinforcing properties, its punishing properties, the opportunity for alternative reinforcers, and the timing of provision are theorized to jointly determine the reinforcing value of alcohol, the putative final common pathway to drinking. These processes are

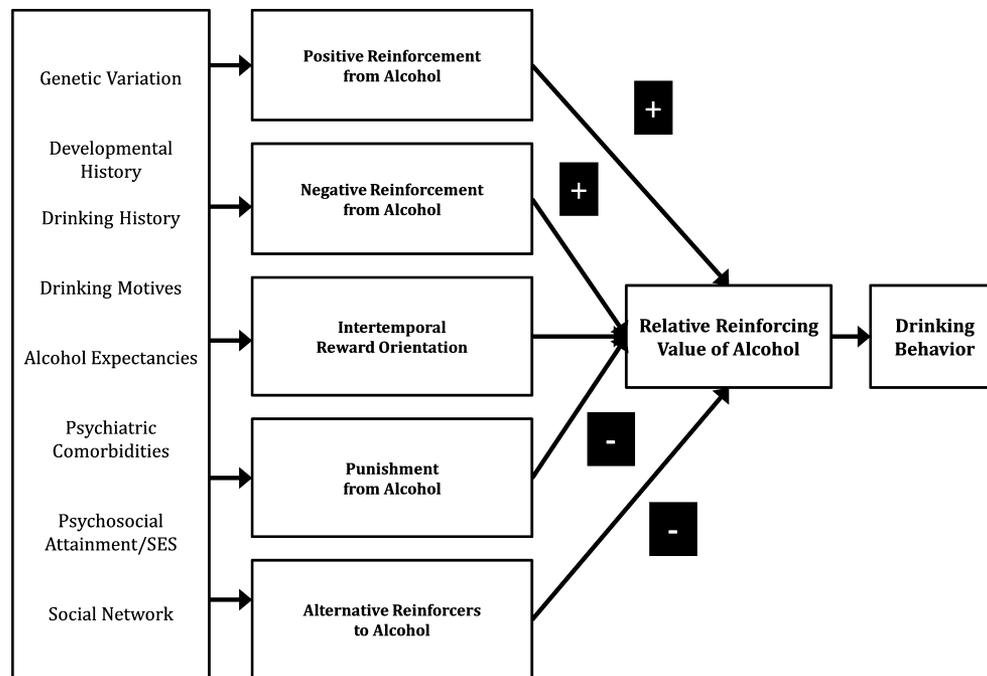


Fig. 1. A simplified conceptual theoretical framework for an operant/behavioral economic perspective on drinking behavior. Diverse classes of influences are theorized to impinge on different facets of alcohol's reinforcing value, with the aggregated reinforcing value proximally determining drinking behavior. Note that the classes of influences on the far left are not assumed to be independent of one another, and the arrows from those influences do not link to the specific aspects of reinforcement. Note also that relative reinforcing value refers to the hypothetical construct, not any single specific operationalization as an intervening variable.

theorized to be the proximal mechanisms by which other known risk factors contribute to drinking behavior.

The critical catalyst for integrating operant learning principles and economic methods, however, was Herrnstein's matching law (Herrnstein, 1961, 1970), which sought to describe behavior in operant environments with more complex reinforcement contingencies. Specifically, the matching law proposes that, over time, behavioral rates of responding scale to (match) the available reinforcement schedules. In turn, selectively allocating finite amounts of behavior for differential outcomes was recognized as basically being a parallel to an economic environment (Hursh, 1980, 1984). Beyond controlled experimental contexts, drinking in the natural environment reflects choices among diverse behavioral options with varying reinforcing properties and behavioral costs. This natural operant environment is highly complex, with many concurrent schedules of reinforcement, but collectively it too can ultimately be understood as a zero-sum behavioral microeconomy within which finite resources are mutually exclusively allocated. For this reason, microeconomic principles and methods have been imported to improve the characterization of operant behavior (Bickel and Vuchinich, 2000; Bickel et al., 1993; Hursh, 1993; Hursh et al., 2005; Vuchinich and Heather, 2003). This approach represents the converse of behavioral economic studies that import psychological processes to understand economic preferences; it is the importation of economic concepts and methods to understand individual consumption behavior.

A second important insight from the matching law was that delay to reward had a similar effect to response cost (Chung and Herrnstein, 1967), indicating that the reinforcing value of an outcome was a function not only of its reinforcing properties, punishment, and alternatives, but also the immediacy of access. For this reason, it is also included in Fig. 1. In addition, it became clear that the temporal valuation of outcomes based on delay tended to be hyperbolic in form (i.e., differentially steep initially and then shallow subsequently) (Mazur, 1987), and a mathematical implication of hyperbolic discounting was a preference reversal as access to a smaller immediate reward approached. In other words, although an individual might report preferring a \$100 larger later reward in 1 month over \$80 in 3 weeks, hyperbolic preferences would predict the smaller sooner reward becoming more appealing and being selected as time to receipt approached. Preference reversals are an exemplar of irrational preferences as they violate the assumption of consistency over time, but, more importantly, dynamic inconsistency in intertemporal choice was viewed as a potential model system for self-control failure in addiction (Ainslie, 1975, 2001; Rachlin and Green, 1972). In turn, a prediction from this interpretation was that individuals with addictive disorders would exhibit particularly hyperbolic time preferences, addressed below.

