INVESTIGATING HOW BOTTOM-UP AND TOP-DOWN SYSTEMS RELATE TO ALCOHOL USE AND ALCOHOL USE DISORDER

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by

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The undersigned, appointed by the Dean of the Graduate School, have examined the dissertation entitled

INVESTIGATING HOW BOTTOM-UP AND TOP-DOWN SYSTEMS RELATE TO ALCOHOL USE AND ALCOHOL USE DISORDER

Presented by Jarrod M. Ellingson

A candidate for the degree of Doctor of Philosophy

And hereby certify that in their opinion it is worthy of acceptance.

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DEDICATION

I owe many thanks to those who have provided me support and guidance throughout my graduate education and dissertation work. I thank my advisor, Wendy Slutske, for her mentorship, teaching, and collaboration since my arrival to the University of Missouri in 2008, and particularly for sticking with me after I returned to the university from a leave of absence. I would not be the researcher I am today without your mentorship, and I hope to someday mentor with the same energy and care that you put into working with your students. I also thank Ian Gizer and Ken Sher, for allowing me to join their lab meetings and learn from them during the last few years, and to Phil Wood for providing extensive quantitative feedback on this and many other projects. I am very grateful to my many peers, including my friend and lab mate, Leah Richmond-Rakerd, and other close friends, including Andrew Littlefield, Alvaro Verges, and Drew Bailey, who have helped to cultivate my enthusiasm for research (and have provided many laughs along the way). I also owe a great deal to my parents and grandparents, for instilling in me a strong work ethic and always providing support. Most of all, I thank my wife, Yuri Kashima-Ellingson, and our daughter, Maisie, for their love, support, and for keeping me balanced.

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Chapter 1: Introduction

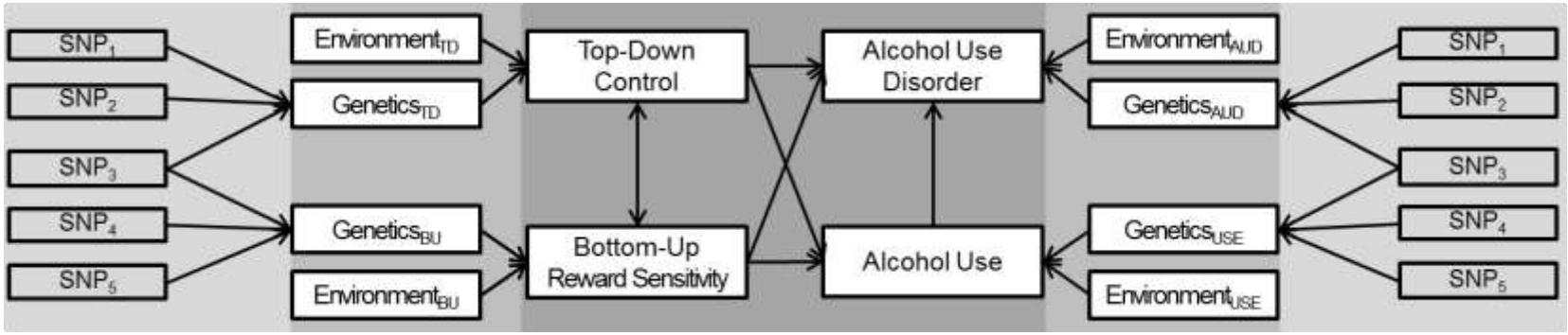
The consequences of excessive alcohol use and alcohol use disorder (AUD) are numerous and often severe. In the U.S. alone, alcohol use results in $223.5 billion in estimated annual costs (e.g., due to lost productivity, healthcare costs, criminal justice costs; Bouchery, Harwood, Sacks, Simon, & Brewer, 2011) and 85,000 annual deaths (Mokdad, Marks, Stroup, & Gerberding, 2004). There is, therefore, a critical need to understand how individuals with problematic alcohol use differ from those with normative use, as well as the ways in which consequences from problematic use can be alleviated. Understanding individual differences associated with AUD may inform the development of effective preventions and interventions.

Dual-systems models of alcohol use and AUD.

Numerous dual-systems models have been posited in which alcohol use and AUD are associated with two complementary systems, a bottom-up, emotion-based system characterized by reward sensitivity (i.e., a strong drive for reinforcing stimuli), and a top-down, cognitive-based system characterized by behavioral dyscontrol (i.e., an inability to control urges for reinforcing stimuli) (Hutchison, 2010; Wiers & Stacy, 2006). The distinction between these systems is, in part, based in neuroscience; whereas bottom-up systems are more primitive (e.g., reward seeking) and implemented by subcortical substrates of the brain (e.g., mesolimbic reward systems; Koob & Le Moal, 2008), top-down systems are more evolved (e.g., decision making) and implemented by cortical substrates (e.g., frontal cortical regions; Goldstein & Volkow, 2011). For consistency with the literature and simplicity, reward sensitivity and behavioral (under)control will refer to the bottom-up and top-down systems throughout the rest of this paper.

Frequently, personality characteristics assess reward sensitivity and behavioral undercontrol. Reward sensitivity maps onto Gray's behavioral approach system (i.e., appetitive motivation; Gray, 1990) and at elevated levels reflect trait sensation seeking. In the current paper, the definition of sensation seeking put forth by Zuckerman (1994) was adopted to describe reward sensitivity: the tendency to seek "varied, novel, complex, and intense sensations and experiences" (p. 27). Behavioral undercontrol maps onto executive functioning and at elevated levels reflect trait impulsivity (Bickel, Jarmolowicz, Mueller, Gatchalian, & McClure, 2012). In the current project, a facet of impulsivity was used to define behavioral undercontrol: the tendency to "act on the spur of the moment and without regard to the consequences" (i.e., lack of planning or premeditation; Whiteside & Lynam, 2001, p. 685). Dual-systems models of alcohol involvement hypothesize that an imbalance between these constructs increases the liability for AUD (see Figure 1, adapted from Hutchison, 2010). Specifically, individuals sensitive to alcohol's rewarding effects and low in self-control are most prone to developing AUD.

Figure 1-1. A heuristic model of the project.



Shaded regions distinguish levels of analysis. The aims of the proposed project are displayed, shaded to distinguish whether the level of analysis is phenotypic (center, darkest box), latent genetic or environmental (intermediate shading), or genotypic (outside, lightest boxes). Aim 1 will investigate whether bottom-up and top-down processes are differentially related to alcohol outcomes at the: phenotypic level (including longitudinally) using the AHB study (Chapter 3), latent genetic and environmental levels using the ATR study (Chapter 4), and genotypic level using the AHB study (Chapter 5). Aim 2 will investigate whether top-down processes moderate the relationship between bottom-up processes and alcohol outcomes at the: phenotypic level using the AHB study (Chapter 6) and latent genetic level using the ATR study (Chapter 7). This diagram is intended to convey the aims of the project and how they relate to one another. Therefore, this diagram is incomplete.

Investigations of dual-systems models have assessed these systems with a wide range of specificity, including measures that tap general (e.g., risky behavior) and specific tendencies (e.g., substance use). Further, whereas some studies use behavioral measures (e.g., Houben & Wiers, 2009), others use self-report measures (e.g., Quinn & Harden, 2013). Consistent with a dual-systems model, lab measures of behavioral control (executive functioning) have moderated the relationship between reward sensitivity (behavioral approach) and problematic alcohol use in adolescents (Thush et al., 2008) and college students (Houben & Wiers, 2009). That is, sensitivity to alcohol's reinforcing effects may be unrelated to alcohol problems unless accompanied by behavioral undercontrol. Notably, this moderation effect has not been extended to studies employing self-reported personality measures, although one study failed to find such an effect using a behavioral measure of control (executive functioning) and a self-report measure of reward sensitivity (alcohol expectancies) (Littlefield, Vergés, McCarthy, & Sher, 2011). Further, there is limited evidence of the applicability of dual-systems models of AUD beyond emerging adulthood (age 18-25), and no studies have investigated a dual-systems model of AUD beyond the phenotypic level, such as at the genetic level.

Dual-systems models of AUD assume that reward sensitivity and behavioral undercontrol are instrumental in the manifestation of, and are distinctly related to, problematic use. That is, each construct is hypothesized to account for a unique proportion of variance in AUD, thus warranting the inclusion and delineation of both systems in models of AUD. These central assumptions, however, have not been tested to clarify whether a more parsimonious model is appropriate. Notably, previous studies have demonstrated that sensation seeking and lack of planning are moderately correlated

with each other (r = .34; Smith et al., 2007), as well as with alcohol use (*r*s for lack of planning = .21–.32, sensation seeking = .22–.36) and alcohol-related problem (*r*s for lack of planning = .26–.37, sensation seeking = .17–.22) (Coskunpinar, Dir, & Cyders, 2013). Therefore, it is plausible that reward sensitivity and behavioral undercontrol explain overlapping variance in alcohol involvement.

The proposed project had two overarching goals covering five specific aims, which were tested in two independent samples (see Figure 1 for a heuristic model of the aims to be tested across these two samples). The first goal was to investigate whether reward sensitivity and behavioral undercontrol are differentially related to alcohol involvement (i.e., alcohol use and AUD) at multiple levels: the phenotypic (including longitudinally; Chapter 3), latent genetic and environmental (Chapter 4), and genotypic (Chapter 5). The second goal was to investigate whether self-report measures of behavioral undercontrol moderate the relationship between reward sensitivity and alcohol involvement at the phenotypic (Chapter 6) and latent genetic (Chapter 7) levels.

Behavior genetic studies.

Latent genetic factors (i.e., the aggregation of unmeasured genetic effects) account for a significant proportion of variance in AUD (50%-61%; Kendler & Prescott, 2006), reward sensitivity (48%-63%; Koopmans, Boomsma, Heath, & Doornen, 1995), and behavioral undercontrol (48%; Bezdjian, Baker, & Tuvblad, 2011). Few studies, however, have investigated the genetic overlap of alcohol involvement with reward sensitivity or behavioral undercontrol. In a study by Slutske and her colleagues (2002), behavioral undercontrol accounted for 28% and 49% of the genetic variation in AUD in

men and women, respectively. There have been no investigations of the genetic or environmental overlap among reward sensitivity and alcohol involvement.

Notably, there has been one bivariate behavior genetic study of reward sensitivity and behavioral undercontrol. Hur and Bouchard Jr (1997) attributed 55% of the genetic variance in behavioral undercontrol to sensation seeking. These findings suggest that a large proportion of genetic markers are shared across these risk factors, but each also has distinct genetic underpinnings. This study, however, used a small sample of twins reared apart (n=106), and there have been no replication attempts. Recent work from our lab attempted to replicate these findings in a larger sample of twins (*n*=4,764); whereas these constructs were associated with common genetic factors in men, each was influenced by a distinct set of genetic factors in women (Ellingson, Verges, Littlefield, Martin, & Slutske, 2013). Notably, it is unclear whether the common genetic influences of reward sensitivity and behavioral undercontrol are related to alcohol involvement (i.e., a trivariate extension of these bivariate studies).

Molecular genetic studies.

Molecular genetic studies have implicated several genotypes (i.e., measured genetic markers) in reward sensitivity and behavioral undercontrol. Reward sensitivity has been associated with dopamine genes, including markers for dopamine transporters (e.g., DAT1/SLC6A3; Enter, Colzato, & Roelofs, 2012) and receptors (e.g., DRD2 and DRD4; Eisenberg et al., 2007). In addition, there may be additive effects across dopamine genes (Derringer et al., 2010), but such effects have been questioned and replication attempts are needed (Powell & Zietsch, 2011). Activity in mesolimbic reward

substrates following alcohol administration has also been associated with an opioid gene (OPRM1; Ramchandani et al., 2011).

Behavioral undercontrol has been linked to serotonergic genes, including markers for serotonin transporters, which are associated with impulsiveness (5-HTTLPR; Lesch et al., 1996) and attention deficits (5-HTR1B; Faraone & Mick, 2010). In addition, behavioral undercontrol, like reward sensitivity, is associated with dopamine genes (e.g., DRD4 and DAT; Congdon, Lesch, & Canli, 2008). Findings of genetic markers unique to reward sensitivity (e.g., OPRM1) and behavioral undercontrol (e.g., 5-HTTLPR) and common to both constructs (e.g., DRD4, DAT) consistent with behavior genetic findings that suggest distinct and overlapping genetic factors (Hur & Bouchard Jr, 1997).

Developmental studies.

Much of the empirical and theoretical work on dual-systems models has focused on adolescence and emerging adulthood, largely informed by the neuroscience literature. Some attribute elevations in risky behavior during adolescence to hyperactivation in subcortical regions associated with emotional reactivity (e.g., amygdala, ventral striatum), prior to maturation of the prefrontal cortical regions associated with executive functioning (Casey, Jones, & Hare, 2008; Somerville, Jones, & Casey, 2010; Steinberg, 2007, 2010). Initial empirical support for this hypothesis came from cross-sectional research, showing age differences in self-reported measures of sensation seeking (e.g., "I sometimes do 'crazy' things just for fun,") and impulsivity/lack of planning (e.g., "I act on the spur of the moment") (Steinberg et al., 2008). Subsequent studies using longitudinal samples, such as the National Longitudinal Survey of Youth (NLSY) yielded further support for these developmental patterns (Harden & Tucker-Drob, 2011; Quinn &

Harden, 2013; Shulman, Harden, Chein, & Steinberg, 2015). Across studies, sensation seeking and other measures of reward sensitivity sharply increase around ages 12-14, whereas lack of planning and other measures of self-control (reverse-scored) decrease gradually at least through age 30 (Harden & Tucker-Drob, 2011; Steinberg et al., 2008). There has been little work investigating developmental patterns of these personality traits further into adulthood.

Despite following distinct developmental patterns, change in sensation seeking appears to be correlated with change in lack of planning. The magnitude of correlated change varies substantially, however, based on how change is modeled and the age of the sample. Analyzing participants age 12–24 in the NLSY, the correlation between linear change in these two traits was small and nonsignificant (r = 0.21, 95 % confidence interval [CI] -0.01, 0.44; Harden & Tucker-Drob, 2011); however, there was moderate correlation when change was modeled as quadratic (r = 0.44, 95 % CI 0.04, 0.78). A more recent paper drawn from the same sample, by the same group, investigated change across a later period (age 15–26), during which there was strong and statistically significant correlated change when modeling non-linear change (r = 0.67) (Quinn & Harden, 2013). Therefore, the way in which change is modeled can have important implications for estimating the developmental overlap between constructs in a dual-systems model, and presumably other outcomes (e.g., alcohol involvement).

Significance of the proposed work.

Clarifying how reward sensitivity and behavioral undercontrol are related to each other and alcohol involvement is important to furthering progress in this area for many reasons. First, if these systems were truly distinct and predictive of alcohol use and/or

AUD, any model including only one of these systems would be incomplete. Further, if these systems account for the same risk in AUD, models including both systems may be unnecessarily complex. Second, understanding the constructs underlying alcohol involvement may inform etiologic models of AUD (e.g., each system may reflect a different risk mechanism of AUD; Magid, MacLean, & Colder, 2007). Third, clarifying the relationship between these systems may lead to uniformity in the ways in which these systems are measured and discussed. For example, some studies have intentionally combined measures of bottom-up and top-down systems, whereas others have intended to measure one system but mistakenly measured, or mislabeled it as, the other (see Magid et al., 2007 for a description of these studies). Fourth, much of the work on dual-systems models focuses on outcomes in adolescence and, less frequently, emerging adulthood. The proposed project will extended this work to alcohol outcomes through young adulthood (age 35-38). Further, an atheoretical analytic approach will be used to identify the best-fitting growth model for these constructs, given that the developmental overlap among these constructs appears to be heavily dependent on how change is modeled. Finally, understanding individual differences associated with alcohol use and AUD may inform the development of effective preventions and interventions. For example, some treatments are thought to specifically target reward sensitivity or cravings (e.g., topiramate; Johnson et al., 2007), and others specifically behavioral control (e.g., working memory training; Bickel, Yi, Landes, Hill, & Baxter, 2011).

The proposed project, therefore, offers to provide important foundational work for translating basic personality and genetic research to applied contexts. In attempting to elucidate the relationship between these systems and alcohol involvement, the current

project applied two research questions across three levels of data. First, are reward sensitivity and behavioral undercontrol differentially related to alcohol involvement? Specifically, this work differentiated risk among the constructs of dual-systems models of alcohol involvement using phenotypic data (including longitudinal; Chapter 3) data, genetically informed data (i.e., latent genetic risk; Chapter 4), and genotypic data (i.e., measured genetic risk; Chapter 5). Therefore, this work tested a central assumption of dual-systems models—that both reward sensitivity and behavioral undercontrol are necessary for explaining alcohol involvement. Second, does behavioral control moderate the relation between reward sensitivity and alcohol involvement, at the phenotypic (Chapter 6) and latent genetic levels (Chapter 7)? Therefore, this work directly tested the dual-systems model of alcohol involvement—that these constructs comprise a non-additive, interaction effect on alcohol involvement (i.e., beyond what is accounted for by two main effects).

Chapter 2: General Methods

Participants.

Australian Twin Registry (ATR). Participants in the ATR were members of a national community-based twin registry who participated in a study primarily focused on gambling addiction (80.4% recruitment rate; for more details, see Slutske et al., 2009). In 2004–2007, 4,764 participants (57% female; age 32-43, *M* age = 38) completed a self-report, paper-pencil questionnaire about personality characteristics and a semi-structured psychiatric telephone interview that assessed alcohol use and AUD symptoms. Participants who denied ever having a drink (i.e., lifetime abstainers) were excluded from analyses in the current paper, as the conceptual model of behavioral undercontrol moderating the influence of reward sensitivity on alcohol involvement does not apply to these individuals. Further, sex-limited expression of genetic risk was beyond the scope of the current project; therefore, participants included only individuals from same-sex twin pairs, resulting in 3,631 participants from 1,473 complete twin pairs (monozygotic females [MZF] = 524, MZ males [MZM] = 349, dizygotic females [DZF] = 371, DZ males [DZM] = 229) and 685 incomplete pairs. The study was approved by the Institutional Review Boards (IRBs) at the University of Missouri—Columbia and the Queensland Institute of Medical Research.

Alcohol, Health, and Behavior Study (AHB). The AHB focused on family history risk for AUDs. Participants were first-year college students in a large, midwestern public university (see Sher, Walitzer, Wood, & Brent, 1991 for more details). In 1987-1988, 489 participants (54% female; 94% Caucasian; age 18-19, *M* age = 18.2) completed self-report, paper-pencil questionnaires and interviews regarding alcohol involvement and various risk factors (e.g., personality). There have since been six

additional waves of data collection (ages 19, 20, 21, 25, 29, and 35). At Wave 7 (in 2003-2004, *M* age = 35), the retention rate was 78%. As in the ATR, lifetime abstainers were excluded from analyses, resulting in 476 participants in the current study. All data collection was approved by the IRB at the University of Missouri.

Although collected in different countries, the ATR and AHB samples are remarkably similar in gender (ATR = 57% female, AHB = 54% female), ethnicity (over 90% European ancestry), and age/generation (ATR = 38 in 2004-2007, AHB = 35 in 2003-2004).

Measures.

Similar measures of alcohol use, AUD, and personality were used in the ATR and AHB samples (see Table 2-1 for makeup of measures, Table 2-2 for descriptive statistics). All alcohol measures were log-transformed to account for non-normality, and personality measures were zero-centered to minimize the influence of collinearity in regression models.

Alcohol Involvement. Both the ATR and AHB measured normative alcohol use with alcohol quantity-frequency (alcohol QF; Jackson & Sher, 2006), the typical quantity (average number of drinks per occasion) multiplied by the frequency of drinking. In addition, both the ATR and AHB had a composite measure of heavy drinking; in the ATR, heavy drinking was the average frequencies of intoxication and hangover, and in the AHB it was the average frequencies of getting "a little high or light-headed on alcohol", "drunk (not just a little high)" and binge drinking. Problematic alcohol use was based on the number of endorsed items from the AUD section of the Composite International Diagnostic Interview in the ATR (Robins et al., 1988) and on the Diagnostic

Interview Schedule in the AHB (DIS-IIIA; Robins, Helzer, Croughan, Williams, & Spitzer, 1985).

Table 2-1. Primary Measures of Alcohol Use, Alcohol Use Disorder, and Personality				
Measures	Sample			
Alcohol Involvement	Australian Twin Registry (ATR)		Alcohol, Health, and Behavior (AHB)	
Alcohol Use				
Alcohol Quantity*Frequency				
	Past Year Drinking Frequency		Past Year Drinking Frequency	
	Past Year Typical Quantity		Past Year Typical Quantity	
Heavy Drinking Composite				
	Past Year Hangover Frequency		Past Month Binge Frequency	
	Past Year Intoxication Frequency		Past Month Drunk Frequency	
			Past Month High (from Alcohol) Freq.	
Alcohol Use Disorder				
Symptom Count	DSM5 Alcohol Use Disorder (without craving) (Composite International Diagnostic Interview; Robins et al., 1988)		DSM-IV Alcohol Dependence (Diagnostic Interview Schedule; Robins, Helzer, Croughan, Williams, & Spitzer, 1985)	
Personality	Scale	Subscale (# of items)	Scale	Subscale (# of items)
Reward Sensitivity				
General Sensation Seeking	ZSS	Disinhibition (10)	EPI	Impulsiveness (4)
	ZSS	Boredom Susceptibility (10)		
	ZSS	Experience Seeking (10)		
	ZSS	Thrill & Adventure Seeking (10)		
Positive Expectancies	ZSS	Disinhibition (4)	Alcohol Expectancies	Activity Enhancement (9)
	ZSS	Experience Seeking (2)		
Behavioral Undercontrol				
	MPQ	Control (20)	EPI	Impulsiveness (4)

Table 2-2. Descriptive statistics of measures from AHB at Wave 7 (age 35; lower diagonal) and ATR (*M* age 38; upper diagonal).

