INDIVIDUAL DIFFERENCES IN THE IMPACT OF STRESS ON ALCOHOL USE, BINGE DRINKING, AND ALCOHOL USE ONSET: THE ROLE OF DEVELOPMENTAL AND BIOLOGICAL VARIATION

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Jessica Wells

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DEDICATION

This work is dedicated to my father.

Justin Lee Wells (1966-2014)

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ABSTRACT

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Previous research suggests that both distal and proximal environmental stressors impact later alcohol use behaviors. Introduction of the stress sensitization hypothesis has highlighted that the effects of these environmental stressors may not be limited to direct effects but, rather, are interactive wherein the impact of proximal life stress are greater for individuals who have experienced distal stress such as childhood abuse (ExE). At the same time, gene-environment (GxE) interaction studies have examined how the effects of both distal and environmental stress is moderated by genetic polymorphisms in two-way interactions. The current study seeks to add to a small body of literature seeking to merge these two processes by examining a genetically moderated stress sensitization hypothesis (GxExE) on alcohol use, binge drinking, and alcohol use onset. The current dissertation further contributes to this body of literature by assessing gender-specific GxExE effects and presenting preliminary models gender-specific alcohol dependence and the role of sex-role identification in alcohol use, binge drinking, and alcohol use onset. Mixed results concerning the serotonergic polymorphisms, MAOA and 5-HTTLPR, two-way and three-way interactions with distal and proximal environmental stress were found. These findings and implications for programming designed to reduce alcohol use are discussed.

KEY WORDS: Childhood abuse, Stress, Stress sensitization, MAOA, 5-HTTLPR, Alcohol use, Binge drinking, Alcohol use onset

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CHAPTER I

Introduction

Although alcohol use is highly prevalent with approximately 62.2% of adult males and 50.1% of adult females over the age of 25 reporting past month alcohol use (Substance Abuse and Mental Health Services Administration, 2014), a number of severe costs to society and individuals result from severe alcohol use patterns. Recent evidence suggests that one in ten deaths of working aged adults occurs as a direct result of alcohol use (Stahre, Roeber, Kanny, Brewer, & Zhang, 2014). Alcohol-related mortality rates between 2006 and 2010 are estimated to be approximately 27.9 per 100,000 people per year (Stahre et al., 2014). Financial costs to society resulting from death, injury, mental and physical health consequences exceed $249 billion per year, with binge drinking being the greatest contributor to the national cost (Sacks, Gonzales, Bouchery, Tomedi, & Brewer, 2015).

Alcohol use is costly not only to society, but also raises the risk for a number of physical and psychological risk factors for the individual. Chronic alcohol use is associated with liver disease and pancreatitis (Warren & Murray, 2013), high-density lipoprotein cholesterol and consequential heart disease (Suh Shaten, Cutler, & Kuller, 1992), and specific types of cancer (Mostofsky, Mukamal, Giovannucci, Stampfer, & Rimm, 2016). Alcohol use also increases risk for anxiety (Kushner, Abrams, & Borchardt, 2000), depression (DeSimone, Murray, & Lester, 1993), and suicide (Swahn, Bossarte, & Sullivent, 2008). Beyond health consequences, the effects of alcohol have been found to reduce school performance (Singleton & Walfson, 2009) and facilitate violent antisocial behavior (Lennings, Copeland, & Howard, 2003; Soyka, 2000; Swahn,

Bossarte, & Sullivent, 2008). Finally, alcohol use and binge drinking increase an individual's likelihood of being the victim of intimate partner violence (Cunradi, Todd, & Mair, 2015), unwanted sexual advances (Novik, Howard, & Boekeloo, 2011), and rape (Champion et al., 2004).

Although alcohol use is not legal until the age of twenty-one in the United States, alcohol use onset largely precedes this age. Adolescents report alcohol use more frequently than the use of any other substance (Windle et al., 2008; Witt, 2010). In descriptive analysis of adolescent alcohol use in the Monitoring the Future data, 41% of 8th graders and 63% of 10th graders report having used alcohol with 20% and 42% reporting having ever been drunk, respectively (Johnston et al., 2006). While a national longitudinal study revealed that alcohol use in the past month has significantly decreased over time (adolescents 12-17 years old: 14.7% in 2009, 11.5% in 2014; early adults 18-25: 61.8% in 2009, 59.6% in 2014; adults, 26 and older: 54.9% in 2009, 56.5% in 2014), underage drinking remains highly problematic with approximately 8.7 million people drinking under the legal drinking age. Further, of those who participate in underage drinking, 60.6% engage in binge drinking. By the time an individual reaches the legal drinking age of 21, 22.8% of individuals will already be a current alcohol drinker and 13.6% will already be involved in binge drinking (CBHSQ, 2015).

With such prevalent use, alcohol use disorders are also widespread. Although estimates vary by measurement, estimates from a national sample in 2014 suggest that approximately 2.7% of adolescents, 12.3% of young adults, and 5.9% of adults met criteria for a DSM-IV alcohol use disorder (CBHSQ, 2015). Research with a focus on sex and gender differences in these prevalence rates suggests that, as compared to females,

adult males both drink alcohol more frequently and have a greater percentage that meet criteria for alcohol-related disorders (Brady & Randall, 1999; Cotto, Davis, Dowling, Elcano, Staton, & Weiss, 2010), although this gender difference has been diminished across time with recent research finding that more recent cohorts (2001-2002) have a diminished gender gap as compared to the gender gap observed when older cohorts were of approximately the same age (1991-1992; Keyes, Martins, Blanco, & Hasin, 2010).

Despite recent trends in reduction of alcohol use, severe patterns of alcohol use behavior resulting in alcohol use disorder and health consequences due to binge drinking remain a challenge for psychologists, criminologists, and public health officials. With heritability estimates of alcohol use disorder approximated at 49% in a recent meta-analysis (Verhulst, Neale, & Kendler, 2015), understanding how biological variation contributes to variation in alcohol use behaviors is critical. In early examinations of the underpinnings of alcohol abuse, it became clear that neither environmental nor genetic factors alone can sufficiently model risk. Rather, environments and genetics interact to explain variation in alcohol abuse. Specifically, employing a behavioral genetic approach, an early adoption study suggested that genetic factors of biological parents, passed to their adopted children were more likely to lead to alcohol abuse in certain risk environments (Cloninger, Bohman, & Sigvardsson, 1981). Several gene-environment (GxE) interaction studies have been published within criminology in the explanation of general antisocial behavior and, specifically, alcohol-related behaviors and disorders, including alcohol use (Covault et al., 2007; Daw et al., 2012; Kim et al., 2014; Kranzler et al., 2012; Laucht et al., 2009; Stogner & Gibson, 2013), binge drinking (Covault et al., 2007; Kim et al., 2014; Kranzler et al., 2012; Laucht et al., 2009; Olsson et al., 2005),

alcohol use age of onset (Kaufman et al., 2012), and alcohol dependence (Copeland et al., 2011; Ducci et al., 2008; Nikulina et al., 2012; Nilsson et al., 2008, 2011). The GxE model examines how the effect of environmental factors on alcohol use varies across genotypes. Overall, the results from these studies are mixed with some studies showing that genes such as MAOA and 5-HTTLPR interact with environmental risk factors to explain alcohol use, binge drinking, and alcohol dependence while others have found no interactive effects.

MAOA and 5-HTTLPR are genetic polymorphisms implicated in the functioning of the serotonin system. Due to their effects on the ability of neurons to send messages via this important neurotransmitter, they have been widely studied in GxE models. In regard to alcohol use, MAOA has been found to interact with childhood sexual abuse (Ducci et al., 2008; Nilsson et al., 2011) and quality of family relation (Nilsson et al., 2008, 2011) to explain alcohol use disorder as well as interact with life stress to explain alcohol use frequency (Stogner & Gibson, 2013). 5-HTTLPR has been found to interact with parental attachment to explain binge drinking (Olsson et al., 2005), as well as interact with life stress (Covault et al., 2007; Kranzler et al., 2012; Laucht et al., 2009), social norms (Daw et al., 2012), and family conflict (Kim et al., 2014) to explain alcohol use frequency and binge drinking.

The current body of GxE literature, however, suffers from some noteworthy limitations. First, many GxE studies focus on childhood maltreatment without specificity for the age at which maltreatment began (see Chapter 2). Childhood maltreatment during different developmental stages has been shown to have differing neurological consequences and thus, the long-term effects of childhood maltreatment on alcohol-

related behaviors may vary depending on when childhood maltreatment was experienced (Edalati & Krank, 2015). Second, studies examining GxE effects among males and females separately find disparate results. Many studies fail to examine the potential limitations to the GxE effects across sex. Third, GxE studies have largely failed to account for developmental processes across the life course. Studies have examined GxE largely within cross-sectional frameworks thus presuming that there is no variation in additive or interactive effects of environmental risk exposure at varying points in the life course. This practice is highly problematic as a large body of research suggests that the effects of proximal stressors (i.e., stressors experienced recently) may be influenced by distal life stressors (i.e., stressors experienced at an earlier age), a process referred to as stress sensitization (Hammen, Henry, & Daley, 2000). This model suggests that experience of early life stress within the normative range better equips individuals when faced with later life stress. Those who experience extremely low stress or extremely high stress environments may be sensitized to the stress, thus leading to increased risk of the deleterious effects of later life stress (Eames et al., 2014; Keyes, McLaughlin, Koenen, Goldmann, Uddin, & Galea, 2012; Kim et al., 2014; Young-Wolff, Kendler, & Prescott, 2012). Importantly, little consideration has been given to how genetic variation may contribute to this stress sensitization process.

A GxExE model has recently been proposed, merging both the stress sensitization and GxE approaches. Homberg and van den Hove (2012) argue that, when examining interactive effects of proximal stressors and genes, it is important to also account for human adaption to stressful early life environments. Thus, explanation of a phenomenon necessitates an examination of how genes may moderate how early life environments

impact the salience of later life environments in explaining behavior or psychological variation. In other words, the genetically moderated stress sensitivity model holds that while exposure to extreme stress in early life increases the impact of later life stress, certain variants of genetic polymorphisms increase the subjective experience of early and later life stress. As such, carriers of environmentally "reactive," or "risk," genetic variants experience more stress sensitization than those with less reactive variants. Examination of this hypothesis, to date, has been extremely rare and limited to examination of variation in depressive outcomes (Grabe et al., 2012; Starr, Hammen, Conway, Raposa, & Brennan, 2014) and criminal and delinquent behavior (Wells, Armstrong, Boisvert, Lewis, Gangitano, & Hughes-Stamm, forthcoming).

As such, the current dissertation proposes a genetically moderated stress sensitization process in relation to alcohol-related behaviors. While this model may be applicable to a number of behavioral outcomes, it may be critical in explanation of alcohol-related behaviors as the developmental course from initiation of use to problem or disordered behavioral patterns. Research suggests that early onset alcohol use potentiates neuronal pathways that may lead to more severe alcohol use trajectories in later life (Chambers, Taylor, & Potenze, 2003). Of note, studies have also suggested that this continuity of use may be largely influenced by genetic factors for males but to a lesser extent for females (McGue, Iacono, Legrand, & Elkins, 2001). Given this, sensitivity to early environmental stress exposure may lead to both increased early alcohol use and stress system sensitization. Such individuals, when faced with later life stress may be more strongly affected by the stress leading to subsequent use. Importantly, these individuals are not only more strongly affected by stress but alcohol use later in life

may lead to more severe patterns of use if they had been engaged in early alcohol use. Thus, the genetically moderated stress sensitization model may explain not only alcohol use but trajectories of use and alcohol dependence.

The goal of the current dissertation is to further examine the processes underlying trajectories of alcohol use, binge drinking, and alcohol use onset from a developmental biosocial perspective. Previous research has highlighted both environmental explanations, biological explanations, and their interactions. Despite this body of literature, much is left unknown about the intricacies of how biology and environments interact across the life course. The current dissertation seeks to address this limitation by reviewing previous literature concerning the effects of distal stress, proximal stress, MAOA, 5-HTTLPR, and GxE models combining these environments and genetic polymorphisms. Previous literature is extended first by application of these GxE models through a longitudinal modeling technique, specifying abuse onset. Second, the current dissertation applies a GxExE model to the explanation of alcohol use, binge drinking, and alcohol dependence, thus modeling the complex interactions of both genes and environments as well as distal environments with proximal environments. To this end, data from the first four waves of the National Longitudinal Study of Adolescent to Adult Health (Add Health) are analyzed.

Chapter 2 begins with a review of literature examining the direct effects of stress on alcohol use, binge drinking, and alcohol dependence. The effects of both proximal and distal stress are reviewed. Further, the varying effects of stress on alcohol use behaviors across biological sex and socialized sex roles is highlighted. Second, Chapter 2 provides a brief primer on the importance of serotonin in the development of trajectories of alcohol

use behaviors and reviews the direct effects of two focal polymorphisms, MAOA and 5-HTTLPR. Third, Chapter 2 provides a systematic review of GxE studies of MAOA and 5-HTTLPR in interaction with distal and proximal stress. Finally, the stress sensitization model and the genetically moderated stress sensitization model are highlighted.

Chapter 3 describes in detail the sampling procedures of the Add Health including targeted sampling for the genetic supplemental sample of siblings. Protocols for genotyping of MAOA and 5-HTTLPR are also provided. Measurement and descriptive statistics of each variable of interest are supplied as well. Chapter 3 concludes with the plan of analysis of the current dissertation.

Chapter 4 displays the results of the analyses. Results begin with bivariate correlations between all variables. Results from growth curve models of alcohol use and binge drinking, and survival analysis of alcohol use age of onset are presented. For each dependent variable, development of modeling strategy is first discussed. Then, ExE and GxExE analyses are presented in text and in tabular formats. Further, results of direct and two-way interactions between MAOA and 5-HTTLPR with distal and proximal stress are discussed in text. Finally, a brief discussion of preliminary findings of gender-specific alcohol dependence models and sex-role specific alcohol use, binge drinking, and alcohol use age of onset is provided.

Chapter 5 discusses these results in context of previous literature and implications of the current dissertation are highlighted. Limitations of the current dissertation are then discussed along with a proposal for future research to extend the current body of knowledge. Finally, this dissertation concludes with a call to examine alcohol use behaviors in light of genetic and environmental influences throughout the life course.

CHAPTER II

Literature Review

Definitional Issues Associated with Alcohol Use Behaviors and Disorders

Collectively, the history of clinical definitions surrounding alcohol-related disorders have undergone three distinct periods. The alcoholism period was largely marked by ambiguity in definition (DSM-I and DSM-II). The dependence/abuse period advanced how alcohol-related disorders were regarded (DSM-III and DSM-IV). This period made a clear distinction between drinking that induced problems in daily life as indicated by abuse from more severe and individualistic drinking issues that were characterized by withdraw, tolerance, and increase use as indicated by dependence. The alcohol use disorders period has recently emerged and has favored one overarching diagnosis as opposed to the dependence/abuse differentiation (DSM-V).

Rationale for merging dependence and abuse into alcohol use disorder has been provided by the DSM-V Substance-Related Disorders Work Group (Hasin et al., 2013). Generally, it is thought that the previous hierarchical structure of the DSM-IV regarding abuse and dependence was problematic. Specifically, if an individual met diagnostic criteria for dependence, a diagnosis of abuse was not to be given. This practice led many to assume abuse always accompanied a diagnosis of dependence, however, this was thought to be a problematic assumption especially in regard to the diagnosis of women who are more likely to present dependence symptoms without the presence of abuse symptoms (Hasin & Grant, 2004; Hasin, Hatzenbueler, Smith, & Grant, 2005). Further, while only the presence of one symptom was necessary for an abuse diagnosis, three or more symptoms were necessary for a dependence diagnosis. As such, the threshold for

diagnosis of abuse was much lower than that of dependence. Thus, many individuals meeting two dependence criteria presented drinking-related problems but were left untreated due to non-diagnosis (Hasin & Paykin, 1998; McBride, Adamson, Bunting, & McCann, 2009; Pollock & Martin, 1999). Specification of severity thus allows for such individuals to meet diagnostic criteria with a lower number of symptoms present. Evidence suggests that diagnosis is relatively stable across DSM-IV and DSM-V criteria with the exception of those meeting only abuse diagnosis with DSM-IV criteria (Slade et al., 2016). Generally, a slightly lower prevalence of diagnosis occurs with DSM-V as compared to DSM-IV criteria (Slade et al., 2016)

Beyond clinical definitions of alcohol-related disorders, researchers have analyzed alcohol-related behaviors through a variety of definitions. Alcohol use generally refers to the frequency with which an individual consumes alcohol (e.g., numbers of days per year) but has also generalized to encompass alcohol consumption (e.g., the amount of alcohol consumed over a time period). Binge drinking is formally defined by 5 or more alcoholic beverages (i.e., 12 ounces of beer, 5 ounces of wine, or 2 ounces of hard liquor) by men within 2 hours or 4 or more alcoholic beverages in 2 hours by women (NIAAA, 2004). Heavy episodic drinking relates similarly to binge drinking but does not make the gender distinction between males and females (i.e., 5 or more alcoholic beverages in 2 hours). Alcohol-related problems and problem drinking generally relate to some external issues surrounding use of alcohol, similar to alcohol abuse definitions from formal DSM criteria. Given the nuances of these definitions, each of these terms will be cited throughout this dissertation in an effort to most precisely identify the definition used by original study authors.

Environmental Influences on Alcohol Use Behaviors: Stress and Gender Variation

The causes and correlates of between individual variation in rates and prevalence of alcohol use and abuse has been widely studied from medical, psychological, and criminological perspectives. The most well studied correlates of alcohol use include peer drinking behavior (Bray, Adams, Getz, & McQueen, 2003; Mason & Windle, 2001), low school attachment (Henry & Slater, 2007), lax parenting styles and low parental support (Hoffmann & Bahr, 2014; Mason & Windle, 2001), and low religiosity (Hoffmann & Bahr, 2014; Mason & Windle, 2001). Additionally, the bulk of explanations concerning the greater use of alcohol among males than females focuses on how these risk factors occur more frequently in males than females. Although these explanations may explain alcohol use, much of their predictive power is limited to adolescent and early adulthood drinking behavior. Of interest in the current dissertation, exposure to both distal and proximal stressors may impact alcohol use throughout the life course. Further, exposure to stress may influence both normative and severe alcohol use trajectories.