A further point about the operant behavioral economic perspective is that it emphasizes the importance of a "molar" perspective on behavior rather than a "molecular" perspective (Vuchinich, 1995; Vuchinich and Tucker, 1988). This dis-

tion refers to investigating temporally extended patterns of behavior as opposed to assessments that are only specific to a particular instance. The perspective is influenced by Herrnstein's matching law to the extent that *rates* of responding matched *rates* of reinforcement, not necessarily instances. Also, more broadly, a molar framework seeks to identify behavioral regularities that are final causes of behavior, rather than the efficient causes of a single instance, one that is potentially not be representative. Although it should be acknowledged that most of the empirical research does not characterize extended temporal sequences of behavior directly, a molar perspective nonetheless informs behavioral economic research on AUDs.

Finally, it is worth noting that the preceding theoretical perspective is entirely distinct from Becker and Murphy's (1988) theory of rational addiction, which comes from the economic tradition of behavioral economics. Although a full discussion of this approach is beyond the scope of this review, the rational addiction perspective argues that addictive behavior, defined as consumption of goods that increase future consumption of the same good can be fundamentally understood as being rational behavior in economic terms. This approach is commonly applied in economics, but not in psychology or psychiatry, and has been criticized on a number of its assumptions (Rogeberg, 2004).

In summary, a behavioral economic approach to AUDs synthesizes concepts and methods from operant behavioral psychology and microeconomics to understand the overconsumption of alcohol. It is informed by both conceptual links to choice behavior in normative behavioral economics and an elaboration of the operant behavioral conceptualization of AUDs. In the following section, 3 core behavioral economic assays will be introduced: delay discounting, alcohol demand, and proportionate alcohol-related reinforcement. These are not the only behavioral economic measures available, but are the ones that have been most extensively applied to AUDs.

THREE CORE BEHAVIORAL ECONOMIC ASSAYS FOR UNDERSTANDING ALCOHOL USE DISORDERS

Delay Discounting

Delay discounting is a measure of intertemporal choice that characterizes preferences for smaller immediate rewards versus larger delayed rewards (i.e., how much a reward is *discounted* by the *delay* to receipt). It is akin to the notion of capacity to delay gratification and is considered a behavioral economic index of impulsivity. Although delay discounting can be assessed for a variety of different commodities and in a number of different formats, the most common strategy is to use money as generalized reinforcer with either iterative permuted decision-making tasks or shorter measures with preconfigured items pertaining to certain levels of discounting. The iterative permuted tasks systematically pose choices between various smaller immediate rewards versus a uniform

larger delayed reward across multiple delay periods (e.g., 1 day, 1 week, 1 month, and 1 year), sometimes using an adaptive format for efficiency. Across trials, an individual's points of indifference (i.e., the point at which the smaller immediate reward is equal to the larger delayed reward) can be ascertained and an overall temporal discounting function can be generated, reflecting the devaluation gradients illustrated in Fig. 2. The most commonly used discounting equation is Mazur's hyperbolic model (1987), but several alternatives exist (e.g., [Green and Myerson, 2004](#); [Rachlin, 2006](#)) and an atheoretical measure of area under the curve is also widely used ([Myerson et al., 2001](#)). Of the measures using preconfigured items, the Monetary Choice Questionnaire (MCQ) ([Kirby et al., 1999](#)) is the most widely used ([MacKillop et al., 2011a](#)). These measures do not permit empirical modeling of the discounting curve, but use the items to infer an estimated discounting function using the hyperbolic model.

Using these various assessments, there is consistent evidence that individuals with AUDs exhibit steeper discounting of future rewards than matched controls ([Bjork et al., 2004](#); [Kirby and Petry, 2004](#); [Mitchell et al., 2005](#); [Petry, 2001](#)). In a meta-analysis of categorical studies, this difference was significant across studies and the effect size was medium ($d = 0.68$) for studies using clinical samples and small ($d = 0.29$) for studies using subclinical samples ([MacKillop et al., 2011a](#)). In studies using continuous designs, greater delay discounting has also been found to be significantly associated with drinking quantity and frequency ([Christiansen et al., 2012](#); [Field et al., 2007](#); [MacKillop et al., 2010a](#)), with medium effect sizes according to statistical conventions.

Etiological causality cannot be addressed in these cross-sectional studies, but an accumulating body of work suggests that steep discounting precedes AUDs and not the other way

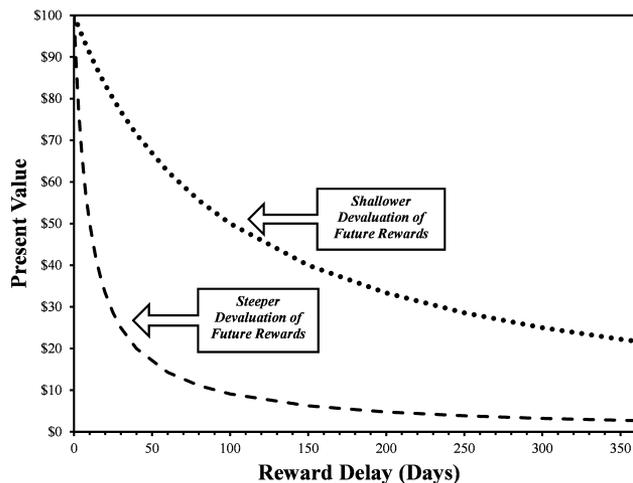


Fig. 2. Prototypic hyperbolic discounting of \$100 available from 1 day to 1 year. The y-axis reflects how much money in the present would be equivalent to \$100 across the future delays (x-axis). More precipitous discounting of larger future rewards reflects greater preference for smaller immediate rewards and is putatively an index of impulsivity.