	Alcohol QF	Heavy Drinking [a]	Alcohol Dependence [b]	Behavioral Undercontrol	General Sensation Seeking	Positive Expectancies
Alcohol QF		.63 (.01)	.39 (.01)	.17 (.02)	.35 (.02)	.49 (.01)
Heavy Drinking [a]	.76 (.02)		.52 (.02)	.24 (.02)	.40 (.02)	.55 (.01)
Alcohol Dependence [b]	.49 (.04)	.51 (.04)		.13 (.02)	.19 (.02)	.31 (.02)
Behavioral Undercontrol	.13 (.05)	.11 (.05)	.11 (.05)		.47 (.02)	.34 (.02)
General Sensation Seeking	.14 (.05)	.18 (.05)	.30 (.05)	.17 (.05)		.67 (.01)
Positive Expectancies	.52 (.04)	.41 (.04)	.39 (.04)	.13 (.05)	.23 (.05)	
Mean (SD)	1.02 (0.91) \ 4.97 (2.27)	0.21 (0.11) \ 1.20 (1.48)	0.29 (0.26) \ 0.18 (0.16)	0.00 (0.08) \ 0.00 (0.04)	0.00 (0.05) \ 0.00 (0.03)	0.01 (0.43) \ 0.00 (0.07)
Skewness	0.87 \ -0.41	2.42 \ 0.84	1.63 \ 2.41	0.69 \ 0.62	1.41 \ 0.11	0.59 \ 0.52
Kurtosis	0.09 \ -0.69	6.22 \ 0.22	1.72 \ 5.53	-0.29 \ -0.13	1.48 \ -0.57	-0.09 \ -0.65

Note: Standard errors are in parentheses. Means, standard deviations, skewness, and kurtosis statistics are presented as AHB \ ATR. Correlations among alcohol measures are outlined in the top-left quadrant of the correlation table, and correlations among personality measures are outlined in the bottom right quadrant. [a] Heavy drinking in AHB was computed as the mean number of days high, drunk, and binge drinking in the previous 30 days, and in the ATR it was computed as the mean number of days intoxicated and hungover in the previous year. [b] Alcohol use Disorder in AHB was based on DSM-IV alcohol dependence, and in the ATR it was based on a DSM-5 symptom count (excluding craving).

As a cross-sectional study, ATR participants were queried on all alcohol measures for the past year and their heaviest drinking period (if it occurred at any time other than the past year). The heaviest drinking period, on average occurred from age 22-26, or between Wave 4 and Wave 5 in AHB. Analyses using heaviest drinking period in the ATR should be interpreted with caution, however, because the nature of these individuals' drinking may bias toward selection effects of heavy drinkers. Indeed, individuals who denied that their heaviest drinking included the last year reported greater levels of current use (alcohol QF; F [1,2093] = 5.70, p = .02) and heavy drinking (F [1,2094] = 29.85, p < .001); however, they unexpectedly reported fewer past-year AUD symptoms (F [1,2095] = 13.43, p < .001). This unexpected finding for AUD symptoms may be driven by individuals whose drinking may have always been high or continues to increase. Individuals whose heaviest drinking did not occur within the last year also reported greater levels of behavioral undercontrol (F [1,1993] = 34.75, p < .001), general SS (F [1,1993] = 114.67, p < .001), and positive expectancies (F [1,1993] = 146.81, p < .001).

As a longitudinal study, AHB participants were queried on all alcohol measures for the past year, including past-year alcohol QF and past-month heavy drinking. For concordance across studies, past-year measures were used in all analyses except behavioral genetic models (Chapter 4), which used measures of peak use and lifetime AUD symptoms.

Personality. Two measures of reward sensitivity were extracted from the ZSS, to assess the positive valence of engaging in risky behavior (i.e., general sensation seeking) and substance use (i.e., positive expectancies). Both were included so that findings from

the current project could be evaluated with respect to prior work on risky behavior (Steinberg et al., 2008) and alcohol involvement (Houben & Wiers, 2009). The limitations of both measures should be considered when interpreting the results. General SS may be a poor indicator of individual differences in the positive valence of substance use, making it inappropriate for dual-systems models of alcohol involvement. In contrast, positive expectancies may be a proxy for problematic substance use, therefore leaving little variance unexplained that may be due to main effects of behavioral undercontrol or non-additive interaction effects.

Mean scores of self-report personality measures were used to assess reward sensitivity and behavioral undercontrol in both samples. Participants in the ATR were administered the 40-item Zuckerman Sensation Seeking Scale (ZSS; Zuckerman, Kolin, Price, & Zoob, 1964). All 40 items from the ZSS were used to measure general sensation seeking (SS). A subset of six ZSS items regarding alcohol and other substance use that assessed the positive valence of substance use measured positive expectancies (example item: "Keeping the drinks full is the key to a good party"). The lower-bound internal consistency (ω; McDonald, 1999) was .93 for general SS and .88 for positive expectancies. Whereas alpha is traditionally used to estimate lower-bound internal consistency, it provides an acceptable estimate under restrictive conditions and typically underestimates internal consistency (Zinbarg, Revelle, Yovel, & Li, 2005). Instead, McDonald's omega is more generalizable across conditions and provides the most accurate measure of internal consistency available for most samples; however, Cronbach's alpha remains the most widely used measure of internal consistency.

The ATR participants were also administered the Multidimensional Personality Questionnaire (MPQ; Tellegen, 1982), from which the 20-item Control scale (reverse-scored) was used to assess behavioral undercontrol (ω=.92). Tellegen and his colleagues have described the MPQ Control scale as a measure of "behavioral control" (Shiner, Masten, & Tellegen, 2002); however, it also is conceptually similar to *lack of planning* and was the strongest loading indicator on *lack of planning* in the original study that developed the UPPS impulsive behavior scale (Whiteside & Lynam, 2001).

The AHB used the Eysenck Personality Inventory (EPI; Eysenck & Eysenck, 1968), from which a 4-item scale assessed behavioral undercontrol in the AHB (ω = .79 – .86 across all waves of AHB). These four items were chosen from a larger 10-item scale previously used in AHB studies (Littlefield, Sher, & Steinley, 2010). Whereas the full 10-item scale is available only at Waves 1, 5, 6, and 7, these four items were selected due to their availability at all seven waves. As with the ATR study, two measures were used to assess reward sensitivity –a measure of general SS was extracted from four items from the EPI (ω =.69 – .81), and a measure of positive expectancies was taken from nine items querying activity enhancement from an alcohol expectancy questionnaire (ω = .84 – .88; Kushner, Sher, Wood, & Wood, 1994; Sher, Wood, Wood, & Raskin, 1996) (see Appendix for full measures).

Measures from AHB and the ATR were administered to an independent sample of undergraduates to compare for concordance. The measures of behavioral undercontrol from the AHB and ATR studies were moderately correlated (r = .49). Similarly, the measures of general SS were moderately correlated (r = .48). A measure of alcohol expectancies was administered as well (Fromme, Stroot, & Kaplan, 1993), however, it

differed from the measure administered in AHB. This measure correlated moderately with the measure of positive expectancies used in the ATR (r = .31). Across measures, behavioral undercontrol was moderately correlated with reward sensitivity (rs = .35 – .48).

Chapter 3: Are reward sensitivity and behavioral undercontrol differentially related to alcohol involvement at the phenotypic level (including longitudinally)?

Methods

Analytic Approach.

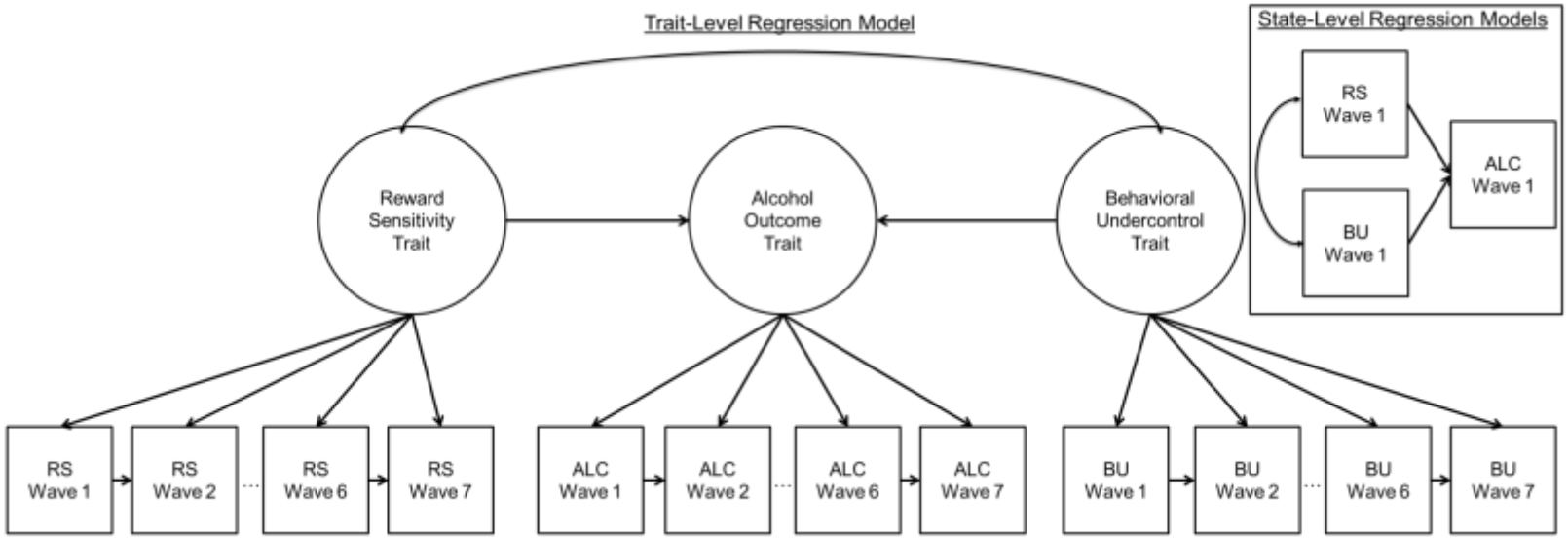
Regression Models. All models for Aim 1 (Chapter 3 – 5) were conducted in Mplus 7.31 (Muthén & Muthén, 1998-2012). Two sets of regression models were conducted to investigate the degree to which reward sensitivity and behavioral undercontrol account for distinct variance in alcohol involvement (alcohol QF, heavy drinking, AUD symptoms). One set of models used general SS as a measure of reward sensitivity, and the other used positive expectancies as a measure of reward sensitivity; both sets of models used the same measure of behavioral undercontrol. Throughout this paper, both measures of reward sensitivity were used to answer each research question. Measures of reward sensitivity and behavioral undercontrol were modeled as correlated independent variables that account for additive variance in alcohol involvement. All seven waves of AHB were analyzed in linear regression models, and data from the ATR (*M* age=38) were used to replicate findings from Wave 7 of AHB (*M* age=35). All phenotypic analyses using the ATR accounted for the non-independence of observations obtained from members of the same family.

State-Trait Models. The seven waves of AHB were analyzed in state-trait models to investigate the relationship between measures of reward sensitivity (general SS, positive expectancies) and behavioral undercontrol with alcohol involvement (alcohol QF, heavy drinking, AUD symptoms) at the state (or wave) and trait (or aggregate) levels. By incorporating several waves, state-trait models decompose variance at the state level into trait (i.e., common variance across states) and error components (i.e., residual

variance at individual states) (Steyer, Ferring, & Schmitt, 1992). Of particular interest was the degree to which trait measures of reward sensitivity and behavioral undercontrol account for the same risk mechanism(s) in alcohol involvement, and whether state-specific associations remain after accounting for risk due to traits.

Multivariate state-trait models were specified with three latent trait variables: a measure of alcohol involvement (alcohol QF, heavy drinking, alcohol dependence), reward sensitivity (general SS, positive expectancies), and behavioral undercontrol. All models included six first-order autoregressive paths for each manifest variable (i.e., Wave 1 to Wave 2, Wave 2 to Wave 3, and so on for each measure in the model). Within multivariate state-trait models, latent traits for reward sensitivity and behavioral undercontrol were modeled as correlated independent variables, predicting latent traits of alcohol involvement (see Figure 3-1). Similarly, residualized state variables for personality measures were modeled as correlated independent variables, predicting state measures of alcohol involvement at each wave. Therefore, each model examined one trait-level association and seven state-specific associations (i.e., Waves 1-7).

Figure 3-1. State-trait measurement models.



Autoregressive paths were included to account for prior personality and alcohol use. Regression analyses conducted on trait measures, with correlated personality measures (reward sensitivity and behavioral undercontrol) predicting alcohol involvement (pictured). Further, regression analyses were conducted on state-specific personality measures (reward sensitivity and behavioral undercontrol) predicting alcohol involvement at each wave (not pictured).

Latent Growth Models. Latent growth models (LGMs) were conducted using AHB to investigate the nature of change, and co-development of, reward sensitivity (general SS, positive expectancies), behavioral undercontrol, and alcohol involvement (alcohol QF, heavy drinking, AUD symptoms) (Meredith & Tisak, 1990). Notably, the developmental literature on reward sensitivity and behavioral undercontrol has not examined this relationship beyond emerging adulthood (Harden & Tucker-Drob, 2011). Further, it is unclear whether change in each system is related to change in alcohol involvement. Analyses addressing this aim were conducted in two steps: 1) exploratory LGMs identified the best fitting growth factor structure; and 2) multivariate LGMs, incorporating the best fitting growth structure, estimated the correlated intercept and change factors.

First, exploratory LGMs were conducted as an atheoretical approach to modeling the growth of personality and alcohol involvement (Grimm, Steele, Ram, & Nesselroade, 2013). This analytic approach consists of two accommodations to determine best fit of growth to the data. First, the combination and number of intercept and growth factors that provide the best fit was determined for each measure. To determine the number of growth factors that best fit the data, a sequence of models were conducted within an exploratory structural equation modeling framework on the seven waves of data: 1) a tau-equivalent model which consisted of an intercept only (i.e., loadings fixed to one for all waves); 2) a 1-factor model (i.e., loadings freely estimated for each wave), 3) a 1-factor + intercept model (i.e., loadings freely estimated on one factor, fixed to one on the intercept); 4) a 2-factor model; 5) a 2-factor + intercept model; 6) a 3-factor model; and 7) a 3-factor + intercept model. For models in which there were multiple factors, factor correlations were

fixed to zero, as each factor is assumed to represent a distinct growth process. The best-fitting model was chosen based on the Confirmatory Fit Index (CFI; Bentler & Bonett, 1980), Tucker-Lewis Index (TLI; Tucker & Lewis, 1973), and root mean square error of approximation (RMSEA; Steiger & Lind, 1980). After determining the number of growth factors that provide the best fit, the indicator loadings on the growth factors were consulted to choose how to model change in each measure (e.g., linear/quadratic, piecewise). Finally, once a LGM was chosen for each variable, multivariate LGMs were conducted to assess the degree of correlated change among intercept and change factors for alcohol and personality measures.

Results

Regression Models

General SS. Correlations between general SS and behavioral undercontrol were weak to moderate across all waves (*r*s = .15 – .22, *p*s ≤ .001), suggesting these may be distinct risk factors. The results of regression models assessing the effects of behavioral undercontrol and general SS on alcohol involvement in AHB are displayed in Table 3-1. General SS demonstrated statistically significant associations with alcohol QF at all waves (*b*s = 0.38 – 0.64 [SEs = 0.18 – 0.23], *p*s < .05); heavy drinking at all waves (*b*s = 0.21 – 0.30 [SEs = 0.07 – 0.08], *p*s < .01) except Wave 2 (*b* = 0.13 [SE = 0.07], *p* = .08); and alcohol dependence at all waves (*b*s = 0.32 – 0.69 [SEs = 0.10 – 0.12], *p*s < .01). Behavioral undercontrol demonstrated associations through Wave 7 (age 25) for alcohol QF (*b*s = 0.50 – 0.93 [SEs = 0.15 – 0.16], *p*s < .01), heavy drinking (*b*s = 0.21 – 0.37 [SEs = 0.05 – 0.07], *p*s < .01), and alcohol dependence (*b*s = 0.17 – 0.36 [SEs = 0.08 – 0.09], *p*s < .05). At Waves 6 (age 29), however, behavioral undercontrol was not

associated with alcohol dependence, and at Wave 7 (age 35) it was not associated with alcohol dependence or heavy drinking. Notably, the magnitude of associations also appears to become smaller across waves for all alcohol measures.

Table 3-1. Regression model estimates of general sensation seeking and behavioral undercontrol on alcohol involvement in the AHB sample.

Personality Measure	Wave 1 (Age 18) *n* = 476	Wave 2 (Age 19) *n* = 471	Wave 3 (Age 20) *n* = 459	Wave 4 (Age 21) *n* = 460	Wave 5 (Age 25) *n* = 444	Wave 6 (Age 29) *n* = 389	Wave 7 (Age 35) *n* = 367
	Alcohol QF						
General Sensation Seeking	0.64 (0.18)***	0.55 (0.18)**	0.55 (0.18)**	0.38 (0.18)*	0.64 (0.19)**	0.55 (0.22)*	0.56 (0.23)*
Behavioral Undercontrol	0.93 (0.15)***	0.77 (0.15)***	0.68 (0.16)***	0.61 (0.15)***	0.50 (0.15)**	0.36 (0.16)*	0.37 (0.18)*
	Heavy Drinking						
General Sensation Seeking	0.26 (0.07)***	0.13 (0.07)	0.29 (0.07)***	0.24 (0.08)**	0.30 (0.07)***	0.21 (0.08)**	0.26 (0.08)**
Behavioral Undercontrol	0.37 (0.06)***	0.21 (0.06)**	0.29 (0.07)***	0.24 (0.06)***	0.21 (0.05)***	0.17 (0.06)**	0.10 (0.06)
	Alcohol Dependence						
General Sensation Seeking	0.35 (0.10)***	0.44 (0.10)***	0.44 (0.10)***	0.37 (0.11)**	0.32 (0.11)**	0.43 (0.12)***	0.69 (0.12)***
Behavioral Undercontrol	0.36 (0.08)***	0.32 (0.08)***	0.32 (0.09)***	0.21 (0.09)*	0.17 (0.08)*	0.16 (0.08)	0.10 (0.09)

Note: *** $p < .001$, ** $p < .01$, * $p < .05$. Estimates are for unstandardized regression coefficients, standard errors are in parentheses. Regression models specified general sensation seeking and behavioral undercontrol as correlated (rs = .15 – .22, ps ≤ .001), centered dependent variables. Thus, these main effects capture associations of each personality measure with alcohol involvement, independent of the effect of the other personality measure. Alcohol measures were log-transformed to account for non-normality.

Table 3-2. Estimates of main effects of general sensation seeking and behavioral undercontrol on alcohol involvement for past year and peak period of use in the ATR sample.

Personality Measure	Peak (Age 22 - 26) *n* = 1,439	Past Year (Age 38) *n* = 3,499
	Alcohol QF	
General Sensation Seeking	1.33 (0.17)***	3.11 (0.17)***
Behavioral Undercontrol	0.48 (0.13)***	0.04 (0.14)
	Heavy Drinking	
General Sensation Seeking	2.17 (0.25)***	2.68 (0.13)***
Behavioral Undercontrol	0.29 (0.18)	0.37 (0.12)**
	Alcohol Use Disorder	
General Sensation Seeking	0.71 (0.13)***	0.39 (0.05)***
Behavioral Undercontrol	0.44 (0.10)***	0.11 (0.04)*

Note: *** $p < .001$, ** $p < .01$, * $p < .05$. Estimates are for unstandardized regression coefficients, standard errors are in parentheses. Regression models specified general sensation seeking and behavioral undercontrol as correlated ($r = .47$, $p < .001$), centered dependent variables. Thus, these main effects capture associations of each personality measure with alcohol involvement, independent of the effect of the other personality measure. Alcohol measures were log-transformed to account for non-normality. Participants were asked about their past-year drinking, and whether there was ever a time when they drank more than in the past year. If participants reported prior use that exceeded current levels, they were also asked about use during that time. Therefore, peak use is based on a subset of participants, and past year is based on the full sample.

Correlations between general SS and behavioral undercontrol were statistically significant and stronger in the ATR ($r = .47$, $p < .001$), relative to AHB, suggesting greater overlap between these risk factors. The results of regression models in the ATR, attempting to replicate findings from AHB's Wave 7 (Age 35) based on past-year reports (*M* age = 38) and Waves 4-5 based on peak alcohol involvement (*M* age 22 – 26), are displayed in Table 3-2. Consistent with findings from AHB, general SS was associated with all alcohol measures during peak use (*b*s = 0.71 – 2.17 [SEs = 0.13 – 0.25], *p*s < .001) and the previous year (*b*s = 0.39 – 3.11 [SEs = 0.05 – 0.17], *p*s < .001). Further,

behavioral undercontrol was associated with peak alcohol QF (b = 0.48 [SE = 0.13], p < .001) and lifetime AUD symptoms (b = 0.44 [SE = 0.10], p < .001), and heavy drinking (b = 0.37 [SE = 0.12], p < .01) and AUD symptoms (b = 0.11 [SE = 0.04], p = .01) during the previous year. As in the AHB, there were weaker associations from peak to past-year alcohol QF (b = 0.48 to 0.04, p = .001 to .79) and lifetime to past-year AUD symptoms (b = 0.44 to 0.11, p = .001 to .01) in the ATR.

Positive Expectancies. In the AHB, the correlations between positive expectancies and behavioral undercontrol were weak at all waves (rs = .13 – .19, ps < .01) and nonsignificant at Waves 5 and 6 (rs = .06 – .09, ps = .05 – .21), suggesting that these may be distinct risk factors. The results of regression models assessing the effects of behavioral undercontrol and positive expectancies on alcohol associations are displayed in Table 3-3. Positive expectancies demonstrated associations at all waves with alcohol QF (bs = 0.63 – 0.89 [SEs = 0.06 – 0.07], ps < .001), heavy drinking (bs = 0.17 – 0.37 [SEs = 0.02 – 0.03], ps < .001), and alcohol dependence (bs = 0.27 – 0.42 [SEs = 0.03 – 0.04], ps < .001). As with models of general SS, behavioral undercontrol was more consistently associated with alcohol involvement at earlier waves. Through Wave 3, behavioral undercontrol was associated with alcohol QF (bs = 0.49 – 0.74 [SEs = 0.13 – 0.14], ps < .001), heavy drinking (bs = 0.14 – 0.30 [SEs = 0.05 – 0.06], ps < .05), and alcohol dependence (bs = 0.27 – 0.28 [SEs = 0.08], ps < .01). Through Waves 4 – 7, associations with alcohol dependence were not significant, except at Wave 5 (bs = 0.10 – 0.18 [SEs = 0.08 – 0.09], ps = .02 – .26). Further, associations with alcohol QF and heavy drinking were not significant at Wave 7 (bs = 0.07 – 0.22 [SEs = 0.06 – 0.15], ps = .15 –

.22). Therefore, there were no statistically significant associations between behavioral undercontrol and alcohol involvement at Wave 7 (age 35).