Stress will be referred to as "the nonspecific response of the body to any demand" (Selye, 1976, p. 53), a definition still highly regarded and largely unchanged across decades. This section will first review the deleterious effects of distal and proximal stress. While these effects are fairly ubiquitous, attention will be given to how gender impacts these experiences. Specifically, prior research that examines whether males and females are differentially affected by the experiences of varying sources of stress will be reviewed. Section two of this chapter will highlight the direct impact of biological factors on alcohol use and dependence with a focus on two polymorphisms in the serotonin system, 5-HTTLPR and MAOA. Section three of this chapter will present a systematic

literature review of how these environmental and biological factors interact. Gene-environment interaction studies (GxE) of 5-HTTLPR and MAOA in interaction with distal and proximal stress will also be detailed. Following, the stress sensitization model will be reviewed and a genetically moderated stress sensitization model will be proposed as the guiding framework for the current research.

Cross sectional effects of stressors. Adverse childhood experiences (ACEs), as established by Felliti et al. (1998) in a seminal study of the effects of children's exposure to risk environments, include both various forms of childhood abuse as well as household dysfunction such as spousal abuse and substance use within the home. These forms of childhood stress have been found to be associated with a host of problematic outcomes both during childhood and later in life including alcohol-related behaviors and disorders. Dube et al. (2003) found that for each additional ACE experienced, the likelihood of early illicit drug initiation more than doubled on average. ACE exposure also increases the risk of early initiation of alcohol use (Dube, Miller, Brown, Giles, Felitti, Dong, & Anda, 2006). Increased risk of early initiation of use is vitally important as early onset alcohol use is associated with later life alcohol use (DeWit, Adlaf, Offord, & OGborne, 2000; Grant & Dawson, 1997; Grant et al., 2006; Labouvie et al., 1997) and alcohol related disorders (Brook, Brook, Zhang, Cohen, & Whiteman, 2002; DeWit, Adlaf, Offord, & OGborne, 2000) even after controlling for genetic and shared environmental influences such as parenting (Grant et al., 2006). Further research into the impact of ACEs has revealed that the effects of these experiences are not limited to early onset of alcohol use; rather, ACE experience is also associated with increases in general drug use, drug addiction, alcohol dependence, and problem drinking (Dube, Anda, Felitti, Edwards,

& Croft, 2002; Dube, Felitti, Dong, Chapman, Giles, & Anda, 2003; Felitti et al., 1998; Pilowsky, Keyes, & Hasin, 2009; Strine et al., 2012).

While ACEs encompass a large number of risk environments, the most salient environmental risk factors are those of abuse. Childhood physical and sexual assault have been found to be positively associated with adolescent alcohol dependence and alcohol abuse (Afifi, Mota, Dasiewicz, MacMillan, & Sareen, 2012; Kilpatrick, Acierno, Saunders, Resnick, Best, & Schnurr, 2000) as well as early onset alcohol use (Hamburger, Leeb, & Swahn, 2008; Rothman, Edwards, Heeren, & Hingson, 2008; Sartor, Lynskey, Bucholz, McCutcheon, Nelson, Waldron, & Heath, 2007). Further, research has suggested that the experience of more than one type of abuse in childhood, known as polyvictimization, increases the risk of DSM-IV criteria alcohol abuse (Ford, Elhai, Connor, Frueh, 2010) and heavy drinking in adolescents (Bensley, Spieker, van Eenwyk, & Schoder, 1999). Those examining childhood sexual abuse specifically have also found significant positive associations between abuse and alcohol dependence (Anda et al., 2002; Molnar, Buka, & Kessler, 2001).

Among adults, childhood abuse and neglect are also important in the explanation of alcohol use behaviors. Childhood maltreatment and parental use of force were found to be associated with excessive alcohol use in a New Zealander sample of emerging adults (Fergusson & Lynskey, 1997). In a nationally representative study of Americans, analyses of Add Health's Wave III data (when participants were between the ages of 18 and 26) found that each type of maltreatment was associated with an increased risk of regular alcohol use and binge drinking (Hussey, Chang, & Kotch, 2006) even after

accounting for age, gender, race, parental monitoring, and parental alcohol use (Shin, Edwards, & Heeren, 2009).

The association between distal stress with alcohol use may depend, in part, on the developmental stage of the individual. Stronger effects of adolescent and persistent maltreatment on combined drug use and problem drinking have been detected when compared to maltreatment isolated in earlier childhood (Ireland, Smith, & Thornberry, 2002; Thornberry, Ireland, & Smith, 2001). Other work also utilizing the Rochester Youth Development Study but analyzing drug and alcohol problems separately have found that while childhood-limited maltreatment is associated with drug use, adolescent maltreatment is associated with both drug use and problem drinking, suggesting that later onset maltreatment of children may be a more salient predictor of later alcohol-related behaviors (Thornberry, Henry, Ireland, & Smith, 2010).

While research suggests that the distal environment of childhood abuse has a lasting effect on alcohol use, proximal stressors such as life stress and negative life events may also be critical in explaining alcohol use. Proximal stressors are those stressors that occur closer in temporal distance between experience of the stressor and alcohol use. Among adults, stressful life events include familial, friendship, or romantic trouble, financial strain, and crime victimization. These stressors along with lab-induced social stress have been found to increase risk of alcohol use and problem drinking (Boden, Fergusson, & Horwood, 2014; Carney, Armeli, Tennen, Affleck, & O'Neil, 2000; Cole, Tucker, & Friedman, 1990; King, Bernardy, & Hauner, 2003; Magrys & Olmstead, 2015). Experiences of assault victimization have also been found to increase the risk of alcohol use (Kilpatrick et al., 2000; Kilpatrick et al., 1997). In a small study of women (n

= 99), life stress was associated with alcohol use even after controlling for childhood sexual abuse exposure (Sartor & O'Malley, 2016). The timing of proximal stressors is also thought to be important. Research suggests that stress-related frequency of drinking is more prominent in early adulthood while the amount of alcohol consumed as a coping mechanism for stress is higher in post-undergraduate stages (Perkins, 1999).

Longitudinal effects of stressors. Research suggests that few individuals abstain from alcohol use across their life course (Kerr, Fillmore, & Bostrom, 2002). Rather, the majority of individuals initiate alcohol use in adolescence, with patterns of heavy drinking typically occurring in the early 20's, followed by rapid desistence thereafter (e.g., Costanzo et al., 2007; Englund, Egeland, Oliva, & Collins, 2008). Of particular interest to the current study is a trajectory that deviates from this common pattern wherein there is an escalation of alcohol use throughout the life course, ultimately leading to alcohol dependence. Similar to the literature on between-individual differences in substance use, research has highlighted many domains of influence on within-individual change in substance use. While studies of the association between childhood abuse and neglect with alcohol use have been largely cross sectional, some evidence suggests that childhood abuse contributes to lifetime alcohol use. In a sample of Mexican women, for example, childhood abuse was found to be associated with lifetime alcohol consumption (Frias-Armenta, 2002).

In an important longitudinal study of the effects of subtypes of childhood abuse over the life course, Shin, Miller, and Teicher (2013) examined the effects of two subtypes of childhood abuse (i.e., physical, emotional) individually and in conjunction with one another reported before the age of 16. Additionally, sexual abuse was examined

but only in conjunction with other subtypes of abuse. Using data from four waves of the Add Health, two-level growth-curve models examined the impact of each of these types of abuse on heavy episodic drinking (HED). Childhood neglect and physical abuse individually and in conjunction with each other were found to be significantly associated with initiation and change in HED across time. No significant effect of sexual abuse in conjunction with other subtypes of abuse was found. Problematically, however, Shin, Miller and Teicher (2013) failed to account for temporal ordering of abuse exposure and HED. That is, abuse was measured by the prevalence and frequency of exposure before the age of 16 while HED was measured in all four waves of which some participants were under the age of 16 in two of these waves. As such, levels of HED and change in HED in Waves I and II may have occurred prior to the exposure of childhood abuse and thus cannot be said to be influenced by future abuse.

Despite this evidence, some literature suggests that while childhood abuse is an important predictor of alcohol use initiation, and that alcohol use initiation is associated with trajectories leading to alcohol dependence (Brook, Brook, Zhang, Cohen, & Whiteman, 2002; DeWit, Adlaf, Offord, & OGborne, 2000), there is no direct association between childhood abuse and alcohol dependence after controlling for this effect (Sartor, Kynskey, Heath, Jacob, & True, 2007; Sartor, Lynskey, Bucholz, McCutcheon, Nelson, Waldron, & Heath, 2007). Further, longitudinal examinations of alcohol use trajectories from middle to late adulthood suggest that the effect of childhood abuse is limited to absolute levels of alcohol use but does not explain variation in the slope of decrease of use across this age range (Leung, Britton, & Bell, 2016).

Confounds. Despite fairly consistent evidence that distal and proximal stressors are associated with increased alcohol use and more deleterious alcohol use trajectories, it is possible that this association may be confounded by factors outside of the measurement of many studies. In regard to the distal stress association, these confounds include correlations between childhood abuse and other risk factors including parental attachment, parental education, socioeconomic status, and shared genetic factors (Grant et al., 2006; Shin, Miller, & Teicher, 2013). Further, evidence suggests that childhood abuse experiences increase the likelihood of future experiences of victimization (Gomez, 2011; Turner, Finkelhor, & Ormrod, 2010), a finding particularly salient among females (Widom, Cqaja, & Dutton, 2014). Given this continuity of victimization experience, it is difficult to determine whether alcohol use behaviors are influenced by childhood abuse, proximal stress, or both.

For the purposes of the current review, the genetic confounds are of primary interest as they are outside the realm of incurring childhood stress and may have long lasting, often unmeasurable effects. In regard to the proximal stress association, these confounds include the presence of depression, and a potential reciprocal relationship wherein stress may lead to alcohol use and, consequently, more stress exposure (Brennan et al., 1999; Hart & Fazaa, 2004). While the presence of depression is often easily controlled for with additional measures, accurate temporal ordering of proximal stress and alcohol use is often unestablished as doing so requires adequate longitudinal data and thus this confound is of primary interest.

As previously discussed, there is a moderate to large heritability component of alcohol-related disorders, with approximately 50% of the variance attributable to genetic

factors (Verhulst, Neale, & Kendler, 2015). Evidence suggests that a passive gene-environment correlation may explain both why individuals with parents who are abusive and parents who use alcohol problematically are themselves at heightened risk for problematic alcohol use behaviors. That is, there is an increased risk for severe patterns of alcohol use that may also explain a heightened likelihood for an individual to be exposed to childhood abuse. Individuals having substance abusing parents have been consistently found to be at an increased risk for exposure to problematic parenting behavior (Anda et al., 2002; Kettinger et al., 2000; Stanger et al., 2004; Suchman et al., 2007, 2008). In fact, Dube et al. (2001) found that the likelihood of ACE experience was between two and thirteen times higher for children raised in families where one or both parents abused alcohol, with the highest risk occurring for children with two alcohol abusing parents.

While this could be explained as a cycle of violence with deference given only to generational exposure to abuse and subsequent problematic alcohol use, other methodological approaches further strengthen the assertion of a potential passive gene-environment correlation. Controlling for ACE exposure, individuals in environments with alcohol dependent parents are more likely to display alcohol abuse (Anda et al., 2002). In a longitudinal study, after controlling for genetic relatedness in female twins, the association between childhood sexual abuse and alcohol-related disorders was not found, leaving to question whether distal environmental risk exposure is causally related to alcohol-related disorders (Bulik, Prescott, & Kendler, 2001). In contrast to these findings, other research suggests that there exists a residual effect of experiencing childhood abuse, beyond passive gene-environment correlations. Studies controlling for parental alcohol

use have found a significant association between childhood abuse and maltreatment with later alcohol-related disorders (Nelson et al., 2002; Shin, Edwards, & Heeren, 2009; Young-Wolff, Kendler, Ericson, & Prescott, 2011).

The ability of stress to influence alcohol use has been challenged by a potential reciprocal relationship. It has been acknowledged that not only may life stress increase alcohol use but also that alcohol use may increase life stress (Brennan et al., 1999). This effect has been termed an alcohol contaminated effect (Hart & Fazaa, 2004). Without the use of sound methodology and statistical modeling, the temporal ordering of the stress-alcohol use association may be unclear. Indeed, in a study examining this potential confounding association, it was found that stressful life events unrelated to alcohol use were associated with alcohol use to a far lesser extent than life events that may be impacted by alcohol use (Hart & Fazaa, 2009). Contrary to the assertions of an alcohol contamination effect, in a comparison of varying longitudinal models, a recent study found a better model fit where stress predicted alcohol use rather than the reciprocal effect (Boden, Fergusson, & Horwood, 2014). As such, while stress may initially precede alcohol use, future stress within the control of the individual may be exacerbated by alcohol use and thus models aiming to evaluate the effects of stress on alcohol use may avoid this confound by modeling longitudinal reciprocal effects or analyzing exposure to stressors that cannot be controlled by the individual.

Gender

While it is clear that distal and proximal stress has deleterious consequences for individuals, evidence suggests that these effects may vary across gender and source of stress. These differences may be the result of gender differences in the number of

stressful experiences and gender differences in the salience of stressful experiences. As such, the role that stress plays in explaining alcohol-related disorders is unlikely to generalize across gender. Rather, the etiology of alcohol-related disorders may differ for males and females.

While general strain theory suggests that all individuals engage in criminal behavior as a coping mechanism for failure to achieve goals (Agnew, 1992), Broidy and Agnew (1997) extend this idea to explain gender differences in the rate of crime. Specifically, they argue that strain may explain gender differences in offending due to variation across males and females in the amount and sources of strain as well as the emotional and behavioral responses to that strain. As will be reviewed, although females typically report greater exposure to strain, Broidy and Agnew (1997) argue that males are more likely to respond with overt criminal and violent behavior whereas females are more likely to cope with strain through introverted mechanisms such as substance use. Although alcohol use frequency has been consistently found to be greater among males, the use of alcohol in response to exposure to strain may be more prevalent among females.

Further, although studies assessing variation in stress and the effects of stress and strain have largely focused on gender, careful consideration of how socialization of sex roles may affect the experience of stress and ultimately gender variation in alcohol-related behaviors is needed. Ultimately, the effects of stress on alcohol-related behaviors may vary as a function of both gender and the socialization of sex roles.

Gender differences in the number of stressful experiences. Research examining the lives of males and females suggests that there are gender differences in the

amount of stress an individual experiences. Peer victimization, such as social and physical bullying, has been found to disproportionately be perpetrated against males (Friedman, Marshal, Guadamuz, Wei, Wong, Saewyc, & Stall, 2011; Seals & Young, 2003; Wolke, Woods Stanford, & Schultz, 2001). Females, on the other hand, have been found to be more greatly victimized by overt types of abuse. Specifically, institutional and community based samples find that females are at greater risk for victimization through physical childhood abuse and childhood sexual abuse (Dube, Anda, Whitfield, Brown, Felitti, Dong, & Giles, 2005; Friedman, Marshal, Guadamuz, Wei, Wong, Saewyc, & Stall, 2011; Lake, 1995; McClellan, Farabee, & Crouch, 1997; but see Thompson, Kingree, & Desaid, 2004). The gender disparity in victimization of childhood abuse is lesser in regard to emotional abuse (Corliss, Cochran, & Mays, 2002).

Generally, research finds that females are also more frequently exposed to proximal stressors. In a longitudinal study of adolescents, females reported greater exposure to stressful life events, particularly social stressors (Hankin, Mermelstein, & Roesch, 2007). In a study examining gender differences in stress, while males and females were found to report the same number of stressful life events, females reported more chronic stress and a higher frequency of minor daily stressors than males (Matud, 2004).

This gender variation in experience of stressful life events may vary as a function of measurement, however. In an analysis of gender differences in specific types of proximal stressors, Kendler et al. (2001) found that while females were disproportionately exposed to social stressors (e.g., social conflicts, illness of or loss of a confidant) males reported higher levels of occupational and financial stress (e.g., loss of a

job, robbery, work problems). Others, however, have reported no gender differences in levels of occupational stress exposure across gender (Galanakis et al., 2009; McLaughlin, Conron, Koenen, & Gilman, 2010). Hatch and Dohrenwend (2007) further report that while males and females experience similar levels of exposure to stressful life events, the sources of stress vary across gender with males reporting more exposure to traumatic life threatening events with the exception of rape and females reporting more romance-related stress and stress related to deaths of others.

Gender differences in the salience of stressful experiences. Not only are females more likely to experience abuse, the salience with which abuse is experienced is generally found to be greater among females as well. That is, abuse among females is generally more likely to result in problematic health and behavior than among males. Variation in biological maturation at varying points in the life course of males and females may contribute to differentiation of stress response (Bale & Epperson, 2015). Measurements of biological reactivity to stress suggest that females have greater stress responsivity than males, particularly concerning social stressors as opposed to performance stressors (Stroud, Papandonatos, D'Angelo, Brush, & Lloyd-Richardson, 2017).

In regard to the varying effects on health, the detrimental effects of childhood physical abuse on long term health were found to be greater among females than males (Thompson, Kingree, & Desai, 2004). In regard to psychological outcomes, psychosis has been found to be predicted by childhood physical and sexual abuse among females but not among males, with a stronger effect for physical abuse (Fisher et al., 2009), while childhood sexual abuse has been found to be more strongly associated with suicide

attempts among females than males (Bebbington, Cooper, Minot, Brugha, Jenkins, Meltzer, & Dennis, 2009).

For substance-related disorders, the interaction between gender and the effects of distal stressors are more nuanced (Fagan, 2001). In a longitudinal study of American adults, an association between childhood sexual assault and binge drinking was found for females but not for males (Skinner, Kristman-Valente, & Herrenkohl, 2015). In a French sample, it has been found that parental control and emotional support have stronger contributions to female alcohol use than males (Choquet, Hassler, Morin, Falissard, & Chau, 2008). MacMillian et al. (2001) found an association of physical or sexual abuse with lifetime prevalence of illicit drug abuse/dependence for females only. In males, the abuse-substance use association was found only between childhood sexual abuse and alcohol abuse/dependence (MacMillan et al., 2001). Conflicting results have been found wherein an association between childhood sexual abuse and alcohol dependence has been found for both males and females but an association with alcohol problems found only among females (Molnar, Buka, & Kessler, 2001). Further evidence suggests that childhood maltreatment is more strongly associated with substance dependence among females than among males (McClellan, Farabee, & Crouch, 1997; Widom & White, 1997).