around. In retrospective studies, steeper discounting has been associated with earlier onset of AUD symptoms (Dom et al., 2006; Kollins, 2003). A number of longitudinal studies have directly addressed delay discounting and drinking over time. For example, 1 longitudinal study found discounting generally predicted subsequent drinking over the course of adolescence, but drinking did not predict subsequent discounting (Fernie et al., 2013). This parallels a longitudinal study in adolescent smokers (Audrain-McGovern et al., 2009). In a second longitudinal investigation, steeper discounting mediated the predictive relationship between working memory and drinking behavior over adolescence (Khurana et al., 2013). Further evidence for longitudinal links between steep delay discounting and alcohol misuse comes from a series of studies using a naturalistic measure of delay discounting, the documented allocation of discretionary financial resources to alcohol (immediate smaller reward) versus savings (future delayed reward). Specifically, this measure has been found to predict natural resolution of drinking problems among untreated heavy drinking adults (Tucker et al., 2002, 2006). This relationship was subsequently replicated in an ecological momentary assessment design using interactive voice response (Tucker et al., 2008, 2012). Also related to etiology, a number of studies have found that family history of alcohol and other drug use is associated with steeper delay discounting (e.g., Acheson et al., 2011; Dougherty et al., 2014; VanderBroek et al., 2016), even among drug-naïve early adolescents, suggesting it may be an intermediate process for the risk conferred by family history, genetic, and/or environmental.

Of note, a number of the aforementioned studies used the MCQ, for which there is an inherent loss of assessment resolution as a result of using preconfigured items. This is both in terms of characterizing exact participant temporal discounting functions and capacity to test alternative models of discounting. However, despite this, the measure has robustly linked addictive behavior and steep discounting (MacKillop

et al., 2011a), suggesting it is nonetheless capturing key variability in preferences. In addition, the MCQ has been shown to have robust psychometric properties, including extended test–retest reliability (Kirby, 2009).

Alcohol Demand

Demand is a fundamental concept in economics and refers to the amount of a commodity that is sought or consumed at a given price. In this case, alcohol demand is an index of the individual's value of alcohol as a reinforcer. Methodologically, demand can be assessed via either operant progressive-ratio or fixed-ratio schedules, or behavioral economic purchase tasks. For the former, participants earn access to alcohol via effortful behavior on an experimental manipulandum (e.g., spacebar presses) at varying levels of response requirement. For the latter, participants report how much alcohol (or other drug) they would consume at a variety of prices that start very low and escalate to very high levels; choices are either for entirely hypothetical outcomes or may be for a consequated outcome that the participant actually receives. For both operant schedules and purchase tasks, motivation for alcohol is conceptually measured by the effects on consumption in the context of the imposition of costs, akin to measuring the momentum of an object by quantifying the resistance needed to stop it. More specifically, the reinforcing value of alcohol can be operationalized using microeconomic demand curve analysis, which formally characterizes the relationship between consumption of a commodity and its cost. Demand curves yield multiple motivational indices, and prototypic demand and expenditure curves are presented in Fig. 3. These indices include consumption at minimum price (i.e., intensity), the price that reduces consumption to zero (i.e., breakpoint), maximum expenditure (O_{max}), and the aggregate slope of the demand curve (i.e., elasticity), which quantifies the degree to which intensity of demand is defended. Most of the preceding can be generated using