Table 3-3. Regression model estimates of positive expectancies and behavioral undercontrol on alcohol involvement in the AHB sample.

Personality Measure	Wave 1 (Age 18) *n* = 476	Wave 2 (Age 19) *n* = 471	Wave 3 (Age 20) *n* = 459	Wave 4 (Age 21) *n* = 460	Wave 5 (Age 25) *n* = 444	Wave 6 (Age 29) *n* = 389	Wave 7 (Age 35) *n* = 367
				Alcohol QF			
Positive Expectancies	0.71 (0.06)***	0.77 (0.06)***	0.80 (0.06)***	0.89 (0.06)***	0.82 (0.07)***	0.63 (0.07)***	0.75 (0.07)***
Behavioral Undercontrol	0.74 (0.13)***	0.58 (0.13)***	0.49 (0.14)***	0.44 (0.12)***	0.44 (0.13)**	0.35 (0.14)*	0.22 (0.15)
				Heavy Drinking			
Positive Expectancies	0.27 (0.02)***	0.26 (0.02)***	0.33 (0.03)***	0.37 (0.03)***	0.26 (0.03)***	0.17 (0.03)***	0.21 (0.02)***
Behavioral Undercontrol	0.30 (0.05)***	0.14 (0.06)*	0.22 (0.06)***	0.18 (0.05)***	0.20 (0.05)***	0.17 (0.05)**	0.07 (0.06)
				Alcohol Dependence			
Positive Expectancies	0.33 (0.03)***	0.32 (0.03)***	0.36 (0.04)***	0.42 (0.04)***	0.38 (0.04)***	0.27 (0.04)***	0.30 (0.04)***
Behavioral Undercontrol	0.28 (0.08)***	0.28 (0.08)***	0.27 (0.08)**	0.16 (0.08)	0.15 (0.08)	0.18 (0.08)*	0.10 (0.09)

Note: *** $p < .001$, ** $p < .01$, * $p < .05$. Estimates are for unstandardized regression coefficients, standard errors are in parentheses. Regression models specified general sensation seeking and behavioral undercontrol as correlated (*r*s = .06 – .21, *p*s = .001 – .21), centered dependent variables. Thus, these main effects capture associations of each personality measure with alcohol involvement, independent of the effect of the other personality measure. Alcohol measures were log-transformed to account for non-normality.

Table 3-4. Estimates of main effects of positive expectancies and behavioral undercontrol on alcohol involvement for past year and peak period of use in the ATR sample.

Personality Measure	Peak (Age 22 - 26) *n* = 1,439	Past Year (Age 38) *n* = 3,499
	Alcohol QF	
Positive Expectancies	1.30 (0.10)***	2.69 (0.09)***
Behavioral Undercontrol	0.44 (0.11)***	0.02 (0.12)
	Heavy Drinking	
Positive Expectancies	1.91 (0.13)***	2.37 (0.07)***
Behavioral Undercontrol	0.30 (0.16)	0.33 (0.10)**
	Alcohol Use Disorder	
Positive Expectancies	0.87 (0.06)***	0.44 (0.03)***
Behavioral Undercontrol	0.34 (0.09)***	0.06 (0.04)

Note: *** $p < .001$, ** $p < .01$, * $p < .05$. Estimates are for unstandardized regression coefficients, standard errors are in parentheses. Regression models specified general sensation seeking and behavioral undercontrol as correlated ($r = .34$, $p < .001$), centered dependent variables. Thus, these main effects capture associations of each personality measure with alcohol involvement, independent of the effect of the other personality measure. Alcohol measures were log-transformed to account for non-normality. Participants were asked about their past-year drinking, and whether there was ever a time when they drank more than in the past year. If participants reported prior use that exceeded current levels, they were also asked about use during that time. Therefore, peak use is based on a subset of participants, and past year is based on the full sample.

The results of regression models in the ATR are displayed in Table 3-4. Positive expectancies and behavioral undercontrol demonstrated stronger correlations in the ATR, relative to AHB ($r = .34$, $p < .001$). Positive expectancies were associated with all measures of alcohol involvement during the period of peak use (*b*s = 0.87 – 1.91 [SEs = 0.06 – 0.13], *p*s < .001) and the previous year (*b*s = 0.44 – 2.69 [SEs = 0.03 – 0.09], *p*s < .001). Behavioral undercontrol was again associated with peak alcohol QF and lifetime AUD symptoms (*b*s = 0.34 – 0.44 [SEs = 0.09 – 0.11], *p*s < .001), but not for past-year measures. In contrast, behavioral undercontrol was associated with heavy drinking during

the previous (b = 0.30 [SEs = 0.16], p = .06) but not during peak use (b = 0.33 [SEs = 0.10], p < .01).

State-Trait Models.

General SS and Behavioral Undercontrol. To test whether associations between alcohol involvement and personality measures are attributable to specific waves or a general trait, state-trait models were conducted in the AHB sample (see Figure 3-1). The trait factors of general SS and behavioral undercontrol were moderately correlated (r = .33, p < .001). Further, there were weak but statistically significant correlations between these personality measures specific to Wave 1 (r = .12, p = .02), Wave 3 (r = .13, p = .03), Wave 4 (r = .16, p = .01), and Wave 6 (r = .12, p = .02), suggesting that there may be some state-specific overlap between these risk factors not accounted for by general traits. Results of state-trait models investigating general SS and behavioral undercontrol are displayed in Table 3-5. The trait factor of general SS was associated with trait factors of heavy drinking (b = 0.27 [SE = 0.11], p < .05) and alcohol dependence (b = 0.41 [SE = 0.15], p<.01), but not alcohol QF (b = 0.35 [SE = 0.26], p = .18). In contrast, the trait factor of behavioral undercontrol was associated with all measures of alcohol involvement (bs = 0.25 – 0.61 [SEs = 0.09 – 0.23], ps < .01). At the state level, there were Wave 1 associations across alcohol measures for general SS (bs = 0.15 – 0.45 [SEs = 0.06 – 0.15], ps < .05) and behavioral undercontrol (bs = 0.22 – 0.65 [SEs = 0.05 – 0.14], ps < .01). At subsequent waves, general SS demonstrated effects at some waves for alcohol QF (Waves 3, 5, 6; bs = 0.24 – 0.45 [SEs = 0.12 – 0.17], ps < .05) heavy drinking (Waves 5, 6; bs = 0.15 – 0.16 [SEs = 0.06 – 0.07], ps < .05), and alcohol dependence (Waves 2, 4, 6, 7; bs = 0.18 – 0.43 [SEs = 0.08 – 0.10], ps < .05). In contrast, behavioral

undercontrol demonstrated a significant association with alcohol QF at Wave 2 (b = 0.21 [SE = 0.10], p = .03), but not at subsequent waves or with any other measures. Therefore, behavioral undercontrol and alcohol involvement were associated at the trait-level and in early adulthood (age 18 – 19).

Table 3-5. State-trait model estimates of main effects of general sensation seeking and behavioral undercontrol on alcohol involvement in the AHB sample.

Personality Measure	Trait (n = 476)	Wave 1 (Age 18) (n = 476)	Wave 2 (Age 19) (n = 471)	Wave 3 (Age 20) (n = 459)	Wave 4 (Age 21) (n = 460)	Wave 5 (Age 25) (n = 444)	Wave 6 (Age 29) (n = 389)	Wave 7 (Age 35) (n = 367)
	Alcohol QF							
General Sensation Seeking	0.35 (0.26)	0.45 (0.15)**	0.14 (0.11)	0.24 (0.12)*	0.25 (0.14)	0.36 (0.17)*	0.45 (0.15)**	-0.04 (0.16)
Behavioral Undercontrol	0.61 (0.23)**	0.65 (0.14)***	0.21 (0.10)*	0.17 (0.11)	0.16 (0.10)	0.22 (0.14)	0.02 (0.11)	0.17 (0.12)
	Heavy Drinking							
General Sensation Seeking	0.27 (0.11)*	0.15 (0.06)*	-0.03 (0.06)	0.09 (0.06)	0.08 (0.06)	0.16 (0.06)*	0.15 (0.07)*	0.06 (0.07)
Behavioral Undercontrol	0.25 (0.09)**	0.27 (0.05)***	0.06 (0.05)	0.09 (0.05)	0.06 (0.05)	0.08 (0.05)	0.08 (0.05)	0.03 (0.05)
	Alcohol Dependence							
General Sensation Seeking	0.41 (0.15)**	0.2 (0.09)*	0.18 (0.08)*	0.09 (0.10)	0.23 (0.10)*	0.15 (0.10)	0.30 (0.10)**	0.43 (0.10)***
Behavioral Undercontrol	0.33 (0.13)**	0.22 (0.08)**	0.13 (0.07)	0.07 (0.08)	-0.04 (0.08)	0.03 (0.08)	0.04 (0.07)	0.00 (0.08)

Note: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. State-trait models included an autoregressive path to account for prior alcohol involvement and personality, and both personality measures were modeled as correlated independent variables at the trait ($r = .33$, $p < .001$) and state levels (rs = .02 – .16, p = .01 – .68). Therefore, associations at each wave assess the association unique to each personality measure, and after accounting for prior personality/alcohol measures.

Positive Expectancies and Behavioral Undercontrol. The trait factors of positive expectancies and behavioral undercontrol were moderately correlated (r = .23, p < .001), however, associations at the state level were negligible (rs = -.02 – .06, ps = .24 – .84). Results of state-trait models investigating positive expectancies and behavioral undercontrol are displayed in Table 3-6. Therefore, the association between these risk factors appears to be due to general trait factors. The trait factor of positive expectancies was associated with trait factors of all alcohol measures (bs = 0.14 – 0.45 [SEs = 0.03 – 0.07], ps < .001). In contrast, the trait factor of behavioral undercontrol accounted for a unique association with heavy drinking (b = 0.14 [SE = 0.06], p = .02) and alcohol dependence (b = 0.19 [SE = 0.09], p = .03), but not with alcohol QF (b = 0.25 [SE = 0.14], p = .08). At the state level, positive expectancies were associated with nearly every alcohol measure at every wave (alcohol QF: bs = 0.22 – 0.54 [SEs = 0.05 – 0.08], ps < .001; heavy drinking: bs = 0.09 – 0.18 [SEs = 0.02 – 0.03], ps < .001; alcohol dependence: bs = 0.05 – 0.27 [SEs = 0.03 – 0.07]). In contrast, behavioral undercontrol was associated with all measures at Wave 1 (bs = 0.21 – 0.64 [SEs = 0.05 – 0.12], ps < .01), and with alcohol QF and alcohol dependence at Wave 2 (bs = 0.14 – 0.20 [SEs = 0.07 – 0.09], ps < .05); however, it demonstrated sparse associations at subsequent waves for all alcohol measures (bs = -0.03 – 0.26 [SEs = 0.05 – 0.13], ps = .04 – .71).

Across both sets of models, behavioral undercontrol was associated with alcohol involvement at the trait level and at Wave 1, but not thereafter. In regard to findings for measures of reward sensitivity, general SS was associated with heavy drinking and alcohol dependence at the trait level and at several waves, but associations with alcohol QF were state-specific. In contrast, positive expectancies were associated with alcohol

involvement at the trait level and at nearly every wave (only the association with alcohol dependence at Wave 3 was not significant).

Table 3-6. State-trait model estimates of main effects of sensation seeking and lack of planning on alcohol involvement in the AHB sample.

Personality Measure	Trait (n = 476)	Wave 1 (Age 18) (n = 476)	Wave 2 (Age 19) (n = 471)	Wave 3 (Age 20) (n = 459)	Wave 4 (Age 21) (n = 460)	Wave 5 (Age 25) (n = 444)	Wave 6 (Age 29) (n = 389)	Wave 7 (Age 35) (n = 367)
	Alcohol QF							
Positive Expectancies	0.45 (0.07)***	0.47 (0.06)***	0.22 (0.05)***	0.28 (0.06)***	0.30 (0.08)***	0.54 (0.07)***	0.24 (0.06)***	0.33 (0.06)***
Behavioral Undercontrol	0.25 (0.14)	0.64 (0.12)***	0.20 (0.09)*	0.17 (0.10)	0.16 (0.09)	0.26 (0.13)*	0.08 (0.11)	0.10 (0.12)
	Heavy Drinking							
Positive Expectancies	0.14 (0.03)***	0.19 (0.02)***	0.09 (0.02)***	0.16 (0.03)***	0.18 (0.03)***	0.18 (0.03)***	0.09 (0.02)***	0.10 (0.02)***
Behavioral Undercontrol	0.14 (0.06)*	0.26 (0.05)***	0.04 (0.05)	0.08 (0.05)	0.06 (0.05)	0.09 (0.05)	0.10 (0.05)*	0.02 (0.05)
	Alcohol Dependence							
Positive Expectancies	0.21 (0.04)***	0.21 (0.04)***	0.11 (0.03)**	0.05 (0.07)	0.16 (0.07)*	0.27 (0.04)***	0.13 (0.04)***	0.15 (0.04)***
Behavioral Undercontrol	0.19 (0.09)*	0.21 (0.07)**	0.14 (0.07)*	0.05 (0.07)	-0.03 (0.09)	0.04 (0.08)	0.08 (0.07)	0.03 (0.08)

Note: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. State-trait models included an autoregressive path to account for prior alcohol involvement and personality, and both personality measures were modeled as correlated independent variables at the trait ($r = .23$, $p < .001$)and state levels (rs = -.02 – .06, ps = .24 – .84). Therefore, associations at each wave assess the association unique to each personality measure, and after accounting for prior personality/alcohol measures.

Latent Growth Models.

Exploratory structural equation modeling (ESEM) was first conducted to inform the growth factor structure of personality and alcohol measures (ages 18-35). Specifically, the following seven models were fit: 1) tau-equivalent; 2) 1-factor; 3) 1-factor + intercept; 4) 2-factor; 5) 2-factor + intercept; 6) 3-factor; and 7) 3-factor + intercept. The 3-factor + intercept model was inestimable for some measures (Alcohol QF, Alcohol Dependence), and it produced untrustworthy standard errors due to a non-positive definite product matrix for all personality measures. Therefore, this model was not considered. The best-fitting model was chosen based on the CFI, TLI, and RMSEA fit statistics (see Table 3-7). To assess RMSEA, the probability that estimate was less than .05 was consulted, rather than the point estimate of the RMSEA, because some RMSEA estimates were unreliable as indicated by large standard errors around the fit statistic. For models producing equivalent fit statistics, the more parsimonious model was favored.

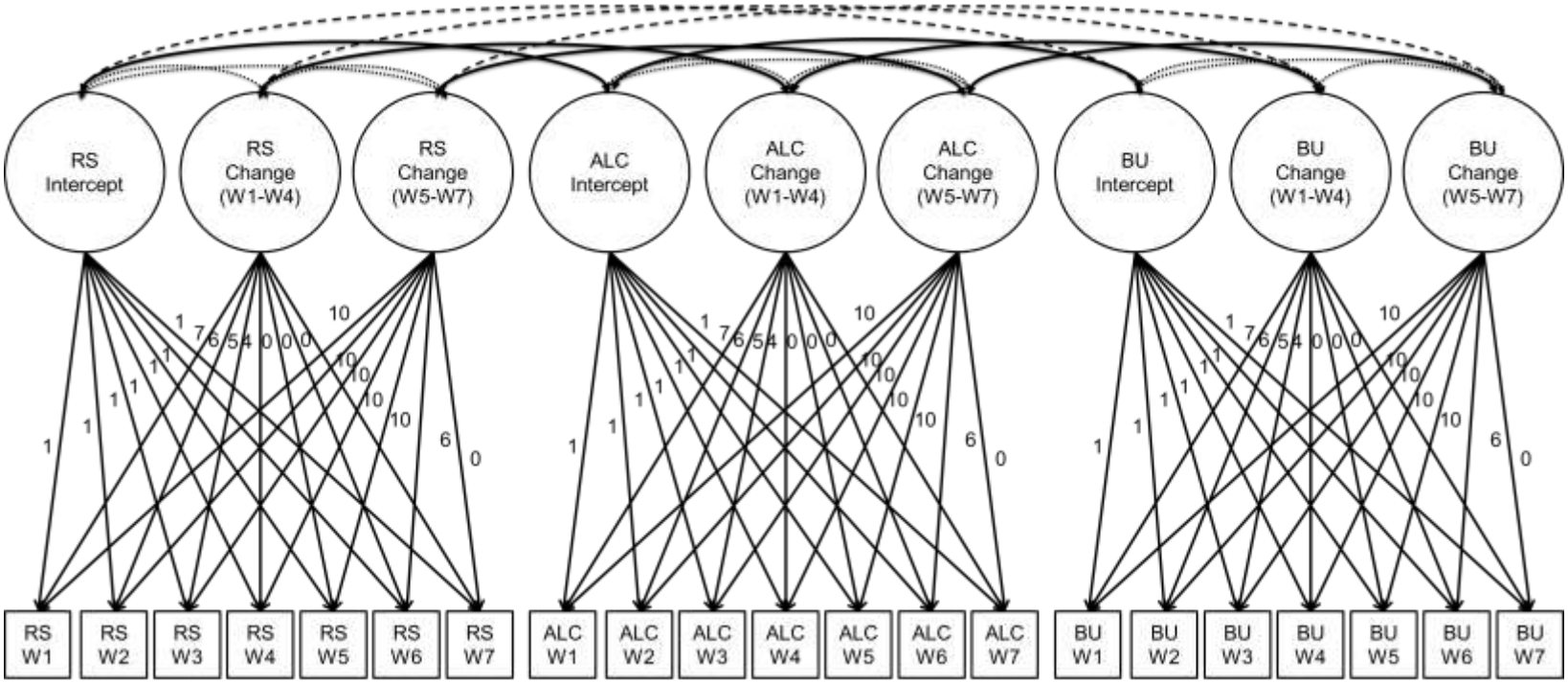
Both the 2-factor + intercept and 3-factor models provided adequate fit. The 2-factor + intercept model provided the best fit for general SS, positive expectancies, heavy drinking, and alcohol dependence; the 3-factor model provided the best fit for behavioral undercontrol and alcohol QF. Notably, among all 3-factor models, the first factor extracted functioned much like an intercept and loaded on all waves (e.g., standardized loadings = .53 – .76 for behavioral undercontrol, .52 – .91 for alcohol QF). Therefore, a 2-factor + intercept LGM was used for all personality and alcohol measures.

Table 3-7. Fit statistics for exploratory structural equation models, determining the best-fitting latent growth model.

Model	CFI	TLI	RMSEA ($p < .05$)
		Behavioral Undercontrol	
Tau-Equivalent	0.903	0.898	0.000
1-Factor	0.919	0.878	0.000
1-Factor + Intercept	0.981	0.970	0.211
2-Factor	0.991	0.976	0.374
2-Factor + Intercept	0.998	0.994	**0.799**
3-Factor	**1.000**	**0.999**	0.751
		General SS	
Tau-Equivalent	0.864	0.858	0.000
1-Factor	0.923	0.884	0.000
1-Factor + Intercept	0.991	0.985	0.744
2-Factor	0.996	0.990	0.788
2-Factor + Intercept	**1.000**	**0.999**	**0.899**
3-Factor	0.995	0.963	0.309
		Positive Expectancies	
Tau-Equivalent	0.839	0.831	0.000
1-Factor	0.851	0.776	0.000
1-Factor + Intercept	0.977	0.963	0.004
2-Factor	0.978	0.942	0.000
2-Factor + Intercept	**0.997**	**0.990**	**0.553**
3-Factor	0.997	0.981	0.285
		Alcohol QF	
Tau-Equivalent	0.769	0.758	0.000
1-Factor	0.801	0.702	0.000
1-Factor + Intercept	0.974	0.958	0.001
2-Factor	0.977	0.940	0.000
2-Factor + Intercept	**1.000**	0.999	0.876
3-Factor	1.000	**1.000**	**0.999**
		Heavy Drinking	
Tau-Equivalent	0.845	0.837	0.000
1-Factor	0.929	0.893	0.000
1-Factor + Intercept	0.982	0.972	0.192
2-Factor	0.986	0.962	0.103
2-Factor + Intercept	**1.000**	**1.000**	0.928
3-Factor	1.000	1.000	**0.976**
		Alcohol Dependence	
Tau-Equivalent	0.808	0.798	0.000
1-Factor	0.847	0.771	0.000
1-Factor + Intercept	0.977	0.962	0.233
2-Factor	0.981	0.949	0.125
2-Factor + Intercept	**0.999**	**0.998**	**0.893**
3-Factor	0.999	0.991	0.652

Note: The best fitting model and statistics are in bold type. In several cases, the lowest RMSEA estimate did not have the highest probability of being below .05. Therefore, the probability that RMSEA estimate was below .05 was used rather than the point estimate.

Figure 3-2. Multivariate latent growth models, estimating factors for the intercept, change at Waves 1 – 4 (ages 18-21), and change at Waves 5-7 (age 25-35), for reward sensitivity, behavioral (under)control, and alcohol involvement.



The parameters of greatest interest were the correlations between intercept and change factors of alcohol involvement and personality measures (reward sensitivity, behavioral undercontrol), depicted by solid, bold slings. All intercept and change factors were allowed to correlate in the model, but only those between reward sensitivity and behavioral undercontrol (dashed slings), and within each construct (dotted slings) are depicted in the figure. In addition, family history and gender were included as covariates for each factor.

The loadings were consulted to determine the growth factor structure, from which a piecewise model (for Waves 1-4 and Waves 5-7) or linear + quadratic change model both appeared appropriate. Models fitting both linear and quadratic change factors were inestimable or fit poorly. Piecewise models (for change at Waves 1-4, and 5-7) provided adequate fit across all measures, except alcohol QF, which was considered poor (CFI = .752, TLI = .721, RMSEA = .191 [90% CI = .177, .205], *p* [RMSEA < .05] < .001), and heavy drinking, which was considered fair (CFI = .967, TLI = .949, RMSEA = .065 [90% CI = .048, .083], *p* [RMSEA < .05] = .001) (see Table 3-8). Therefore, results from LGMs of alcohol QF and heavy drinking should be interpreted with caution. An alternative, free-curve model was also conducted and is presented in Appendix B, which included a linear change factor from ages 18-21 and a factor with freely estimated loadings on all waves (which appears to measure non-linear change in later adulthood).