Results are mixed in regard to gender differences in the salience of proximal stressors. In a study in which men and women reported equal number of experiences of life stress, the negative effects of that stress including psychological distress and somatic symptoms were reported to be higher among females than males (Matud, 2004). Other results examining alcohol use directly also suggest that females are more strongly

impacted by stress than males (Boden, Fergusson, & Horwood, 2014; King et al., 2003; Rospenda et al., 2008). In a laboratory stress test, although no gender difference was found in the change in alcohol cravings pre- and post- stressor, an increase in alcohol cravings was found only among males who reported feeling more stress subjectively (Chaplin, Hong, Bergquist, & Sinha, 2008).

Despite these findings, others contrarily suggest that stress among males is more likely to lead to alcohol use than stress among females (Dawson, Grant, & Ruan, 2005; San Jose, Van Oers, Van De Mheen, Garretsen, & Mackenbach, 2000), particularly in regard to occupational stress. For example, more thorough examination of the effects of stress on alcohol-related behaviors suggests that gender differences in the effects of stress may depend on the source of stress. In an examination comparing general life stress and occupational sexual and general harassment, life stress was more strongly associated with alcohol use among females than among males whereas harassment was more strongly associated with alcohol use among males (Rospenda, Fujishiro, Shannon, & Richman, 2008).

Biological sex and socialization of gender. Both biological sex and socialized sex roles may influence variation in stress and alcohol use. Literature consistently finds that males are more likely to engage in alcohol use than females (Brady & Randall, 1999; Cotto, Davis, Dowling, Elcano, Staton, & Weiss, 2010) although this gap is diminishing (Keyes et al., 2010). One explanation for this finding is that alcohol use is engrained in stereotypical male behavior in that alcohol use is one expression of masculinity (Landrine, Bardwell, & Dean, 1988).

This association, however, may be more nuanced. A recent comprehensive review of the literature found that while femininity is largely negatively associated with alcohol use, low adherence to femininity is a protective factor for alcohol use disorder (Brady, Iwamoto, Grivel, Kaya, & Clinton, 2016). Some contrary evidence suggests that diminished sex role differentiation, however, is a risk factor. In a case-control comparison of 120 alcoholic and non-alcoholic women, non-alcoholic women were characterized by higher levels of masculinity while alcoholic women were characterized by undifferentiated sex role expression (Sorell, Silvia, & Busch-Rossnagel, 1993; see also Kroft & Leichner, 1987). As such, while drinking behaviors may be encouraged by masculine stereotypes, more chronic alcohol-related disorders may be associated with a lack of sex role expression.

Some have suggested that the differentiation of sex roles explains variation in stress experiences rather than a true biological difference (Lundberg, 2005) although results from current literature are inconclusive. In an analysis of the amount of variance explained by sex and sex roles, Gianakos et al. (2002) did not find an association between femininity and masculinity as measured by the Bem Sex Role Inventory (BSRI) with alcohol use. They did, however, find that males were more likely to use alcohol than females in a college sample (Gianakos et al., 2002). Also using a college sample, Lengua and Stormshak (2000) found no gender difference in substance abuse but a positive association between masculinity and substance abuse. Others have sought to explain this association beyond direct effects. Specifically, Huselid and Cooper (1992) sought to explain how gender influences alcohol use through sex roles. Among adolescents, sex roles mediate the association between gender and alcohol use (Huselid & Cooper, 1992).

Sex roles may impact alcohol use beyond direct gender differences as adherence to sex roles may influence exposure to various types of stress. For example, quality of employment is significantly lower among females than males (Stier & Yaish, 2014). Because stress is experienced more greatly in lower level positions through both an imbalance of job demand and control as well as work effort and reward (Bakker & Demerouti, 2007; Campos-Serna, Ronda-Perez, Arazcoz, Moen, & Benavides, 2012), the gender roles that contribute to variation in career placement may contribute to the amount of stress experienced (Mayor, 2015).

Finally, as previously discussed, general stress exposure is associated with an increase in alcohol use (Boden, Fergusson, & Horwood, 2014; Carney, Armeli, Tennen, Affleck, & O'Neil, 2000; Cole, Tucker, & Friedman, 1990; King, Bernardy, & Hauner, 2003; Magrys & Olmstead, 2015). Variation in gender norms surrounding alcohol expectancies may influence the likelihood that an individual will engage in alcohol use as a coping mechanism for stress. In a sample of adult drinkers (n = 1316) examining gender differences in the stress-alcohol use association, it has been found that males who anticipated positive outcomes of alcohol use drank more following stress while, for females, alcohol expectancies did not influence the stress-alcohol use association (Cooper, Russell, Skinner, Frone, & Mudar, 1992). These findings have since been replicated in multiple small samples of adults (n = 88: Armeli, Carney, Tennen, Affleck, & O'Neil, 2000), college students (n = 84: Kidorf & Lang, 1999) and adolescents (n = 184: Laurent, Catanzaro, & Callan, 1997). In a longitudinal study of 485 individuals, the effect of alcohol expectancies on heavy drinking has been found to not only be limited to males, but also to those very near age 21 (S.D. = .93; Rutledge & Sher, 2001).

Overall, the greater prevalence and salience of stressful experiences among females is directly contrary to the greater prevalence of alcohol use and dependence among males and masculine gender roles. This juxtaposition has been explained largely through evidence suggesting that femininity is associated with higher levels of engaging in more effective coping mechanisms (Gonzalez-Morales, Peiro, Rodriguez, & Greenglass, 2006; Ogus, Greenglass, & Burke, 1990; Vermeulen & Mustard, 2000) although some research suggests that this varies by gender rather than sex role (Gianakos, 2000).

Summary

As has been discussed, childhood abuse has been consistently found to increase both adolescent and adult alcohol use. Similarly, but with less consistency, life stress increases risk for alcohol use. Both biological sex and sex role expression have been found to contribute to both an individual's level of stress exposure and the salience of such exposure on alcohol use. Cumulatively, distal and proximal stressors are critical in the development of alcohol use behaviors. Additionally, as will be reviewed in the following section, risks for alcohol use are not limited to environmental risk exposure. Rather, certain biological factors may contribute both to alcohol use as well as affect the salience of stress on alcohol use.

The Role of Biology in Alcohol Use and Dependence

While distal and proximal stress are important antecedents of alcohol use disorders, the etiology of alcohol use extends beyond these environmental associations. Estimates of the heritability of alcohol dependence range from 40% to 60% (Heath et al., 1997; Kendler, Prescott, Neale, & Pedersen, 1997; Prescott & Kendler, 1999) with a

recent meta-analysis finding that approximately 49% of the variance in alcohol use disorders were attributable to additive genetic factors (Verhulst, Neale, & Kendler, 2015). With such a significant portion in the variance in alcohol dependence being attributable to genetic components, close examination in how specific genetic factors infer risk or protection from alcohol dependence is necessary to fully understand the etiology of this disorder and alcohol-related behaviors that contribute to this disorder. This section will detail the neurobiological underpinnings of alcohol related behaviors and disorders.

Neurobiology of addiction: A brief introduction. Adolescence characterizes a critical period of experimentation and learning for humans. Overlapping neurological developmental processes prime individuals for reduced harm avoidance and increased motivation (Casey & Jones, 2010; Chambers, Taylor, & Potenza, 2003). These two routes of information processes are referred to as top-down and bottom-up processing, respectively. Top-down processing refers to mechanisms designed to control behavior and direct goal-oriented behaviors and is particularly guided by prefrontal cortical regions. Bottom-up processing refers to mechanisms designed to enhance motivation. Models of development of these neurological processes have supported varying maturational trajectories of top-down and bottom-up processing wherein maturation of top-down processing follows a linear trajectory into adulthood while bottom-up processing matures much quicker, peaking in early adolescence, on average (Casey & Jones, 2010; Ernst, Pine & Hardin, 2006; Geier & Luna, 2009; Steinberg, 2008). Indeed, this developmental trajectory of top-down and bottom-up processing mirrors that of self-report impulsivity and sensation seeking, respectively (Steinberg et al., 2008). As such, the motivation to seek sensations such as those provided by alcohol use is not adequately

controlled by cortical regions responsible for curbing decisions leading to problematic decisions concerning use (Casey & Jones, 2010; Chambers, Taylor, & Potenza, 2003). Motivational and incentive based reward systems are activated above that in the already heightened normal range for adolescents with the use of substances (Hardin & Ernst, 2009).

This is highly problematic given evidence that adolescent-onset substance abuse is a risk factor for increased use into adulthood (DeWit, Adlaf, Offord, & OGborne, 2000; Grant & Dawson, 1997; Grant et al., 2006; Labouvie et al., 1997). This encoding of alcohol use behavioral patterns may be related to disruption of myelination processes and neurogenesis and synaptic pruning that occurs throughout adolescence (Blakemore & Choudhurt, 2006; Witt, 2010). Myelination, or the growth of myelin sheaths which allow for quicker transmission of neuronal signals, continues to occur in the prefrontal cortical neurons into adolescence (Barnea-Goraly et al., 2005; Sowell, Thompson, Holmes, Jernigan, & Toga, 1999). As such, disruption of this process may have long term effects on control of alcohol related behaviors. Further, through a process of synaptic pruning, neuronal connections that are infrequently used are abandoned (Crews & Hodge, 2007) while those that are used remain. Thus, neuronal pathways associated with alcohol related behaviors may be reinforced by early frequent alcohol use due to an increased frequency of use of such pathways. Synaptic pruning occurs throughout the life course but occurs at a greater rate at younger ages (Gogtay et al., 2004) and thus early onset alcohol use may impact processes of synaptic pruning more than alcohol use later in life. Together, these processes suggest that early onset alcohol use, or use above normative levels may contribute to long term patterns of alcohol related behaviors and disorders (Chambers,

Taylor, & Potenze, 2003). As such, understanding of the genetic and environmental influences to variation in alcohol use onset is critical to understanding of trajectories of alcohol use onset.

Beyond continuity and escalation of use, adolescent alcohol use is also associated with neurodegeneration within brain regions responsible for learning and memory such as the hippocampus and prefrontal cortex (De Bellis et al., 2000; Witt, 2010; Zeigler et al., 2005) and thus may consequently lead to a failure to encode negative memories associated with alcohol use. For instance, in a matched case-control design of those with alcohol use disorder and normal controls, De Bellis et al. (2000) found reduced hippocampal volumes among those with alcohol use disorder, a brain region critical in the formation of memory. Even into adulthood, age of use moderates the association between alcohol use and diminished memory formation (Acheson, Wtein, & Swartzwelder, 1998). This can contribute to a failure to encode memories concerning the negative effects of alcohol and thus prolong or intensify alcohol use trajectories.

The role of serotonin and serotonergic genes in addiction. To date, dopaminergic function has been of central focus in the etiology of alcohol dependence. Dopamine has been a central focus due to its critical role in motivation (Di Chiara, 1995; Wise, 2004) and alteration in dopamine reception following prolonged alcohol use (Bowirrat & Oscar-Berman, 2005; Noble, Blum, Ritchie, Montgomery, & Sheridan, 1991; Volkow et al., 1996). Dopamine function is highly important in the formation of addictive related behaviors (e.g., see Conner, Pinquart, & Gamble, 2009; Munafo, Matheson, & Flint, 2007).

While dopaminergic functioning may be crucial to the continuation of use, dopamine is unable to account for the consistent association found between distal and proximal stress exposure and alcohol-related behavior initiation and progression. The current study is thus focused upon the role of serotonergic polymorphisms due to the role of serotonin in the stress response system that may lead to alcohol use. Serotonin and serotonergic polymorphisms are critically important in processing stress (Caspi, Hariri, Holmes, Uher, & Moffitt, 2010; Cloninger, 1987; Fuller, 1992; Mueller, Crocke, Fries, Lesch, & Kirschbaum, 2010). Indeed, a recent meta-analysis of studies from 11 datasets found that s/s homozygotes of 5-HTTLPR displayed increased hypothalamic-pituitary-adrenal (HPA) axis reactivity to stress, indicating that s/s homozygotes were more physiologically affected by the presence of stress (Miller, Wankerl, Stalder, Kirschbaum, & Alexander, 2013). As such, s/s homozygous individuals may be more affected by the presence of environmental stressors than individuals carrying s/l or l/l genotypes of 5-HTTLPR. As will be discussed in a subsequent section, because certain variants of polymorphisms implicated in serotonergic functioning increase stress reactivity, examination of how serotonin affects alcohol use is critical, particularly in light of interactions between 5-HTTLPR and stress in alteration of hippocampal volume, critical to development of addictive behaviors (Rabl et al., 2014).

5-HTTLPR. A variable number tandem repeat polymorphism within the promoter region of the serotonin transporter gene (SLC6A4), 5-HTTLPR, has been implicated in serotonergic functioning (Lesch et al., 1996; Heinz et al., 2000; Little et al., 1998) with some evidence of gender-specific effects in that female MAOA-L carriers show varied neurological processing of negative emotions as compared to MAOA-L males (Williams

et al., 2003). Because serotonergic functioning may be related to alcohol use, and because 5-HTTLPR genotype influences serotonergic function, 5-HTTLPR may be related to alcohol-related behaviors. A discussion of results pertaining to how 5-HTTLPR relates to psychological and behavioral outcomes including alcohol-related behaviors follows.

Functionally, 5-HTTLPR is responsible for signaling messenger RNA (mRNA) to transcribe the gene encoding for serotonin transporter (5-HTT) from DNA to RNA and ultimately to production of serotonin transporters. The two most common variants of 5-HTTLPR are a short (s) allele and a long (l) allele (Heils et al., 1996). The s-allele is approximately 14 repeats and 376 base pairs in length while the l-allele is approximately 16 repeats and 419 base pairs in length (Heils et al., 1996). Allele frequencies have varied by ethnicity. Gelernter, Kranzler, and Cubells (1997) reported that among African Americans, European Americans, and Japanese samples, s-alleles accounted for 25.4%, 40.4%, and 80.2% of all 5-HTTLPR alleles, respectively. In examining genotype frequencies, as each individual carries two 5-HTTLPR alleles with the most common genotypic frequencies being s/s, s/l, and l/l, a comparison of Caucasian and Japanese allele frequencies found that approximately 20.3% and 61.9% were s-allele homozygotes, 31.1% and 0.8% were l-allele homozygotes, and 69.1% and 31.4% were s/l heterozygotes, respectively (Nakamura, Ueno, Sano, & Tanabe, 2000). Even among populations of European decent, significant cross-ethnic variation in genotypic frequency have been found (Noskova et al., 2008). There appears to be no significant cross-gender genotypic frequency (Noskova et al., 2008; Szekely et al., 2004) though there is some evidence for variation in cross-gender functionality wherein male MAOA-L carriers process anger and negative emotions primarily in the medial frontal, parietal, and

superior temporo-occipital regions of the brain while females process these emotions disproportionately in the superior occipital cortex (Williams et al., 2003).

Due to reduced signaling from the s-allele, less transcription of the serotonin transporter gene occurs as compared with the increased signaling from the l-allele and thus greater transcriptional efficacy (Ehli et al., 2012; Heils et al., 1996; Hu et al., 2006; Iurescia et al., 2015; Lesch et al., 1996). As such, s-alleles of the 5-HTTLPR polymorphism have been associated with a reduction in 5-HTT and thus a reduction in serotonin reuptake (Heils et al., 1995; Lesch & Mossner, 1998).

As one of the most widely studied polymorphisms in the human genome, several studies have examined whether 5-HTTLPR polymorphism is associated with alcohol-related behaviors. A recent meta-analysis of 11 studies has suggested that the homozygous s-allele is associated with increased risk of alcohol dependence (Oo, Aung, Jenkins, & Win, 2016; see also Feinn, Nellissery, & Kranzler, 2005). These findings echoed those of previous meta-analyses of alcohol dependence (McHugh, Hofmann, Asnaani, Sawyer, & Otto, 2010) and those extending the outcome variable of interest beyond alcohol dependence to include alcohol abuse and severe alcoholism (Cao, Hudziak, & Li, 2013). Although in one meta-analysis, no association between 5-HTTLPR and Type II alcoholism was detected, a subtype of alcoholism characterized by stronger intergenerational effects as compared to the more environmentally influenced Type I alcoholism (Cao, Hudziak, & Li, 2013). Importantly, while analyses suggest an association between the s-allele and alcohol-related behaviors, the genotype inferring risk varied across population ethnicity with African American populations showing a positive association between the l-allele of 5-HTTLPR for illicit drug use as compared to the s-

allele in European, Asian, and Mexican populations (Cao, Hudziak, & Li, 2013; but see McHugh et al., 2010).

In studies not included in this meta-analysis that examined the effects of 5-HTTLPR on binge drinking, results concerning the association between 5-HTTLPR and alcohol-related behaviors have been mixed. In examination of the relationship between 5-HTTLPR and alcohol-related behaviors, studies suggest increased risk of binge drinking and frequency of alcohol use for s/s homozygotes in a college sample (Herman, Philbeck, Vasilopoulos, & Depetrillo, 2003). In longitudinal analysis of the effects of the s-allele on persistent binge drinking, however, additional s-alleles were associated with a decrease in the odds of persistent binge drinking (Olsson et al., 2005). Importantly, subsequent analyses revealed a gene-environment interaction wherein the effects of the s-allele varied across environmental exposure. The previous literature regarding gene-environment interactions will be discussed in subsequent sections.

MAOA. Another polymorphism implicated in the serotonergic system which has been examined in relation to alcohol-related behaviors is the monoamine oxidase-A upstream variable number tandem repeat (MAOA-uVNTR), a variable number tandem repeat polymorphism located on the X chromosome (Sabol, Hu, & Hamer, 1998). Previous research suggests that variants on MAOA include 2-, 3-, 3.5-, 4-, and 5- repeats of 30 base pairs (Deckert et al., 1999; Sabol, Hu, & Hamer, 1998). The 3- and 4- repeat variations are the most frequently occurring polymorphisms across populations, although the proportion of each variant has been reported to fluctuate across populations. For example, Sabol, Hu, and Hamer (1998) found that while less than 1.8% of participants carried the 3.5- or 5-repeat variants and no participants carried the 2-repeat variant,

61.0% and 59.1% of Asian and African Americans carried the 3-repeat variant and 37.8% and 36.4% carried the 4-repeat variant, respectively. This is in contrast to 33.1% and 29.3% of White and Hispanic participants carrying the 3-repeat allele and 64.8% and 70.7% carrying the 4-repeat variant, respectively (Sabol, Hu, & Hamer, 1998).