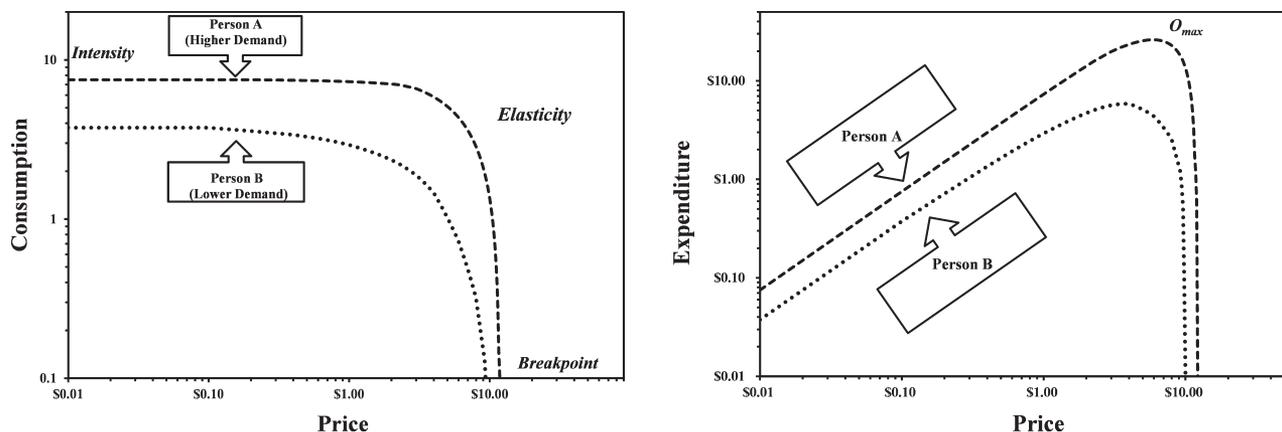


Fig. 3. Prototypic demand and expenditure curves for 2 hypothetical individuals exhibiting higher and lower demand for alcohol. The demand curve is presented on the left, and the expenditure curve is depicted on the right. Consumption refers to numbers of standard drinks; price refers to cost per drink. Intensity refers to demand at very low or zero price, and breakpoint refers to the price that first suppresses consumption to zero; elasticity refers to the aggregated slope of the demand curve, and O_{max} refers to the maximum expenditure on alcohol, the peak of the expenditure curve.

observed participant responses, but elasticity is typically derived via nonlinear regression of an exponential model of demand ([Hursh and Silberberg, 2008](#)). This single parameter model has largely replaced earlier 2-parameter models ([Hursh and Winger, 1995](#); [Hursh et al., 1988](#)).

These indices putatively capture important variability in the value of alcohol as a reinforcer for the individual, both being conceptually related to each other (all reflecting some aspect of alcohol's reinforcing value) but also being distinct (reflecting different points on the demand and expenditure curve). Persistently high alcohol demand is theorized to be an important recursive etiological marker for the development of alcohol misuse in emerging adults ([MacKillop et al., 2011b](#); [Murphy et al., 2007b](#); [2012b](#)). In other words, following initial exposure to alcohol, increasing alcohol involvement with reinforcing consequences is theorized to increase the reinforcing value of alcohol reciprocally, in a feedforward loop. Among recreational drinkers, alcohol's reinforcing value theoretically terminates before significant negative consequences, but among individuals with AUDs, alcohol's reinforcing value persists and escalates despite the adverse effects of drinking.

Considerable empirical research supports this hypothesis, primarily from studies using the purchase task paradigm. Numerous cross-sectional studies have found robust associations between alcohol demand and alcohol misuse in emerging adults. For example, in categorical comparisons, individuals at higher levels of alcohol misuse exhibit significantly higher demand for alcohol ([Murphy and MacKillop, 2006](#); [Smith et al., 2010](#); [Teeters and Murphy, 2015](#); [Teeters et al., 2014](#)). These relationships are also evident in continuous designs, where indices of alcohol demand are significantly associated with levels of alcohol consumption, symptoms of alcohol dependence, and alcohol-related problems ([Bertholet et al., 2015](#); [Gray and MacKillop, 2014b](#); [MacKillop et al., 2010a](#); [Murphy et al., 2009](#); [Smith et al., 2010](#)). Indeed, in meta-analyzing continuous associations in cross-sectional studies, indices of alcohol demand were highly significantly associated with alcohol misuse at moderate effect size magnitudes ([MacKillop et al., 2015b](#)). Demand indices have also been applied to understand common comorbidities between AUDs and other forms of psychopathology. For example, young adult drinkers with depressive or posttraumatic stress disorder symptoms exhibit higher alcohol demand ([Murphy et al., 2013](#)); in both cases, these relationships putatively reflect augmented alcohol demand as a result of heightened motivation for its negatively reinforcing properties, although that indirect effect has not been demonstrated empirically. Similarly, smokers exhibit elevated alcohol demand ([Yurasek et al., 2013](#)), potentially reflecting the known potentiating effects of concurrent alcohol and nicotine consumption ([Doyon et al., 2013](#); [Funk et al., 2006](#)). Also of note, the indices of demand from the Alcohol Purchase Task and other purchase tasks have been shown to have good psychometric properties, including test-retest and internal reliability ([Amlung and MacKillop, 2012,](#)

[2015](#); [Amlung et al. 2012](#); [Few et al., 2012](#); [Murphy et al., 2009](#)).

The preceding relationships pertain to a trait-like perspective on alcohol demand (i.e., preferences that are generally stable over time, *ceteris paribus*), but a second application of alcohol demand has been in augmenting the assessment of state motivation in laboratory studies. Historically, the primary dependent variable in laboratory studies is subjective craving, which is subject to a number of measurement limitations ([Sayette et al., 2000](#)). The use of purchase tasks in laboratory studies has been intended to translate acute motivation into putatively more objective measures of consumption, expenditure, and price sensitivity. The findings to date have been promising. State-oriented alcohol purchase tasks have revealed acute increases in demand in response to alcohol cues ([MacKillop et al., 2010b](#)) and stress manipulations ([Amlung and MacKillop, 2014](#); [Owens et al., 2015](#)), and similar findings have been reported regarding motivation for tobacco ([Acker and MacKillop, 2013](#); [MacKillop et al., 2012](#)) and food ([Stojek et al., 2015](#)). Although not using in vivo manipulations, 2 studies have used manipulations in the instructional sets of alcohol purchase tasks to explore differences in demand based on the presence of psychosocial consequences the following day (e.g., an exam in university drinkers) ([Gentile et al., 2012](#); [Skidmore and Murphy, 2011](#)). In both cases, these instructional changes were found to substantially affect demand and sensitivity to this manipulation was subsequently linked to the presence of a family history of alcohol ([Murphy et al., 2014](#)). Collectively, this work illustrates the viability of examining alcohol demand as assessed via a purchase task as an individual difference measure (effectively an independent variable), an outcome measure (a dependent variable), and as a platform for implementing experimental manipulations.

