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Biphasic Effects of Alcohol on Delay and Probability Discounting

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Abstract

Delay discounting and probability discounting are behavioral economic indices of impulsive and risky decision making that have been associated with addictive behavior, but the acute biphasic effects of alcohol on these decision-making processes are not well understood. This study sought to investigate the biphasic effects of alcohol on delay and probability discounting across the ascending and descending limbs of the breath alcohol concentration (BAC) curve, which are respectively characterized by the stimulant and sedative effects of alcohol. Delay and probability discounting were measured at four time points (Baseline, Ascending, Descending, and Endpoint) across the BAC curve at two target alcohol doses (40 mg/dl and 80 mg/dl) in healthy adults ($N = 23$ and 27 , for both doses, respectively). There was no significant effect of alcohol on delay discounting at either dose. Alcohol significantly affected probability discounting, such that reduced discounting for uncertain rewards was evident during the descending limb of the BAC curve at the lower dose ($p < .05$) and during both the ascending and descending limb of the BAC curve at the higher dose ($p < .05$). Thus, alcohol resulted in increased risky decision making, particularly during the descending limb which is primarily characterized by the sedative effects of alcohol. These findings suggest that the biphasic effects of alcohol across the ascending and descending limbs of the BAC have differential effects on behavior related to decision-making for probabilistic, but not delayed, rewards. Parallels to and distinctions from previous findings are discussed.

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Keywords

delay discounting; probability discounting; impulsivity; alcohol use; behavioral economics

Introduction

There is considerable evidence associating behavioral economic decision-making biases with alcohol misuse and other forms of addictive behavior (e.g., MacKillop et al., 2011; Madden, Petry, & Johnson, 2009). One well-studied decision-making domain is delay discounting (DD), a behavioral economic index of impulsivity. DD measures the individual's preference for smaller immediate rewards relative to larger delayed rewards, akin to the ability to delay gratification. More specifically, DD reflects the degree to which delayed rewards diminish in subjective value. In human studies DD is typically quantified through a series of choices between a fixed larger amount of (hypothetical) money (e.g., \$100) that is available at a delay (e.g., 1 week, 1 month, 6 months) and a systematically varying smaller amount of (hypothetical) money (e.g., \$99, \$95, \$90...) that is available with no delay.

A behavioral economic perspective proposes that alcohol use disorders (AUD) are at least partially a function of persistently impulsive DD. For example, compared with controls, higher levels of impulsive discounting have been found in alcohol dependent individuals who currently drink and alcohol dependent individuals who are currently abstinent, with the highest levels found among current users (Petry, 2001). Similarly, DD has been associated with continuous measures of AUDs including the severity of AUD symptoms (MacKillop et al., 2010) and higher levels of alcohol use (Courtney et al., 2012). Addressing the question of whether DD is associated with addictive behaviors beyond categorical diagnoses, a recent meta-analysis reported evidence of a medium effect size across alcohol studies of delay discounting, with studies of clinical samples (e.g. those having an AUD) evidencing significantly larger effect sizes than studies of subclinical samples (e.g. heavy drinkers who do not meet criteria for an AUD) (MacKillop et al., 2011). Further, DD has been linked to acquisition of substances (Audrain- McGovern et al., 2009) and clinical outcomes, including poorer smoking cessation in problem drinkers (MacKillop & Kahler, 2009; Sheffer et al., 2012). Taken together, these findings have led to the proposal that excessive DD may be a fundamental process of addictive behavior (Bickel & Johnson, 2003).

Probability discounting (PD) is a related, but less well-studied decision making process. PD is a behavioral economic index that characterizes the reduction in value for a reward as a function of the probability of receiving the reward. PD measures the individual's preference between relatively larger, but less certain rewards, and relatively smaller, but more certain rewards (e.g. Green, Myerson, & Ostaszewski, 1999). Whereas greater (i.e., steeper) discounting of delayed rewards is consistently associated with substance abuse and other addictive behaviors, the relationship between PD and addictive activities has been not been consistent across studies. Steep or greater discounting of probabilistic rewards implies a lower value of larger but uncertain outcomes (Rachlin, Raineri, & Cross, 1991). Two studies suggest that pathological gamblers evidence less steep discounting of probabilistic rewards