Functionally, research suggests that the shorter variants of MAOA (2- and 3-repeats) are associated with reduced transcriptional efficacy whereas the 3.5-, 4-, and 5-repeat alleles are associated with increased transcriptional efficacy although findings are mixed in regard to the 5-repeat allele (Deckert et al., 1999; Denny, Koch, & Craig, 1999; Sabol, Hu, & Hamer, 1998). Greater encoding of the MAOA gene results in greater concentrations of MAOA, a catabolizing agent of monoamines including serotonin, dopamine, and norepinephrine with a preference for serotonin (Shih & Thompson, 1999). As such, low expressing variants of MAOA lead to a reduced concentration of this catabolizing agent and thus higher serotonin concentrations and greater neurological reactivity as compared to high expressing MAOA variants.

Because of MAOA-uVNTR's location on the X chromosome, much debate exists concerning the functionality of MAOA among females. Due to X-linked inactivation (i.e., random inactivation of one copy of each gene located on female's two X chromosomes), many studies have excluded females from analyses of the MAOA-uVNTR. In vitro analyses of X-linked inactivation of the MAOA gene, conducted outside of a living organism, largely suggest complete inactivation of one copy of the gene (Benjamin, Van Bakel, & Craig, 2000; Carrel & Willard, 2005; Nordquist & Oreland, 2006; Xue et al., 2002). Some have argued, however, that the MAOA gene may not undergo such inactivation or only partial inactivation (Carrell & Willard, 2005). In vivo

studies of the influence of MAOA on serotonergic function, conducted from living organisms, have found that MAOA is associated with cerebral spinal fluid 5-HIAA levels, the main serotonin metabolite, levels in men but not women (Williams et al., 2003).

In contrast to direct effects of 5-HTTLPR on alcohol use and alcohol disorders, there appears to be little evidence of a direct effect of MAOA-uVNTR on alcohol related behaviors. In a recent meta-analysis of eight studies, no significant association was found between MAOA genotype and alcohol dependence, controlling for racial stratification (Forero, Lopez-Leon, Shin, Park, & Kim, 2015). The bulk of evidence, however, suggests that the association between MAOA and alcohol-related disorders depends largely on the profile of the disorder. When differentiating types of alcoholism (e.g., the presence of co-occurring antisocial behavior) or the presence of personality traits associated with this differentiation, more low expressing alleles have been found among antisocial alcoholics than non-antisocial alcoholics and controls (Samochowiec et al., 1999). Similarly, in a sample of Germans, a disproportionate number of low expressing alleles was found within male antisocial alcoholics but not anxious-depressive or unspecified alcoholic males. In a Finnish male sample, however, no difference was observed in allele distribution of MAOA among Type I alcoholics, Type II alcoholics, or normal controls (Saito et al., 2002). Among females, no difference in MAOA allele distribution was found for any type of female alcoholic (Schmidt, Sander, Kuhn, Smolka, Rommelspacher, Samochowiec, & Lesch, 2000) while an early study found significantly more MAOA low expressing alleles among a mixed sex sample of European alcoholics

than controls (Parsian, Suarez, Tabakoff, Hoffman, Ovchinnikova, Fisher, & Cloninger, 1995).

Interactive Effects of Distal Stress, Proximal Stress, and Serotonin Genes

As discussed, both environmental and genetic risk factors contribute to alcohol use behaviors and disorders. Although these risk factors have largely been examined in isolation, evidence suggests that genes and environments do not operate in isolation. Rather, gene-environment interaction studies (GxE) suggest that the effects of environments on alcohol use vary by genotype. That is, meta-analytic studies suggest that some genetic variants such as the low expressing MAOA alleles and short 5-HTTLPR alleles increase the effect of environmental risk exposure on a variety of behaviors including antisocial behavior (Byrd & Manuck, 2014; Fick & Waldman, 2014), childhood developmental outcomes such as depression, negative emotionality, and other emotional problems (Van IJzendoorn, Belsky, & Bakermans-Kranenburg, 2012), and childhood mental health outcomes (Kim-Cohen et al., 2006). As such, the following section reviews the existing GxE literature examining the interactive effects of distal and proximal environmental stress exposure with MAOA and 5-HTTLPR independently in understanding alcohol use and alcohol disorders. A systematic literature review was conducted in an effort to obtain all relevant studies.

Systematic literature review of gene-environment interaction studies. Two genetic polymorphisms involved in functioning of the serotonergic system, a variable number tandem repeat polymorphism of monoamine oxidase-A (MAOA), and a length polymorphism found in the promoter region of the serotonin transporter gene (5-HTTLPR) have been widely studied in GxE research generally (Byrd & Manuck, 2014;

Kart, Burmeister, Shedden, & Sen, 2011; Kim-Cohen, Caspi, Taylor, Williams, Newcombe, Craig, & Moffit, 2006; Miller, Wankerl, Stalder, Kirschbaum, & Alexander, 2013; Risch et al., 2009; Schinka, Busch, & Robichaux-Keene, 2004; Simon, Czobor, Balint, Meszaros, & Bitter, 2009), and GxE inquiries into alcohol-related behaviors (Cao, Hudziak, & Li, 2013; Feinn, Nellissery, & Kranzler, 2005; Forero, Lopez-Leon, Shin, Park, & Kim, 2015McHugh, Hofmann, Asnaani, Sawyer, & Otto, 2010; Oo et al., 2016). The following systematic literature review examines the current state of knowledge concerning how these two polymorphisms interact with distal and proximal stress independently to explain alcohol use and alcohol dependence.

The systematic literature review is critical in order to ensure that all current studies of the topic are observed. This was accomplished by searching the following ten databases using identical key word searches: Academic Search Complete, Biological Abstracts, JSTOR, Psychology and Behavioral Sciences Collection, Psych Articles, Psych INFO, Sage Journals Online, Science Direct, Web of Science, and Wiley. The 6 key term phrases used were as follows: "'gene environment interaction' AND alcohol AND serotonin," "'gene environment interaction' AND alcohol AND 5httlpr," "'gene environment interaction' AND alcohol AND MAOA," "GxE AND alcohol AND serotonin," "GxE AND alcohol AND 5httlpr," "GxE AND alcohol AND MAOA." Additionally, reference searches were conducted of all returned studies and any GxE studies of MAOA and 5-HTTLPR with distal or proximal stressors were included. Studies of rodents and non-human primates were omitted from this review. Categorization of distal stress was defined by stressors that occurred more than a year prior to alcohol use measure. Categorization of proximal stress was defined by stressors

that included past year exposure, with the exception of lifetime prevalence of stress exposure. Studies of lifetime stress exposure were omitted from this review. This search resulted in 13 unique, relevant studies being captured. The following analysis of these studies first outlines the results of studies examining distal environmental GxE studies followed by proximal environmental GxE studies.

Distal environmental stress. Table 1 displays the specifics of GxE studies examining the interaction between 5-HTTLPR and distal environmental stressors on alcohol-related behaviors. The outlined methods returned three studies with four effect sizes that met inclusion criteria. Laucht et al.'s (2009) study of New York emerging adults examined the interactive effects of 5-HTTLPR and early family adversity as measured by pre-birth family adversity including parental education, early and unwanted pregnancy, chronic unemployment, one parent and overcrowded home to explain the number of drinks consumed and the number of days participants reported binge drinking. Multiple regression analyses suggested that the effects of this distal environmental stressor did not vary by genotype. The absence of a GxE effect in Laucht et al. (2009) may be due to the severity and timing of the distal environment. Although there may be some effect of these prenatal stressors directly and as a proxy for very early life environment, the timing or severity of these distal environments may not be sufficient to lead to a marked change.

Kaufman et al. (2012) analyzed the effects of childhood abuse on early onset alcohol use in a case-control sample of children removed from maltreatment homes and community controls. Children with maltreatment were found to be at greater risk for initiation of early alcohol use if carrying a 5-HTTLPR s-allele. Overall, few conclusions about whether and how 5-HTTLPR interacts with distal environmental stressors to

explain alcohol-related behaviors can be drawn due to the limited number of studies. Generalizability of these findings across gender also cannot be made due to the low number of studies examining 5-HTTLPR and distal environmental stressors on alcohol use behaviors. As compared to the results in Laucht et al. (2009) of fairly mild stressors before birth, interaction between 5-HTTLPR and stress may occur only when stressors are severe such as in Kaufman et al. (2012). Nilsson et al. (2005) examined the interaction between 5-HTTLPR and family relations categorized as good or poor from in-depth interviews. A significant interaction was found in explanation of frequency of intoxication. Post-hoc analyses revealed that the s/l genotype was significantly more reactive to the effects of poor family relations.

Table 1

5-HTTLPR x Distal Stress on Alcohol-Related Problems Studies

Authors (year)	Sample	N	Sex	Mean Age	Race/ Ethnicity	5-HTTLPR Coding	Distal Environment	Dependent Variables	Model	"Risk" Allele/Genotype
Kaufman et al. (2012)	SAFE Homes	127	Mixed	T1: 10.5; T2:12.5	Mixed	s-carrier	Substantiated Maltreatment	Alcohol Use Onset	GEE	s-carrier
Laucht et al. (2009)	Mannheim Study of Children at Risk	309	Mixed	19	Unspecified	l-carrier	Early Family Adversity (during pregnancy)	Number of Drinks	OLS	N.S.
Laucht et al. (2009)	Mannheim Study of Children at Risk	309	Mixed	19	Unspecified	l-carrier	Early Family Adversity (during pregnancy)	Days Binge Drinking	OLS	N.S.
Nilsson et al. (2005)	Survey of Adolescent Life in Vestmanland 2006	66	Male	T1: 16 & 19; T2: 19 & 22	Caucasian	s/s, s/l, l/l	Quality of Family Relations (before T1)	Intoxication Frequency	GLM	s/l

Note: N.S. = Not Significant; OLS = Ordinary Least Squares Regression; GEE = Generalized Estimating Equation; GLM = Generalized Linear Model

Table 2 displays the specifics of GxE studies examining the interaction between MAOA-uVNTr and distal environmental stressors on alcohol-related problems. Inclusion criteria returned five studies examining this GxE with eleven effect sizes. In a sample of Native American females, significant variation was found between those with alcohol use disorder (AUD) and controls among those that had experienced childhood sexual abuse (Ducci et al., 2008). Among sexually abused participants, carriers of the MAOA-L allele were more frequently found in individuals with AUD than controls, suggesting heightened reactivity of those MAOA-L carriers to childhood sexual abuse. In a mixed race, mixed gender sample, Nikulina et al. (2012) found no significant interaction between MAOA and court substantiated reports of childhood neglect, physical, sexual, or multiple maltreatment experiences on the number of alcohol abuse symptoms when participants were followed into adulthood (mean age = 41, S.D. = 3.85).

Table 2

MAOA x Distal Stress on Alcohol-Related Problems Studies

Authors (year)	Sample	N	Sex	Mean Age	Race/ Ethnicity	MAOA-L Coding	MAOA-H Coding	Distal Environment	Dependent Variables	Model	"Risk" Allele
Ducci et al. (2008)	Southwest Indian Tribe	291	Female	37.80	Native American	3R[c]	4R	Childhood Sexual Abuse (before 16 y. o.)	AUD	Chi-Square	MAOA-L
Nikulina et al. (2012)	Proprietary Sample	575	Mixed	41	Mixed	3R (1)[c]	4R (0)	Physical abuse (court substantiated before 11 years old)	Number of DSM-III Alcohol Abuse Symptoms	OLS	N.S.
Nikulina et al. (2012)	Proprietary Sample	575	Mixed	41	Mixed	3R (1)[c]	4R (0)	Sexual abuse (court substantiated before 11 years old)	Number of DSM-III Alcohol Abuse Symptoms	OLS	N.S.
Nikulina et al. (2012)	Proprietary Sample	575	Mixed	41	Mixed	3R (1)[c]	4R (0)	Neglect (court substantiated before 11 years old)	Number of DSM-III Alcohol Abuse Symptoms	OLS	N.S.
Nikulina et al. (2012)	Proprietary Sample	575	Mixed	41	Mixed	3R (1)[c]	4R (0)	Multiple Maltreatment (court substantiated before 11 years old)	Number of DSM-III Alcohol Abuse Symptoms	OLS	N.S.

(continued)

Authors (year)	Sample	N	Sex	Mean Age	Race/ Ethnicity	MAOA-L Coding	MAOA-H Coding	Distal Environment	Dependent Variables	Model	"Risk" Allele
Nilsson et al. (2007)	Survey of Adolescent Life in Vestmanland 2006	66	Male	T1: 16 & 19; T2: 19 & 22	Caucasian	3R (1)	4R (0)	Quality of Family Relations (before T1)	Alcohol-related problem behavior	GLM	N.S.
Nilsson et al. (2007)	Survey of Adolescent Life in Vestmanland 2006	66	Male	T1: 16 & 19; T2: 19 & 22	Caucasian	3R (1)	4R (0)	Maltreated/abused/sexually abused (before T1)	Alcohol-related problem behavior	GLM	N.S.
Nilsson et al. (2008)	Survey of Adolescent Life in Vestmanland 2006	114	Female	T1: 16 & 19; T2: 19 & 22	Caucasian	3R (1)[a]	4R (0)	Quality of Family Relations (before T1)	AUD	GLM	MAOA-H
Nilsson et al. (2008)	Survey of Adolescent Life in Vestmanland 2006	114	Female	T1: 16 & 19; T2: 19 & 22	Caucasian	3R (1)[a]	4R (0)	Quality of Family Relations (before T1)	Alcohol-related problem behavior	GLM	MAOA-H
Nilsson et al. (2008)	Survey of Adolescent Life in Vestmanland 2006	114	Female	19-22	Caucasian	3R (1)[a]	4R (0)	Maltreated/abused/sexually abused (before T1)	AUD	GLM	N.S.
Nilsson et al. (2008)	Survey of Adolescent Life in Vestmanland 2006	114	Female	T1: 16 & 19; T2: 19 & 22	Caucasian	3R (1)[a]	4R (0)	Maltreated/abused/sexually abused (before T1)	Alcohol-related problem behavior	GLM	N.S.

Note: a = heterozygotic females included as L, b = heterozygotic females included as H, c = heterozygotic females included separately; N.S. = Not Significant; AUD = Alcohol Use Disorder; OLS = Ordinary Least Squares Regression; GLM = Generalized Linear Modeling

The results of three studies of the same sample of Swedish adolescents are also presented in Table 2 (Nilsson et al., 2007, 2008). The earliest of these found no significant interaction of MAOA with quality of family relations or abuse experience in explanation of alcohol-related problem behavior among a small subsample of males (n = 66; Nilsson et al., 2007). A follow up study of a sub-sample of Swedish females also did not find a significant MAOA x abuse interaction in explaining alcohol-related problem behavior or AUD (Nilsson et al., 2008). Among these female participants, however, a significant interaction was found between MAOA and quality of family relations, a measure mimicking the DSM-IV Psychosocial and Environmental Problems scale including parental depression, intimate partner violence, and general family functioning, on alcohol-related problem behavior and AUD (Nilsson et al., 2008).

There appears to be some moderation of MAOA x distal stress effects by gender. In the majority of studies reporting a significant interactive effect, with one exception, these are all found within female-specific samples (Nilsson et al., 2008). Interestingly, however, these effects are limited to quality of family relations (Nilsson et al., 2008) and to those with histories of sexual abuse (Ducci et al., 2008; Nilsson et al., 2011). The MAOA allele associated with environmental sensitivity also varies by study, with only one study (Ducci et al., 2008) reporting findings consistent with initial theories of environmental sensitivity of the MAOA-L allele (see Caspi et al., 2002). At the same time, however, meta-analytic results of MAOA-environmental interactions have suggested that the MAOA-H allele confers environmental sensitivity leading to antisocial behavior among females (Byrd & Manuck, 2014). The inclusion of “alcohol-related problem behavior” may be capturing some of this effect toward antisocial behavior (e.g.,

see Nilsson et al., 2008). However, MAOA-H also appears to confer sensitivity to environments in the explanation of AUD (see Nilsson et al., 2008). While these studies present much heterogeneity in results, somewhat more consistent interactive effects, like those found when examining 5-HTTLPR x distal stress, are found for more severe outcome variables.

Proximal environmental stress. Table 3 displays the specifics of six GxE studies examining twenty-six effect sizes of the interaction between 5-HTTLPR and proximal environmental stressors on alcohol-related behaviors. Results from a mixed sex sample of college students suggest that past year stressful life events significantly increase drinking frequency, frequency of binge drinking, and intentions to consume alcohol more strongly for s/s homozygotes when the sample was restricted to Caucasian participants (Covault et al., 2007). Further, after controlling for previous year drinking behavior, being an s-carrier as compared to an l/l homozygote increases the risk of alcohol-use behaviors following stressful life events (Covault et al., 2007). Utilizing data from the same sample, Kranzler et al. (2012) found that female, but not male, s-allele carriers were more reactive to the effects of stressful life events on drinking frequency, and frequency of binge drinking when the sample was restricted to American students of African descent. In contrast, Laucht et al. (2009) found no significant interactive effect between 5-HTTLPR and stressful life events as measured by the Munich Event List, and the number of drinks or the number of days participants binge drank among females. However, they found that males with the l/l genotypes were significantly more reactive to stressful life events for both dependent variables (Laucht et al., 2009). Kim et al. (2015) examined the interactive effect of being an s-allele carrier with family conflict (i.e., conflict with the child and

conflict viewed by the child) in adolescent samples from the United States and the United Kingdom. In the US sample, a significant interaction was found between 5-HTTLPR and family conflict in explanation of intoxication frequency but not alcohol use frequency (Kim et al., 2015). Similarly, in the UK sample, a significant interaction was found between 5-HTTLPR and family conflict for binge drinking frequency but not alcohol use frequency for the maximum number of drinks consumed (Kim et al., 2015). In an Australia sample, the effects of parental attachment were found to be significantly greater among s-allele carriers than l/l homozygotes to explain variation in binge drinking from age 14 to age 24 (Olsson et al., 2005). Finally, in a sample from the National Longitudinal Study of Adolescent to Adult Health, analysis in Wave II males and females examined the interaction between 5-HTTLPR and drinking and smoking school norms to explain alcohol use behaviors (Daw et al., 2013). The effects of school substance use prevalence was significantly greater for those s-allele carriers in the explanation of the number of drinks consumed but not drinking frequency (Daw et al., 2013).