In the foregoing work, alcohol demand was often referred to as a superordinate construct, generally reflecting alcohol's reinforcing value, but it is important to note that the demand indices are considered distinct from one another. It is beyond the scope of this review to unpack the specific findings on an index-by-index basis, but, in general, the largest effect sizes in the studies to date have tended to be for intensity and O_{\max} , with somewhat smaller relationships for breakpoint and elasticity (e.g., [MacKillop et al., 2015b](#)). In terms of interrelationships, the correlations among the indices vary considerably, ranging from negligible to very high (e.g., [Herschel et al., 2012](#); [Murphy and MacKillop, 2006](#); [Murphy et al., 2013](#)). However, 2 studies examined the latent structure of these relationships and have found a binary factor structure to the data, with intensity and O_{\max} loading on 1 factor and elasticity, breakpoint, and O_{\max} loading on the other (O_{\max} loading on both) ([Bidwell et al., 2012](#); [MacKillop et al., 2009](#)). These factors were named *amplitude* (i.e., maximum amount of alcohol consumed and money spent) and *persistence* (i.e., sensitivity to escalating prices), respectively, and broadly scaled to the x - and y -axes of the demand curve. This suggests that there are some natural latent inter-

relationships among the indices and, based on effect sizes, it appears that the indices comprising amplitude measures are most salient to AUDs. However, it would be premature to identify any demand indices as being clearly preferable or superior at this point. Indeed, it is unclear whether that would ever be desirable as a cardinal advantage of using full alcohol demand curve analysis is the availability of high resolution and precision in describing different aspects of reinforcement.

Proportionate Alcohol-Related Reinforcement

The third behavioral economic index that is highly relevant to alcohol misuse is a molar measure of proportionate alcohol-related reinforcement. This is defined as the relative allocation of time and enjoyment that is associated with alcohol use compared to alcohol-free behavior (Murphy et al., 2005, 2006, 2007a). High proportionate alcohol reinforcement is theorized to be an indicator of disproportionate reliance on alcohol-related reinforcement compared to alternative reinforcers. This parallels neurobiological allostatic dysregulation models of addiction in which diminished dopamine response to naturally occurring substance-free rewards such as food or pleasant events is viewed as a key feature (Koob, 2015; Koob and Le Moal, 2008; Koob and Volkow, 2010; Volkow and Baler, 2014). In practice, it is assessed via the Alcohol-related Reinforcement Scale (ARRS) (Correia et al., 1998), which quantifies engagement in a variety of different reinforcing activities and the extent to which alcohol is involved in each. On one hand, alcohol use may be high, but restricted to specific contexts and part of an extensive portfolio of reinforcing psychosocial activities; on the other, alcohol may be a part of all reinforcing activities in a person's life, meaning changing drinking will generally attenuate reinforcing recreational activities. Figure 4 illustrates the nature of the index.

There is considerable empirical evidence that proportionate alcohol-related reinforcement plays an important

role in AUDs. For example, numerous human laboratory studies have shown that substance use decreases if access to alternative reinforcers is increased (Bigelow, 2001; Higgins et al., 2004). Similarly, in preclinical models, contexts devoid of substance-free sources of reinforcement have been consistently found to promote high rates of substance use (Carroll et al., 2009). Pertaining to alcohol misuse in young adults, there is evidence that heavy drinkers report less reinforcement from nondrug activities compared to matched controls (Correia et al., 1998, 2003). In continuous designs, alcohol-free reinforcement is significantly negatively associated with alcohol misuse and vice versa (Correia et al., 1998, 2002; MacKillop and Murphy, 2007; Murphy et al., 2005, 2009). Longitudinally, alcohol-related reinforcement has been shown to predict ongoing drinking and problem resolution in middle-aged AUD+ adults (Tucker et al., 1995, 2002, 2008, 2009; Vuchinich and Tucker, 1996).

With regard to the overlap between alcohol's reinforcing value as measured by alcohol demand and proportionate alcohol-related reinforcement, the two are related but nonetheless distinct. In psychological terms, it can be thought of as the drug's endogenous motivational significance for the individual. In contrast, proportionate alcohol-related reinforcement is an assay of the individual's allocation of behavior across diverse environmental reinforcement contingencies. It characterizes the reinforcement context within which drinking takes place. In psychological terms, it is the molar reinforcement context of alcohol use for the individual. In addition to these conceptual differences, several empirical studies indicate that the 2 are generally quantitatively distinct (MacKillop and Murphy, 2007; Murphy et al., 2009; Skidmore et al., 2014).