and thus place greater value on uncertain outcomes (Holt, Green, & Myerson, 2003; Madden et al., 2009), reflecting an underlying preference for greater risk taking. However, a third study found that this pattern of risk-taking on probability discounting measures was associated with better response to gambling treatment (Petry, 2012). In addition, tentative evidence exists for a causal relationship between alcohol use and PD from animal studies showing that rats exposed to high quantities of alcohol as adolescents showed a greater preference for risky choices later in life (Nasrallah, Yang, & Bernstein, 2009). In contrast, Reynolds et al. (2004) found that smokers showed more risk-averse behavior and devalued uncertain rewards to a greater extent (steeper probability discounting) than non-smokers. However, other studies have shown no relationship between PD and smoking (Mitchell, 1999; Ohmura, Takahashi, & Kitamura, 2005; Reynolds, Karraker, Horn, & Richards, 2003). Thus, the relationship between PD and addictive activities is less clear than for DD.

Although the conceptualization of probability discounting as an index of risky decision-making, with greater discounting akin to less risk taking, has received support, some researchers have proposed that delay and probability discounting share common features (Rachlin et al., 1991), which is supported by positive correlations between these assessments in some studies (e.g. Reynolds, 2006; Reynolds et al., 2003; Richards, Zhang, Mitchell, & de Wit, 1999). For example, in the natural environments of human and non-human animals outcomes often become less probable with increasing delay to occurrence; therefore, delay may be equated with uncertainty (Green & Myerson, 2004; Stevenson, 1986), and steep delay and probability discounting might both reflect a maladaptive decision making bias. As applied to drug abuse, drugs typically provide an immediate and relatively certain source of reinforcement (e.g. euphoria or stress reduction) whereas alternatives to drug use such as good health and academic/vocational outcomes (e.g., obtaining a satisfying career or remaining healthy into old age) are both delayed and uncertain. Therefore, individuals who devalue delayed or uncertain outcomes may show a preference for drug use relative to many alternatives.

Despite some apparent overlap, empirical research generally indicates that delay and probability discounting are not highly correlated (Andrade & Petry, 2012; Holt et al., 2003; Madden et al., 2009; Ohmura et al., 2005; Petry, 2012; Reynolds, Richards, Horn, & Karraker, 2004). In addition, differential associations with addictive behavior have been evident in some cases. For example in Madden et al., (2009) pathological gambling was associated with less steep PD but no differences in DD. In another study, pathological gamblers with a history of substance use showed steeper DD, but no differences in PD, as compared to gamblers without a substance use history (Andrade & Petry, 2012). These findings support the idea that PD and DD reflect different dimensions of impulsivity and may be differentially involved in underlying processes related to addictive behavior.

With considerable trait-level evidence supporting the role of discounting in addictive behaviors, there has recently been increasing interest in the studies of dynamic changes in discounting and the question of how powerful drug state effects may further exacerbate discounting. For example, acute smoking abstinence increased DD for monetary gains and losses, but did not affect DD for cigarettes or PD for either money or cigarettes (Yi & Landes, 2012). Similarly, it is important to understand the impact of acute intoxication on

delay and probability discounting. Indeed, clinically relevant decisions about *how much* alcohol or drugs to consume (e.g., whether or not to have a 2nd or 5th drink), and whether or not to engage in high risk behaviors such as driving or unprotected sex (which are associated with adverse outcomes that are both uncertain and delayed), are often made after an individual has ingested the substance. Alcohol's acute effects have been theorized to dynamically affect discounting, making individuals more impulsive, but laboratory findings are mixed. In support of this theory, alcohol intoxication increased DD on the Experiential Delay Discounting Task (EDT), a "real-time" discounting task that uses small monetary rewards administered during the session (Reynolds, Richards, & de Wit, 2006). However, another study reported alcohol intoxication was associated with less discounting on a hypothetical DD task at trend level, suggesting that alcohol may lead to more cautious decision making at least under certain conditions (Ortner, MacDonald, & Olmstead, 2003). Other studies have reported no effect of alcohol on either DD or PD (Dougherty, Marsh-Richard, Hatzis, Nouvion, & Mathias, 2008; Richards et al., 1999).