Table 3-8. Fit statistics for confirmatory latent growth models, estimating an intercept factor and change factors from ages 18-21 and 25-35 in the AHB sample.

Measure	CFI	TLI	RMSEA (*p* fit < .05)
General Sensation Seeking	0.982	0.972	0.790
Positive Expectancies	0.980	0.970	0.175
Behavioral Undercontrol	0.992	0.988	0.935
Alcohol QF	0.752	0.711	< .001
Heavy Drinking	0.967	0.949	0.070
Alcohol Dependence	0.982	0.992	0.979

Note: Models included family history of alcohol use disorder and gender as covariates.

Due to the generally adequate fit and the interpretability of these change factors (during college at Waves 1–4 , and after college at Waves 5–7), multivariate LGMs

estimated the correlations between intercept and piecewise growth factors using this measurement model for all constructs (see Figure 3-2). The LGM was constructed with an intercept factor, with loadings fixed to 1 at Waves 1–7. Wave 7 was chosen as a reference point, on which all loadings from the change factors fixed to 0, and loadings on all other Waves were fixed with reference to Wave 7 (i.e., age 35). Therefore, loadings across change factors on 1) Wave 1 (age 18) summed to 17 (i.e., 18 + 17 = 35); Wave 2 (age 19) summed to 16; Wave 3 (age 20) summed to 15; Wave 4 (age 21) summed to 14; Wave 5 (age 25) summed to 10; Wave 6 (age 29) summed to 6; and Wave 7 (age 35) summed to 0. The factor accounting for change during college loaded only on Waves 1–4 (based on the time between each wave and Wave 7), and loadings on Waves 5–7 were fixed to 0. The factor accounting for change after college loaded on Waves 1–4 at a fixed value equivalent to the loading on Wave 5 (10) to account for the prior influence of alcohol/personality on subsequent change, and loadings on Waves 5–7 were fixed based on the time between each wave and Wave 7.

General SS and Behavioral Undercontrol. Multivariate LGMs included three variables: general SS as a measure of reward sensitivity, behavioral undercontrol, and alcohol involvement (see Table 3-9). The fit across multivariate LGMs was adequate (CFIs = .976 – .985, TLIs = .970 – .981, RMSEAs = .023 – .033 [95% CIs = .012, .040]). Behavioral undercontrol and general SS were correlated at the intercept (r = .28, p < .001) and change at Waves 1-4 (r = .29, p = .04), but not change at Wave 5-7 (r = .09, p = .59). For all alcohol measures, the intercept was correlated with the intercepts for behavioral undercontrol (rs = .13 – .15 [SEs = 0.06 – 0.07], ps = .02 – .04) and general SS (rs = .19 – .41 [SEs = 0.08 – 0.09], ps < .05). Change in behavioral undercontrol at

Waves 1 – 4 was correlated with change during the same period for alcohol QF (r = .46 [SE = .09], p < .001) and heavy drinking (r = .50 [SE = .13], p < .001), but not alcohol dependence (r = .17 [SE = .11], p = .11). Further, at Waves 5-7, change in behavioral undercontrol was associated with change in heavy drinking (r = .30 [SE = .15], p = .048), but no other alcohol measure. Change in general SS was correlated with change in all alcohol measures at Waves 1 – 4 (rs = .34 – .54 [SEs = 0.11 – 0.16], ps < .01), but none at Waves 5-7 (rs = -.04 - .26 [SEs = 0.18 – 0.25], ps = .15 – .87).

Given the correlated intercept and slope factors between behavioral undercontrol and SS, follow-up models investigated whether associations between personality and alcohol measures persisted after regressing out the variance in the other personality factor (see Table 3-10). After regressing out the variance in general SS, the intercept of behavioral undercontrol was no longer correlated with the intercepts for alcohol involvement (rs = .07 – 0.11 [SEs = 0.06 – 0.07], ps = .07 – .29). The correlated change at Waves 1-4, however, remained statistically significant for alcohol QF (r = .40 [SE = 0.11], p < .001) and heavy drinking (r = .45 [SE = 0.15], p < .01). The correlated change at Waves 5-7 between behavioral undercontrol and heavy drinking was moderate in magnitude but not statistically significant (r = .35 [SE = 0.19], p = .07); however, the magnitude of this correlation actually increased (from r = .30) and the statistical significance was similar (from p = .048), relative to the model without regressing variance in general SS (see Table 3-9). Therefore, the association between behavioral undercontrol and alcohol involvement at the intercept (i.e., capturing liability across all waves) does not appear to be distinct from risk conferred by general SS; however, the correlated change at Waves 1-4 remained significant after this more rigorous test.

Table 3-9. Correlation estimates among intercept and slope parameters from multivariate latent growth models including alcohol involvement, behavioral undercontrol, and a measure of reward sensitivity.

Alcohol Involvement	Behavioral Undercontrol	General Sensation Seeking	Positive Expectancies
		Intercept Correlations	
Alcohol QF	0.15 (0.06)*	0.19 (0.08)*	0.57 (0.05)***
Heavy Drinking	0.14 (0.07)*	0.24 (0.09)**	0.46 (0.06)***
Alcohol Dependence	0.13 (0.07)*	0.41 (0.08)***	0.46 (0.06)***
		Slope Correlations (Waves 1-4)	
Alcohol QF	0.46 (0.09)***	0.50 (0.11)***	0.70 (0.07)***
Heavy Drinking	0.50 (0.13)***	0.54 (0.16)***	0.91 (0.10)***
Alcohol Dependence	0.17 (0.11)	0.34 (0.13)**	0.54 (0.08)***
		Slope Correlations (Waves 5-7)	
Alcohol QF	0.17 (0.10)	0.21 (0.18)	0.53 (0.12)***
Heavy Drinking	0.30 (0.15)*	-0.04 (0.25)	0.53 (0.18)**
Alcohol Dependence	0.04 (0.10)	0.26 (0.18)	0.36 (0.11)**

Note: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. One set of models included behavioral undercontrol and general sensation seeking, and another set included behavioral undercontrol and positive expectancies. Behavioral undercontrol and general sensation seeking were correlated at the intercept ($r = .28$, $p < .001$) and change at Waves 1-4 ($r = .29$, $p = .04$), but not change at Wave 5-7 ($r = .09$, $p = .59$). Behavioral undercontrol and positive expectancies were correlated at the intercept ($r = .14$, $p = .02$), but not change at Waves 1-4 ($r = .12$, $p = .24$) or change at Wave 5-7 ($r = .17$, $p = .13$).

Table 3-10. Correlation estimates among intercept and slope parameters from multivariate latent growth models including alcohol involvement, behavioral undercontrol, and a measure of reward sensitivity (general sensation seeking, positive expectancies), after regressing out variance in reward sensitivity from behavioral undercontrol, and vice versa.

	Behavioral Undercontrol		General Sensation Seeking	Positive Expectancies
Alcohol Involvement	Residualized General Sensation Seeking	Residualized Positive Expectancies	Residualized Behavioral Undercontrol	
		Intercept Correlations		
Alcohol QF	0.11 (0.06)	0.09 (0.07)	0.14 (0.08)	0.56 (0.05)***
Heavy Drinking	0.08 (0.07)	0.09 (0.07)	0.18 (0.09)*	0.45 (0.06)***
Alcohol Dependence	0.07 (0.07)	0.08 (0.07)	0.37 (0.09)***	0.45 (0.06)***
		Slope Correlations (Waves 1-4)		
Alcohol QF	0.40 (0.11)***	0.48 (0.11)***	0.35 (0.14)*	0.67 (0.08)***
Heavy Drinking	0.45 (0.15)**	0.70 (0.27)**	0.41 (0.20)*	0.92 (0.12)***
Alcohol Dependence	0.14 (0.11)	0.12 (0.12)	0.25 (0.14)	0.5 (0.09)***
		Slope Correlations (Waves 5-7)		
Alcohol QF	0.18 (0.11)	0.03 (0.15)	0.21 (0.18)	0.51 (0.13)***
Heavy Drinking	0.35 (0.19)	0.13 (0.36)	-0.05 (0.30)	0.51 (0.21)*
Alcohol Dependence	0.04 (0.11)	-0.09 (0.15)	0.27 (0.19)	0.34 (0.11)**

Note: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. Each column represents a model, wherein intercept and change correlations between personality measures and alcohol involvement were estimated while regressing out variance in the other.

This same approach was taken to investigate whether the correlated change between general SS and alcohol involvement persists, after accounting for behavioral undercontrol. After regressing out the variance in behavioral undercontrol, the intercept of general SS remained statistically significant for heavy drinking (r = .18 [SE = 0.09], p = .049) and alcohol dependence (r = .37 [SE = 0.09], p < .001), but not alcohol QF (r = .14 [SE = 0.08], p = .09). The correlated change at Waves 1-4 remained statistically significant for alcohol QF (r = .35 [SE = 0.14], p = .02) and heavy drinking (r = .41 [SE = 0.2], p = .04), but not alcohol dependence (r = .25 [SE = 0.14], p = .08). Therefore, both behavioral undercontrol and reward sensitivity measures accounted for distinct risk in changes in alcohol involvement during the college years.

Positive Expectancies and Behavioral Undercontrol. To investigate the developmental overlap between positive expectancies, behavioral undercontrol, and alcohol involvement, similar multivariate LGMs were fit (see Table 3-9). Behavioral undercontrol and positive expectancies were correlated for the intercept (r = .14, p = .02), but not for change at Wave 1-4 (r = .12, p = .24) or Wave 5-7 (r = .17, p = .13). Correlations among intercept factors of positive expectancies and alcohol involvement were significant and moderate in magnitude (rs = .46 – .57 [SEs = 0.06 – 0.07], ps < .001). Similarly, correlations among the change factors for Waves 1 – 4 were significant and moderate to large (rs = .54 – .91 [SEs = 0.07 – 0.10], ps < .001). Notably, confidence intervals around the correlation estimate for change between expectancies and heavy drinking during college included 1.00. This may suggest that change in heavy drinking and positive expectancies are inseparable at Waves 1-4; however, the subpar fit of heavy drinking to the LGM warrants caution in interpreting these results. Finally, correlations

among the change factors for Waves 5 – 7 were significant and moderate (*r*s = .36 - .53 [SEs = 0.11 – 0.18], *p*s < .01).

Follow-up models again investigated whether associations between personality and alcohol measures persisted after regressing out the variance in the other personality factor (see Table 3-10). After regressing out the variance in positive expectancies, the intercept of behavioral undercontrol was no longer correlated with the intercepts for alcohol involvement (*r*s = .08 – .09 [SEs = 0.07], *p*s = .16 – .23), but the correlation between the change factors at Waves 1–4 remained statistically significant (*r*s = .48 – .70 [SEs = 0.11 – 0.27], *p*s < .01). In contrast, the correlation between positive expectancies and alcohol involvement remained statistically significant for the intercept (*r*s = .45 – .56 [SEs = 0.05 – 0.06], *p*s < .001), change at Waves 1–4 (*r*s = .50 – .92 [SEs = 0.08 – 0.12], *p*s < .001), and change at Waves 5 – 7 (*r*s = .34 – .51 [SEs = 0.11 – 0.21], *p*s < .05).

Summary of Findings

These analyses were conducted to disentangle the effects of behavioral undercontrol from reward sensitivity, given the weak to moderate correlation between the measures. Across three analytic approaches (linear regression, latent state-trait models, and latent growth models), and two independent samples (AHB and ATR), the associations between behavioral undercontrol and alcohol involvement were more robust in early adulthood (18-21 in AHB, 22-26 in ATR) relative to later in adulthood (25-35 in AHB, 38 in ATR). In regression models, main effects of behavioral undercontrol on alcohol involvement were generally significant up to age 25 in AHB and 26 in ATR, but not thereafter. Main effects of reward sensitivity (general SS, positive expectancies) were statistically significant across almost all outcomes and ages. State-trait models yielded

similar findings for behavioral undercontrol; main effects were found for the latent trait of behavioral undercontrol on alcohol involvement, and some main effects were found at Waves 1 and 2 (ages 18-19), but not thereafter. In contrast, positive expectancies demonstrated robust trait and state effects, but general SS yielded less consistent effects. Finally, multivariate LGMs found robust associations of behavioral undercontrol and reward sensitivity on the intercept and change factors (at ages 18-21). Notably, evidence suggests that the correlated change in alcohol involvement attributable to each personality measures was distinct and persisted under rigorous tests.

Chapter 4: Are reward sensitivity and behavioral undercontrol differentially related to alcohol involvement at the latent genetic and environmental level?

Methods

Analytic Approach.

Univariate Behavioral Genetic Analyses. Structural equation models (SEMs) were fit in Mplus to estimate the proportion of variance in personality and alcohol phenotypes that was associated with additive genetic (A), common environmental (C), and unique environmental (E) factors. These models use genetically-informed data and impose variance and covariance constraints, from which latent variables are assumed to represent the biometrical (ACE) factors. Specifically, the correlation between A factors is fixed to 1.0 for MZ twin pairs and 0.5 for DZ twin pairs (reflecting differences in genetic relatedness); the correlation between C factors is fixed to 1 for all twin pairs (i.e., environmental factors that affect both twins in the same way); and the correlation between E factors was fixed to 0 for all twin pairs (i.e., environmental factors that affect twins differently). Thus, behavioral genetic models estimated the covariances between MZ- (calculated as A+C) and DZ-twin pairs (calculated as 0.5*A+C) and the percentage of phenotypic variance attributable to the biometrical factors.

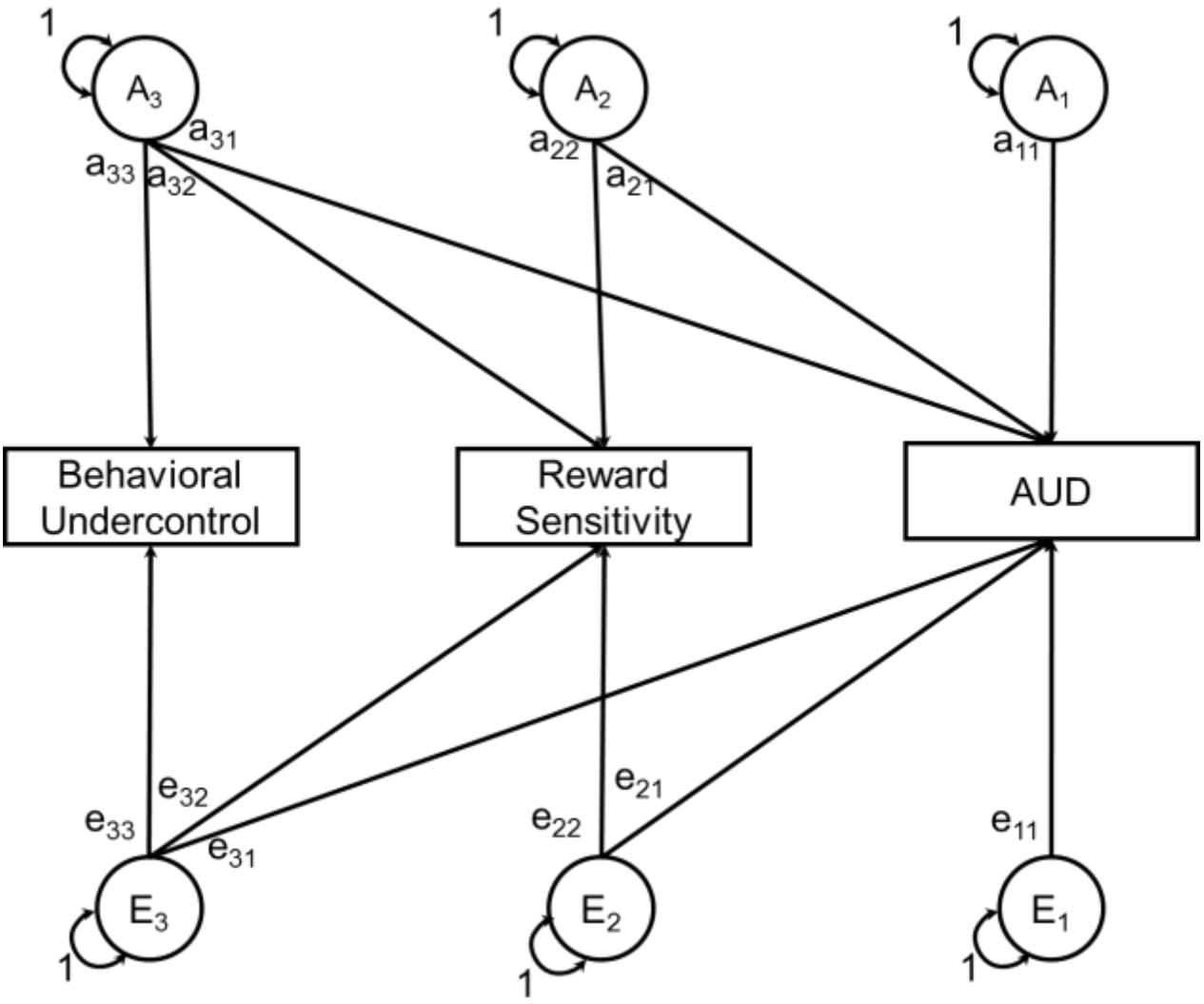
Multivariate Behavioral Genetic Analyses. SEMs were then fit to estimate the proportion of covariance between personality and alcohol phenotypes that was associated with the biometrical factors. Trivariate models were based on the Cholesky decomposition approach (see Figure 4-4), from which three 3x3 triangular matrices containing parameter estimates for the biometrical factors were derived (Loehlin, 1996; Neale & Cardon, 1992). Each matrix contained six elements, three on the diagonal accounting for the variance in each phenotype and three on the off-diagonal accounting

for the covariance between each pair of phenotypes. Thus, the variances and covariances were decomposed into the biometrical factors. In the current study, the proportion of genetic and environmental variance in alcohol phenotypes due to behavioral undercontrol and reward sensitivity (general SS, positive expectancies) was decomposed via the tracing rules (Loehlin, 2004).

All analyses were first run to allow parameter estimates to vary across males and females, and subsequent models constrained parameter estimates across sexes. The fit of these models to the data were compared using chi-square difference tests. These parameter constraints resulted in a worse fit for all multivariate behavior genetic models. Therefore, male and female twin pairs were estimated as separate groups.

Multivariate models provided point estimates and significance estimates for the proportion of variance in alcohol involvement specific to each personality measure (i.e., the measure entered second into the model, after the first accounted for all possible variance) and due to other factors. Therefore, the variance specific to behavioral undercontrol and reward sensitivity, and the variance unexplained by either were directly available from model estimates. Further, by subtracting these estimates from the total variance (i.e., 1), a point estimate of the proportion of explained variance explained by both behavioral undercontrol and reward sensitivity was available, but reliable standard errors and significance estimates were unavailable.

Figure 4-1. Multivariate Cholesky models decomposing the variance in alcohol involvement into latent genetic and environmental variance



Phenotypic variance was decomposed into genetic and environmental variance attributable to behavioral undercontrol (a_{31}^2, e_{31}^2), reward sensitivity (a_{21}^2, e_{21}^2), and other factors (a_{11}^2, e_{11}^2). Variables and path estimates for only one twin are depicted, and correlations between A factors are omitted (MZ = 1, DZ = 0.5), because parameters were constrained to be equal across twins.

Results

Twin Correlations. Table 4-1 displays phenotypic and cross-twin, cross-trait (personality measures with alcohol involvement) twin correlations for MZ and DZ pairs. Phenotypic correlations between behavioral undercontrol and alcohol involvement were weaker than those for measures of reward sensitivity. Among both men and women, cross-trait twin correlations were consistently stronger among MZ pairs than DZ pairs for behavioral undercontrol (MZ = .13 – .20, DZ = .02 – .10), general SS (MZ = .17 – .29, DZ = .06 – .20) and positive expectancies (MZ = .30 – .40, DZ = .10 – .23). Therefore, familial factors appear to be involved in the overlap between all personality measures and alcohol involvement.

Table 4-1. Phenotypic and cross-twin, cross-trait correlations between measures of personality and alcohol involvement.

	Phenotypic Correlation		Twin Correlations			
Alcohol Phenotype	Females (n = 2,035)	Males (n = 1,474)	MFZ (647 pairs)	MZM (469 pairs)	DZF (526 pairs)	DZM (411 pairs)
			Behavioral Undercontrol			
Alcohol QF	.20 (.15, .24)	.17 (.11, .23)	.15 (.09, .22)	.13 (.05, .21)	.06 (-.01, .14)	.05 (-.06, .15)
Heavy Drinking	.22 (.18, .27)	.19 (.13, .24)	.20 (.14, .26)	.19 (.11, .27)	.06 (-.02, .14)	.02 (-.09, .13)
AUD Symptoms	.23 (.19, .28)	.23 (.17, .28)	.18 (.11, .24)	.20 (.12, .28)	.09 (.01, .17)	.10 (-.01, .21)
			General Sensation Seeking			
Alcohol QF	.35 (.31, .39)	.25 (.19, .30)	.27 (.21, .33)	.19 (.12, .27)	.20 (.12, .27)	.07 (-.04, .18)
Heavy Drinking	.35 (.31, .39)	.30 (.25, .36)	.29 (.23, .34)	.22 (.14, .29)	.20 (.13, .28)	.08 (-.03, .19)
AUD Symptoms	.32 (.28, .37)	.23 (.18, .29)	.23 (.17, .29)	.17 (.09, .25)	.13 (.04, .21)	.06 (-.05, .17)
			Positive Expectancies			
Alcohol QF	.50 (.46, .54)	.44 (.39, .49)	.37 (.31, .43)	.34 (.28, .41)	.23 (.15, .31)	.12 (.01, .23)
Heavy Drinking	.49 (.45, .52)	.46 (.41, .50)	.40 (.34, .45)	.35 (.28, .42)	.18 (.10, .26)	.16 (.05, .27)
AUD Symptoms	.47 (.43, .51)	.42 (.37, .46)	.34 (.28, .40)	.30 (.23, .38)	.10 (.01, .18)	.19 (.09, .30)

Note: 95% confidence intervals are in parentheses.

Table 4-2. Estimates of the proportion of variance in measures of personality and alcohol involvement attributable to genetic and environmental factors.