It is also worth noting that the assessment of proportionate alcohol-related reinforcement is qualitatively different from alcohol demand or delay discounting, both are measured by tasks that permit the quantitative analysis of behavior. In addition, demand and discounting tasks both permit

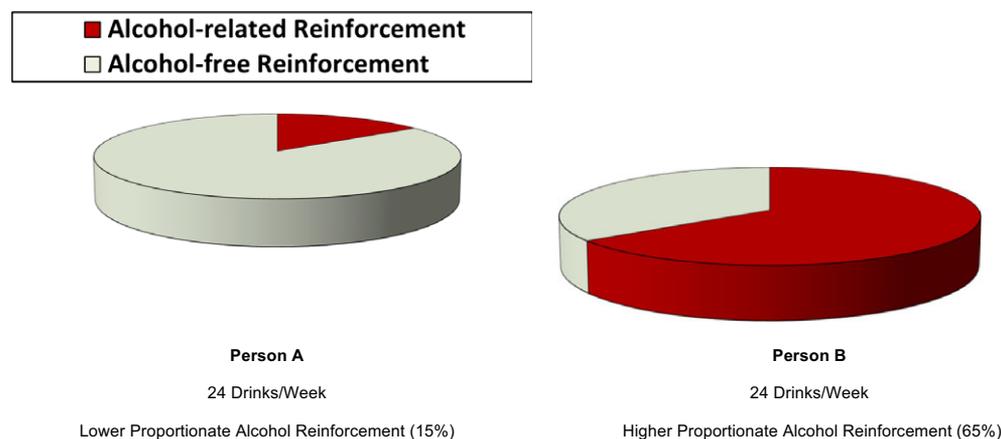


Fig. 4. Prototypic proportionate alcohol-related reinforcement for 2 hypothetical individuals. This index provides a quantitative measure of the relative prominence of alcohol reinforcement within a person's psychosocial/behavioral repertoire. It is distinct from drinking itself, as shown in the 2 examples with equal drinking but substantially different proportions of alcohol-related reinforcement.

the assessment of the *process* of decision making in vivo. In contrast, the ARRS is an entirely retrospective report of activities with and without the presence of alcohol and the associated reinforcement. As such, it is more similar to traditional retrospective self-report inventories than behavioral tasks. To be fair, trait-level alcohol demand often uses the instructional set of drinking during a typical episode, which involves some level of retrospection also, and proportionate alcohol-related reinforcement is quantitatively derived as a ratio rather than being exclusively self-attributions. Nonetheless, proportionate alcohol-related reinforcement as measured by the ARRS is fundamentally a historical measure and there would be value in the development of a task that validly captures the construct (e.g., a concurrent reinforcement schedule pitting alcohol reinforcement against diverse forms of alternative reinforcement).

CLINICAL APPLICATIONS

From a behavioral economic theoretical perspective, altering the reinforcement contingencies for drinking is a critical strategy in treating AUDs and this has been directly investigated using the community reinforcement approach (CRA) and contingency management (CM). Given the deleterious consequences of drinking, it is not uncommon for an individual with an AUD to have substantially impoverished reinforcing opportunities beyond drinking. Loss of recreational activities, jobs, and relationships can create a “vicious cycle” of drinking because of dwindling options, until none remain. Based on this, the CRA’s strategy is to restructure the environmental contingencies to increase the value of sobriety via mutually exclusive alternative reinforcers and thereby also increase the costs of drinking. By doing so, the goal is to make abstinence more reinforcing than drinking. In terms of clinical outcomes, initial trials of the CRA were very positive ([Azrin, 1976](#); [Hunt and Azrin, 1973](#); [Meyers and Miller, 2001](#)) and these outcomes have subsequently generalized from a traditional adult inpatient sample to homeless individuals with AUDs ([Smith et al., 1998](#)) and a young adult AUD sample ([Smith et al., 2011](#)). Across studies, the CRA has been found to be efficacious in treating AUDs ([Miller and Wilbourne, 2002](#); [Roizen et al., 2004](#)) and also other addictive disorders (for a comprehensive review, see [Meyers et al., 2011](#)). An adaptation of the CRA for family members has also been developed, termed Community Reinforcement Approach Family Training (CRAFT). The rationale behind CRAFT is that many individuals with AUDs are ambivalent or unmotivated to modify their drinking and family members may benefit from strategies for modifying the reinforcement contingencies around drinking to encourage treatment. Although the number of randomized controlled trials (RCTs) is small, CRAFT outcomes have been positive for both AUDs ([Dutcher et al., 2009](#); [Miller et al., 1999](#); [Sisson and Azrin, 1986](#)) and other substance use disorders ([Meyers et al., 2011](#)).

In contrast to the macrocosmic perspective of the CRA, CM uses incentives to directly reinforce protreatment outcomes, such as attendance and sobriety (for a review, see [Stitzer and Petry, 2006](#)). From a theoretical standpoint, this strategy increases the opportunity cost of substance use, thus increasing the reinforcing value of protreatment behavior. Given steep delay discounting among individuals with AUDs, an added advantage is that these contingencies are in high temporal proximity. A recent meta-analysis reported CM to be generally efficacious for substance use disorders ([Prendergast et al., 2006](#)). Only 2 studies of CM have been conducted on AUDs, but both have been supportive ([Petry et al., 2000, 2012](#)). A challenge in implementing CM for AUDs is that breath alcohol is the standard biomarker for drinking and is highly transient, but recent studies have used continuous transdermal monitoring systems and ethyl glucuronide, a longer-lasting urinary biomarker, to verify contingencies over longer periods of time ([Barnett et al., 2011](#); [McDonnell et al., 2012](#)).