One limitation of studies to date is that they have focused on the peak effects of alcohol. The drug is known to have distinct biphasic effects across the breath alcohol concentration (BAC) curve. Initially, euphoric-like stimulant effects are reported as blood alcohol levels are rising during the ascending limb of the curve whereas the depressant-like sedative effects, although present during the ascending limb, become more predominant as blood alcohol levels are falling during the descending portion (Earleywine & Erblich, 1996; Erblich J., Earleywine, Erblich B., & Bovbjerg 2003; Holdstock & de Wit, 1998; Martin, Earleywine, Musty, Perrine, & Swift, 1993). These differences across the BAC curve are important because the experiences of stimulation vs. sedation may have different motivational and behavioral significances. For example, stimulation during the ascending limb may be associated with greater impulsivity and higher levels of discounting for delayed or uncertain rewards. Similarly, the sedative experiences associated with the descending limb may attenuate risk taking. In addition, a second limitation is that most of the previous studies in this area have only used a single dose of alcohol, providing only a relatively narrow perspective.

Thus, some of the ambiguity in prior work may be due to the emphasis on the peak of the alcohol administration curve, which comingles alcohol's biphasic stimulating and sedative effects, or the use of only a single dose of alcohol. The current study addresses these prior limitations by focusing on both the ascending and descending limb of the BAC during alcohol administration at two target doses (.40 and .80 mg/dl), using what is referred as the Mellanby paradigm (Martin & Moss, 1993). In order to assess the biphasic effects of alcohol on two types of discounting decision making, DD and PD were analyzed at key time points across the ascending and descending limbs of the BAC curve. We also tested whether alcohol across the BAC influenced discounting differently in male and female participants. To verify the biphasic effects of alcohol in the current sample, we also measured stimulant and sedative effects of alcohol at each time point using the Biphasic Alcohol Effects Scale (BAES; Martin et al., 1993) and examined the relationships among the BAES subscales and measures of DD and PD.

Method

Participants

Participants were 43 non-alcohol dependent participants between the ages of 21 and 65 who were recruited from the Providence, RI community. The final sample of participants who attend all experimental sessions was 40 (20 male and 20 female). Participants were required to be at least 21 years old and to have consumed at least 6 alcoholic drinks on a single occasion without experiencing any problems. Exclusion criteria included: a history of cardiac problems; use of medications contraindicated for alcohol; past or current history of alcohol or drug dependence; Short Michigan Alcohol Screening Test (SMAST; Seltzer, Vinokur, & Van Rooijen, 1975) score >2 ; heavy alcohol consumption defined as greater than 14 standard drinking unit (SDUs)/week for women or 21 SDUs/week for men (Piccinelli et al., 1997); positive urine toxicology screen for benzodiazepines, cocaine, opiates, or marijuana; or abnormal values for liver function tests. Pregnant or nursing females were excluded from the study, and all women of childbearing potential were required to use an effective method of birth control. Because of variability in the duration of the BAC, our final sample included 27 and 23 subjects who had complete data across the ascending and descending limbs of the BAC for the .40 mg/dl dose and .80 mg/dl dose, respectively. Demographic variables and alcohol use characteristics for these individuals are included in Table 1. The study was approved by the Institutional Review Boards of Brown University and Providence VA Medical Center.

Procedures

After a telephone screen, participants attended an in-person baseline session involving informed consent and a clinical interview with a physician to assess history of drug, alcohol, and health problems; physical exam, review of concomitant medications, and medical and psychiatric history. Other baseline assessments included: breath alcohol testing; demographics questionnaire; the SMAST to assess past and current alcohol problems; Timeline Follow Back method (Sobell & Sobell, 1992) to assess baseline level of alcohol consumption in the past 30 days; and laboratory evaluations including urine toxicology, pregnancy screen, and liver function tests.

Participants then attended two experimental sessions that began at 9 am and were generally scheduled within two weeks of each other. Prior to both sessions, participants were asked to fast beginning midnight the day before. The sessions included one of two target alcohol dosages (40mg/dl peak and 80mg/dl peak). As required by the IRB due to safety concerns, the 40mg/dl peak dose was always given in the first experimental session. Quantity of alcohol required to reach target peak alcohol concentrations was determined by the participant's height, weight, gender, and age according to the calculations outlined in Watson (1989). For example, a male participant aged 31-50 years who was 170 cm tall and weighed 80 kg, received 21.9 g of alcohol for the 40 mg/dl target dose. 95% grain alcohol served was served with 4:1 mix of cranberry or orange juice. Subjects were instructed to ingest the alcohol within 10 minutes for the .40 mg/dl dose and 20 minutes for the .80 mg/dl dose. After consumption, subjects rinsed their mouths with water and were assessed for BAC every ten minutes. The ascending limb assessment was triggered at 30 mg/dl for Dose