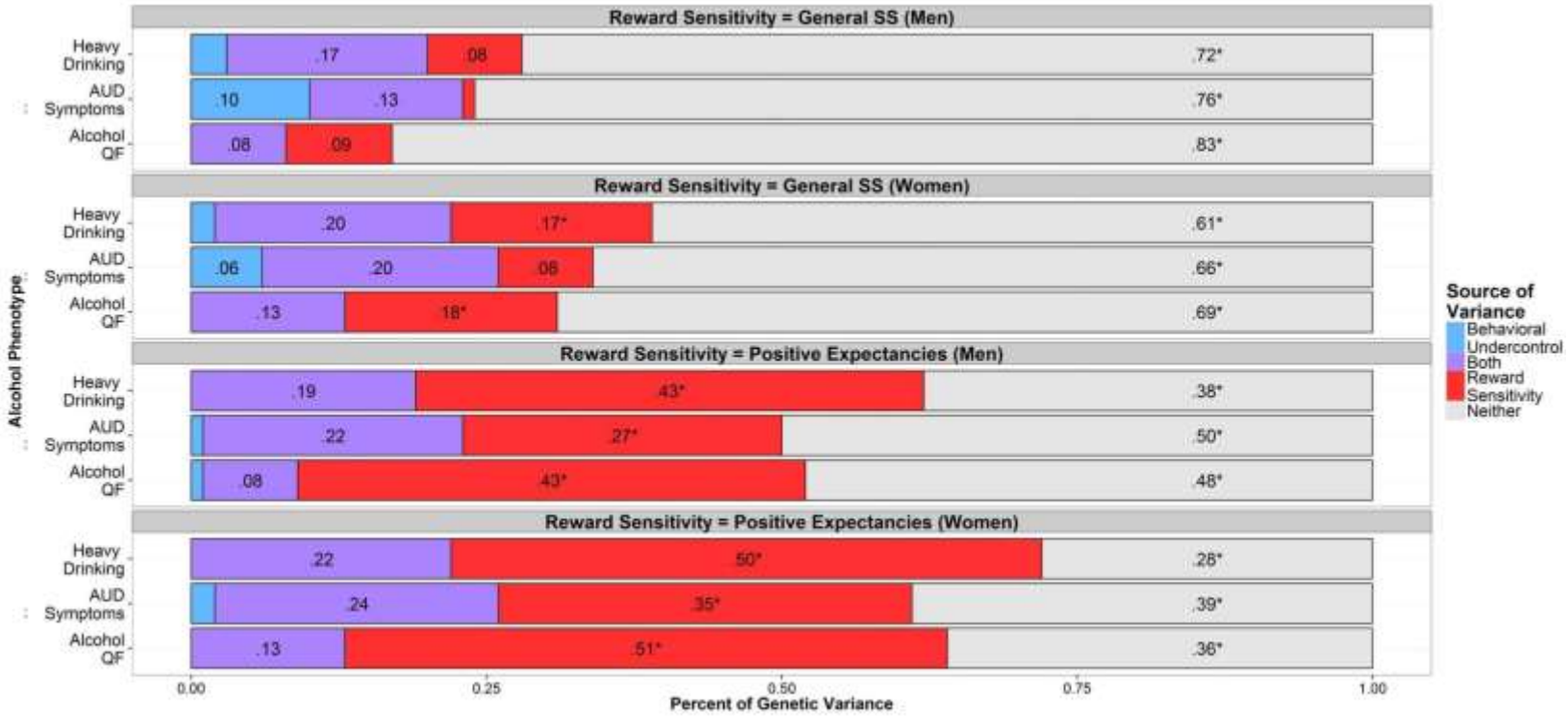
	Women			Men		
Phenotype	Additive Genetics	Shared Environment	Unique Environment	Additive Genetics	Shared Environment	Unique Environment
Personality						
Behavioral Undercontrol	.12 (-.15, .40)	.17 (-.06, .39)	.71 (.62, .80)	.40 (.30, .50)	.00 (.00, .00)	.60 (.50, .71)
General Sensation Seeking	.33 (.08, .58)	.14 (-.08, .36)	.53 (.45, .60)	.38 (.00, .76)[a]	.04 (-.31, .38)	.58 (.49, .68)
Positive Expectancies	.38 (.12, .64)	.06 (-.17, .28)	.57 (.49, .64)	.40 (.04, .76)	.04 (-.28, .37)	.56 (.46, .65)
Alcohol Involvement						
Alcohol QF	.34 (.11, .57)	.15 (-.05, .35)	.51 (.44, .58)	.48 (.40, .56)	.00 (.00, .00)	.52 (.44, .60)
Heavy Drinking	.40 (.16, .64)	.06 (-.15, .27)	.54 (.47, .61)	.43 (.34, .52)	.00 (.00, .00)	.57 (.48, .66)
AUD Symptoms	.38 (.31, .46)	.00 (.00, .00)	.62 (.54, .69)	.43 (.34, .52)	.00 (-.01, .01)	.57 (.48, .66)

Note. 95% confidence intervals are in parentheses. [a] Lower-bound confidence interval was .001; $p = .049$.

Univariate Models. Table 4-2 displays estimates of the proportion of variance in personality and alcohol phenotypes associated with genetic and environmental factors. In men, additive genetic factors accounted for a significant proportion of variance in behavioral undercontrol (A = .40), general SS (A = .38), positive expectancies (A = .40), and all alcohol phenotypes (A = .43 – .48). In women, additive genetic factors accounted for a negligible proportion of variance in behavioral undercontrol (A = .12) but a significant proportion for general SS (A = .33), positive expectancies (A = .38), and all alcohol phenotypes (A = .34 – .40). Unique environmental factors explained the largest proportion of variance in all phenotypes (E = .51 – .71). Notably, shared environmental factors accounted for a negligible proportion of the variances among men (C = .00 – .04) and women (C = .00 – .17). Therefore, multivariate models constrained the effect of C to 0 (as omitted from Figure 4).

Multivariate Models. The genetic variance in alcohol involvement was partitioned into factors attributable to the personality measures (see Figures 4-1 and 4-2). The total variance due to each measure (e.g., behavioral undercontrol accounted for .23 of the genetic variance in AUD symptoms in men) can be calculated by summing variance specific to that measure (e.g., .10 of the genetic variance in AUD symptoms in men was specific to behavioral undercontrol) and the variance due to both personality measures (e.g., .13 of the genetic variance in AUD symptoms in men was due to both behavioral undercontrol and general SS).

Figure 4-2. Cholesky model estimates of the proportion of genetic variance in alcohol phenotypes attributable to behavioral undercontrol and reward sensitivity.



The displayed proportions are estimates of the genetic variance *specific* to each risk factor. Estimates were obtained by running models where behavioral undercontrol was entered second, and then general sensation seeking was entered second into the model (i.e., after the other accounted for all possible genetic variance). The statistical significance of the proportion attributable to both (i.e., variance common to behavioral undercontrol and general sensation seeking) could not be determined, but point estimates were inferable from the model.

Note: * $p < .05$. Estimates of .00 or .01 are not shown.

Behavioral undercontrol accounted for a significant proportion of total genetic variation in alcohol involvement (.12 – .27, except alcohol QF in men [.17]), but a non-significant proportion of genetic variation was distinct from reward sensitivity measures (.00 – .10). Further, a statistically significant proportion of genetic variance was unique to general SS in women, except for AUD symptoms (.08 - 18), but not in men (.01 – .09). Variance unique to positive expectancies accounted for a large and statistically significant proportion of genetic variation in women (.35 – .51) and men (.27 – .43). Together, behavioral undercontrol and general SS accounted for about a quarter of the genetic variance in alcohol phenotypes (.17 – .39), and behavioral undercontrol with positive expectancies accounted for over half (.50 – .72).

Summary of Findings

These findings suggest that behavioral undercontrol is not a distinct risk process from reward sensitivity, with regard to alcohol involvement. Specifically, all genetic variance in alcohol involvement associated with behavioral undercontrol was also associated with reward sensitivity measures, whereas reward sensitivity typically accounted for unique variation in alcohol involvement (beyond behavioral undercontrol). Findings varied, however, depending on which measure of reward sensitivity was used; positive expectancies accounted for a larger proportion of genetic variation. Further, among men, general SS accounted for a negligible proportion of genetic variation in alcohol involvement, apart from behavioral undercontrol.

Chapter 5: Are reward sensitivity and behavioral undercontrol differentially related to alcohol involvement at the genotypic level.

Methods

Measures

Genotypic measures. Genetic data were collected in Wave 7 of AHB (age 35) and were available for 274 participants. Participants selected a location where a phlebotomist obtained a blood sample, which was returned via mail. Genotyping was conducted by Illumina using GoldenGate technology on 1,537 single nucleotide polymorphisms (SNPs) from 130 candidate genes for addiction (Hodgkinson et al., 2008). The analytic approach (see below) also incorporated genome wide association results with alcohol consumption (gram per day per kilogram of bodyweight), from an independent sample (n = 26,316; Schumann et al., 2011), using 1,290 SNPs that were also available in AHB. After quality control procedures, 246 SNPs were dropped due to high missingness (> 5%) and 98 SNPs were dropped due to an ambiguous strand orientation. Further, of the 274 participants with genetic data, phenotype data were missing for 7 participants. Therefore, 946 SNPs in 267 participants were analyzed. Latent trait variables (alcohol involvement, behavioral undercontrol, reward sensitivity), from the state-trait models described above (see *Chapter 3, State-Trait Models*), were used as target phenotypes.

Analytic Approach.

Polygenic risk score (PRS) analyses were conducted using PRSice (‘precise’; Euesden, Lewis, & O'Reilly, 2015), a command-line program that uses results from association analyses to calculate PRSs in PLINK (Purcell et al., 2007), and evaluates and plots associations between PRSs and phenotypes in R. A PRS is the aggregate of the

effects of a subset of genotypes, below a statistical significance threshold (e.g., all SNPs with $p < .10$) and weighted by the effect size (Amin, Van Duijn, & Janssens, 2009). In the current study, PRSice first iteratively applied results from association analyses to the AHB across a range of statistical significance thresholds ($p = .000 – .500$, by .001) to identify the best-fitting PRS to each phenotype. The results from these analyses were plotted in R to show the change in fit across statistical significance thresholds, and the predictive validity of best-fitting PRS was plotted for each phenotype (the change in phenotype across quantiles of the PRS).

Genetic Association Analyses. Association analyses were first conducted in AHB on the 946 available SNPs for measures of behavioral undercontrol, reward sensitivity (general SS, positive expectancies), and alcohol involvement (alcohol QF, heavy drinking, and alcohol dependence). Based on results from PRSice, the SNPs that maximized the proportion of variation explained were identified and extracted as the top hits. These top hits across measures were then compared across measures, to identify potential markers that influence both risk processes.

PRS Analyses. As second set of analyses were conducted using association results from a discovery sample (Schumann et al., 2011), the largest GWAS of alcohol dependence conducted to date ($n = 47,501$, labeled here as the Schumann Study), which were applied to the 946 SNPs available in AHB. PRS analyses identified significance thresholds to maximize the proportion of variation explained in latent traits, and the PRSs were extracted. These PRSs are conceptually similar to the latent genetic factors identified in twin analyses (e.g., Chapter 4), with knowledge of the genetic markers that

comprise the total genetic risk. Therefore, PRSs were incorporated into analyses attempting to replicate findings on the latent genetic risk from the ATR.

Results

Genetic Association Analyses.

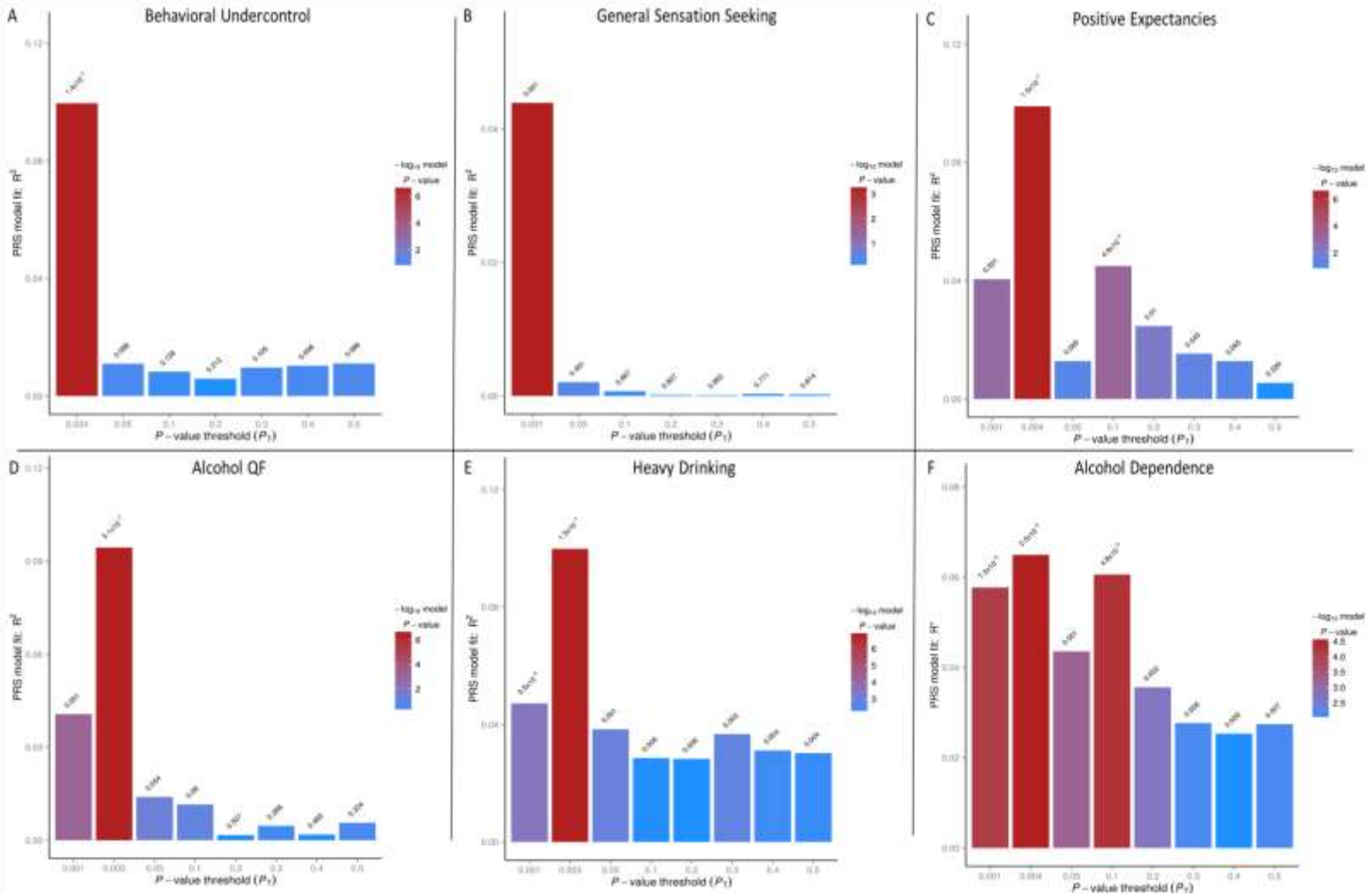
Genetic association analyses on the 946 SNPs were conducted in PLINK for the latent traits of behavioral undercontrol, reward sensitivity, and alcohol involvement. For all phenotypes, no marker reached statistical significance after accounting for multiple testing ($p < 5.3E^{-05}$). These results were used to identify the statistical significance threshold and top hits for each measure (see Figure 5-1). The significance cutoffs were very low among almost all measures (*p*s = .003 – .004, *n* SNPs = 4 – 9 R^2s = .065 – .100), except behavioral undercontrol (*p* = .024, *n* SNPs = 20, R^2 = .100). Further, examination of the plots fitting the PRSs shows sharp increase and decreases in fit, due to analyses capitalizing on chance from using association results from AHB and applying those results to AHB.

Altogether, eight SNPs across six genes were top hits for multiple measures (see Table 5-1). The effect sizes for top hits were in the same direction across measures. Three SNPs were top hits for alcohol dependence and heavy drinking (*rs1070487*, *rs2037547*, *rs11919783*). For positive expectancies, there were three top hits common to alcohol involvement, *rs851011* (alcohol dependence, alcohol QF), *rs1563945* (alcohol QF), and *rs3755557* (alcohol dependence). There was also a common top hit between general SS and alcohol dependence (*rs10488683*). Finally, there was a common top hit between general SS and behavioral undercontrol (*rs3219203*). There were no shared top hits between behavioral undercontrol and any alcohol measures.

Table 5-1. SNPs classified as a top hit for multiple alcohol or personality measures in the AHB sample.

CHR	SNP	Gene	Position (bp)	Phenotype	*β*	SE	R^2	*p*
6	rs851011	MAPK14	36145961	Positive Expectancies	0.21	0.06	0.041	0.00094
				Alcohol Dependence	0.13	0.04	0.045	0.00050
				Alcohol QF	0.30	0.09	0.038	0.00145
11	rs10488683	TPH1	18010121	General SS	-0.04	0.01	0.044	0.00057
				Alcohol Dependence	-0.08	0.03	0.036	0.00188
8	rs1563945	PNOC	28230805	Positive Expectancies	-0.17	0.06	0.031	0.00390
				Alcohol QF	-0.28	0.08	0.041	0.00092
3	rs3755557	GSK3β	121297647	Positive Expectancies	-0.19	0.07	0.032	0.00327
				Alcohol Dependence	-0.12	0.04	0.032	0.00337
5	rs3219203	GABRG2	161427430	General SS	-0.06	0.02	0.031	0.00379
				Behavioral Undercontrol	-0.08	0.03	0.027	0.00750
16	rs1070487	GRIN2A	10143493	Alcohol Dependence	0.11	0.03	0.059	0.00006
				Heavy Drinking	0.08	0.02	0.038	0.00129
3	rs2037547	GSK3β	121027305	Alcohol Dependence	-0.12	0.03	0.050	0.00024
				Heavy Drinking	-0.10	0.03	0.047	0.00035
3	rs11919783	GSK3β	121229323	Alcohol Dependence	-0.14	0.04	0.042	0.00077
				Heavy Drinking	-0.11	0.03	0.035	0.00234

Figure 5-1. The proportion of variance explained by significance thresholds used to compute polygenic risk scores within AHB.



Variance explained is displayed on the y-axis, and the significance threshold is displayed on the x-axis. Polygenic risk scores were computed from all SNPs falling below that threshold. Association analyses were conducted in AHB and then applied to AHB, as a means of determining a cutoff for the top hits of each measure.

PRS Analyses.

Results from the Schumann study were applied to the genotypic data in AHB as part of PRS analyses. The variance explained in AHB measures, across different statistical significance thresholds, are displayed in Figure 5-2 and Table 5-2. Given that these associations are from an independent sample, a larger number of SNPs are required to maximize the variance explained (*p*s = .016 – .393, *n* SNPs = 20 – 326), and a smaller proportion of variance is explained (R^2s = .009 – .043; see Figure 5-3 for plots of PRS quantiles across latent trait scores). Unexpectedly, a larger proportion of variance was explained in positive expectancies than any measure of alcohol involvement. Further, the same number of SNPs and threshold provided the best fit for heavy drinking and alcohol dependence (i.e., the same regression weights from the discovery sample were applied to the same SNPs in AHB), which resulted in the identical PRSs scores for heavy drinking and alcohol dependence in AHB participants. Therefore, subsequent analyses investigated the association between PRSs for alcohol QF and heavy drinking/alcohol dependence with personality measures (i.e., PRSs were the exact same for heavy drinking and alcohol dependence).

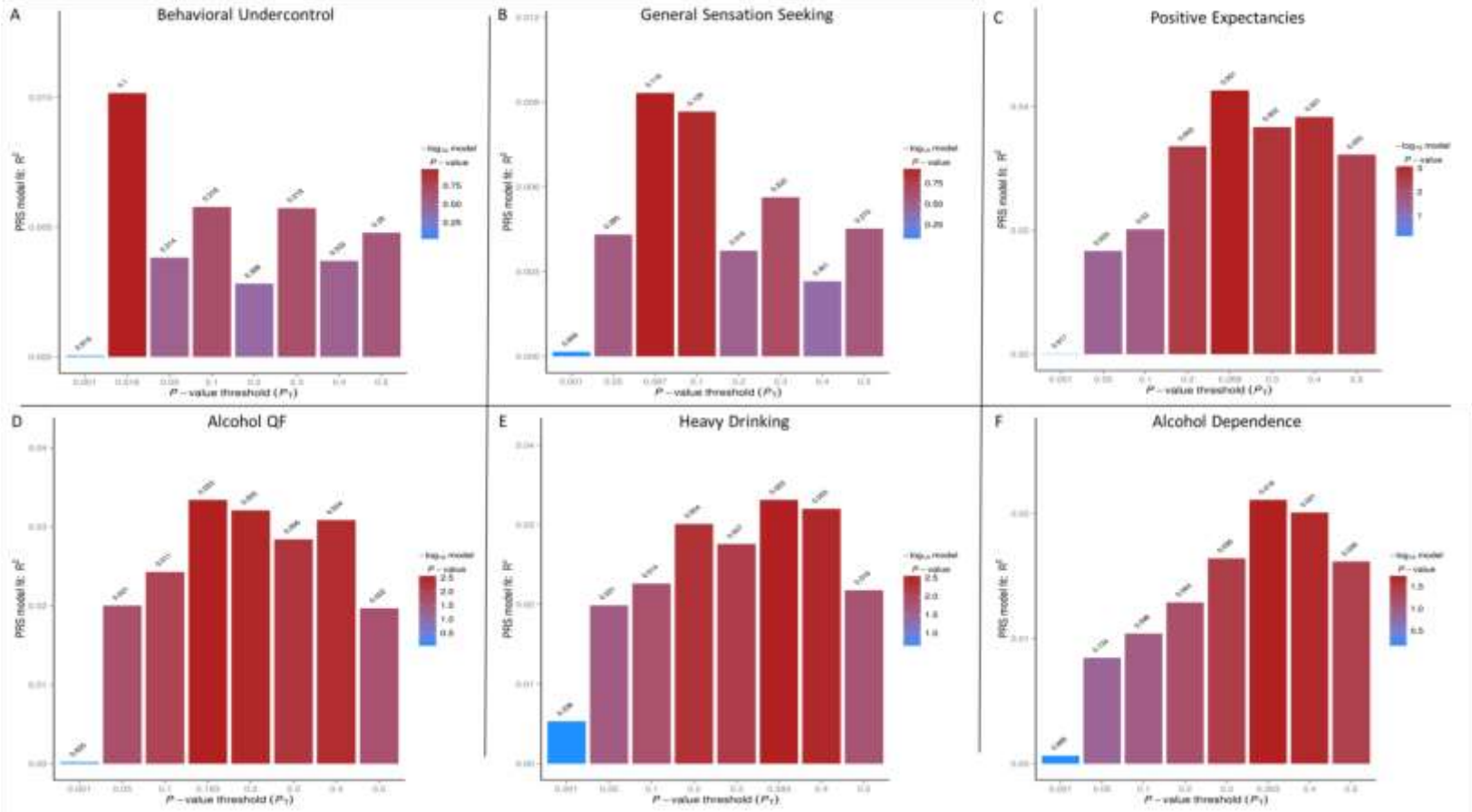
The PRSs for neither behavioral undercontrol (βs = 0.04 – 0.05 [SEs = .06], *ps* = .44 – .59) nor general SS (βs = 0.05 – 0.07 [SEs = .07], *ps* = .33 – .44) were associated with the PRSs for any of the alcohol measures. The PRS for positive expectancies, however, was associated with PRSs for alcohol QF (β = 0.18 [SE = .06], *p* = .003) and heavy drinking/alcohol dependence (β = 0.20 [SE = .06], *p* = .001).