Table 3

5-HTTLPR x Proximal Stress on Alcohol Related Problems Studies

Authors (year)	Sample	N	Sex	Mean Age	Race/Ethnicity	5-HTTLPR Coding	Proximal Environment	Dependent Variables	Model	"Risk" Allele/Genotype
Covault et al. (2007)	Proprietary College Sample (see also, Kranzler et al., 2012)	295	Mixed	18.7	Non-Hispanic Caucasian	s/s, s/l, l/l	Life Events Scale for Students (past year)	Drinking Frequency	OLS	Year 1: s/s; Year 2: s-allele
Covault et al. (2007)	Proprietary College Sample (see also, Kranzler et al., 2012)	295	Mixed	18.7	Non-Hispanic Caucasian	s/s, s/l, l/l	Life Events Scale for Students (past year)	Binge Drinking Frequency	OLS	Year 1: N.S.; Year 2: s/s
Covault et al. (2007)	Proprietary College Sample (see also, Kranzler et al., 2012)	295	Mixed	18.7	Non-Hispanic Caucasian	s/s, s/l, l/l	Life Events Scale for Students (past year)	Drinking Intentions	OLS	Year 1: s/s; Year 2: s-allele
Daw et al. (2013)	AddHeatlh (W1 & W2)	14560	Mixed	16.3	Mixed	s-carrier	School Smoking and Drinking Norms (current)	Number of Drinks	Multilevel linear regression modeling	s-allele
Daw et al. (2013)	AddHeatlh (W1 & W2)	14560	Mixed	16.3	Mixed	s-carrier	School Smoking and Drinking Norms (current)	Drinking Frequency	Multilevel linear regression modeling	N.S.

(continued)

Authors (year)	Sample	N	Sex	Mean Age	Race/Ethnicity	5-HTTLPR Coding	Proximal Environment	Dependent Variables	Model	"Risk" Allele/Genotype
Kim et al. (2015)	US: Project inSight	175	Mixed	T1: 15.05; T2: 15.38	Mixed	s-carrier	Family Conflict (at T1)	Alcohol use frequency	Path Analysis	Time 1: N.S.; Time 2: N.S.
Kim et al. (2015)	US: Project inSight	175	Mixed	T1: 15.05; T2: 15.38	Mixed	s-carrier	Family Conflict (at T1)	Intoxication frequency	Path Analysis	T1: s-carrier; T2: s-carrier
Kim et al. (2015)	UK: Avon Longitudinal Study of Parents and Children (ALSPAC)	4916	Mixed	T1: 12.8; T2: 15.4	Caucasian	s-carrier	Family Conflict (past 3 months)	Alcohol use frequency	Path Analysis	Time 1: N.S.; Time 2: N.S.
Kim et al. (2015)	UK: Avon Longitudinal Study of Parents and Children (ALSPAC)	4916	Mixed	T1: 12.8; T2: 15.4	Caucasian	s-carrier	Family Conflict (past 3 months)	Binge Drinking Frequency	Path Analysis	Time 1: s-carrier
Kim et al. (2015)	UK: Avon Longitudinal Study of Parents and Children (ALSPAC)	4916	Mixed	T1: 12.8; T2: 15.4	Caucasian	s-carrier	Family Conflict (past 3 months)	Maximum number of drinks	Path Analysis	Time 1: N.S.; T2: N.S.

(continued)

Authors (year)	Sample	N	Sex	Mean Age	Race/Ethnicity	5-HTTLPR Coding	Proximal Environment	Dependent Variables	Model	"Risk" Allele/Genotype
Kranzler et al. (2012)	Proprietary College Sample (see also, Covault et al., 2007)	393	Split	20.1	African decent	s-carrier	Life Events Scale for Students (past year)	Drinking Frequency	GLM with binomial distribution and log link function	Males: N.S.; Females: s-carrier
Kranzler et al. (2012)	Proprietary College Sample (see also, Covault et al., 2007)	393	Split	20.1	African decent	s-carrier	Life Events Scale for Students (past year)	Days Binge Drinking	GLM with binomial distribution and log link function	Males: N.S.; Females: s-carrier
Laucht et al. (2009)	Mannheim Study of Children at Risk	309	Mixed	19	Unspecified	l-carrier	Current Stressful Life Events (past 4 years)	Number of Drinks	Multiple Regression	Males: l/l; Females: N. S.
Laucht et al. (2009)	Mannheim Study of Children at Risk	309	Mixed	19	Unspecified	l-carrier	Current Stressful Life Events (past 4 years)	Days Binge Drinking	Multiple Regression	Males: l/l; Females: N. S.
Olsson et al. (2005)	Victorian Adolescent Health Cohort Study	752	Mixed	W1: 15.5 W2: 16 W3: 16.5 W4: 17 W5: 17.5 WV6: 18 W7: 20.5 W8: 24	Unspecified	Number of s-alleles	Parental Attachment (W8)	Persistent Binge Drinking Prevalence	Logistic Regression	s-allele

Note: N.S. = Not Significant; OLS = Ordinary Least Squares Regression; GLM = Generalized Linear Modeling

Generalizability of 5-HTTLPR x proximal stress environment effects on alcohol related problems across gender is not adequately addressed in the current literature. Of the five studies examined, only two examined cross-gender effects with mixed results. Kranzler et al. (2012) found female-specific interactive effects while Laucht et al. (2009) found male-specific interactive effects of stressful life events in the past year and four years, respectively. Comparison of Caucasian-specific and African decent-specific results from the proprietary sample of Covault et al. (2007) and Kranzler et al. (2012) suggest a potential racially specific gender moderation of this GxE. Specifically, in the analysis of Caucasian participants, no significant GxE was found (Covault et al., 2007) but in the analysis of participants of African descent, a significant GxE was found in female participants.

As was suggested in the G x distal environmental stress studies, severity of the alcohol-related behavior appears to have an effect on 5-HTTLPR x proximal stress results but less markedly so. For example, Kim et al. (2015) found that this GxE was significantly associated with intoxication frequency in a US sample and binge drinking in a UK sample but not drinking frequency in either. This echoes previous G x distal environmental stress findings, suggesting that GxE effects are more likely among more severe patterns of alcohol-related behavior. However, the results of others find significant interactions regardless of dependent variable measure (Covault et al., 2007; Kranzler et al., 2012; Laucht et al., 2009). Further, while AUD is of clinical importance, no study of 5-HTTLPR x proximal stress examined whether these findings hold in regard to this deleterious disorder.

No GxE studies examining the interaction between MAOA and proximal environmental stressors were found.

Summary. A growing body of literature (n = 14) has examined the interactive effects of 5-HTTLPR and MAOA in interaction with distal and proximal stressors in the explanation of alcohol-related behaviors. MAOA x distal stressor and 5-HTTLPR x proximal stressor are the most frequently studied (n = 6, n = 5, respectively). There is a clear need to further examine MAOA x proximal stressor and 5-HTTLPR x distal stressor effects on alcohol related behaviors. Across all studies examining these interactions, the results suggest that male and female processes are not uniform. Further, severity of the outcome measure (i.e., frequency of alcohol use as compared to AUD) affects GxE results with significant GxE results emerging in studies of more severe patterns of behavior such as binge drinking and AUD. As a whole, much is left unknown about how 5-HTTLPR and MAOA interact with distal and proximal stressors to explain alcohol-related behaviors.

Stress sensitization. While both distal and proximal environmental stressors are directly important in understanding levels and trajectories of alcohol use and dependence, a recent model of stress sensitization suggests that distal and proximal environmental stressors may also interact. Initially hypothesized by Hammen, Henry and Daley (2000) in relation to depression, the stress sensitization model suggests that the effect of proximal stressors varies depending on stress exposure early in life. It is suggested that individuals who are exposed to high levels of distal stress have a diminished capacity to successfully overcome proximal stress. Thus, the effects of proximal stress are greater for those who have been exposed to chronic or traumatic distal stress.

Neurologically, experiences of distal stressors may alter neurodevelopment and thus may amplify the effects of proximal life stress (Heim et al., 1997; Heim et al., 2000; Heim & Nemeroff, 2001). Specifically, distal stress exposure may increase hypothalamic-pituitary-adrenal (HPA) axis reactions to stressors (Heim & Nemeroff, 2001). In brief, activation of the HPA axis results in the release of a series of hormones that effectively signal to the individual that they are in danger or threatened in some way. When presented with a stressor, corticotrophin releasing hormone is secreted, triggering the release of adrenocorticotropic hormone, and ultimately the release of cortisol from the adrenal glands (Tarullo & Gunner, 2006). Cortisol then signals physiological and neurological changes that increase physical performance and memory formation. Importantly, a negative feedback loop exists whereby glucocorticoid receptors detect cortisol and, in effect, "turn off" the stress response. Chronic exposure to cortisol due to prolonged or traumatic stress diminishes the effect of cortisol on the glucocorticoid receptors (Frodl & O'Keane, 2013). As such, those with exposure to chronic or traumatic distal stress have a reduced ability and increased time to return to homeostasis following exposure to stress later in life. As a result of this process, the effect of stress among these individuals is greater and thus may be more likely to lead to negative psychological and behavioral problems.

While stress sensitization has largely been applied to psychological constructs including depression (e.g., see Harkness, Bruce, & Lumley, 2006; McLaughlin, Conron, Koenen, & Gilman, 2010; Rudolph & Flynn, 2007) and post-traumatic stress disorder (Shao et al., 2015), this model has also been applied to behavioral phenotypes, including intimate partner violence perpetration (Roberts, McLaughlin, Conron, & Koenen, 2011),

antisocial behavior (Wells, Armstrong, Boisvert, Gangitano, Lewis, & Hughes-Stamm, forthcoming), and as reviewed below, alcohol use and alcohol dependence.

Previous studies examining the stress sensitization hypothesis on alcohol use have largely supported that distal environmental exposure increases the effects of proximal stress on alcohol use. In a sample from Detroit, childhood maltreatment was found to interact with neighborhood disorder to explain binge drinking and overall number of drinks consumed (Keyes, McLaughlin, Koenen, Goldmann, Uddin, & Galea, 2012). In examining the effects of childhood maltreatment, maltreatment was found to interact with stressful life events to explain variation in alcohol cravings among a sample of drinkers, even controlling for parental alcoholism (Kim et al., 2014)

Gender-specific analyses have suggested that males and females may not be equally sensitized to stress given distal environmental stress exposure. In a study that conducted gender-specific analyses, a stress sensitization effect was found for women but not men (Young-Wolff, Kendler & Prescott, 2012). This stress sensitization effect was found only in regard to proximal stressors outside the control of the individual and did not extend to controllable stressors as determined by in-depth interview. For example, job loss was categorized as an uncontrollable stressor unless the loss was within the control of the individual while interpersonal issues, such as divorce, were categorized as controllable unless otherwise indicated. In a male only sample, however, childhood trauma interacted with life stress to explain drinking severity (Eames et al., 2014). In another gender-specific analysis, no stress sensitization effect was found among men or women in explanation of heavy drinking behaviors (Colman et al., 2013).

A genetically moderated stress sensitization model of alcohol use and dependence. Merging the stress sensitization hypothesis with gene-environment interaction perspectives, a genetically moderated stress sensitization (GxExE) model has been proposed. Originally formulated by Homberg and van den Hove (2012), the GxExE model contends that the degree to which an individual will be sensitized to proximal stress by distal stress varies across genotype. Although originally modeled on variants of 5-HTTLPR (Homber & van den Hove, 2012), this model may extend to other genetic polymorphisms associated with variation in stress responsivity. Genetic variants associated with higher degrees of stress responsivity (i.e., those variants that increase the impact of stress) will lead to a higher degree of stress sensitization under this model. As such, carriers of 5-HTTLPR's s-allele and MAOA's low expressing alleles should experience stress to a higher degree than l-allele and high expressing allele carriers. Further, among those with more reactive genotypes, those who experience distal stress should be more reactive to proximal stress than those without such exposure.

In a direct test of GxExE, Lynch, Manly, and Cicchetti (2015) examined stress reactivity in their sample of 186 children via respiratory sinus arrhythmia (RSA), an indicator of parasympathetic activity. RSA levels were significantly associated with an interaction between childhood maltreatment and neighborhood crime levels. Moreover, this ExE interaction was moderated by the examined polymorphisms, eNOS and GABRA6. This direct measure of stress reactivity both supports the GxExE model as well as suggests that it may be applied to other genetic polymorphisms of interest.

The utility of the GxExE model in explaining depression has been supported in one cross-sectional study (Grabe et al., 2012). In a sample of 1974 German adults,

depression was significantly associated with a three-way interaction between 5-HTTLPR, childhood abuse, and adult traumatic experiences. An analysis of longitudinal data also supports a GxExE effect in explaining depression. In a study of 705 males and females followed for 20 years, experiencing childhood abuse before the age of 5 was found to increase the effect of proximal stress on depression (Starr, Hammen, Conway, Raposa, & Brennan, 2014). Further, this effect was found to be moderated by 5-HTTLPR wherein s-allele carriers were more strongly sensitized than homozygotic l-allele carriers.

The GxExE model has also been applied to behavioral outcomes (Wells, Armstrong, Boisvert, Lewis, Gangitano, & Hughes-Stamm, forthcoming). Using two samples, one sample of college students and one sample from the Add Health Wave III, MAOA was found to interact with childhood abuse and stressful life events to explain crime and delinquency. The effect of stressful life events was found to be significantly greater for those with childhood abuse among male MAOA-L carriers. This line of evidence suggests that stress sensitization may be moderated by MAOA and 5-HTTLPR genotypes in explanation of behavior as well as psychological outcomes.

Purpose of Dissertation

The GxExE model thus has utility in explaining how genetic polymorphisms, distal, and proximal stress may impact alcohol use and alcohol disorders. The current dissertation applies this framework to longitudinally examine levels of alcohol use, binge drinking, and alcohol use age of onset. Specifically, the current dissertation will test whether distal and proximal environments interact to explain alcohol use, binge drinking, and alcohol use age of onset, and whether 5-HTTLPR and MAOA moderate this ExE effect across time. Due to previous research suggesting that ExE and GxE effects vary by

gender, these analyses will also be conducted in male-only and female-only subsamples. Preliminary analyses will examine the GxExE effects, by gender, on alcohol dependence. Finally, as previously discussed, evidence suggests that sex-roles, rather than gender, may differentiate the antecedents of alcohol use behaviors. Preliminary evidence will be presented examining the GxExE model across sex-role stratified subsamples.

Research questions.

1. Do MAOA and 5-HTTLPR interact with distal stress as measured by abuse at varying periods of childhood to explain alcohol use, binge drinking, and age of onset of alcohol use? (G x DE)

2. Do MAOA and 5-HTTLPR interact with proximal stress as measured by victimization and vicarious victimization experiences to explain alcohol use, binge drinking, and age of onset of alcohol use? (G x PE)

3. Do MAOA and 5-HTTLPR interact with distal and proximal stress to explain alcohol use, binge drinking, and age of onset of alcohol use? (G x DE x PE)

4. Do these two-way and three-way interactions explain variation in life-time prevalence of alcohol dependence? (preliminary)

4. Do these effects vary across gender?

6. Do these effects vary by sex-role identification? (preliminary)

CHAPTER III

Methods

In order to test the genetically moderated stress sensitization model of alcohol use, binge drinking, and alcohol use age of onset, longitudinal data from the National Longitudinal Study of Adolescent to Adult Health (Add Health) was analyzed. To date, four waves of data have been drawn from individuals in a nationally representative sample of school youth in grades 7-12 between 1994 and 1995. Due to the use of genotypic data at Wave III, analyses were conducted only on the restricted-use sample. Specific information regarding sampling techniques and restricted-use data is outlined below. Access to data to support this dissertation was made available by Add Health personnel for my analyses under the license and guidance of Dr. Danielle Boisvert. Approval for this project was granted through the Institutional Review Board at Sam Houston State University. This chapter will outline sampling procedures of the Add Health, the measures included in the current dissertation, and the analytic plan.

Sampling

Individuals eligible to participate in the Add Health were selected through a stratified multi-stage cluster sampling technique of high schools and middle/feeder schools. Specifically, 80 high schools were selected from the Quality Education Database, stratified by size. Eligible schools included those that served 11th grade students and enrolled more than 30 students. From each of these selected high schools, one middle/feeder school was selected, weighted by contribution of the number of students to the high school. Failure to participate resulted in replacement of the originally chosen school by another middle/feeder school. In 28 cases, the high school selected

served 7th to 8th grade students thus feeder schools were not selected in these cases. With a 79% rate of agreement to participate, data were collected from individuals in 132 schools from 80 communities varying by urbanicity and with student populations ranging from less than 100 to 3000.

Wave I. Data for adolescent period 1 was collected from in-home interviews between September 1994 and April 1995 when participants were between the ages of 12 and 20. For less sensitive items, data was collected via interview with Computer-Assisted Person Interview (CAPI). For more sensitive information, participants answered self-administered questionnaires using Audio Computer-Assisted Self Interview (ACASI). Each interview spanned approximately 90 minutes. Approximately 17 students were chosen from each of 12 sampling frames determined by sex and grade (including those that did not participate in the in-school survey) from selected schools with a resulting sample of approximately 200 students from each selected school pair. This resulted in a core sample of 12105 in-home questionnaires collected in Wave I with a 79% response rate. Additionally, several supplemental samples were targeted including individuals with disabilities, African American participants with highly educated parents, ethnic oversampling of Cuban, Puerto Rican, and Chinese participants and a genetic supplemental sample resulting in a 20745 total in-home participants at Wave I.

Wave II. Data for adolescent period 2 was collected from in-home Wave II interviews approximately one year later in the same manner as Wave I between April and August of 1996 when participants were between the ages of 12 and 21. The same individuals sampled in Wave I were targeted with the exception of those in the 12th grade unless part of the genetic supplemental sample. Participants from the individuals with

disabilities supplemental sample were not followed. An addition of 65 individuals that were not surveyed in Wave I but who were part of the genetic supplemental sample were added resulting in an 88.6% response rate. This translated in data collected from 14738 participants. Those that aged out of the sample (12^{th} grade at Wave I) and who were not in the genetic sample did not participate in the Wave II collection.

Wave III. Data for the transition to adulthood period was collected from in-home Wave III interviews, collected in the same manner as Wave I between August 2001 and April 2002 when participants were between the ages of 18 and 26 although 24 participants were between in ages of 27 and 28 years old. Again, the same participants were targeted with the exception of those that were located outside of the United States. This resulted in the collection of 15170 interviews from original Wave I respondents with a 77.4% response rate.

Wave IV. In-home interview data for Wave IV were collected in the same manner as Wave I in 2008 when participants were generally between the ages of 24 and 32 years old, although 52 participants were between 33 and 34 years old. Again, the same participants were targeted, resulting in successful location of 92.5% of original participants and an 80.3% overall response rate.