The third area where progress has been made applying behavioral economic theory in clinical settings is as an enhancement to brief motivational interventions (BMIs) for young adult drinkers. Typical BMIs are single session interventions that provide personalized feedback within a motivational interviewing framework. Several studies have evaluated the addition of a behavioral economic supplement that focuses on reducing the value of alcohol by fostering increases in substance-free reinforcement and increasing the salience of delayed rewards. In an initial within-subjects pilot study, the supplement was associated with robust reductions in drinking ([Murphy et al., 2012c](#)). Subsequently, in an RCT using an active control group, the supplement was again associated with significantly greater reductions in alcohol problems ([Murphy et al., 2012a](#)). However, a subsequent version of the supplement that was attenuated and focused on both alcohol and other drugs did not enhance drinking outcomes, suggesting the full supplement may be necessary ([Yurasek et al., 2015](#)). A promising aspect of this latter study was that the behavioral economic supplement did significantly reduce marijuana use compared to the control condition.

A final notable application of behavioral economics in clinical studies of alcohol is in mechanistic research, either using indices for predicting treatment response or directly examining treatment effects. This work has largely taken place in the context of BMIs for young adult drinkers. Early studies using within-subjects designs reported that both indices of alcohol demand and proportionate alcohol-related reinforcement were significantly associated with intervention response ([MacKillop and Murphy, 2007](#); [Murphy et al., 2005](#)). In both cases, higher pretreatment reinforcing value was associated with worse follow-up drinking. Taking a different tack, 1 investigation has used indices of alcohol demand to investigate whether one of the mechanisms of naltrexone was via alternations to the reinforcing value of

alcohol (Bujarski et al., 2012). In that study, naltrexone did indeed significantly reduce intensity, O_{\max} and breakpoint compared to placebo. More recently, Dennhardt and colleagues (2015) reported that a BMI acutely reduced alcohol demand (intensity, O_{\max} , elasticity) and the acute reductions in demand were predictive of 6-month outcomes. Similarly, a second study recently reported that 2 baseline demand indices (intensity and O_{\max}) significantly predicted follow-up drinking and alcohol problems, that these indices exhibited acute reductions in response to the interventions, and that those changes were predictive of intervention response (Murphy et al., 2015). In addition, this study also assessed relative discretionary expenditures on alcohol and found that this index predicted baseline alcohol problems and follow-up drinking that reductions in expenditure predicted follow-up outcomes. These findings collectively suggest behavioral economic indices are highly promising prognostic variables and mechanisms of behavior change.

THE NEUROECONOMICS OF ALCOHOL USE DISORDERS

The field of neuroeconomics has existed for just over a decade and started primarily with proof-of-concept studies demonstrating that key decision-making phenomena could be characterized at all using neuroimaging (e.g., McClure et al., 2004; Sanfey et al., 2003). Increasingly, neuroeconomic approaches have been applied to clinical populations, including individuals with AUDs. The dominant methodology is functional magnetic resonance imaging (fMRI), which indirectly characterizes neural activity via the blood-oxygen-level-dependent (BOLD) signal, and much of the empirical neuroeconomic research on AUDs has focused on the neural correlates of delay discounting. In an early case-control study of delay discounting and AUDs, individuals with AUDs exhibited steeper discounting behaviorally and greater neural activity in dorsolateral prefrontal cortex (dlPFC), posterior parietal cortex (PPC), and parahippocampal gyrus (Boettiger et al., 2007). Similar findings were present in a subsequent study using the same design, with individuals with AUDs exhibiting greater devaluation of future rewards behaviorally and significantly greater activity in bilateral dlPFC (Amlung et al., 2014). Differences in PPC were not observed in that study, although significantly greater activity in the precuneus and parietal cortex was present. In general, these findings are similar to studies of individuals with methamphetamine and nicotine dependence compared to controls that found significantly greater frontoparietal activity in the addiction criterion groups (Clewett et al., 2014; Monterosso et al., 2007). In contrast, in a study using a continuous design, significant associations were detected between severity of AUD and neural activity in the anterior insula, inferior frontal gyrus, anterior cingulate, cuneus, and inferior parietal lobule (Claus et al., 2011). Moving away from

region-of-interest-based designs, a recent study examined functional connectivity in individuals with AUDs and controls, finding significantly greater connectivity in salience, default mode, orbitofrontal, and executive networks in the AUD group (Zhu et al., 2015). In addition, in individuals with AUDs, level of delay discounting was significantly associated with connectivity in the executive control, default mode, and salience networks. Although only a small number of studies have been conducted, one common theme has been significant differences in frontoparietal regions, suggesting important differences in the interactions between executive faculties and prospective thinking/consciousness. In addition, an interesting theme is that the significant findings to date have revealed greater brain activity and functional connectivity among individuals with AUDs, and not the other way around. Although intuition might predict deficits in activity during delay discounting, the studies to date suggest greater activity and functional connectivity, despite more impulsive behavioral output. Although definitive conclusions cannot be drawn given the relatively small number of studies to date, these studies provide potentially important initial insights into this disrupted form of decision making in AUDs.