Table 5-2. Characteristics of the best-fitting polygenic risk scores for personality and alcohol measures in the AHB sample.

Measure	*p-cutoff*	*n* SNPs	*r*	R^2	*p*
Behavioral Undercontrol	0.016	20	0.101	0.010	0.1003
General SS	0.087	78	0.097	0.009	0.1155
Positive Expectancies	0.268	238	0.206	0.043	0.0007
Alcohol QF	0.193	171	0.183	0.033	0.0027
Heavy Drinking	0.393	326	0.182	0.033	0.0028
Alcohol Dependence	0.393	326	0.145	0.021	0.0176

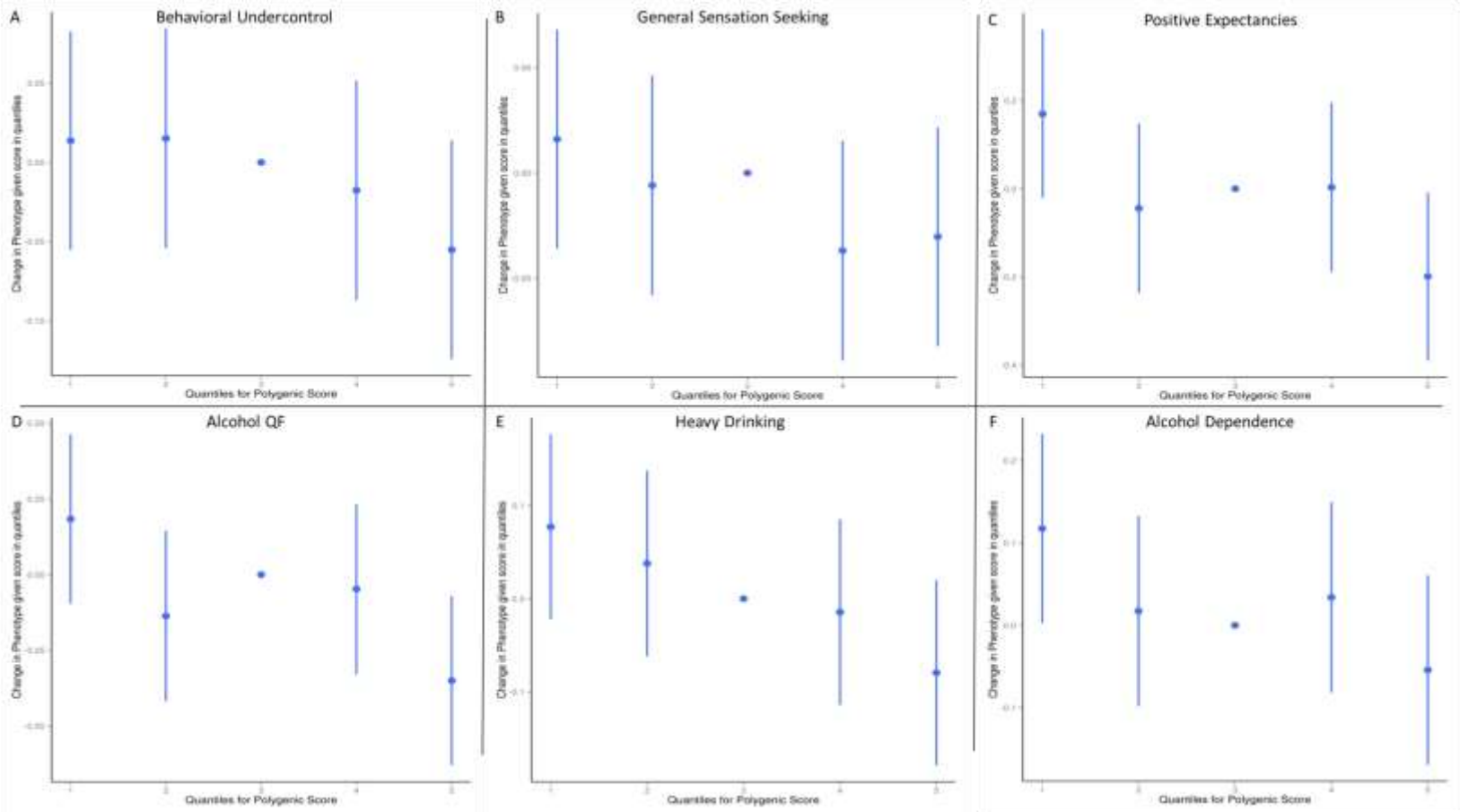
Note: Results show the significance cutoff and number of SNPs from the discovery sample (Schumann et al., 2011), which comprise the PRSs that explain the maximum variance (r, R^2) in measures of personality and alcohol involvement in the AHB data. Personality measures demonstrate discriminant validity of results from Schumann et al (2011), a genomewide association study of alcohol consumption; however, the discovery sample explained the largest proportion of variance in positive expectancies.

Figure 5-2. The proportion of variance explained by significance thresholds used to compute polygenic risk scores in AHB from GWAS results for alcohol consumption in an independent sample (Schumann et al., 2011).



Variance explained is displayed on the y-axis, and the significance threshold is displayed on the x-axis. Polygenic risk scores were computed from all SNPs falling below that threshold. Association analyses were from an independent, discovery sample (Schumann et al., 2011) and applied to the AHB data. Plots were used to identify the cutoff for calculating polygenic risk scores for each measure. Personality measures were include primarily to demonstrate discriminant validity of results from Schumann et al (2011), a genomewide association study of alcohol consumption; however, the discovery sample explained the largest proportion of variance in positive expectancies.

Figure 5-3. Quantile plots demonstrating the predictive validity of polygenic risk scores on levels of alcohol involvement.



Quantile groups of ascending polygenic risk scores are displayed on the x-axis, with the middle group as the reference group. Standardized levels of each measure are displayed on the y-axis, with the reference group mean set to 0. That is, the increase/decrease in standard deviations from the reference group are displayed.

Summary of Findings

Although association analyses failed to identify any SNPs that met statistical significance after accounting for multiple testing, there were eight SNPs across six genes that were among the top hits for multiple phenotypes. Further, PRSs from the Schumann sample explained 2-4% of the variance in alcohol involvement and positive expectancies. Regression analyses conducted on the PRSs should be interpreted with caution, however, given that strong genetic association found for positive expectancies from the discovery sample results. Although it is possible that positive expectancies are predictive of genetic risk for alcohol involvement, this may also be due to chance.

Chapter 6: Does behavioral undercontrol moderate the relation between reward sensitivity and alcohol involvement at the phenotypic level?

Methods

Analytic Approach.

Interaction models were tested in SAS 9.3 (SAS Institute, 2002-2010). Interaction effects (Judd, Kenny, & McClelland, 2001) were tested to investigate moderation effects of behavioral undercontrol on associations between reward sensitivity and alcohol involvement, as demonstrated with behavioral measures in adolescents and emerging adults (e.g., Thush et al., 2008). The use of longitudinal data from ages 18-35 has the advantage over previous studies of elucidating this functional relationship across adulthood. Again, data from the ATR were used to replicate findings from Wave 7 of the AHB. Given that AHB queried recent alcohol involvement, the ATR measures assessing past year, instead of peak year, involvement were used. Regression models included sex as a covariate, as well as quadratic effects to control for spurious interactions (Lubinski & Humphreys, 1990). For both samples, outliers were dropped if they had both high leverage (greater than twice the sample mean for leverage) and high influence (Cook's D greater than $\frac{4}{n-2-1}$) on the model results (Chatterjee & Hadi, 1986). In addition, participants who abstained from alcohol use were not included in analyses.

Results

General SS. The results of the regression models assessing associations between behavioral undercontrol, general SS, and their interaction with alcohol associations are displayed in Table 6-1. After participants were dropped due to missingness, and excessive influence and leverage on model results, there were 445 participants analyzed at Wave 1, reduced to 325 participants at Wave 7 of AHB. Main effects of behavioral

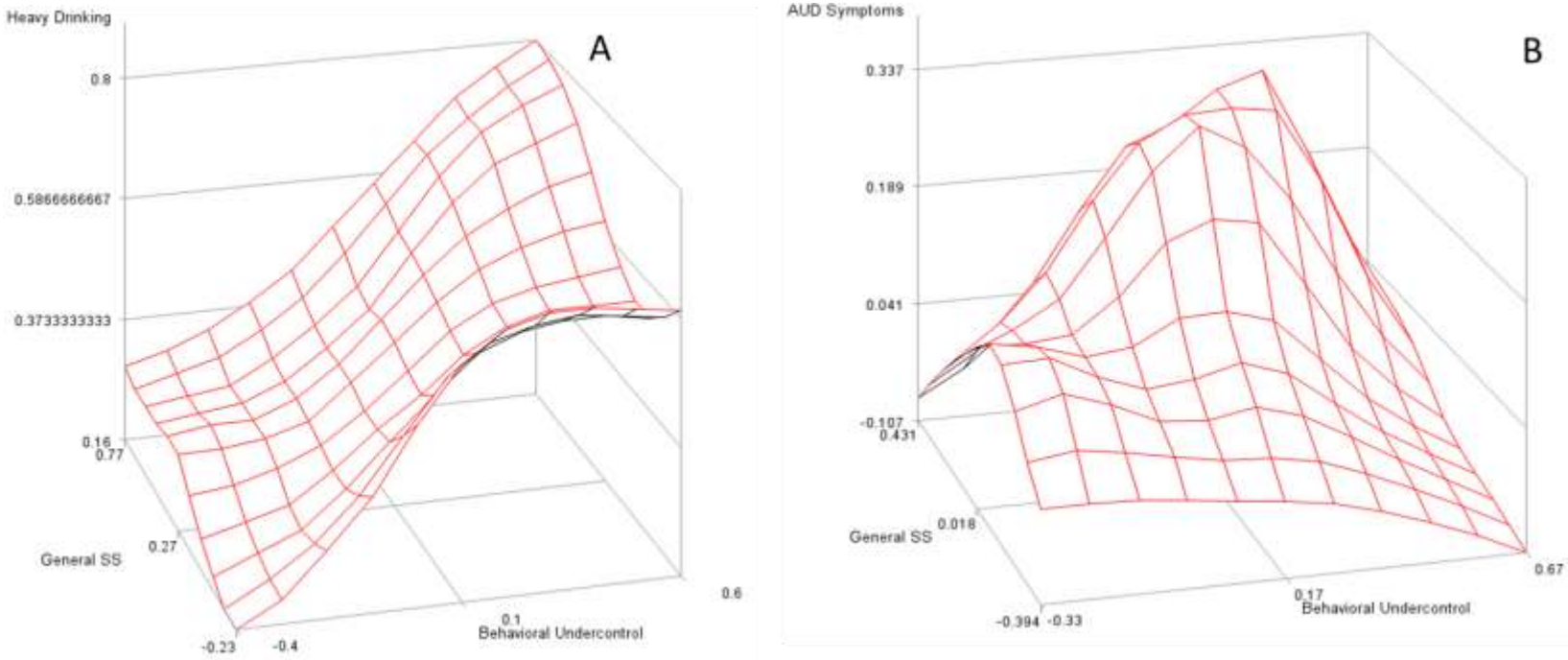
undercontrol were consistently associated with Alcohol QF (*b*s = 0.36 – 0.89 [SEs = 0.14 – 0.20], *p*s < .05) and heavy drinking through Wave 6 (*b*s = 0.17 – 0.38 [SEs = 0.06], *p*s < .01), but only through Wave 4 for alcohol dependence (*b*s = 0.19 -0.36 [SEs = 0.08 – 0.09], *p*s < .05). General SS was less consistently associated with alcohol QF (Waves 1, 5, 6; *b*s = 0.42 – 0.68 [SEs = 0.18 – 0.30], *p*s < .05) and heavy drinking (Waves 1, 3-5; *b*s = 0.18 – 0.35 [SEs = 0.07 – 0.09], *p*s < .05); however, it demonstrated associations with alcohol dependence at all waves (*b*s = 0.28 – 0.89 [SEs = 0.10 – 0.19], *p*s < .01). Regarding whether behavioral undercontrol moderates associations between reward sensitivity and alcohol involvement, interaction effects reached statistical significance only for heavy drinking at Waves 2 (*b* = -0.65 [SE = 0.26], *p* < .05) and 5 (*b* = 0.60 [SE = 0.21], *p* < .01). Notably, the interaction effect at Wave 2 was in the opposite direction of what is proposed by dual-systems models.

Table 6-1: Regression coefficients for main and interaction effects of behavioral undercontrol and general sensation seeking on alcohol involvement across waves of the AHB study and the ATR.

	AHB Wave 1 (Age 18) *n* = 445	AHB Wave 2 (Age 19) *n* = 441	AHB Wave 2 (Age 20) *n* = 436	AHB Wave 4 (Age 21) *n* = 430	AHB Wave 5 (Age 25) *n* = 415	AHB Wave 6 (Age 29) *n* = 357	AHB Wave 7 (Age 35) *n* = 325	ATR (*M* Age = 38) *n* = 3,175
				Alcohol QF				
General Sensation Seeking	0.42 (0.18)*	0.25 (0.19)	0.26 (0.20)	0.35 (0.20)	0.68 (0.24)**	0.62 (0.30)*	0.41 (0.36)	2.53 (0.18)***
Behavioral Undercontrol	0.89 (0.15)***	0.83 (0.15)***	0.70 (0.16)***	0.48 (0.14)***	0.36 (0.16)*	0.48 (0.18)**	0.45 (0.20)*	0.07 (0.15)
Interaction	-0.56 (0.58)	-0.99 (0.65)	-0.43 (0.61)	0.06 (0.57)	0.42 (0.62)	-0.79 (0.85)	-0.46 (0.93)	-0.45 (0.92)
				Heavy Drinking [a]				
General Sensation Seeking	0.18 (0.07)*	0.11 (0.08)	0.19 (0.08)*	0.19 (0.09)*	0.35 (0.09)***	0.15 (0.11)	0.21 (0.13)	2.40 (0.13)***
Behavioral Undercontrol	0.38 (0.06)***	0.19 (0.06)**	0.26 (0.06)***	0.23 (0.06)***	0.17 (0.06)**	0.19 (0.06)**	0.12 (0.07)	0.26 (0.11)*
Interaction	-0.19 (0.24)	-0.65 (0.26)*	-0.09 (0.25)	-0.12 (0.25)	0.60 (0.21)**	-0.44 (0.29)	0.51 (0.35)	1.18 (0.69)
				Alcohol Use Disorder [b]				
General Sensation Seeking	0.28 (0.10)**	0.36 (0.11)***	0.36 (0.12)**	0.37 (0.13)**	0.44 (0.14)**	0.59 (0.17)***	0.89 (0.19)***	0.25 (0.04)***
Behavioral Undercontrol	0.31 (0.08)***	0.36 (0.09)***	0.34 (0.09)***	0.19 (0.09)*	0.11 (0.09)	0.16 (0.10)	0.11 (0.11)	0.11 (0.04)**
Interaction	-0.27 (0.33)	0.03 (0.35)	0.14 (0.37)	-0.42 (0.37)	0.55 (0.36)	-0.49 (0.49)	0.19 (0.55)	0.96 (0.22)***

NOTE: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. [a] Heavy drinking in AHB was computed as the mean number of days high, drunk, and binge drinking in the previous 30 days, and in the ATR it was computed as the mean number of days intoxicated and hungover in the previous year. [b] Alcohol use Disorder in AHB was based on DSM-IV alcohol dependence, and in the ATR it was based on a DSM-5 symptom count (excluding craving).

Figure 6-1: The nature of interaction effects between general sensation seeking (SS) and behavioral undercontrol on alcohol involvement in AHB and ATR.



The interaction effect from AHB was at Wave 5 (age 25; Panel A), and the ATR was at age 38 (Panel B). Interactions effects reached statistical significance. In AHB (A), the effect of general SS on heavy drinking appears to be mitigated at lower levels of behavioral undercontrol (i.e., higher control). In ATR (B), there appears to be a quadratic, or blunted, effect on AUD symptoms at lower levels of behavioral undercontrol, and the effect of general SS on AUD symptoms is more pronounced in the middle-higher range of behavioral undercontrol. No other interaction effects reached statistical significance and were in the hypothesized direction.

After participants were dropped due to missingness and excessive influence and leverage on model results, there were 3,175 participants analyzed from the ATR. Main effects of behavioral undercontrol were associated heavy drinking (b = 0.26 [SEs = 0.11], p = .02) and AUD symptoms (b = 0.11 [SEs = 0.04], p < .01), but not Alcohol QF (b = 0.07 [SEs = 0.15], p = .65). In addition, general SS displayed associations with all alcohol measures (bs = 0.25 – 2.53 [SEs = 0.04 – 0.18], ps < .001). Regarding whether behavioral undercontrol moderated associations between reward sensitivity and alcohol involvement, interaction effects reached statistical significance for AUD (b = 0.95 [SE = 0.22], p < .001) and approached statistical significance for heavy drinking (b = 1.18 [SE = 0.69], p = .09), but not for alcohol QF (b = -0.45 [SE = 0.92], p = .63). The nature of interactions effects between behavioral undercontrol and general SS on alcohol involvement are displayed in Figure 6-1, wherein associations between general SS and alcohol involvement are mitigated among those low in behavioral undercontrol (i.e., high in control).

Positive Expectancies. The results of the regression models assessing associations between behavioral undercontrol, positive expectancies, and their interaction with alcohol associations are displayed in Table 6-2. After participants were dropped due to missingness and excessive influence and leverage on model results, there were 449 participants analyzed at Wave 1, reduced to 327 participants at Wave 7 of AHB. Main effects of behavioral undercontrol were similar to those observed with general SS and are not described again. Positive expectancies were associated with all alcohol measures at all waves (bs = 0.14 – 0.95 [SEs = 0.03 – 0.08], ps < .0001). Regarding whether behavioral undercontrol moderated associations between reward sensitivity and alcohol

involvement, interaction effects reached statistical significance at Wave 5 for heavy drinking (b = 0.18 [SE = 0.08], p = .03) and alcohol dependence (b = 0.33 [SE = 0.13], p = .01).

After participants were dropped due missingness and excessive influence and leverage on model results, there were 3,148 participants from the ATR analyzed. Main effects of behavioral undercontrol were found for heavy drinking (b = 0.20 [SEs = 0.09], p = .03), but not Alcohol QF (b = -0.08 [SEs = 0.13], p = .54) or AUD symptoms (b = 0.04 [SEs = 0.04], p = .27). Positive expectancies were associated with all alcohol measures (bs = 0.39 – 2.77 [SEs = 0.03 – 0.11], ps < .001). Regarding whether behavioral undercontrol moderates associations between reward sensitivity and alcohol involvement, interaction effects reached statistical significance for heavy drinking (b = 0.64 [SE = 0.32], p = .04), but not for alcohol QF (b = -0.002 [SE = 0.41], p = .99) or AUD (b = 0.15 [SE = 0.14], p = .27). The nature of interactions effects between behavioral undercontrol and positive expectancies on alcohol involvement was similar to that shown for behavioral undercontrol and general SS (see Figure 6-2).

Summary of Findings

There was little evidence of a moderation effect of behavioral undercontrol on measures of reward sensitivity, with only 5 of 42 models yielding statistically significant interactions in the expected direction (i.e., reward sensitivity was most problematic among individuals low in self-control). Of these five interaction effects, however, two were replications between AHB and ATR (positive expectancies and behavioral undercontrol on heavy drinking). Notably, an additional interaction effect was statistically significant but in the opposite direction proposed by the dual-systems model;

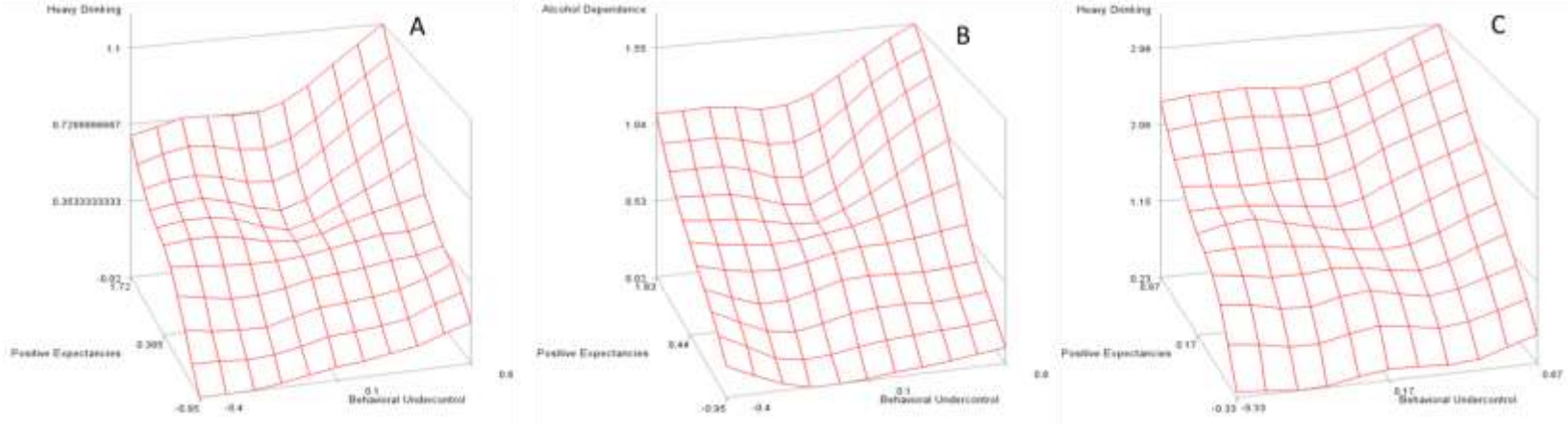
at Wave 1 in AHB, general SS was more strongly associated with heavy drinking among individuals low in behavioral control. Measures for which there was a significant interaction were followed up in Chapter 7.