A and 60 mg/dl for Dose B; the descending limb assessment was triggered at 30 mg/dl for both doses. At each of five time points [baseline (prior to consumption), ascending limb, peak, descending limb, and endpoint], participants completed the following measures:

Biphasic Alcohol Effects Scale—(BAES; Martin et al., 1993). To verify the biphasic effects of alcohol in the current sample, the BAES was used to measure subjective experiences of stimulation and sedation at time points across the BAC curve. The BAES is a 14 item unipolar adjective rating scale designed to measure both stimulant and sedative effects of alcohol.

Delay and Probability Discounting Assessment—For the computerized discounting assessments (Reynolds et al. 2003), the first half of the choice trials assessed Delay Discounting and consisted of one smaller, immediate reward and one larger, delayed reward (e.g., \$50 now versus \$100 in 180 days). The task was used to determine indifference points for five different delay intervals: 1, 2, 30, 180, and 365 days. The larger delayed reward was \$100 across all trials, and smaller amount of immediate money was titrated by the program based on participant responses to previous questions. Adjustments in amount of immediate money were made in a manner as to narrow the range of values on successive choice trials until an indifference point was determined (cf. Reynolds et al., 2003). The second half of the choices assessed Probability Discounting and consisted of a sure amount of money and an uncertain amount of money (e.g., \$50 for sure and 85% chance of \$100). Indifference points were determined in a similar manner for five different probability values: 1.0, 0.9, 0.75, 0.5, and 0.25. All rewards were hypothetical. The instructions described the nature of the task and encouraged subjects to regard each trial as though it were the only choice they faced.

Data Analysis

We individually reviewed the BAC time course data for each participant in order to establish sufficient fit to the ascending and descending limbs of the BAC curve. Mean BACs for each time point on the alcohol administration curve are reported in Figure 1. Due to variability in the BAC and difficulty collecting BAC directly at peak due to our dynamic assessment protocol, only 5 and 16 subjects had complete data at all 5 time points for the .40 mg/dl dose and .80 mg/dl dose, respectively. Given that the focus of the study was on the biphasic differences across the BAC curve and the importance of complete data, we completed our final analysis on the 27 and 23 subjects who had complete data at baseline, ascending, descending, and endpoint (BADZ) time points.

Points of indifference were initially generated in both the delay and probability discounting tasks. Then, analysis of the delay and probability discounting was implemented using an area-under-the-curve (AUC), which has the advantage of avoiding assumptions about the form of the underlying data and model-fitting error (Myerson, Green, & Warusawitharana, 2001). For DD, higher AUC values reflect less discounting of delayed rewards; thus, higher AUCs reflect lower levels of impulsivity for DD. For PD, higher AUCs reflect greater valuation of uncertain rewards (i.e., lower discounting and greater risk taking). To test for any baseline differences between the two sessions, we used one-way two-level within subjects analyses of variance (ANOVAs) to compare baseline performance at the 40 mg/dl

dose and .80 mg/dl dose for both DD and PD. Effects of the .40 mg/dl dose and .80 mg/dl dose on BAES, DD, and PD were based on mixed factor two-way ANOVAs with the four-level BAC time point variable as the within subjects factor and gender as the two-level between subjects factor. Where significant omnibus main effects or interactions were present, follow-up pairwise t-tests were used to determine the nature of the effects. Because of the within-subject design, sphericity was evaluated using Mauchly's W and, where violated, a Greenhouse-Geisser correction was implemented and adjusted degrees of freedom are provided in the text. Pearson product-moment (r) correlations tested the relationships between 1) discounting measures (DD and PD) and the sedation and stimulation subscales of the BAES and 2) DD and PD at the four time points across the BAC. Skewness or kurtosis was violated (e.g. greater than ± 3) for eight of the BAES variables and in these cases Spearman's rho correlations were used to test associations with PD and DD. The AUC analysis was implemented using GraphPad Prism and the ANOVAs and correlations were implemented using SPSS 19.0.