Beyond delay discounting, 1 study has investigated the neural correlates of alcohol demand decision making (MacKillop et al., 2014). In that study, male heavy drinkers underwent an extended protocol combining an fMRI scan with a bar laboratory self-administration session. Participants completed an adapted demand paradigm in the scanner, choosing how many drinks they would consume at various prices within a \$15 “bar tab.” (Immediately following the scan, the participants received one of their choices and the associated money and alcohol in a bar laboratory.) The study characterized the neural activity associated with 3 different types of choices: inelastic choices (i.e., maximum alcohol consumption selected across prices), elastic choices (i.e., some alcohol consumption selected, but lower than maximum), and suppressed demand (no alcohol consumption selected). Decisions to drink in general (inelastic and elastic) were associated with frontoparietal activity, putatively reflecting executive functioning, deliberation, and prospective thinking. Elastic demand decisions, reflecting reductions in preferences but not complete suppression, elicited the largest magnitude differences in activation. These choices were characterized by differential frontostriatal activity and insular activity, appearing to capture the interplay among subjective reward value in the striatum, interoceptive visceral processing via the insula, and the external contingencies represented in dlPFC. In addition, elastic demand drinking decisions were associated with significant deactivation in regions associated with default mode network activity. This apparent default mode network suppression appears to reflect the greater cognitive load associated with these decisions. Although this is clearly just a single study, it provides proof of concept that alcohol demand can be characterized in a neuroimaging environment.

GAPS IN KNOWLEDGE AND FUTURE DIRECTIONS

The preceding sections reveal the numerous ways behavioral economics and neuroeconomics have been applied to AUDs, but significant gaps in knowledge remain. In the case of the behavioral studies on delay discounting, alcohol demand, and proportionate alcohol reinforcement, a significant limitation is that the vast majority of the work is cross-sectional in nature. In particular, no longitudinal risk studies have leveraged indices of alcohol demand or proportionate alcohol reinforcement, and only a small number of investigations have focused on delay discounting. This leaves unanswered significant scientific questions about whether these processes are causal or consequential, and undermines the unique molar theoretical orientation of behavioral economics. A second gap in the behavioral literature is that although behavioral economic variables appear to reveal novel aspects of acute motivation in laboratory studies, the incremental value of these additional facets remains an open question.

At the clinical end of the spectrum, although behavioral economic interventions are well supported, the total number of trials on CRA, CM, and augmented BMIs is small and generalizing the efficacy of these approaches to additional populations is a natural step forward. In addition, with the exception of the brief intervention studies, the previous CRA and CM trials have not systematically examined behavioral economic mediators and moderators of treatment effects to address whether the positive effects are for the predicted reasons and whether outcomes systematically differ based on task performance. For example, proportionate alcohol-related reinforcement is an obvious putative mechanism for positive CRA effects, given the program's theorized influence on non-alcohol-related reinforcement. Another future clinical direction is a focus on delay discounting as a novel treatment target. Several recent studies have identified methods for acutely attenuating steep discounting (e.g., [Bickel et al., 2011](#); [Daniel et al., 2013](#); [Radu et al., 2011](#)) and, although the generalizability is not clear at this point, these strategies may contribute to improving treatment response. However, a recent review reported evidence of a rate-dependent effect in studies attempting to reduce delay discounting behaviorally ([Bickel et al., 2015](#)). This effect was such that the most robust effects were present for the most impulsive individuals, suggesting an individual's discounting rate itself is a potentially powerful moderating variable.

Substantial gaps in knowledge also remain at the more basic end of the translational spectrum. The neuroimaging studies on delay discounting have provided novel and unique perspectives on the neural correlates of this form of maladaptive decision making, but the literature is largely descriptive, not predictive in terms of change over time or prescriptive in terms of identifying specific forms of neural activity to target. In other words, these

approaches need to be integrated into etiological and clinical research more fully. Similarly, the recent study using fMRI to study alcohol demand is not an end unto itself, but rather part of the foundation for future questions, such as differences in neural processing of alcohol demand among individuals with AUDs versus social drinkers or in response to experimental manipulations. Similarly, there is a line of inquiry about delay discounting is whether it is a mechanism by which genetic variation confers risk for addictive disorders (i.e., an endophenotype) ([Gottesman and Gould, 2003](#); [MacKillop and Munafò, 2013](#)). Recent studies using animal models and twin designs have established that delay discounting appears to be relatively robustly heritable ([Anokhin et al., 2011, 2015](#); [Richards et al., 2013](#); [Wilhelm and Mitchell, 2009](#)). In addition, a small number of molecular genetic studies have reported associations between steep discounting and dopamine-related polymorphisms ([Boettiger et al., 2007](#); [Eisenberg et al., 2007](#); [Gray and MacKillop, 2014a](#); [MacKillop et al., 2015a,b](#); [Paloyelis et al., 2010](#)). This is a nascent area of the field and considerable further progress will be needed to characterize genetic influences on delay discounting and, ultimately, whether discounting mediates the relationship between specific forms of genetic variation and risk for AUDs. It is also possible that alcohol demand may serve as a mechanism linking genetic variation and AUD risk, but this has received only very limited investigation to date ([Lamb and Daws, 2013](#); [Owens et al., 2015](#); [Wahlstrom et al., 2012](#)).

CONCLUSIONS

Considered collectively, behavioral economics and neuroeconomics provide a powerful framework for studying the nature of AUDs. Importing theories and tools from a variety of disciplines, these approaches attempt to conceptualize the problem from a unique vantage point, the value of which is supported by a substantial and robust empirical literature. The body of work to date provides a deep and broad foundation upon which to build and addressing the gaps identified has the potential to make major contributions to understand the AUDs and other addictive disorders.

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CONFLICTS OF INTEREST

None.

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