Table 6-2: Regression coefficients for main and interaction effects of behavioral undercontrol and positive expectancies on alcohol involvement across waves of the AHB study and the ATR.

	AHB Wave 1 (Age 18) *n* = 449	AHB Wave 2 (Age 19) *n* = 442	AHB Wave 3 (Age 20) *n* = 441	AHB Wave 4 (Age 21) *n* = 438	AHB Wave 5 (Age 25) *n* = 415	AHB Wave 6 (Age 29) *n* = 358	AHB Wave 7 (Age 35) *n* = 327	ATR (*M* age = 38) *n* = 3,148
				Alcohol QF				
Positive Expectancies	0.72 (0.06)***	0.88 (0.06)***	0.95 (0.08)***	0.87 (0.07)***	0.86 (0.07)***	0.66 (0.07)***	0.78 (0.07)***	2.77 (0.10)***
Behavioral Undercontrol	0.76 (0.13)***	0.64 (0.13)***	0.51 (0.13)***	0.39 (0.12)**	0.30 (0.14)*	0.41 (0.16)**	0.30 (0.17)	-0.08 (0.13)
Interaction	-0.06 (0.19)	0.29 (0.19)	0.22 (0.21)	-0.10 (0.20)	0.20 (0.22)	-0.06 (0.24)	0.07 (0.24)	0.00 (0.41)
				Heavy Drinking [a]				
Positive Expectancies	0.28 (0.03)***	0.30 (0.03)***	0.36 (0.03)***	0.34 (0.03)***	0.24 (0.03)***	0.14 (0.03)***	0.22 (0.03)***	2.31 (0.07)***
Behavioral Undercontrol	0.30 (0.05)***	0.15 (0.06)**	0.24 (0.06)***	0.19 (0.05)***	0.15 (0.05)**	0.18 (0.06)**	0.08 (0.07)	0.20 (0.09)*
Interaction	0.12 (0.08)	0.10 (0.08)	0.15 (0.09)	0.00 (0.09)	0.18 (0.08)*	0.07 (0.09)	-0.01 (0.10)	0.64 (0.32)*
				Alcohol Use Disorder [b]				
Positive Expectancies	0.32 (0.04)***	0.31 (0.04)***	0.42 (0.05)***	0.42 (0.05)***	0.37 (0.05)***	0.25 (0.04)***	0.30 (0.05)***	0.39 (0.03)***
Behavioral Undercontrol	0.29 (0.08)***	0.31 (0.08)***	0.28 (0.09)**	0.17 (0.08)*	0.04 (0.09)	0.17 (0.09).	0.12 (0.11)	0.04 (0.04)
Interaction	0.01 (0.11)	-0.10 (0.12)	0.14 (0.13)	-0.06 (0.15)	0.33 (0.13)*	-0.02 (0.14)	0.04 (0.16)	0.15 (0.14)

NOTE: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. [a] Heavy drinking in AHB was computed as the mean number of days high, drunk, and binge drinking in the previous 30 days, and in the ATR it was computed as the mean number of days intoxicated and hungover in the previous year. [b] Alcohol use Disorder in AHB was based on DSM-IV alcohol dependence, and in the ATR it was based on a DSM-5 symptom count (excluding craving).

Figure 6-2: The nature of interaction effects between positive expectancies and behavioral undercontrol on alcohol involvement in AHB and ATR.



The interaction effect from AHB was at Wave 5 (Panels A and B) and in the ATR (Panel C). All interactions displayed reached statistical significance. Interaction effects were such that associations between positive expectancies and alcohol involvement were tempered among individuals lower in behavioral undercontrol (i.e., higher in control). No other interaction effects approached statistical significance across other waves of AHB.

Chapter 7: Does behavioral undercontrol moderate the relation between reward sensitivity and alcohol involvement at the latent genetic level?

Methods

Analytic Approach.

DeFries-Fulker regression models were employed using twin data (with groups classified by zygosity, as in the classical twin study), in which one twin's behavioral undercontrol moderates the relation between their own reward sensitivity and their co-twin's alcohol involvement. Analyses only included same-sex twin pairs, because the involvement of sex-limited genetic effects was beyond the scope of the current project. To investigate the involvement of genetic factors on main and interaction effects, a constant value is given to each twin pair to represent their genetic relatedness (G; MZ = 1, DZ = 0.5). Analyses modeled main effects (behavioral undercontrol, reward sensitivity, G) two-way interaction effects (behavioral undercontrol * reward sensitivity, behavioral undercontrol * G, reward sensitivity * G, gender * G), quadratic effects moderated by genetic relatedness to account for spurious higher-order effects (behavioral undercontrol * behavioral undercontrol * G, reward sensitivity * reward sensitivity * G), and a three-way interaction effect (behavioral undercontrol * reward sensitivity * G). The three-way interaction effect was of primary interest. If significant, this would provide evidence that the moderator effect previously demonstrated at the phenotypic level in studies of the dual-systems model (e.g., Houben & Wiers, 2009) is at least partially due to genetic factors. Alternatively, failure to find a significant difference between zygosity groups in the strength of moderation would suggest that the relation between reward sensitivity and alcohol involvement is not moderated by behavioral undercontrol at the latent genetic level. Demonstrating the action of the dual-systems model of personality on

alcohol involvement at the latent genetic level could inform future research investigating interactions of specific genetic risk factors for reward sensitivity and behavioral undercontrol (e.g., measured GxG).

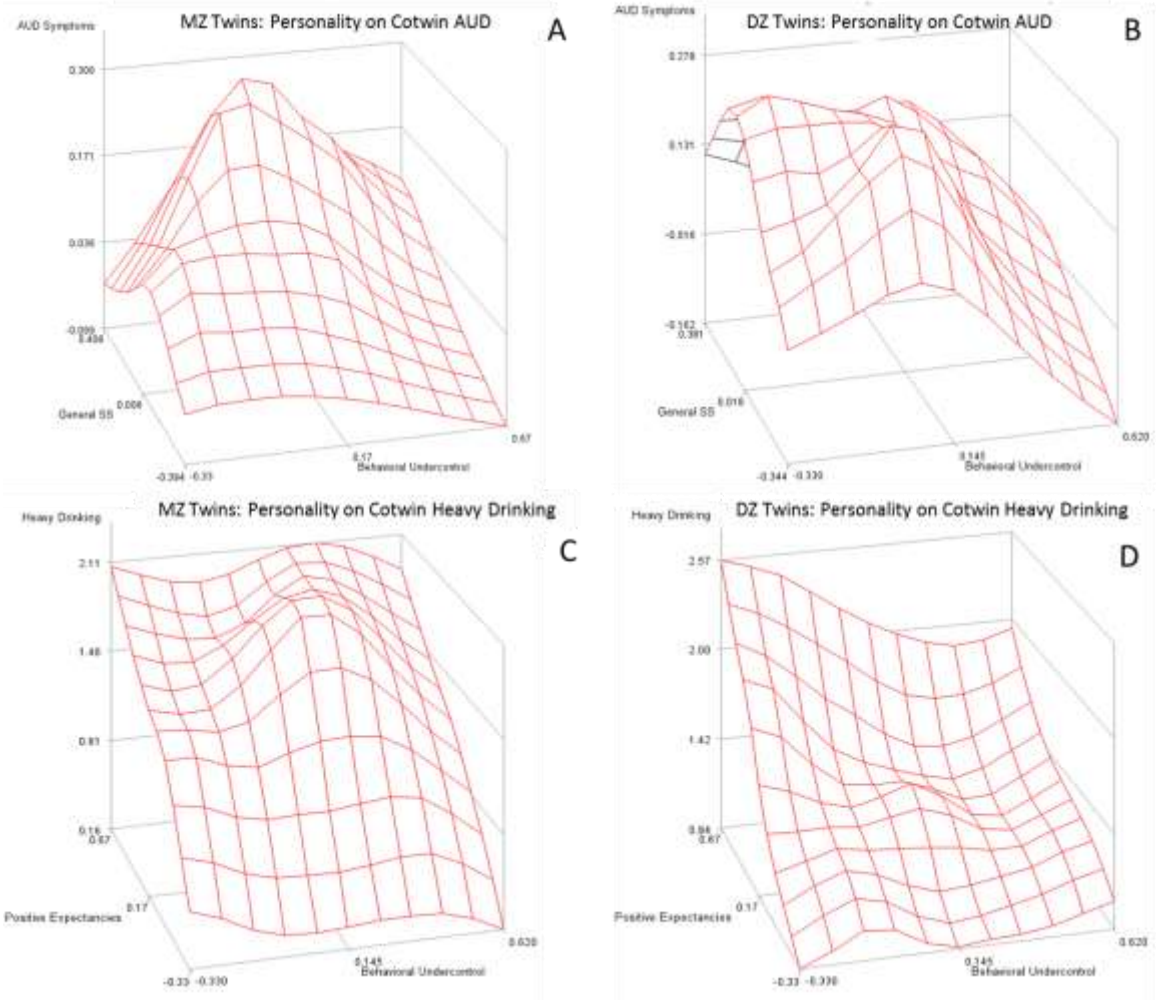
Results

The significant interaction effects found in Chapter 6 with the ATR (general SS * behavioral undercontrol on AUD symptoms; positive expectancies * behavioral undercontrol on heavy drinking) were followed up in Chapter 7 using the ATR. For general SS, there was a significant three-way interaction of behavioral undercontrol and twin zygosity on AUD symptoms (b = 3.04 [SE = 0.72], $p < .001$). For positive expectancies, however, the three-way interaction on heavy drinking was not statistically significant (b = 1.41 [SE = 1.42], p = 0.32). The difference in associations between personality measures on cotwin alcohol involvement, across MZ and DZ twin pairs, are displayed in Figure 7-1.

Summary of Findings

Latent genetic factors appear to be involved in the moderated association between general SS and AUD symptoms by behavioral undercontrol. This was not found, however, for the moderated effect of positive expectancies on heavy drinking.

Figure 7-1: The nature of interaction effects, from DeFries Fulker Models, between measures of reward sensitivity and behavioral undercontrol on cotwin alcohol involvement in the ATR.



There was evidence of the involvement of genetic factors on the moderation effect of behavioral undercontrol on the association between general SS and AUD symptoms (Panels A and B), but not on the moderation effect of behavioral undercontrol on the association between positive expectancies and heavy drinking (Panels C and D).

Chapter 8: General Discussion

The studies in the current paper were broken into two separate aims: those investigating the degree to which reward sensitivity and behavioral undercontrol are distinct risk processes for alcohol involvement (Aim 1), and those investigating whether behavioral undercontrol moderates associations between reward sensitivity and alcohol involvement (Aim 2). Therefore, Aim 1 tested a key assumption of dual-systems models of alcohol involvement, and Aim 2 directly tested this model. Findings from the current study found limited support for the assumption that these are distinct risk processes, particularly after emerging adulthood. The variance in alcohol involvement due to behavioral undercontrol was often not distinct from variance due to reward sensitivity, except at younger ages (ages 18-21), but reward sensitivity accounted for distinct variance in alcohol involvement, separate from behavioral undercontrol. The current studies also found limited support for the dual-systems model, when using self-report measures to assess these risk factors in two independent samples. Only 5 out of 42 interaction effects were significant and in the hypothesized direction. However, of the two statistically significant interactions in the ATR, genetic factors were implicated in this interaction.

Summary of Aim 1: Reward sensitivity and behavioral undercontrol accounted for distinct risk in alcohol involvement in early adulthood (18-22), but not middle adulthood (25-38).

In Chapter 3, behavioral undercontrol demonstrated consistent associations with alcohol involvement before age 25, but measures of reward sensitivity (both general SS and positive expectancies) were associated with most alcohol measures at most waves. Similarly, there were some state-specific associations between behavioral undercontrol

and alcohol involvement at ages 18 and 19, and measures of reward sensitivity were associated with alcohol involvement throughout the seven waves of AHB. Further, trait factors of nearly all personality measures were associated with all alcohol outcomes, suggesting much of the risk is constant across ages 18-35. Finally, LGMs found correlated change between all personality measures and alcohol involvement primarily during college (ages 18 - 21), but only with positive expectancies demonstrated during later adulthood (ages 25 – 35).

In Chapter 4, behavioral genetic investigations of these associations found no evidence of behavioral undercontrol as a distinct genetic risk process for alcohol involvement. Both measures of reward sensitivity, however, accounted for distinct genetic risk (except general SS in males). Finally, in Chapter 5, several genetic markers were top hits for alcohol involvement and reward sensitivity, but not behavioral undercontrol. These analyses were limited, however, by a small, candidate set of genes (946 SNPs). As part of Chapter 5, PRSs from AHB were incorporated to extend analyses of latent genetic variance in the ATR (Chapter 4). Analyses found associations between PRSs of alcohol involvement and trait measures of positive expectancies, but not behavioral undercontrol or general SS. Therefore, there were associations with reward sensitivity specific to alcohol (i.e., positive expectancies), but not with a broader measure of reward sensitivity (i.e., general SS) or behavioral undercontrol. Consistent with findings from the ATR, these findings suggest that genetic risk due to reward sensitivity may account for distinct genetic risk, beyond what is due to behavioral undercontrol.

Summary of Aim 2: Self-report measures of behavioral undercontrol rarely moderated associations between reward sensitivity and alcohol involvement, but genetic factors may be involved when interaction effects occur.

In Chapter 6, there was limited support for the dual-systems model of alcohol involvement. In AHB, interaction effects were found only at Wave 5 (age 25). Notably, there was a statistically significant interaction effect at Wave 2, in the opposite direction as hypothesized by the model, wherein individuals high in behavioral undercontrol (i.e., low in self-control) demonstrated weaker associations between general SS and heavy drinking. This effect is possibly spurious and may not be unexpected, given that there were 42 moderation effects tested altogether. Further, isolated effects in both directions may be expected if a true effect is not present. Consistent with this possibility, half of the interaction coefficients in the current study were positive (7 in Table 16; 14 in Table 17), and half were negative (14 in Table 16, 7 in Table 17), indicating a roughly normal distribution around zero. Unexpectedly, interaction effects were more common in the ATR (2 of 6 were significant), and one of these was a replication from the AHB study (positive expectancies and behavioral undercontrol on heavy drinking). Finally, findings from Chapter 7 suggest that genetic factors may be involved when these interactions do occur.

Comparing and Contrasting Findings from Aims 1 and 2.

Although similar approaches were used across these aims, there is a distinction between their interpretation. In particular, regression models were central to both Aims 1 and 2. The regression models conducted to investigate Chapter 3 (Aim 1), whether reward sensitivity and behavioral undercontrol are differentially related to alcohol

involvement, modeled these as correlated independent variables with additive risk (i.e., risk specific to reward sensitivity, risk specific to behavioral undercontrol, and risk accounted for by both constructs). In contrast, the regression models conducted to investigate Chapter 6 (Aim 2), whether behavioral undercontrol moderates associations between reward sensitivity and alcohol involvement, assumed a non-additive interaction between these constructs that cannot be captured by summing their main effects.

The practical benefit of including non-additive interaction between these constructs can be evaluated by comparing these models (see Table 8-1). Among models in which interaction effects reach statistical significance, the variance explained in alcohol involvement (R^2s = .027 – .310 [SEs = 0.005 – 0.039]) increased by just 0.3% to 2.6%, relative to models in which these constructs were modeled as correlated independent variables (R^2s = .037 – .307 [SEs = 0.007 – 0.038]). In one case, the interaction model explained less variance than the additive model. Therefore, even when interaction effects are statistically significant, the incremental validity beyond a simpler, additive model is questionable.

Table 8-1. The variance explained in an additive, correlated independent variables model (Chapter 3), versus a moderation, interacting independent variables model (Chapter 6).

				R^2 (SE)	
Sample	Age	Alcohol Outcome	Personality Measures	Chapter 3: Additive Model Correlated Variables	Chapter 6: Moderation Model Interacting Variables
AHB	25	Heavy Drinking	General SS & Behavioral Undercontrol	.088 (.027)	.114 (.032)
AHB	25	Heavy Drinking	Positive Expectancies & Behavioral Undercontrol	.215 (.038)	.223 (.039
AHB	25	AUD Symptoms	Positive Expectancies & Behavioral Undercontrol	.144 (.029)	.161 (.031)
ATR	38	AUD Symptoms	General SS & Behavioral Undercontrol	.037 (.007)	.027 (.005)
ATR	38	Heavy Drinking	Positive Expectancies & Behavioral Undercontrol	.307 (.015)	.310 (.014)

Note: Standard errors are in parentheses. Chapter 6 dropped participants with undue influence and leverage on the model results. Therefore, the samples used across the two analytic approaches are not identical.

Finally, when interaction effects were modeled, several effects of general SS on alcohol involvement were no longer significant (i.e., comparing Table 3-1 – 3-4 with Tables 6-1 – 6-2). This did not occur for either behavioral undercontrol or positive expectancies. Although this may be due to the interaction itself being modeled, outliers were dropped from interaction models and may also be involved in this discrepancy.

Implications: Developmental Considerations

A primary aim of the current studies was to build on work investigating the co-development of behavioral undercontrol, reward sensitivity, and alcohol involvement. Evidence suggested that the development of behavioral undercontrol in adulthood is largely independent of positive expectancies, but not general SS in emerging adulthood. In regard to the development of alcohol involvement, measures of use (alcohol QF, heavy drinking) were associated with behavioral undercontrol and reward sensitivity at ages 18-21, but problems (dependence) were associated only with the development of reward sensitivity during this same period.

Although these findings suggest that there is co-development among behavioral undercontrol, reward sensitivity, and alcohol involvement, the developmental interplay remains unclear. For example, there is strong evidence to suggest that alcohol effects executive functioning, particularly when exposure is chronic (Pitel et al., 2007), which may decrease inhibitory control over time. Similarly, some have hypothesized that a reward dependency syndrome may develop after years of engaging in substance use (Koob, 2013), which may manifest in a more positive evaluation of substance use or risky behavior. It is also plausible, however, that poor self-control and/or strong reward sensitivity precede alcohol involvement (Slutske, Moffitt, Poulton, & Caspi, 2012).

Incorporating transactional models with AHB and similar studies may provide important insight into the temporal relationship between these risk processes and alcohol involvement. Further, identifying which risk process comes online first may be particularly informative for early intervention efforts.

Implications: Behavioral Genetic Considerations

An additional aim of the current paper was to differentiate behavioral undercontrol and reward sensitivity as genetic risk factors for alcohol involvement. Multivariate behavioral genetic analyses found no evidence that behavioral undercontrol accounts for distinct risk in alcohol involvement, apart from reward sensitivity. The genetic overlap between these systems is consistent with growing neuroimaging evidence suggesting that, despite being implemented by separate neural substrates, projections between bottom-up (Koob & Le Moal, 2008) and top-down systems (Goldstein & Volkow, 2011) are critical to the development of psychiatric outcomes. For example, white matter projections from the prefrontal cortex to the striatum are associated with trait measures of behavioral undercontrol (e.g., persistence; Lei et al., 2014), as well as behavioral measures in healthy (e.g., delay discounting; Peper et al., 2013) and alcohol dependent samples (response inhibition; Courtney, Ghahremani, & Ray, 2013). Considering the current findings in light of this research, it is possible that genetic factors for the top-down system are associated with alcohol involvement indirectly, solely via projections to the bottom-up system. That is, the involvement of behavioral undercontrol in the genetic risk for alcohol involvement may be entirely attributable to corticolimbic projections, and reward sensitivity may account for additional risk via activity within the mesolimbic system.

The molecular genetic findings from the current study are interesting and identified possible genetic markers that may account for risk in alcohol involvement via reward sensitivity. A review of the literature suggests mechanisms by which these markers may confer risk. Of the markers of interest in the current paper, *rs851011* (on the *MAPK14* gene) was a top hit for three of six phenotypes (positive expectancies, alcohol QF, and alcohol dependence) and has been previously associated with alcohol outcomes in the Missouri Adolescent Female Twin Study (Agrawal et al., 2011). The *MAPK14* gene, which is located on chromosome 6 and encodes for a MAP kinase protein involved in various cellular processes (e.g., proliferation, differentiation, transcription regulation), has also been implicated in brain volume deficits via marijuana use in schizophrenia patients (Onwuameze et al., 2013).

In addition, three of the eight markers fell on the GSK3β gene (*rs3755557* for positive expectancies and alcohol dependence and *rs2037547* and *rs11919783* both for alcohol dependence and heavy drinking), which is on chromosome 3 and encodes for a protein involved in neuronal development. These markers have been implicated in schizophrenia (Li et al., 2011), particularly medication and medication side effects (Souza et al., 2010; Souza et al., 2008), and bipolar disorder (Luykx et al., 2010). Considering the function of this gene and the diverse psychiatric outcomes associated with it, it is plausible that the *GSK3β gene* broadly confers transdiagnostic risk for many psychiatric disorders.

The other markers identified have been linked with diverse outcomes, including suicidality and psychotic, mood, and addictive disorders (*TPH1 gene*); pain disorders and postpartum depression (*PNOC gene*); epilepsy and seizures (*GABRG2 gene*); and

cognitive functioning and speech (*GRIN2A gene*). Inferences about these findings should be made with caution, because significant associations have often been followed by numerous null findings (Munafò & Flint, 2011). Further, it is becoming increasingly evident that behavioral traits are influenced by many polymorphisms with very small effects ($R^2 \leq 1\%$) (Vinkhuyzen, Wray, Yang, Goddard, & Visscher, 2013). Therefore, larger studies, in regard to sample size and genome coverage, will be important for advancing this line of research.