Results

Effects of Alcohol

Table 2 contains the Means (S.E.M.) for the stimulation and sedation subscales of BAES. Sphericity was violated for both stimulation (.40 mg/dl dose: $W = .006$, $p < .001$; .80 mg/dl dose: $W = .050$, $p < .001$) and sedation (.40 mg/dl dose: $W = .392$, $p = .001$; .80 mg/dl dose: $W = .283$, $p < .001$). Mixed factorial ANOVAs indicated a significant effect of both alcohol doses on the stimulation and sedation subscales of the BAES (Stimulation .40 mg/dl dose ($F [1.093, 25.143] = 12.974$, $p < .001$); Stimulation .80 mg/dl dose ($F [1.229, 24.588] = 13.295$, $p = .001$); Sedation .40 mg/dl dose ($F [1.995, 45.887] = 20.872$, $p < .001$); Sedation .80 mg/dl dose ($F [1.779, 35.589] = 10.042$, $p = .001$)). For sedation, this reflected a significant difference between baseline and the experiences of sedation at all other time points (See Table 2; p 's range from .002 to $< .001$). For stimulation, this reflected a significant difference between baseline and the experiences of stimulation at the ascending and descending time points (See Table 2; p 's range from .02 to $< .001$).

On the sedation subscale, a main effect of gender [.40 mg/dl dose ($F [1,23] = 13.65$, $p < .001$); .80 mg/dl dose ($F [1, 20] = 5.67$, $p = .027$) and a gender $\times$ BAC interaction [.40 mg/dl dose ($F [1.995, 45.887] = 6.917$, $p = .002$); .80 mg/dl dose ($F [1.779, 35.589] = 2.859$, $p = .08$] was present such that male participants experienced greater overall sedation particularly during the descending limb of the BAC. These gender main effects and gender $\times$ BAC interactions were present for both doses, albeit the gender $\times$ BAC interaction was significant only at trend level for the 80 mg/dl dose. No gender main or interaction effects were present on the stimulation subscale at either dose.

Delay and Probability Discounting

No baseline differences were present between the 40 mg/dl dose and .80 mg/dl dose sessions for either DD ($F [1,21] = .116$, $p = .737$) or PD ($F [1,21] = .113$, $p = .740$). For the 40mg/dl dose, sphericity was violated for both delay ($W = .468$, $p < .01$) and probability ($W = .540$, $p = .01$) discounting. No effect of alcohol was evident on DD ($F [1.954, 48.841] = .216$, $p = .$

80). However, a significant effect of alcohol was present for PD ($F [2.074, 51.850] = 4.004$, $p = .02$). This reflected a significant difference between baseline and the decision-making during the descending time point (Mean difference (SD) = .02 (.01), $p=.02$) and a trend-level difference between baseline and the return to baseline (Mean difference (SD) = .03 (.02), $p=.05$). In addition, statistical trends were also evident between the ascending limb and the descending limb (Mean difference (SD) = .04 (.02), $p=.07$), and between the descending time point and the return to baseline (Mean difference (SD) = .03 (.02), $p=.09$). Each of these relationships reflected more risky decision-making during the descending limb. There was no main effect of gender nor was there a gender $\times$ BAC interaction for either DD or PD at the 40mg/dl dose.

Similarly, for the .80 mg/dl dose, sphericity was again present for both delay ($W = .629$, $p = .01$) and probability discounting ($W = .427$, $p < .01$). Again no effect of alcohol was present for DD ($F [2.355, 49.457] = 1.115$, $p = .34$), but a significant effect of alcohol was evident for PD ($F [1.939, 40.721] = 3.508$, $p = .04$). This effect reflected significantly more risky decision-making compared to baseline during the ascending limb (Mean difference (SD) = .03 (.01), $p=.02$) and the descending limb (Mean difference (SD) = .05 (.02), $p=.03$), and a trend-level difference between baseline and the return to baseline (Mean difference (SD) = .04 (.02), $p=.07$). There was no main effect of gender nor was there a gender $\times$ BAC interaction for either DD or PD at the 80mg/dl dose. However, there was a trend level gender by BAC interaction for PD ($F [1.939, 40.721] = 2.89$, $p = .07$), that suggested that alcohol increased risky decision-making during both the ascending and descending limbs in males, but primarily during the descending limb in females.