Genetic Data

Genetic data was first collected from individuals in the genetic supplemental sample which targeted the twins, full-, half-, and non-related siblings of original participants. To be eligible for inclusion, the sibling had to be enrolled in school between grades 7 and 12. While all siblings were included in the in-home interview, Wave III saliva samples for DNA genotyping were only collected from those siblings who were

full siblings or twins with 3787 eligible individuals. Buccal cells were collected via saliva samples and genotyped using the following protocols at the Institute for Behavioral Genetics in Boulder, CO. DNA was extracted from saliva samples following manufactured protocols using ZymoResearch (Irvine, CA) Silicon A plates with a 500 uL Oragene solution, a 1:20 ratio in Tris-EDTA and a resulting 8.0 pH (Smolen et al., 2013). Quantification of samples was accomplished using Picogreen (Invitrogen, Carlesbad, CA).

MAOA-uVNTR was sequenced by slightly modifying a previously published protocol (Haberstick et al., 2005; Sabol et al., 1998) using the following 5' to 3' primer sequence: forward: 6FAM ACA GCC TGA CCG TGG AGA AG; reverse: GAA CGG ACG CTC CAT TCG GA. See Table 4 for allelic frequencies of MAOA-uVNTR by sex. The serotonin transporter gene polymorphism, 5-HTTLPR, was sequenced by modification of a previously published protocol (Anchordoquy et al., 2003; Lesch et al., 1996) using the following 5' to 3' primer sequence originally published by Gelernter et al. (1999): forward: NED ATG CCA GCA CCT AAC CCC TAA TGT, reverse: GGA CCG CAA GGT GGG CGG GA. See Table 4 for allelic frequencies of 5-HTTLPR by sex.

Table 4

MAOA and 5-HTTLPR Allelic Distributions among Males and Females

	Males		Females	
	n	%	n	%
MAOA				
2R	11	0.91	1	0.00
3R	428	35.28	195	18.59
3.5R	8	0.66	0	0.00
4R	587	48.39	430	40.99
5R	15	1.24	0	0.00
2R/3R	0	—	13	1.24
2R/3.5R	0	—	0	0.00
2R/4R	0	—	16	1.53
2R/5R	0	—	0	0.00
3R/3.5R	0	—	7	0.67
3R/4R	0	—	510	48.62
3R/5R	0	—	8	0.76
3.5R/4R	0	—	14	1.33
3.5R/5R	0	—	1	0.00
4R/5R	0	—	18	1.72
5-HTTLPR				
s/s	217	20.69	226	18.63
s/l	488	46.52	556	45.84
l/l	344	32.79	431	35.53

Analytic Sample

The final analytic sample for main analyses included 1049 male and 1213 female participants. Of the 3787 individuals eligible for inclusion of DNA data, DNA was collected and analyzed for 2574 (68%). Of these, 5-HTTLPR analysis procedures failed for 16 individuals and MAOA analysis procedures failed for 35 individuals (3 individuals failed both) resulting in 2526 individuals with complete DNA information in Wave III. Of these, 2262 individuals were retained in Wave IV. Observations were omitted from analysis if dependent or independent variable information was missing for that wave. Further, female carriers of cross-functioning alleles (discussed above) were omitted from MAOA analyses only (Model 2, n = 552).

The average age for participants at each wave was as follows: Wave I = 15.57, Wave II = 16.48, Wave III = 21.90, Wave IV = 28.39. Among male participants, 307 (29.29%) reported some childhood abuse at Wave I, 343 (32.73%) at Wave II, 398 (37.98%) at Wave III, and 398 (37.98%) at Wave IV. Among female participants, 443 (36.55%) reported some childhood abuse at Wave I, 489 (40.35%) at Wave II, 604 (49.83%) at Wave III, and 604 (49.83%) at Wave IV. Proximal stress among males was reported by 102 (9.75%) at Wave I, 62 (6.34%) at Wave II, 69 (6.58%) at Wave III, and 174 (16.62%) at Wave IV. Proximal stress among females was reported by 104 (8.59%) at Wave I, 59 (5.14%) at Wave II, 61 (5.03%) at Wave III, and 216 (17.81%) at Wave IV. Some alcohol use was reported by 465 (44.54%) of males in Wave I, 448 (45.74%) in Wave II, 779 (74.76%) in Wave III, and 795 (76.00%) in Wave IV. Alcohol use was reported by 530 (43.73%) of females in Wave I, 497 (43.39%) in Wave II, 860 (71.19%) in Wave III, and 799 (65.87%) in Wave IV. Binge drinking was reported by a minority of

participants in every wave for females and in Wave I and Wave II for males (male: Wave I = 293, 27.98%, Wave II = 324, 33.20%, Wave III = 602, 57.72%, Wave IV = 590, 56.46%; female: Wave I = 267, 22.05%, Wave II = 281, 24.54%, Wave III = 472, 39.27%, Wave IV = 450, 37.13%). Alcohol use onset for females was an average age of 17.25 and alcohol use onset for males was an average age of 16.46.

Measures

Distal stress. Similar to Shin, Miller, and Teacher's (2013) abuse prevalence measure, distal stress was measured by the prevalence of physical, sexual, or emotional childhood abuse. Abuse was captured at Wave IV when participants were asked three questions pertaining to the prevalence of sexual, physical, and emotional abuse experiences before the age of 18. Specifically, participants were asked, "Before your 18th birthday, how often did a parent or other adult caregiver . . ." 1. "hit you with a fist, kick you, or throw you down on the floor, into a wall, or down stairs," 2. "touch you in a sexual way, force you to touch him or her in a sexual way, or force you to have sexual relations," and 3. "say things that really hurt your feelings or made you feel like you were not wanted or loved" with potential response categories of "this has never happened," "one time," "two times," "three to five times," "six to ten times," and "more than ten times." Responses to these questions were then dichotomized and coded as "0" = no abuse, "1" = abuse to create three dichotomous measures of abuse: physical abuse, sexual abuse, and emotional abuse.

Following the prevalence questions, participants were asked to report the age at which the abuse began. These were then categorized into early childhood abuse, middle childhood abuse, and late childhood abuse. Early, middle, and late childhood age ranges

were determined based upon previous research examining the impact of childhood abuse on hippocampal volume. In a case-control comparison of the effects of sexual abuse on hippocampal volume among females, it has been suggested that the greatest effects of childhood abuse occur between the ages of 3 and 5 years old and 11 and 13 years old (Andersen et al., 2008), an important finding for the current study, given the association between hippocampal volume trajectories of alcohol use disorders (De Bellis et al., 2000). Conversely, others have argued that the effects of traumatic experiences, such as childhood abuse, may be greatest until approximately the age of 10 due to increased dendritic and axonal branching in early life (Hart & Rubia, 2012; Sowell, Peterson, Thompson, Welcome, Henkenuius, & Toga, 2003).

As such, early childhood abuse was measured as abuse beginning before the age of 11, middle childhood abuse was coded as beginning between the ages of 11 and 13, and late childhood abuse was coded as beginning between the ages of 14 and 18. Dichotomous measures were created for each abuse type, at each developmental period, for each wave. Sexual, physical, and emotional abuse were coded as "0" = had not occurred, "1" = had occurred in early (before age 11), middle (between 11 and 12.9 years old), and late (from 13 to 18 years old) childhood. To assure correct temporal ordering, values for the abuse measures were coded as 0 until the age at which the abuse had occurred and coded 1 for each wave thereafter. For example, coding of a participant reporting physical abuse with an onset of 17 who was age 14 at Wave I, 15 at Wave II, 21 at Wave III, and 27 at Wave IV would be as follows for the late physical abuse onset variable: Wave I: 0, Wave II: 0, Wave III: 1, Wave IV: 1. These measures were then

collapsed into composite abuse measures of any abuse in early childhood, any abuse in middle childhood, and any abuse in late childhood for each wave.

See Table 5 for descriptive statistics of each categorization of onset by abuse type across waves. Across all four waves, 47.86% (n = 1061) of the sample reported at least some form of childhood abuse with 411 (18.19%) reporting any early childhood abuse, 251 (11.11%) reporting middle childhood abuse, and 474 (20.97%) reporting late childhood abuse. Of those that reported each type of abuse, 342 (13.32%) participants reported physical abuse with a mean age of onset of 10.82, 106 (4.49%) reported sexual abuse with a mean age of onset of 8.23, and 920 (29.74%) reported emotional abuse with a mean age of onset of 11.99. Because individuals could report differing onset ages for each type of abuse, 75 participants reported staggered onset of different types of abuse (e.g., sexual abuse started in “early” childhood and physical abuse started in “middle” childhood).

Table 5

Distal Stress, Childhood Abuse Onset Frequency by Wave

	Wave I		Wave II		Wave III		Wave IV		Total	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
Physical Abuse										
Early	2069	156	2069	156	2069	156	2069	156	2069	156
Middle	2161	58	2159	65	2159	66	2159	66	2159	66
Late	2155	44	2128	71	2105	120	2105	120	2105	120
Total	—	—	—	—	—	—	—	—	2225	342
Sexual Abuse										
Early	2180	76	2180	76	2180	76	2180	76	2180	76
Middle	2242	10	2241	13	2241	15	2241	15	2241	15
Late	2247	6	2246	9	2241	15	2241	15	2241	15
Total	—	—	—	—	—	—	—	—	2256	106
Emotional Abuse										
Early	1861	312	1861	312	1861	312	1861	312	1861	312
Middle	1973	185	1971	198	1971	202	1971	202	1971	202
Late	1942	164	1874	232	1767	406	1767	406	1767	406
Total	—	—	—	—	—	—	—	—	2173	920
Overall Abuse										
Early	1849	411	1849	411	1849	411	1849	411	1849	411
Middle	2034	226	2014	246	2009	251	2009	251	2009	251
Late	2060	200	1981	279	1786	474	1786	474	1786	474
Total	—	—	—	—	—	—	—	—	1156	1061

Proximal stress. As the current study seeks to analyze longitudinal effects of proximal stress, measurement of proximal stress must be equal across all waves of data collection. That is, that which individuals may find stress inducing in adolescence may not largely overlap with those which individuals find stress inducing in adulthood. To develop a uniform measure of proximal stress throughout the life course, events related to victimization or observation of victimization of another were indexed to measure proximal stress. Victimization and observation of victimization (including death or illness of loved ones) are common elements of many commonly used stressful life events scales including the Stressful Life Events Screening Questionnaire (Goodman, Corcoran, Turner, Yuan, & Green, 1998), the Schedule of Recent Events and Social Readjustment Rating Scale (Holmes & Rahe, 1967). The victimization aspect of the stressful life events scales, unlike that of financial strain, employment, or living situations does not suffer from variation in importance from adolescence to adulthood.

Victimization and observation of victimization experiences were measured with the following items for prevalence in the past 12 months: 1. “You saw someone shoot or stab another person,” 2. “Someone pulled a knife or gun on you,” 3. “Someone shot you.” 4. “Someone cut or stabbed you,” 5. “Have any of your friends tried to kill themselves?” and 6. “Have any of your family members tried to kill themselves.” While all of these questions appear in each of the four waves, three alterations in questioning exist. First, item 2 was separated into two items concerning knife and gun threats during Wave III only. Second, items 4 and 5 were combined into a single measure in Wave IV. Third, items 5 and 6 were combined into a single measure in Wave IV.

Due to fluctuation in measurement and low prevalence of occurrence of each item (see Table 6), proximal stress was measured as a prevalence index for any of these victimization or observation of victimization items. Participants reported the greatest amount of proximal stress in Wave IV (17.26%) when they were an average age of 28.39, followed by Wave I (8.87%) when they were an average age of 15.57, and nearly the same amount of proximal stress in Wave II (5.71%) at an average age of 16.48 and Wave III (5.65%) at an average age of 21.90.

Table 6

Prevalence of Victimization and Observation of Victimization Items

	Wave I n (%)	Wave II n (%)	Wave III n (%)	Wave IV n (%)
Friend Attempted Suicide	209 (16.26)	289 (12.20)	165 (6.56)	—
Family Member Attempted Suicide	112 (4.45)	72 (3.04)	70 (2.78)	—
Friend of Family Attempted Suicide	—	—	—	137 (6.06)
Saw Shooting/Stabbing	238 (9.56)	164 (6.93)	118 (4.69)	168 (8.16)
Gun Pulled on You	—	—	108 (4.29)	—
Knife Pulled on You	—	—	82 (3.26)	—
Gun/Knife Pulled on you	283 (11.25)	205 (8.66)	—	126 (6.12)
Someone Shot You	34 (1.35)	29 (1.23)	16 (.64)	—
Someone Stabbed You	108 (4.30)	59 (2.49)	16 (.64)	—
Someone Shot/Stabbed You	—	—	—	69 (3.35)
Total Proximal Stress	222 (8.87)	135 (5.71)	142 (5.65)	390 (17.26)

Serotonergic Polymorphisms

5-HTTLPR. Sex specific allelic distribution of 5-HTTLPR can be seen in Table 4. All individuals carry two 5-HTTLPR alleles of either a 14 repeat, 376 base pair s-allele or 16 repeat, 419 base pair l-allele, although some rare extra-long variants were detected in the current sample and elsewhere (Nakamura et al., 2000). Due to the rarity of these variants, a lack of direct evidence concerning the functionality of extra-long alleles, and the desire to directly compare the current study with previous literature that did not include these variants, those carriers of extra-long variants were not included in analyses. This resulted in the heterozygous condition (s/l) being the most prominent genotype (47.14%) followed by l/l (33.96%) and s/s (18.90%). This distribution represents a significant departure from Hardy-Weinberg Equalibrium (HWE; chi-square = 6.463, p = .01), which will be discussed in the limitations section.

MAOA-uVNTR. Sex specific allelic distribution of MAOA can be seen in Table 4. Based on previous research, the alleles were collapsed into two categories, low expressing alleles, 2-repeat, 3-repeat, and 5-repeat, and high expressing alleles, 3.5-repeat and 4-repeat (Denney et al., 1999; Sabol et al., 1998). While the 5-repeat allele will be coded as low expressing following previous research (Kim-Cohen et al., 2006; Wakschlag et al., 2010), due to some conflicting research concerning the functionality of the 5-repeat allele (Deckert et al., 1999; Sabol et al., 1998), analyses will be replicated with the omission of those carriers of the 5-repeat allele (n = 42).

Because MAOA-uVNTR is located on the X chromosome, males were assigned to a category based on their hemizygotic status (MAOA-L: n = 454, 43.28%; MAOA-H: n = 595, 56.72%). Females, however carry two copies of this polymorphism. Due to

random inactivation of genes located on the X chromosome (Benjamin, Van Bakel, & Craig, 2000; Carrel & Willard, 2005; Nordquist & Oreland, 2006; Xue et al., 2002), it is currently not possible to assign a category to those participants with a cross-functioning genotype (i.e., one low expressing allele and one high-expressing allele). As such, female genotype categories were only assigned to those with matching allelic functionality (i.e., 2 low expressing alleles or 2 high expressing alleles), a procedure that has appeared elsewhere in the literature (e.g., Widom & Brzustowicz, 2006; Williams et al., 2009). Classified in this manner, 552 female participants were excluded from the analyses with the most common cross-functioning genotype of 3R/4R (n = 510, 42.04%). After classification, 217 (32.83%) of females were coded as MAOA-L and 444 (67.17%) were coded as MAOA-H. Due to the rarity of some variants, such as the 2R, 3.5R and 5R alleles accounting for only 42, 30, and 41 of the observed 3475 alleles, the overall distribution of the MAOA-uVNTR significantly departed from HWE (chi-square = 2400.437, $p < .00$), which will be discussed in the limitations section. Racial distributions of MAOA and 5-HTTLPR are displayed in Table 7.

Table 7

Sample Demographic Statistics by Race

	African American (%)	Caucasian (%)	Hispanic (%)	Other (%)	Total (%)
MAOA-L	189 (56.59)	368 (31.75)	114 (40.86)	87 (58.39)	758 (39.46)
MAOA-H	145 (43.41)	791 (68.25)	165 (59.14)	62 (41.61)	1163 (60.54)
5-HTTLPR-s/s	38 (8.58)	267 (17.85)	103 (27.47)	88 (45.13)	469 (18.90)
5-HTTLPR-s/l	154 (35.76)	739 (49.40)	195 (52.00)	82 (42.05)	1170 (47.14)
5-HTTLPR -l/l	251 (56.66)	490 (32.89)	77 (20.53)	25 (12.82)	843 (33.96)

Dependent Variables

Alcohol use frequency. Frequency of alcohol use was measured in each wave of data collection. Specifically, participants were asked "during the past 12 months, on how many days did you drink alcohol?" Descriptive statistics for each of the dependent variables are presented in Table 8. As can be seen, the modal response category for each wave was "never" with one exception; Wave IV males equally reported "never" drinking and drinking "1-2 days per week." Male participant alcohol use frequency was an average of 1.07 (S.D. = 1.52) in Wave I, 1.22 (S.D. = 1.64) in Wave II, 2.52 (S.D. = 1.87) in Wave III, and 2.61 (S.D. = 1.87) in Wave IV. Female participants' alcohol use averaged 0.93 (S.D. = 1.34) in Wave I, 1.01 (S.D. = 1.44) in Wave II, 1.87 (S.D. = 1.58) in Wave III, and 1.80 (S.D. = 1.65) in Wave IV. For males, alcohol use frequency increases over the life course while, for females, alcohol use peaks in Wave III and slightly declines in Wave IV. Wave-to-wave correlations suggest the largest growth occurred between Wave II and Wave III for both males and females (male: WI-WII, $r = .51$, $p < .001$, WII-WIII, $r = .25$, $p < .001$, WIII-WIV, $r = .48$, $p < .001$; female: WI-WII, $r = .55$, $p < .001$, WII-WIII, $r = .33$, $p < .001$, WIII-WIV, $r = .45$, $p < .001$). Throughout all four waves, 92 (8.77%) males and 129 (10.63%) females reported having abstained from alcohol use in the 12 months prior to data collection across all four waves.