Implications: Applied Considerations

The current findings may also have important treatment implications. Given that much of the risk due to behavioral undercontrol was shared with reward sensitivity, particularly after emerging adulthood, AUD interventions targeting control may be effective via indirect influences on urges to use alcohol (e.g., mindfulness-based interventions; Garland et al., 2014). In contrast, AUD interventions targeting reward sensitivity (e.g., naltrexone; Maisel, Blodgett, Wilbourne, Humphreys, & Finney, 2013) may act independent of control. Therefore, although a combination of interventions targeting both systems may be effective at addressing AUD, the current findings suggest that even interventions targeting control may function via indirect effects on reward sensitivity.

The nuance of stronger associations between behavioral undercontrol and alcohol involvement in emerging adulthood should also be considered. Specifically, targeting self-control in addition to reward sensitivity may be important for limiting the effects of harmful alcohol use in the college environment (Slutske, 2005). Others have speculated that physical or cognitive exercise regimens may be beneficial to increasing self-control

(Littlefield, Sher, & Wood, 2009). The current findings build on this and suggest that it may also be beneficial to target reward sensitivity. For example, there may be benefit to universities in providing many opportunities for students to engage in entertaining, non-alcohol-related activities.

Limitations and Future Directions

The measurement of bottom-up urges and top-down control should be considered when applying the current findings to dual-systems models of alcohol involvement. A fundamental concern when interpreting these models is whether our measurement of these risk processes are adequate. Typically, studies of dual-systems models use behavioral measures, some of which correlate weakly with analogous self-report measures (Cyders & Coskunpinar, 2012; King, Patock-Peckham, Dager, Thimm, & Gates, 2014), and neuroimaging is often incorporated with these measures as a direct measure of these bottom-up and top-down processes. Self-report measures, such as those used in the current paper, have been shown to yield different interactions than implicit, behavioral measures (Thush et al., 2008).

A similar measurement concern has to do with the scope of the measures used. The current study included both specific and general measures of reward sensitivity, but only a general measure to assess risk related to behavioral undercontrol. Assessing reward sensitivity specific to alcohol is consistent with some investigations of the dual-systems model (e.g., Houben & Wiers, 2009 used an alcohol version of the implicit association task), but it is unclear whether general or specific measures best represent these systems. For example, it is possible that alcohol-specific measures of behavioral undercontrol best capture risk for AUD, but general measures of self-control are typically

used (e.g., Houben & Wiers, 2009 used the standard stroop task). Therefore, understanding the optimal operationalizations of these risk processes will be important for better understanding how reward sensitivity and behavioral undercontrol relate to alcohol involvement.

To further stress the importance of better measurement methods, advancing an understanding of the genetic underpinnings of psychiatric outcomes depends on adequate phenotypic measurement. Further, taking advantage of stronger phenotype measures, recent advances in molecular and statistical genetics may allow for more flexibility in data collection, such as recruiting individuals rather than twin pairs (Yang, Lee, Goddard, & Visscher, 2011).

Summary

There has been an increasing focus on investigating dual-systems models of risky behavior, which assume that bottom-up approach urges and top-down control are distinct risk process for alcohol involvement and AUD (Casey, Tottenham, Liston, & Durston, 2005; Harden & Tucker-Drob, 2011; Quinn & Harden, 2013; Somerville et al., 2010; Steinberg, 2010). The current findings suggest that, although conceptually distinct, behavioral undercontrol is not a distinct risk process, apart from reward sensitivity, for alcohol involvement after emerging adulthood. Further, there was limited evidence of an interaction between behavioral undercontrol and reward sensitivity on alcohol involvement, and the incremental validity of statistically significant correlations was questionable. Further research will be needed to elucidate how these systems influence alcohol independently of, and possibly in tandem with, the other. Additional work is needed to extend these findings to better understand the functional relationship between

these constructs and addictive behavior, and improved measurement of these constructs will also be critical.

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APPENDIX A: Scales

Reward Sensitivity

ATR: General Sensation Seeking

Each of the items below contains two choices A and B. By choosing the letter A or B, please indicate which most describes <u>your likes</u> or the way you feel. In some cases you may find items in which both choices describe your likes or feelings. <u>Please choose the one that better describes your likes or feelings.</u> In some cases you may find items in which you do not like either choice. In these cases choose the option that you dislike least. It is important that you respond to all items with only one choice, A or B. We are interested only in your likes or feelings, not in how others feel about these things or how one is supposed to feel. There are no right or wrong answers as in other kinds of tests. Be frank and give an honest appraisal of yourself.

Please try to respond to the statements even if you are not sure of the answer. Don't spend too much time deciding on the answer.

1.
    a. I like "wild" uninhibited parties.
    b. I prefer quiet parties with good conversation.
2.
    a. There are some movies I enjoy seeing a second or even third time.
    b. I can't stand watching a movie that I've seen before.
3.
    a. I often wish I could be a mountain climber
    b. I can't understand people who risk their necks climbing mountains.
4.
    a. I dislike all body odors.
    b. I like some of the earthy body smells.
5.
    a. I get bored seeing the same old faces.
    b. I like the comfortable familiarity of everyday friends.
6.
    a. I like to explore a strange city or section of town by myself, even if it means getting lost.
    b. I prefer a guide when I am in a place I don't know well.
7.
    a. I dislike people who do or say things just to shock or upset others.
    b. When you can predict almost everything a person will do and say he or she must be a bore.

8.

a. I usually don't enjoy a movie or play where I can predict what will happen in advance.
b. I don't mind watching a play or movie where I can predict what will happen in advance.

9.

a. I have tried marijuana or would like to.
b. I would never smoke marijuana.

10.

a. I would not like to try any drug which might produce strange and dangerous effects on me.
b. I would like to try some of the drugs that produce hallucinations.

11.

a. A sensible person avoids activities that are dangerous.
b. I sometimes like to do things that are a little frightening.

12.

a. I dislike "swingers" (people who are uninhibited and free about sex).
b. I enjoy the company of real "swingers".

13.

a. I find that stimulants make me uncomfortable.
b. I often like to get high (drinking liquor or smoking marijuana).

14.

a. I like to try new foods that I have never tasted before.
b. I order the dishes with which I am familiar so as to avoid disappointment and unpleasantness.

15.

a. I enjoy looking at home movies, videos, or travel slides.
b. Looking at someone's home movies, videos, or travel slides bores me tremendously.

16.

a. I would like to take up the sport of water skiing.
b. I would not like to take up water skiing.

17.

a. I would like to try surfboard riding.
b. I would not like to try surfboard riding.

18.

a. I would like to take off on a trip with no preplanned or definite routes, or timetable.
b. When I go on a trip I like to plan my route and timetable fairly carefully.

19.

a. I prefer the “down to earth” kinds of people as friends.
b. I would like to make friends in some of the “far out” groups like artists or “punks”.

20.

a. I would not like to learn to fly an airplane.
b. I would like to learn to fly an airplane.

21.

a. I prefer the surface of the water to the depths.
b. I would like to go scuba diving.

22.

a. I would like to meet some persons who are homosexual (men or women).
b. I stay away from anyone I suspect of being “gay” or “lesbian”.

23.

a. I would like to try parachute jumping.
b. I would never want to try jumping out of plane, with or without a parachute.

24.

a. I prefer friends who are excitingly unpredictable.
b. I prefer friends who are reliable and predictable.

25.

a. I am not interested in experience for its own sake.
b. I like to have new and exciting experiences and sensations even if they are a little frightening, unconventional, or illegal.

26.

a. The essence of good art is in its clarity, symmetry of form, and harmony of colors.
b. I often find beauty in the “clashing” colors and irregular forms of modern paintings.

27.

a. I enjoy spending time in the familiar surroundings of home.
b. I am very restless if I have to stay at home for any length of time.

28.

a. I like to dive off the high board.
b. I don’t like the feeling I get standing on the high board (or I don’t go near it at all).

29.

a. I like to date persons who are physically exciting.
b. I like to date persons who share my values.

30.

a. Heavy drinking usually ruins a party because some people get loud and boisterous.
b. Keeping the drinks full is the key to a good party.

31.

a. The worst social sin is to be rude.
b. The worst social sin is to be a bore.

32.

a. A person should have considerable sexual experience before marriage.
b. It's better if two married persons begin their sexual experience with each other.

33.

a. Even if I had the money, I would not care to associate with flighty rich persons in the "jet set".
b. I could conceive of myself seeking pleasures around the world with the "jet set".

34.

a. I like people who are sharp and witty even if they do sometimes insult others.
b. I dislike people who have their fun at the expense of hurting the feelings of others.

35.

a. There is altogether too much portrayal of sex in movies.
b. I enjoy watching many of the "sexy" scenes in movies.

36.

a. I feel best after taking a couple of drinks.
b. Something is wrong with people who need liquor to feel good.

37.

a. People should dress according to some standard of taste, neatness, and style.
b. People should dress in individual ways even if the effects are sometimes strange.

38.

a. Sailing long distances in small sailing crafts is foolhardy.
b. I would like to sail a long distance in a small but seaworthy sailing craft.

39.

a. I have no patience with dull or boring persons.
b. I find something interesting in almost every person I talk to.

40.

a. Skiing down a high mountain slope is a good way to end up on crutches.
b. I think I would enjoy the sensations of skiing very fast down a high mountain slope.

ATR: Positive Expectancies (subset from the full General Sensation Seeking items)

1) A: I find that stimulants make me uncomfortable.
B: I often like to get high (drinking liquor or smoking marijuana).
2) A: I would not like to try any drug which might produce strange and dangerous effects on me.
B: I would like to try some of the drugs that produce hallucinations.
3) A: I like "wild" uninhibited parties.
B: I prefer quiet parties with good conversation.
6) A: I have tried marijuana or would like to.
B: I would never smoke marijuana.
7) A: Heavy drinking usually ruins a party because some people get loud and boisterous.
B: Keeping the drinks full is the key to a good party.
11) A: I feel best after taking a couple of drinks.
B: Something is wrong with people who need liquor to feel good.

AHB: General Sensation Seeking

Please answer the following questions by indicating either "Yes" or "No" for each question. There are no right or wrong answers, and no trick questions.

Work quickly and do not think too long about the exact meaning of the question.

Response Format:

A. Yes
B. No

41. I often long for excitement.
42. At times I have a strong urge to do something harmful or shocking.
43. I would do almost anything for a dare.
44. At time, I very much wanted to leave home.

AHB: Positive Expectancies

The following list describes some effects of alcohol. Because alcohol affects people in different ways, we would like to know which of these effects you experience when you drink alcohol. Based on your own drinking experience, how much do you expect each of these effects when drinking alcohol? (If you have never consumed alcohol, indicate how you might expect alcohol to affect you if you had several drinks.)

Response Format:

0) Not At All
1) A Little Bit
2) Somewhat
3) Quite A Bit
4) A Lot

1. alcohol tastes good
2. drinking makes celebration more enjoyable
3. drinking adds enjoyment to a good meal
4. drinking makes many activities more enjoyable
5. drinking helps me fall asleep at night
6. drinking can be exciting
7. drinking makes sports events more enjoyable
8. drinking makes listening to music more enjoyable
9. drinking is a good way to kill time

Behavioral Undercontrol

ATR

Instructions: These items are statements that you might use to describe your attitudes, opinions, interests, feelings, or other characteristics. After most of the items there are two choices, True (T) or False (F). If the statement or item is true for you (or more true than false), then choose T. If the statement or item is false for you (or more false than true) then choose F.

Please try to respond to the statements even if you are not sure of the answer. Don't spend too much time deciding on the answer.

Response Format:

0. False
1. True

1) I keep close track of where my money goes.
2) I often stop one thing before completing it and start on another.
3) When forced with a decision I usually take time to consider and weigh all possibilities.
4) I often act without thinking.
5) I often prefer to "play things by ear" rather than to plan ahead.
6) I don't like to start a project until I know exactly how to do it.
7) I am more likely to be fast and careless than to be slow and plodding.
8) I tend to value and follow a rational, "sensible" way of doing things.
9) I am often not as cautious as I should be.
10) I plan and organize my work in detail.
11) I often start projects with little idea of what the end result will be.
12) People say that I am well-organized (that I do things in a systematic manner).
13) I am a cautious person.
14) I am very level headed and always like to keep my feet on the ground.
15) Whenever I go out to have fun I like to have a pretty good idea of what I'm going to do.
16) Before I get into a new situation I like to find out what to expect from it.
17) Whenever I decide anything I try to remember the basic rules of right and wrong.
18) I very much dislike it when someone breaks the rules of good conduct.

AHB

This inventory consists of numbered statements. Read each statement and decide whether it is true as applied to you or false as applied to you. If a statement is true or mostly true, circle the True response "T". If a statement is false or not usually true as applied to you, circle the False response "F". There are no right or wrong answers, and no trick questions.

Response Format:

0. False
1. True

1) I think things over before doing anything.
2) I am usually carefree.
3) I do and say things without stopping to think.
4) I often do things on the spur of the moment.

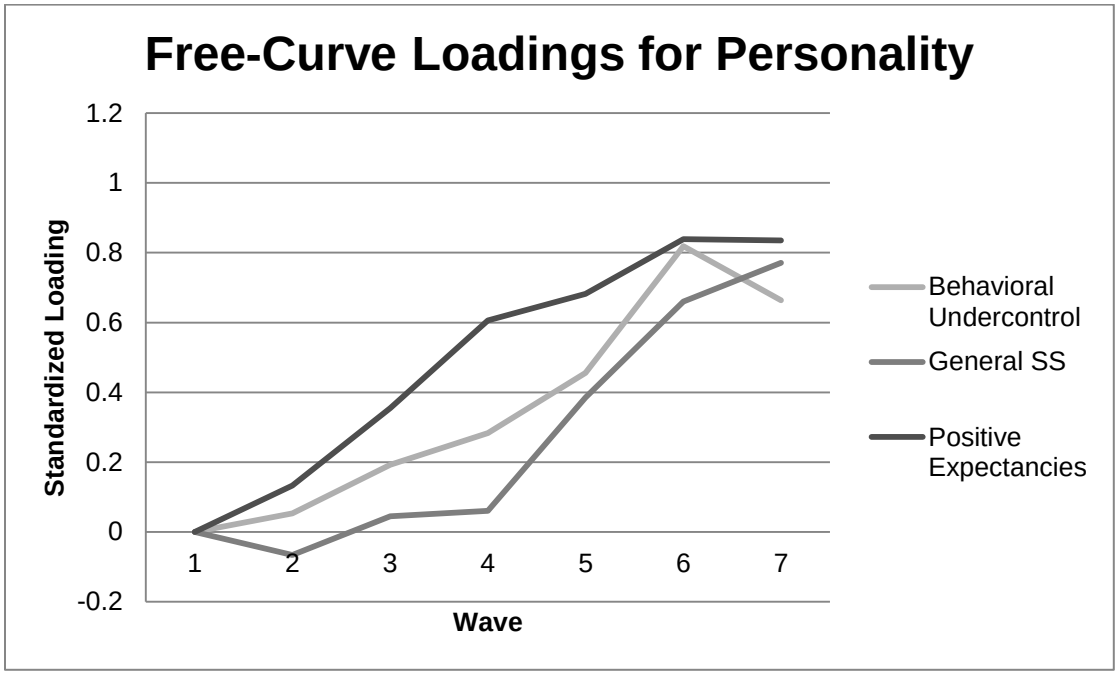
APPENDIX B: Free-Curve, Latent Growth Model Results

Table B-1. Fit statistics for free-curve latent growth models, estimating an intercept factor, change factor of linear change at ages 18-21, and a free-curve factor from 18-35 in the AHB sample.

Measure	CFI	TLI	RMSEA (p fit < .05)
General Sensation Seeking	0.990	0.981	0.877
Positive Expectancies	0.987	0.976	0.362
Behavioral Undercontrol	0.984	0.971	0.593
Alcohol QF	0.993	0.988	0.772
Heavy Drinking	0.994	0.989	0.907
Alcohol Dependence	0.997	0.995	0.979

Note: Models included family history of alcohol use disorder and gender as covariates.

Standardized factor loadings on the free-curve change factor for personality and alcohol measures.



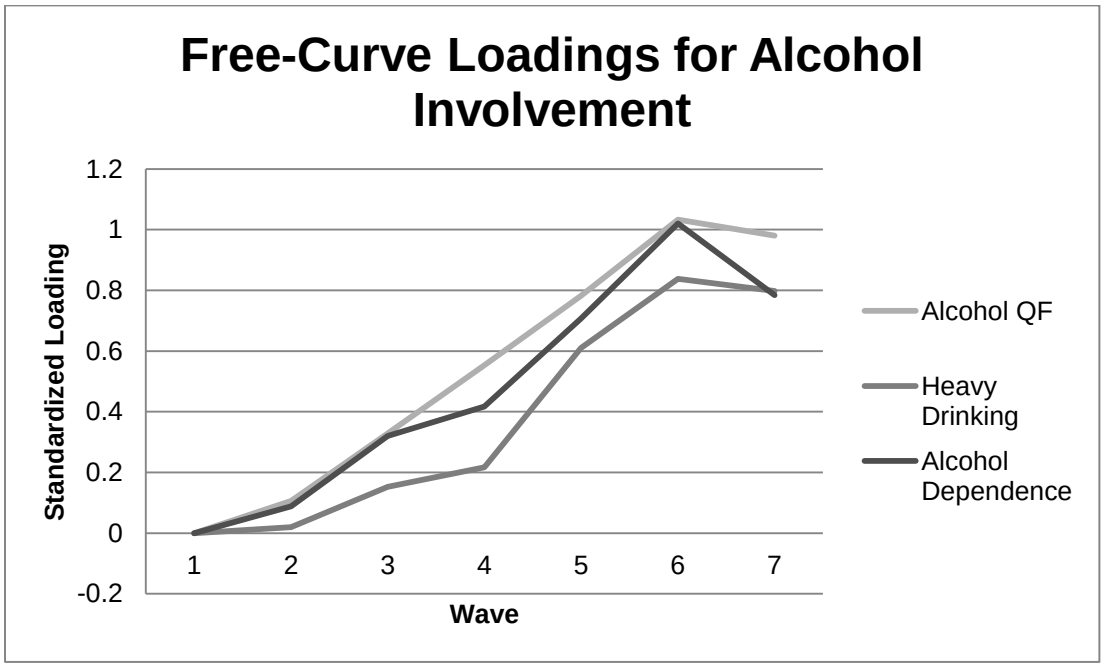


Table B-2. Correlation estimates among intercept and slope parameters from multivariate latent growth models including alcohol involvement, behavioral undercontrol, and a measure of reward sensitivity.

Alcohol Involvement	Behavioral Undercontrol	General Sensation Seeking	Positive Expectancies
		Intercept Correlations	
Alcohol QF	0.41 (0.05)***	0.29 (0.06)***	0.67 (0.04)***
Heavy Drinking	0.44 (0.06)***	0.31 (0.06)***	0.70 (0.04)***
Alcohol Dependence	0.39 (0.06)***	0.41 (0.07)***	0.64 (0.05)***
		Linear Change (Waves 1-4)	
Alcohol QF	0.33 (0.17)	0.04 (0.20)	0.56 (0.11)***
Heavy Drinking	0.65 (0.25)*	0.48 (0.31)	0.70 (0.13)***
Alcohol Dependence	0.36 (0.27)	0.83 (0.57)	0.74 (0.16)***
		Free-Curve Slope	
Alcohol QF	0.38 (0.07)***	0.39 (0.08)***	0.65 (0.05)***
Heavy Drinking	0.44 (0.08)***	0.49 (0.09)***	0.62 (0.07)***
Alcohol Dependence	0.26 (0.08)**	0.47 (0.10)***	0.54 (0.07)***

Note. *** $p < .001$, ** $p < .01$, * $p < .05$. Estimates were obtained from multivariate latent growth curve models.

Table B-3. Correlation estimates among intercept and slope parameters from free-curve, multivariate latent growth models including alcohol involvement, behavioral undercontrol, and a measure of reward sensitivity (general sensation seeking, positive expectancies), after regressing out variance in reward sensitivity from behavioral undercontrol, and vice versa.

	Behavioral Undercontrol		General Sensation Seeking	Positive Expectancies
Alcohol Involvement	Residualized General Sensation Seeking	Residualized Positive Expectancies	Residualized Behavioral Undercontrol	
		Intercept Correlations		
Alcohol QF	0.39 (0.05)***	0.36 (0.06)***	0.21 (0.07)**	0.66 (0.04)***
Heavy Drinking	0.41 (0.06)***	0.4 (0.07)***	0.24 (0.07)**	0.69 (0.04)***
Alcohol Dependence	0.34 (0.07)***	0.34 (0.07)***	0.33 (0.07)***	0.62 (0.05)***
		Linear Change (Waves 1-4)		
Alcohol QF	ne	-0.01 (0.77)	-0.73 (2.74)	0.5 (0.14)***
Heavy Drinking	ne	ne	-0.17 (1.87)	0.63 (0.22)**
Alcohol Dependence	ne	ne	ne	0.69 (0.19)***
		Free-Curve (Waves 1-7)		
Alcohol QF	0.36 (0.07)***	0.34 (0.08)***	0.35 (0.09)***	0.63 (0.05)***
Heavy Drinking	0.4 (0.09)***	0.38 (0.1)***	0.46 (0.1)***	0.6 (0.07)***
Alcohol Dependence	0.23 (0.09)*	0.2 (0.09)*	0.44 (0.1)***	0.52 (0.07)***

Note: Standard errors are in parentheses. *** $p < .001$, ** $p < .01$, * $p < .05$. ne = Not Estimable. Each column represents a model, wherein intercept and change correlations between personality measures and alcohol involvement were estimated while regressing out variance in the other.

VITA

Jarrod Ellingson was born in Mitchell, South Dakota, where he was raised by his parents as an only child. Growing up, he spent a majority of his time playing, talking about, or thinking about baseball. Notably, his first exposure to statistics came from the backs of baseball cards. Jarrod attended the University of Northern Iowa, where he majored in Psychology and minored in Journalism. Prior to attending the University of Missouri, he conducted research through a summer internship at the Mayo Clinic (Rochester, MN) and received a Master's degree in Psychology from San Diego State University, where he met his wife, Yuri. Jarrod took a one-year leave of absence from Missouri to work at Indiana University, while he and Yuri married and she finished her doctorate. Together, Jarrod and Yuri raise their one-year-old daughter, Maisie.