Associations among Delay and Probability Discounting Assessments and BAES subscales—DD did not significantly correlate with either of the BAES subscales at any of the time points (BADZ). For Dose A, PD at endpoint (Z) was positively correlated with the stimulation subscale of the BAES ($r = .48$; $p = .01$). No other correlations with discounting and BAES subscales across the BAC curve were significant. DD and PD were significantly (positively) correlated at each time point for both alcohol doses. Table 3 lists the correlations between AUC for DD and PD for the .40 mg/dl and .80 mg/dl dose BAC curves.

Discussion

The results of this laboratory study of the biphasic effects of alcohol on behavioral economic decision-making processes suggest no effect of alcohol intoxication on DD and a significant effect of alcohol on PD across the BAC curve. For PD, the .40 mg/dl dose resulted in higher AUCs, which reflect a greater valuation of uncertain outcomes, during the descending limb of the BAC, and the .80 mg/dl dose resulted in higher AUCs during both the ascending and descending limbs of the BAC. Thus, as overvaluing uncertain rewards is considered an indicator of risky decision-making (Holt et al., 2003; Madden et al., 2009), these findings suggest increased risky decision-making under the influence of alcohol, particularly during the descending limb of the BAC curve which is associated with alcohol's sedative effects. In addition, PD and DD were positively correlated across the BAC curve. In other words, there

was a tendency for individuals who placed less value on immediacy of reward to place less value on certainty (i.e., probability) of reward across the alcohol administration curve.

Although DD and PD were moderately positively correlated across the BAC curve, only PD, primarily on the descending limb, was increased by alcohol intoxication. This suggests that, despite common features between DD and PD (Rachlin et al., 1991), the effects of alcohol during the descending limb of the BAC may uniquely affect decisions related to discounting of uncertain rewards. To our knowledge this is first the study to observe more risky decision-making on a probability discounting task during alcohol intoxication. This finding is consistent with commonly reported clinical and naturalistic observations that alcohol intoxication can lead to increased levels of a variety of risk-taking behaviors (e.g., risky sexual activities, fighting, other drug use, gambling, or unsafe driving). Similarly, there is robust evidence that alcohol acutely impairs inhibitory control on Stop-Signal and Go/No-go tasks (e.g. de Wit, Crean, & Richards, 2000; Marczinski, Abrams, Van Selst, & Fillmore, 2005). Taken together, these findings suggest that alcohol may differentially affect various aspects of decision-making and underscore the importance of examining multiple impulsivity constructs in a single study.

In general, these results are consistent with several other studies that have not found significant effects of acute alcohol administration on delay discounting tasks (Dougherty et al., 2008; Richards et al., 1999). The only prior study to observe the expected association between alcohol intoxication and impulsivity included a delay discounting task (the EDT) that used very small reward outcomes that were administered real time in session (Reynolds et al., 2006). Interestingly, the EDT also incorporates elements of probability discounting in that some of the rewards are probabilistic. Thus, the bulk of the evidence generated from controlled laboratory studies of delay discounting and alcohol administration suggest that acute alcohol use does not increase impulsive discounting. However, discounting for probabilities or using a combination of delayed and probabilistic rewards may be more sensitive than delay alone to alcohol's acute effects. Further, there are many methods of assessing discounting with multiple varying parameters, such as those related to the magnitude of delayed/uncertain rewards and length of delay, that are likely to impact consistency of findings. Studies should strive to match discounting assessments with those of prior work in order to directly compare findings.

In the current study, alcohol produced the expected biphasic effects of stimulation and sedation across the ascending and descending limbs of the BAC curve, such that the ascending limb was primarily characterized by stimulation experiences for both doses, whereas, the descending limb was primarily characterized by sedation. Consistent with prior research, increases in sedation were also present during the ascending limb and did not significantly differ from those reported during the descending limb (Erblich et al., 2003). Surprisingly, self-reported sedation did not significantly associate with measures of PD or DD taken at corresponding time points. Self-reported stimulation was positively associated with PD at the endpoint of the .40 mg/dl dose BAC curve, suggesting that increased PD on the descending limb may have been in part due to lingering levels of alcohol-related stimulation. However, this finding was not consistent across doses and should be interpreted cautiously given the low levels of stimulation reported at endpoint.