Table 8

Frequency of Alcohol Use, Binge Drinking, and Prevalence of Alcohol Dependence in the past 12 Months by Sex and Wave

	Males				Females			
	WI	WII	WIII	WIV	WI	WII	WIII	WIV
Alcohol Use Frequency								
Never	579	529	263	251	682	649	348	414
1-2 Days	164	123	82	73	229	169	192	152
3-12 Days	119	108	127	134	129	135	227	218
2-3 Days per Month	71	76	183	170	81	93	216	196
1-2 Days per Week	71	81	239	251	66	68	167	169
3-5 Days per Week	24	49	105	127	20	22	50	50
Every Day or Almost Every Day	16	9	43	40	5	10	8	14
Mean Alcohol Use Frequency	1.07	1.22	2.52	2.61	.93	1.01	1.87	1.80
(Standard Deviation Alcohol Use Frequency)	1.52	1.64	1.87	1.87	1.34	1.44	1.58	1.65
Binge Drinking Frequency								
Never	754	652	441	455	944	864	730	762
1-2 Days	87	85	171	174	108	102	191	178
3-12 Days	67	65	106	136	64	60	111	105

(continued)

	Males				Females			
	WI	WII	WIII	WIV	WI	WII	WIII	WIV
2-3 Days per Month	52	61	128	116	43	55	82	95
1-2 Days per Week	51	66	130	111	29	41	66	53
3-5 Days per Week	22	31	52	41	16	13	20	16
Every Day or Almost Every Day	14	16	15	12	7	10	2	3
Mean Binge Drinking Frequency	.74	.94	1.57	1.45	.50	.59	.86	.81
(Standard Deviation Binge Drinking Frequency)	1.42	1.58	1.72	1.64	1.14	1.25	1.33	1.29
Alcohol Use Age of Onset								
Mean Age	—	—	—	16.46	—	—	—	17.25
(Standard Deviation)	—	—	—	.05	—	—	—	.05
Alcohol Dependence								
Prevalence	—	—	—	109	—	—	—	66

Binge drinking frequency. Participants reported the frequency with which they binge drank at each of the four waves of data collection. Binge drinking was measured by asking "over the past 12 months, on how many days did you drink five or more drinks in a row?" Aligning this measure with current definitions of binge drinking (e.g., see NIAAA, 2004), Wave IV specified the threshold of binge drinking by sex. That is, male participants were asked about the frequency of drinking five or more drinks in a row while females were asked about the frequency of drinking four or more drinks in a row. The delay in altering this item to be sex specific may slightly impact results; Waves I, II, and III measures may capture slightly more severe binge drinking among females. Male binge drinking averaged 0.74 (S.D. = 1.42) in Wave I, 0.94 (S.D. = 1.58) in Wave II, 1.57 (S.D. = 1.72) in Wave III, and 1.45 (S.D. = 1.64) in Wave IV. Females binge drinking averaged 0.50 (S.D. = 1.14) in Wave I, 0.59 (S.D. = 1.25) in Wave II, 0.86 (S.D. = 1.33) in Wave III, and 0.81 (S.D. = 1.29) in Wave IV. Like alcohol use frequency, wave-to-wave correlations indicate that the largest change in binge drinking occurred between Wave II and Wave III (male: WI-WII, $r = .45$, $p < .001$, WII-WIII, $r = .19$, $p < .001$, WIII-WIV, $r = .40$, $p < .001$; female: WI-WII, $r = .46$, $p < .001$, WII-WIII, $r = .24$, $p < .001$, WIII-WIV, $r = .44$, $p < .001$).

Alcohol use onset. Onset of alcohol use was measured in Wave IV. Participants were first asked whether they had ever had a single occasion of drinking. To assess this, participants were asked "have you had a drink of beer, wine, or liquor more than two or three times? Do not include sips or tastes from someone else's drink." Those that responded in the affirmative were asked a follow-up question assessing the age at which alcohol use began. Specifically, participants were asked "how old were you when you

first had an alcoholic drink? By drink, we mean a glass of wine, a can or bottle of beer, a wine cooler, a shot glass of liquor, or a mixed drink, not just sips or tastes from someone else's drink." Responses to this follow up question ranged from 5 to 30 among males and 8 to 30 among females. Of participants reporting alcohol use onset, males average age of onset was 16.45 (S.D. = 3.09) while female average age of onset was 17.25 (S.D. = 17.25). In models that include alcohol use onset as a control variable, individuals who reported no alcohol use onset were coded to "onset" at the maximum reported age, as this method is preferable to excluding all individuals without alcohol use onset.

Alcohol dependence. Lifetime prevalence of alcohol use disorders was measured in Wave IV. Due to collection of Wave IV data occurring in 2008, diagnostic criteria from the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) was used (American Psychiatric Association, 2000). DSM-IV alcohol use disorders include alcohol dependence and alcohol abuse. As reviewed above, significant variation in DSM diagnostic criteria has occurred over time, including between the then-current DSM-IV criteria and the current DSM-V criteria (American Psychiatric Association, 2013). Due to these changes, the current analysis will focus solely on alcohol dependence for three primary reasons. First, previous literature has primarily focused on alcohol dependence rather than alcohol abuse, possibly due to the heightened severity of alcohol dependence as compared to alcohol abuse. That is, dependence incorporates symptoms indicative of alteration of biological functioning whereas abuse incorporates symptoms focused upon the social consequences of use. DSM-IV criteria for dependence is met if the individual experienced clustering of three or more symptoms within a twelve month period broadly including tolerance, withdrawal, escalation in amount and attention toward use, and

reduced attention to non-alcohol-related activities. Criteria for abuse was met if the individual experienced one or more symptom within a twelve month period broadly including experiences of problems at work, school, family, and friends, legal problems, or engaging in high-risk situations due to use. Second, while many changes have occurred to the diagnostic criteria of alcohol dependence and alcohol abuse throughout DSM revisions, the diagnostic criteria for alcohol dependence has been more stable than that of alcohol abuse. As such, results from the current dissertation may be at a greater advantage of being useful when examining alcohol dependence defined by current DSM-V criteria for alcohol use disorders and with future revisions of the DSM.

As such, alcohol dependence was coded as "0" = no alcohol dependence, "1" = alcohol dependence if at least 3 of the following experiences occurred together in a twelve month period: 1. "Have you ever found that you had to drink more than you used to in order to get the effect you wanted?" 2. "Has there ever been a period when you spent a lot of time drinking, planning how you would get alcohol, or recovering from a hangover?" 3. "Have you often had more to drink or kept drinking for a longer period of time than you intended?" 4. "When you decided to cut down or quit drinking, were you able to do so for at least one month?" 5. "Has there ever been a period of time when you wanted to quit or cut down on your drinking?" 6. "During the first few hours of not drinking, do you experience withdrawal symptoms such as the shakes, feeling anxious, trouble getting to sleep or staying asleep, nausea, vomiting, or rapid heartbeats?" 7. "Have you ever continued to drink after you realized drinking was causing you any emotional problems (such as feeling irritable, depressed, or uninterested in things or having strange ideas) or causing you any health problems (such as ulcers, numbness in

your hands/feet or memory problems)?" or 8. "Have you ever given up or cut down on important activities that would interfere with drinking like getting together with friends or relatives, going to work or school, participating in sports, or anything else?"[1] Of the 1049 male participants and 1213 female participants, 109 and 66 met criteria for alcohol dependence measured at Wave IV, respectively. Of note, because this measure captured life time prevalence, temporal ordering of this dependent variable and proximal stress cannot be established. As such, results of models containing proximal stress will be presented as preliminary evidence only.

Control Variables

To account for the previously mentioned confounds, control variables for the analyses will closely follow that of Shin, Miller, and Teicher's (2013) longitudinal analysis of childhood abuse on heavy episodic drinking in the Add Health data. As such, there are four control variables in the current study: age, race, parental relationship quality, and depression. Age was measured as a continuous variable at each of the four waves. As previously discussed, due to racial stratification of the functionality of the serotonin polymorphisms, models will contain controls for race. Further, analyses will be replicated in race-specific sub-samples to ensure that results do not fluctuate as a function of race. Previous literature also suggests that males and females may vary in serotonin polymorphism functionality as well as the impact of distal and proximal stress. As such, all analyses will be stratified by sex and results will be presented for male-only and female-only subsamples.

[1] Item 4 was asked only if the person reported attempting to quit (skip pattern item not shown). Item 5 was asked only if the person reported not attempting to quit.

Quality of relationship with parents was measured in Wave I by the average score of four items asking participants “how close do you feel” and “how much do you think s/he cares about you” with each item assessed for the mother and father. Potential responses were captured on a Likert-type scale with 1 = not at all, 2 = very little, 3 = somewhat, 4 = quite a bit, and 5 = very much. For participants reporting parental quality of only one parent, the average of the two scores for that parent were computed as parental quality. The average for the parental quality measure was 4.62 (S.D. = .51).

Depression will also be controlled for. Similar to childhood abuse measures, depression diagnosis was measured in Wave IV by asking participants, “has a doctor, nurse or other health care provider ever told you that you have or had depression?” with 326 (14.42%) reporting yes and 1935 (85.58%) reporting no. For those that reported yes, a follow up question measured the age at which the depression began with an average diagnosis given at 21.5 years old. Depression was then coded for each wave as having been diagnosed = 1 and no previous diagnosis = 0 for each wave. Coded in this way, depression will be coded as 1 for each wave following onset.

Finally, as previously discussed, it is largely unknown whether variation in the association between stress and alcohol use is due to differences in biological sex or social sex roles. In Wave III, Bem Sex-Role Inventory (BSRI) scores were obtained from a subsample of the Add Health participants (n = 4159) of which 16.88% (n = 702) were also included in the genetic supplemental sample. BSRI data was collected using a short form version (30 items) of an original 60 item scale. The BSRI was originally developed by Bem and Allen (1974) to measure the degree to which individuals identify with masculine and feminine sex roles. Females reported a significantly greater level of

femininity (mean = 57.22, S.D. = 10.93) than males (mean = 50.76, S.D. = 13.66; t = 6.61, $p < .001$). No significant difference was observed, however, in level of masculinity between males (mean = 50.48, S.D. = 11.83) and females (mean = 49.69, S.D. = 10.77; t = -0.88, $p > .05$).

Sex role adherence was categorized into four dichotomous variables. Participants were divided into "masculine," "feminine," "androgynous," and "undifferentiated" subsamples based on the relative score of masculinity and femininity. Consistent with prior research (Bem, 1977; Berdahl, 2007; Daigle & Mummert, 2014; Fischer & Narus, 1981; Hoffman & Borders, 2001; Kopper, 1996), participants were coded as "masculine" if their masculinity score was above the median masculinity score and their femininity score was below the median. Conversely, participants were coded as "feminine" if their femininity score was above the median and their masculinity score was below the median. Those whose masculinity and femininity scores were both above the median of their respective scores were coded as "androgynous" while those that scored below their respective medians were coded as "undifferentiated." Among males, this resulted in 62 (26.61%) participants being coded as masculine, 24 (10.3%) as feminine, 65 (27.90%) as androgynous, and 82 (35.19%) as undifferentiated. Among females, this resulted in 50 (14.49%) participants being coded as masculine, 87 (25.22%) as feminine, 119 (34.49%) as androgynous, and 89 (25.80%) as undifferentiated. Males were significantly more likely to be categorized as masculine (t = -3.65, $p < .001$) and undifferentiated (t = -2.44, $p < .05$) and females were significantly more likely to be categorized as feminine (t = 4.54, $p < .001$). As will be discussed in the plan of analysis, due to significant reduction in sample size, only preliminary models will be presented analyzing the GxExE model on

alcohol use, binge drinking, and alcohol dependence stratified by masculinity and femininity as indicated by BSRI scores.

Plan of Analysis

Analyses of data will begin with bivariate statistics evaluating direct associations between distal stress, proximal stress, alcohol use and binge drinking frequency, and alcohol use age of onset in each wave and alcohol dependence in Wave IV. Following, three sets of models will be estimated to test the GxExE model of 1. alcohol use frequency, 2. binge drinking frequency, and 3. alcohol use onset. Growth Curve Modeling (GCM) will be used for the model sets one and two. Model set three will be estimated via survival analysis using Cox regression. Preliminary analyses of sex-role stratified subsamples will be presented for each of these three model sets as well. Additionally, analyses will include preliminary models of alcohol dependence in gender-specific subsamples.

For model sets one and two, GCM is ideal to analyze both between individual differences and within individual change in alcohol use behaviors. This approach is preferable to traditional change scores, as greater power is available in GCM models (Curran, Obeidat, & Losardo, 2010; Muthen & Curran, 1997). For model set three, Cox regression will be used to estimate the time to “failure” of first alcohol use. This approach is preferable to traditional ordinary least square regression as it accounts for censorship of individuals that have not used alcohol and thus for whom age of onset is not applicable. Preliminary alcohol dependence models will be estimated using binary logistic regression given the dichotomous nature of alcohol dependence diagnosis. Importantly, as alcohol dependence is measured as a lifetime prevalence, models assessing the effect of proximal

stress should be viewed with extreme caution, as temporal ordering of stress preceding alcohol dependence criteria cannot be established.

As many individuals in the analytic sample are from the shared households, these models will be estimated using a three level multilevel modeling approach (level 1 = dependent variable observation at each wave; level 2 = individual; level 3 = family). As previously discussed, literature suggests that stress and genetic factors may not equally affect female and male alcohol use. Because single group GCM assumes no systematic difference in parameters (Curran, Obeidat, & Losardo, 2010), multiple group GCMs will be estimated, grouped by biological sex, allowing parameters of interest to vary freely across groups.

Model set 1 will include the following steps: step 1: distal environment, step 2: proximal environment, step 3: distal environment and proximal environment directly and in interaction. Model set 2 will include the following steps: step 1: direct genetic effect of MAOA, step 2: MAOA and distal environment directly and in interaction, step 3: MAOA and proximal environment directly and in interaction, step 4: MAOA, distal environment, proximal environment directly, in all combinations of 2-way interactions, and in 3-way interaction. Model set 3 will include the following steps: step 1: direct genetic effect of 5-HTTLPR, step 2: 5-HTTLPR and distal environment directly and in interaction, step 3: 5-HTTLPR and proximal environment directly and in interaction, step 4: 5-HTTLPR, distal environment, proximal environment directly, in all combinations of 2-way interactions, and in 3-way interaction. In an effort to be direct, only step 3 from model set 1 and step 4 from models sets 2 and 3 will be presented in tables while the remaining models will be discussed in text when appropriate. All models will be estimated with controls for age,

race, parental relationship quality, and depression while model sets 1 and 2 will also include controls for alcohol-use onset.

CHAPTER IV

Results

Analyses began with bivariate correlations between each independent variable at each wave and each dependent variable at each wave. The correlation matrices for males and females are presented for Waves I through IV in Tables 9 through 12, respectively. Male correlations are presented in the lower, left-hand side of the tables while female correlations are presented in the upper, right-hand side of the tables. Following, models testing direct and two-way interactions with MAOA and 5-HTTLPR are discussed in text, but not presented in tabular form. Then, ExE and GxExE models are presented in text and in tables (Tables 15 through 21) for alcohol use, binge drinking, and alcohol onset (step 3 from model set 1 and step 4 from models sets 2 and 3). Finally, results of preliminary models for alcohol dependence and sex-role analyses are discussed in text with tables available in Appendices A through D.

Bivariate Results

Childhood abuse did not directly correlate with male binge drinking or alcohol use age of onset in any wave, but was significantly associated with an increase in male alcohol use frequency in Wave III (early onset: $r = .07$, $p < .05$) and alcohol dependence among males in Wave IV (early onset: $r=.15$, $p<.001$; middle onset: $r=.07$, $p<.05$). In females, early-onset childhood abuse was associated with alcohol use frequency in Wave IV ($r = .08$, $p < .01$). Middle-onset childhood abuse was associated with significantly higher binge drinking frequency in Wave I ($r = .06$, $p < .05$). Late-onset childhood abuse was associated with significantly greater frequency of alcohol use in Waves I and II (WI:

r = .09, p < .01; WII: r = .11, p < .001) and binge drinking in Waves I and II (WI: r = .10, p < .001; WII: r = .08, p < .01).

Proximal stress was associated with an increase in male alcohol use in Waves I and II (WI: r = .12, p < .001; WII: r = .16, p < .001) and binge drinking in Waves I and II in the expected direction (WI: r = .13, p < .001; WII: r = .15, p < .001) and Wave IV in the opposite than expected directions (WVI: r = -.06, p < 05). Proximal stress was associated with decreased age of alcohol use onset in Wave II (r = -.11, p < .001) among males. No significant correlation between proximal stress and alcohol dependence was found for males in Wave IV. Among females, proximal stress was associated with greater frequency of alcohol use (r = .14, p < .001) and binge drinking in Wave I (r = .17, p < .001) and lower age of alcohol use onset in Wave IV (r = -.06, p < .05). Proximal stress did not significantly correlate with alcohol dependence among females in Wave IV.

For the candidate genes of interest among males, MAOA-L carriers reported significantly less alcohol use (r = -.08, p < .05) and binge drinking (r = -.08, p < .01) in Wave III. No significant correlation was found between MAOA and alcohol use age of onset or alcohol dependence. All male correlations between 5-HTTLPR and alcohol use, binge drinking, alcohol use age of onset, and alcohol dependence were non-significant. For females, MAOA-L carriers reported significantly less binge drinking in Wave I (r = -.10, p < .01) but significantly greater levels of alcohol use (r = .11, p < .01) and binge drinking (r = .08, p < .05) in Wave IV. Female 5-HTTLPR, s/l genotype was associated with significantly greater alcohol use (r = .06, p < .05) and binge drinking (r = .06, p < .05) while l/l genotype was associated with significantly lower levels of alcohol use (r = -.07, p < .05) and binge drinking (r = -.08, p < .01) in Wave III. No significant correlation

was found between MAOA and 5-HTTLPR with alcohol use age of onset or alcohol dependence.

Of the control variables, for males, parental quality was negatively associated with alcohol use in Waves I, II, and III (WI: $r = -.14$, $p < .001$; WII: $r = -.12$, $p < .001$; WIII: $r = -.07$, $p < .05$) and binge drinking in Waves I and II (WI: $r = -.16$, $p < .001$; WII: $r = -.10$, $p < .01$). For females, parental quality was associated with a decrease in alcohol use frequency in Waves I and II (WI: $r = -.13$, $p < .001$; WII $r = -.10$, $p < .001$) and binge drinking Waves I, II, and III (WI: $r = -.11$, $p < .001$; WII: $r = -.13$, $p < .001$; WIII: $r = -.06$, $p < .05$). Depression was not significantly associated with alcohol use or binge drinking in any wave for males, but was significantly positively associated with binge drinking in females in Wave I ($r = .09$, $p < .01$).