Gender analyses revealed that alcohol did not have differing effects on discounting in male and female participants. However, there was a trend-level gender $\times$ BAC interaction at the higher dose of alcohol suggesting that males may have increased risky-decision making during both the ascending and descending limbs, whereas female participants primarily increased risky-decision making during the descending limb. Male participants also reported greater sedation across the BAC curve (during both the ascending and descending limbs), then female participants, who primarily reported sedation experiences during the descending limb. Therefore, it is possible that the greater sedation experienced by male participants during both the ascending and descending limbs may have impacted males' riskier decision making during those same time points, although, as previously mentioned, self-reported sedation did not correlate with PD during either the ascending or descending limbs. Taken together, these results suggest that males and females may have different patterns of experience when it comes to the biphasic effects of alcohol, and further, that there may be gender differences in the effects of alcohol on discounting across the BAC curve. As the initial BAES validation studies examined predominantly males with moderate social drinking backgrounds (Earleywine & Erblich, 1996; Martin et al., 1993), gender differences on the BAES subscales are understudied and the gender differences reported here with the BAES and PD should be followed up with a sample adequately powered to detect such effects.

Methodological Considerations

The findings should be interpreted in the context of several limitations and methodological considerations. The absence of a placebo condition leaves open the possibility that the effects reported are related to the effect of time or repeated administration on the measured variables. In addition, alcohol doses were not counterbalanced and participants were not blind to alcohol dose, which could have influenced expectancies across the two alcohol doses. The study tested hypothetical measures of monetary discounting and did not include experiential measures of discounting that include real time or drug related rewards. Non-hypothetical or primary reinforcers may reflect properties more consistent with reinforcers sought during intoxication in the real world. However, there is also considerable evidence that discounting decisions for hypothetical outcomes have a strong correspondence with choices for actual outcomes (e.g. Bickel, Pitcock, Yi, & Angtuaco, 2009; Lagorio & Madden, 2005; Madden et al., 2004), suggesting that this would not be expected to drastically affect the findings. Another consideration is that this was a study of non-problem drinkers. The effects of alcohol on impulsive and risky decision-making may differ in important ways in heavy or problem drinkers and may be exacerbated by more general cognitive deficits associated with chronic substance use.

Another aspect of the methodology that is worth discussing further is the missing data. This suboptimal outcome was due to heterogeneity of the breath alcohol curve and our dynamic assessment protocol that focused deploying assessments in maximal proximity to the target BACs during the ascending and descending limbs. Together these resulted in the assessment time windows being missed more often than expected. This illustrates the challenges in implementing Mellanby protocols, which are essential for evaluating acute alcohol effects at specified levels during the ascending and descending limbs, but are relatively unusual

because of some of the challenges present in the current study. There are several strategies that may be useful in refining this approach in future studies. First, the calculation of the temporal parameters of alcohol intoxication are increasingly established (Brick, 2006) and could be used to implement a standardized assessment rather than dynamically-triggered assessments. While this approach would virtually eliminate missing data, it is likely to introduce more BAC variability. However, this variability could be statistically modeled. Second, focusing on a higher peak dose would permit greater clarity with regard to the ascending and descending limbs. For example, peak BACs of 60 mg/dl and 100 mg/dl might be necessary for improved resolution of effects at 30 mg/dl and 60 mg/dl. A final option is the use of the intravenous alcohol clamp (Ramchandani & O'Connor, 2006), which permits considerably more experimenter control over blood alcohol levels and would eliminate pharmacokinetic variability. This, however, is a more invasive and costly paradigm, and removing pharmacokinetic variability diminishes potentially important participant-level variability. Oral alcohol challenges remain the more naturalistic option.

Despite these methodological considerations, this study is among the first to examine the biphasic effects of alcohol intoxication on impulsive and risky decision-making. Our finding that alcohol intoxication did not affect DD and resulted in less steep PD, particularly during the descending limb of the BAC, suggests that alcohol may result in more risky approaches to decision-making under certain conditions, despite intact consideration of the future. Further, our study underscores the importance of examining multiple types of discounting decision-making at various critical time points during alcohol intoxication. Taken together, these results support the idea that delay and probability discounting measures may reflect related, but unique aspects of decision-making that may be differentially affected during alcohol intoxication and other drug states. Delay discounting may be most relevant as a molar level risk factor that influences patterns of decisions to drink, instead of engaging in alternatives associated with delayed outcomes, over time. Acute alcohol intoxication may not generate myopic decision-making, but may enhance preference for larger riskier rewards.

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Figure 1. Mean (S.E.M.) Breath Alcohol Concentration (BAC) for the 40mg/dl dose and 80mg/dl dose at each time point on the alcohol administration curve for the full sample ($N = 40$).

Table 1

Sample demographics and alcohol use variables.

<i>Demographic Variables</i>	<i>.40 mg/dl dose</i>	<i>.80 mg/dl dose</i>
Gender, <i>N</i> (%)		
Male/Female	13/14 (48.1/51.9%)	11/12 (47.8/52.2%)
Ethnicity, <i>N</i> (%)		
White (non-Hispanic)	19 (70.4%)	14 (60.9%)
Black (non-Hispanic)	2 (7.4%)	2 (8.7%)
Hispanic	2 (7.4%)	3 (13.0%)
Asian	2 (7.4%)	2 (8.7%)
Other	2 (7.4%)	2 (8.7%)
Age, <i>M</i> (<i>SD</i>)	29.0 (11.4)	30.0 (8.3)
BMI, <i>M</i> (<i>SD</i>)	26.9 (8.2)	27.9 (8.3)
Years of Education, <i>M</i> (<i>SD</i>)	14.5 (2.2)	14.3 (2.3)
<i>Alcohol Use Variables</i>		
Average standard drinking units per week past 30 days, <i>M</i> (<i>SD</i>)	8.2 (8.1)	7.4 (5.4)
Number of drinking days past 30 days, <i>M</i> (<i>SD</i>)	6.5 (4.4)	6.9 (4.8)
Number of heavy drinking days past 30 days, <i>M</i> (<i>SD</i>)*	3.4 (0.7)	3.0 (3.0)

Note. .40 mg/dl dose *N*=27; .80 mg/dl dose *N*=23; Full sample *N*=40;

* Heavy for male > 4.5 standard drinking units, heavy for female > 3.5 standard drinking units.

Table 2

Biphasic Alcohol Effects Scale (Means (S.E.M)) and Area Under the Curve (Means (S.E.M)) for Delay and Probability Discounting Tasks for Baseline, Ascending, Descending, and Endpoint Assessments by Alcohol Dosage

	Biphasic Alcohol Effects Scale				Area Under the Curve			
	Sedation		Stimulation		Delay Discounting		Probability Discounting	
	Dosage A	Dosage B	Dosage A	Dosage B	Dosage A	Dosage B	Dosage A	Dosage B
Baseline	0.3 (0.26)	0.0 (0.00)	0.4 (0.41)	0.0 (0.00)	.54 (.050)	.50 (.061)	.28 (.023)	.30 (.037)
Ascending	9.0** (2.01)	8.3** (1.82)	8.1* (2.07)	13.1** (3.07)	.56 (.051)	.54 (.061)	.30 (.028)	.33* (.040)
Descending	7.6** (1.53)	8.0** (1.66)	2.5 (0.87)	3.2* (1.36)	.56 (.053)	.52 (.065)	.34* (.038)	.35* (.047)
Endpoint	4.4** (1.16)	4.7** (1.43)	1.6 (0.57)	1.9 (1.04)	.56 (.054)	.51 (.062)	.31 [†] (.032)	.34 [†] (.048)

Note.

**
p < .01

*
p < .05

[†] p < .10 when compared to baseline; Dosage A: Target of 40mg/dl (n=27); Dosage B: Target of 80mg/dl (n=23).

Table 3

Correlations between Delay and Probability Discounting Area Under the Curve Measures across the .40 mg/dl dose and .80 mg/dl dose Breath Alcohol Concentration Curves.

Delay Discounting	Probability Discounting			
	Baseline	Ascending	Descending	Endpoint
Baseline	.53 [*] /.52 [*]	.58 [*] /.54 [*]	.33 [*] /.53 [*]	.49 [*] /.57 [*]
Ascending	.58 [*] /.58 [*]	.63 [*] /.63 [*]	.45 [*] /.59 [*]	.57 [*] /.63 ^{**}
Descending	.70 [*] /.64 [*]	.81 ^{**} /.69 ^{**}	.72 ^{**} /.67 ^{**}	.81 ^{**} /.69 ^{**}
Endpoint	.66 [*] /.62 [*]	.70 ^{**} /.64 ^{**}	.55 [*] /.62 ^{**}	.70 ^{**} /.68 ^{**}

Note: .40 mg/dl dose = left side of hash; .80 mg/dl dose = right side of hash;

*
p-value < 0.01;

**
p-value < 0.001.