Table 9

Wave I Correlation Matrix

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
1. Alcohol Use Frequency	—	.73***	-.24***	.21***	.11***	-.09**	.02	-.10***	-.13***	.05	.02	.04	.09**	.14***	-.03	.05	.01	-.05
2. Binge Drinking Frequency	.81***	—	-.15***	.15***	.09**	-.08**	.01	-.06*	-.11***	.09**	.03	.06*	.10***	.17***	-.10**	.04	-.02	-.00
3. Alcohol Use Onset	-.19***	-.14***	—	.11***	-.21***	.21***	.03	.06*	.04	-.01	-.10***	-.02	-.01	-.00	-.00	-.01	-.03	.04
4. Age	.27***	.26***	.11***	—	-.02	-.06*	.05	.07*	-.08**	.03	.04	.00	.27***	-.02	.02	.07*	.03	-.09**
5. White	.06*	.06	-.25***	-.00	—	-.59***	-.50***	-.33***	.05	.05	.00	-.02	-.00	-.02	-.27***	-.02	.05	-.04
6. Black	-.07*	-.09**	.18***	-.05	-.56***	—	-.20***	-.13***	.02	-.01	-.03	.02	-.02	.00	.22***	-.15***	-.10***	.23***
7. Hispanic	.06	.09**	.07*	.04	-.53***	-.18***	—	-.11***	-.03	-.03	.00	-.02	.02	.03	.00	.05	.05	-.10***
8. Other	-.10***	-.11***	.11***	.02	-.35***	-.12***	-.12***	—	-.08**	-.04	.04	.03	.01	-.03	.18***	.20***	-.01	-.15***
9. Parental Quality	-.14***	-.16***	.11**	-.12***	-.08*	.08**	.04	-.03	—	-.03	-.08**	-.08**	-.14***	-.10***	-.10**	-.01	-.02	.03
10. Depression	.02	.03	-.03	.06	.05	-.03	-.02	-.03	-.02	—	.06*	-.01	.02	.06	-.00	.02	-.09**	.08**
11. Early Childhood Abuse	.01	.01	-.10**	.01	-.01	-.02	.00	.04	-.12***	.12***	—	.02	-.07*	.10***	.06	.03	-.03	.01
12. Middle Childhood Abuse	.00	.02	.01	.00	.04	.00	-.05	.00	-.06*	.03	.01	—	-.02	.03	-.07	-.01	-.00	.01

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
13. Late Childhood Abuse	.03	.04	.05	.23***	-.04	.01	.02	.05	-.06	.03	-.03	-.00	—	-.03	.04	-.00	.01	-.02
			-.03															
14. Proximal Stress	.12***	.13***	.02	.02	.00	-.03	.04	-.02	-.07*	-.04	.01	.04	.02	—	-.04	-.06	-.00	.01
15. MAOA-L	.04	.04	.03	.03	-.13***	.14***	.01	.02	.03	-.05	.00	-.02	-.03	-.01	—	-.44	-.06	.00
16. S/S	-.05	-.06	-.01	-.01	-.09**	-.13***	.09**	.22***	.01	.01	.07	.03	.08	.05	-.02	—	-.44***	-.36***
17. S/L	-.01	.00	.02	.02	.09**	-.11***	.03	-.05	-.02	-.00	-.01	-.03	-.02	.00	-.05	-.48***	—	-.68***
18. L/L	.06	.05	-.01	-.01	-.02	.23***	-.11***	-.13***	.02	-.00	.05	.01	-.05	-.04	.08*	-.36***	-.65***	—

Note: * $p < .05$; ** $p < .01$; *** $p < .001$.

Table 10

Wave II Correlation Matrix

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
1. Alcohol Use Frequency	—	.78 ***	-.33 ***	.18 ***	.14 ***	-.11 ***	-.01	-.09 **	-.10 ***	.02	.04	-.02	.11 ***	.03	-.01	.04	.02	-.04
2. Binge Drinking Frequency	.85 ***	—	-.24 ***	.09 **	.12 ***	-.11 ***	-.00	-.05	-.13 ***	.03	.01	-.01	.08 **	.06	-.07	.03	.01	-.03
3. Alcohol Use Onset	-.24 ***	-.17 ***	—	.11 ***	-.21 ***	.21 ***	.03	.06 *	.04	-.00	-.10 ***	-.03	.00	.01	-.00	-.01	-.03	.04
4. Age	.31 ***	.28 ***	.12 ***	—	-.01	-.07 *	.04	.08 *	-.09 **	.04	.04	-.05	.23 ***	-.05	.00	.07 *	.03	-.09 **
5. White	.13 ***	.16 ***	-.25 ***	-.01	—	-.59 ***	-.50 ***	-.33 ***	.05	.06 *	.00	-.02	-.02	-.03	-.27 ***	-.02	.05	-.04
6. Black	-.16 ***	-.17 ***	.18 ***	-.06	-.56 ***	—	-.20 ***	-.13 ***	.02	-.02	-.03	.02	-.00	-.03	.22 ***	-.15 ***	-.10 ***	.23 ***
7. Hispanic	.02	.02	.07 *	.05	-.53 ***	-.18 ***	—	-.11 ***	-.03	-.04	.00	-.02	.02	.06 *	.00	.05	.05	-.09 ***
8. Other	-.04	-.07 *	.11 ***	.03	-.35 ***	-.12 ***	-.12 ***	—	-.08 **	.04	.04	.04	.02	.01	.18 ***	.20 ***	-.01	-.15 ***
9. Parental Quality	-.12 ***	-.10 **	.11 **	-.11 ***	-.08 *	.08 **	.04	-.03	—	-.07 *	-.08 **	-.08 **	-.15 ***	-.11 ***	-.10 **	-.01	-.02	.03

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
10. Depression	.04	.06	-.04	.07 *	.06	-.01	-.04	-.04	-.01	—	.06	.00	.03	.01	-.04	.01	-.03	.03
11. Early Childhood Abuse	.02	.03	-.10 **	.03	-.01	-.02	.00	.04	-.12 ***	.09 **	—	.02	-.07 *	.00	.06	.03	-.03	.01
12. Middle Childhood Abuse	.03	.06	-.00	-.04	.02	.01	-.05	.02	-.07 *	.09 **	.01	—	-.06	-.00	.07	-.01	-.01	.01
13. Late Childhood Abuse	.02	.01	.04	.19 ***	-.05	.04	.01	.03	-.08 *	.04	-.03	-.03	—	-.01	.04	-.00	.00	-.00
14. Proximal Stress	.16 ***	.15 ***	.02	-.00	.04	-.01	.09 **	-.04	-.03	-.03	.01	.03	.03	—	-.09 *	.00	-.01	.01
15. MAOA-L	.02	.05	.02	.03	-.13	.14 ***	.01	.02	.03	-.03	.00	-.01	-.01	-.01	—	.08 *	-.06	.00
16. S/S	-.01	-.02	.04	-.01	-.09 **	-.13 ***	.09	.22 ***	.01	-.01	.07 *	.04	.04	.01	-.02	—	-.44 ***	-.36 ***
17. S/L	.00	.02	-.01	.03	.09 **	-.11 ***	.03	-.05	-.02	-.01	-.01	-.04	-.01	-.02	-.05	-.47 ***	—	-.68 ***
18. L/L	.00	-.00	-.02	-.03	-.02	.23 ***	-.11 ***	-.13 ***	.02	.02	-.05	.00	-.03	.01	.08 *	-.36 ***	-.65 ***	—

Note: * p < .05; ** p < .01; *** p < .001.

Table 11

Wave III Correlation Matrix

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
1. Alcohol Use Frequency	—	.69 ***	-.47 ***	.06 *	.20 ***	-.21 ***	-.04	-.01	-.04	.04	.02	-.05	-.04	-.03	.06	.02	.06 *	-.07 *
2. Binge Drinking Frequency	.76 ***	—	-.36 ***	-.02	.19 ***	-.21 ***	-.01	-.03	-.03	.03	-.00	-.03	-.01	-.02	.02	.02	.06 *	-.08 **
3. Alcohol Use Onset	-.43 ***	-.33 ***	—	.11 ***	-.21 ***	.21 ***	.03	.06 *	.04	-.04	-.10 ***	-.04	.00	.01	-.00	-.01	-.03	.04
4. Age	.03	-.05	.08 **	—	-.02	-.08 **	.06 *	.08 **	-.07 **	.01	.03	-.06 *	-.02	-.01	.01	.09 **	.04	-.11 ***
5. White	.23 ***	.22 ***	-.25 ***	.01	—	-.59 ***	-.50 ***	-.33 ***	.04	.16 ***	.00	-.02	-.06	-.05	-.27 ***	-.02	.05	-.04
6. Black	-.18 ***	-.16 ***	.18 ***	-.07 *	-.56 ***	—	-.20 ***	-.13 ***	.02	-.09 **	-.03	.02	.02	.01	.22 ***	-.15 ***	-.10 ***	.23 ***
7. Hispanic	-.10 **	-.08 **	.07 *	.05	-.53 ***	-.18 ***	—	-.11 ***	-.03	-.08 **	.00	-.03	.05	.04	.00	.05	.05	-.10 ***
8. Other	-.04	-.07 *	.11 ***	.01	-.35 ***	-.12 ***	-.12 ***	—	-.08 **	-.05	.04	.04	.00	.01	.18 ***	.20 ***	-.01	-.15 ***
9. Parental Quality	-.07 *	-.04	.11 **	-.11 ***	-.08 *	.08 **	.04	-.03	—	-.06	-.08 **	-.08 **	-.09 **	-.04	-.10 **	-.01	-.02	.03

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.
10. Depression	.06	.05	-.00	.05	.08**	-.03	-.05	-.06	-.07*	—	.09**	.07*	-.00	-.01	-.09*	-.01	-.02	.03
11. Early Childhood Abuse	.07*	.01	-.10**	.03	-.01	-.02	.00	.04	-.12***	.08**	—	.02	-.14***	-.00	.06	.03	-.03	.01
12. Middle Childhood Abuse	.06	.04	-.01	-.04	.02	.01	-.04	.02	-.07*	.05	.01	—	-.08**	.00	-.06	-.01	-.01	.01
13. Late Childhood Abuse	-.01	-.01	.04	-.02	-.06*	.06	.01	.01	-.08**	.01	-.08*	-.00	—	.01	-.01	-.00	.00	-.00
14. Proximal Stress	-.02	-.00	.01	-.00	-.02	.04	-.01	-.00	.01	.00	-.02	.02	-.02	—	-.02	-.00	.01	-.01
15. MAOA-L	-.08*	-.08**	.02	.02	-.13***	.14***	.01	.02	.03	-.01	.00	-.01	.02	-.01	—	.08*	-.06	.00
16. S/S	.01	-.01	.04	-.01	-.09**	-.13***	.09**	.22***	-.01	-.01	.07*	.05	.05	.02	-.02	—	-.44***	-.36***
17. S/L	.02	.02	-.01	.03	.09**	-.11***	.03	-.05	-.02	-.02	-.01	-.04	-.01	.01	-.05	-.48***	—	-.68***
18. L/L	-.03	-.01	-.02	-.02	-.02	.23***	-.11***	-.13***	.02	.02	-.05	.00	.03	.00	.08*	-.36***	-.65***	—

Note: * p < .05; ** p < .01; *** p < .001.

Table 12

Wave IV Correlation Matrix

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	19.
1. Alcohol Use Frequency	—	.70 ***	-.64 ***	.26 ***	-.08 **	.12 ***	-.13 ***	-.01	-.02	-.01	.04	.08 **	.01	-.01	-.00	.11 **	.01	.02	-.03
2. Binge Drinking Frequency	.71 ***	—	-.42 ***	.37 ***	-.07 *	.09 **	-.12 ***	.04	-.03	-.06 *	.04	.04	.01	.03	.02	.08 *	.01	.01	-.02
3. Alcohol Use Onset	-.64 ***	-.46 ***	—	-.19 ***	.13 ***	-.21 ***	.21 ***	.03	.06	.04	-.07 *	-.10 ***	-.04	.00	.05	-.00	-.01	-.03	.04
4. Alcohol Dependence	.23 ***	.32 ***	-.24 ***	—	-.06 *	.05	-.05	-.00	-.01	-.04	.13 ***	.08 **	.05	.01	.04	.02	.02	.01	-.02
5. Age	-.05	-.08 *	.11 ***	-.05	—	-.03	-.06 *	.06 *	.08 **	-.07 *	.01	.02	-.07 *	-.04	-.01	.01	.08 **	.02	-.08 **
6. White	.18 ***	.13 ***	-.25 ***	.12 ***	-.00	—	-.59 ***	-.50 ***	-.33 ***	.04	.15 ***	.00	-.02	-.06	-.03	-.27 ***	-.02	.05	-.04
7. Black	-.12 ***	-.12 ***	.18 ***	-.09 **	-.04	-.56 ***	—	-.20 ***	-.13 ***	.03	-.09 **	-.03	.02	.02	.02	.22 ***	-.15 ***	-.10 ***	.23 ***
8. Hispanic	-.06 *	-.04	.07 *	-.04	.04	-.53 ***	-.18 ***	—	-.11 ***	-..03	-.06 *	.00	-.03	.05	.05	.00	.05	.05	-.10 ***
9. Other	-.08 **	-.02	.11 ***	-.04	.00	-.35 ***	-.12 ***	-.12 ***	—	-.07 **	-.06 *	.04	.04	.00	-.04	.18 ***	.20 ***	-.01	-.15 ***

	1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.	14.	15.	16.	17.	18.	19.
10. Parental Quality	-.04	-.05	.11**	-.09**	-.11***	-.08*	.08**	.04	-.03	—	-.02	-.08**	-.08**	-.09**	-.04	-.10**	-.01	-.02	.03
11. Depression	.01	.02	-.05	.15***	-.02	.13***	-.06	-.07*	-.06	-.09**	—	.13***	.10***	.00	-.03	-.08*	.01	-.02	.02
12. Early Childhood Abuse	.02	-.00	-.10**	.15***	.01	-.01	-.02	.00	.04	-.12***	.09**	—	.02	-.14***	-.00	.06	.03	-.03	.01
13. Middle Childhood Abuse	-.01	-.01	-.01	.07*	-.04	.02	.01	-.04	.02	-.07*	.11***	.01	—	-.08**	.00	-.06	-.01	-.01	.01
14. Late Childhood Abuse	-.00	.02	.04	-.00	-.01	-.06*	.06	.01	.01	-.08**	.08*	-.08*	-.00	—	-.01	-.01	-.00	.00	-.00
15. Proximal Stress	-.06	-.06*	-.01	-.00	-.07*	-.04	.07*	.01	-.05	-.04	.07*	-.03	-.01	.00	—	-.01	-.01	.01	.00
16. MAOA-L	.00	-.03	.02	-.02	.02	-.13***	.14***	.01	.02	.03	-.02	.00	-.01	.02	-.02	—	.08*	-.06	.00
17. S/S	-.05	-.01	.04	.00	-.02	-.09**	-.13***	.09**	.22***	.01	-.02	.07*	.05	.05	-.03	-.02	—	-.44***	-.36***
18. S/L	-.00	.01	-.01	.03	.03	.09***	-.11***	.03	-.05	-.02	-.03	-.01	-.04	-.01	-.01	-.05	-.48***	—	-.68***
19. L/L	.04	-.01	-.02	-.04	-.02	-.02	.23***	-.11***	-.13***	.02	.05	-.05	.00	-.03	.03	.08*	-.36***	-.65***	—

Note: * p < .05; ** p < .01; *** p < .001.

To ensure that data could support gene-environment interaction analyses, correlations between MAOA and 5-HTTLPR and childhood abuse and proximal stress were analyzed and are presented in Table 13 for males and females. GxE findings can be problematic when large, significant correlations are found between genetic polymorphisms and the environments they interact with. As can be seen in Table 13, among males, the only significant gene-environment correlations were found for the S/S 5-HTTLPR genotype. S/S was significantly associated with more early childhood abuse in Waves II, III, and IV ($r = .05$, $p < .05$) and late childhood abuse at Wave I ($r = .08$, $p < .05$). Among females, S/S was associated with higher levels of early childhood abuse at Wave I ($r = .07$, $p < .05$) and MAOA-L was associated with higher levels of proximal stress in Wave II ($r = .09$, $p < .05$). Although these correlations were found to be significant, because they are very weak, analyses were conducted as outlined in the plan of analysis although this is a limitation of the current dissertation.

Table 13

Gene-Environment Correlations between MAOA, 5-HTTLPR and Alcohol Use Behaviors across Wave and Sex

	Males				Females			
	MAOA-L	S/S	S/L	L/L	MAOA-L	S/S	S/L	L/L
Early Childhood Abuse								
WI	.00	.03	-.03	.01	.06	.07*	-.01	-.05
WII	.00	.07*	-.01	-.05	.06	.03	-.03	.01
WIII	.00	.07*	-.01	-.05	.06	.03	-.03	.01
WIV	.00	.07*	-.01	-.05	.06	.03	-.03	.01
Middle Childhood Abuse								
WI	-.02	.03	-.03	.00	-.07	-.01	-.00	.01
WII	-.01	.04	-.04	.00	-.07	-.01	-.01	.01
WIII	-.01	.05	-.04	.00	-.06	-.01	-.01	.01
WIV	-.01	.05	-.04	.00	-.06	-.01	-.01	.01
Late Childhood Abuse								
WI	-.03	.08*	-.02	-.05	.04	.01	.01	-.02
WII	-.01	.04	-.01	-.03	.04	-.00	.00	-.00
WIII	.02	.05	-.01	-.03	-.01	-.00	.00	-.00
WIV	.02	.05	-.01	-.03	-.01	-.00	.00	-.00
Proximal Stress								
WI	-.01	.05	.00	-.04	-.04	-.01	-.00	.01
WII	-.01	.01	-.02	.01	-.09*	.00	-.01	.01
WIII	-.01	-.02	.01	.00	-.02	-.00	.01	-.01
WIV	-.02	-.03	-.01	.03	-.01	-.01	.01	.00

Note: * $p < .05$; ** $p < .01$

Alcohol Use Frequency

Model specifications. To analyze the impact of the covariates of interest on growth of alcohol use across time, determination of the shape of the growth curve was first established. Visual analysis of the mean trajectory of alcohol use across sex suggested non-linear growth for both males and females (see Figure 1). Models compared a linear, quadratic, and cubic function of growth. Comparison of change in model fit indices suggested that the quadratic model provided the best fit while remaining parsimonious as large gains in model fit were achieved between the linear and quadratic model but only a small gain was had with the addition of a cubic term. Further, likelihood ratio tests revealed that a significant improvement in the model was gained from the linear to the quadratic (male: LR Chi-Square = 252.46, $p < .001$; female: LR Chi-Square = 209.83, $p < .001$) but no significant improvement was made between the quadratic and cubic (male: LR Chi-Square = .17, $p = .68$; female: LR Chi-Square = 1.25, $p = .26$). See Table 14 for specific model fit indices for each of these functions.

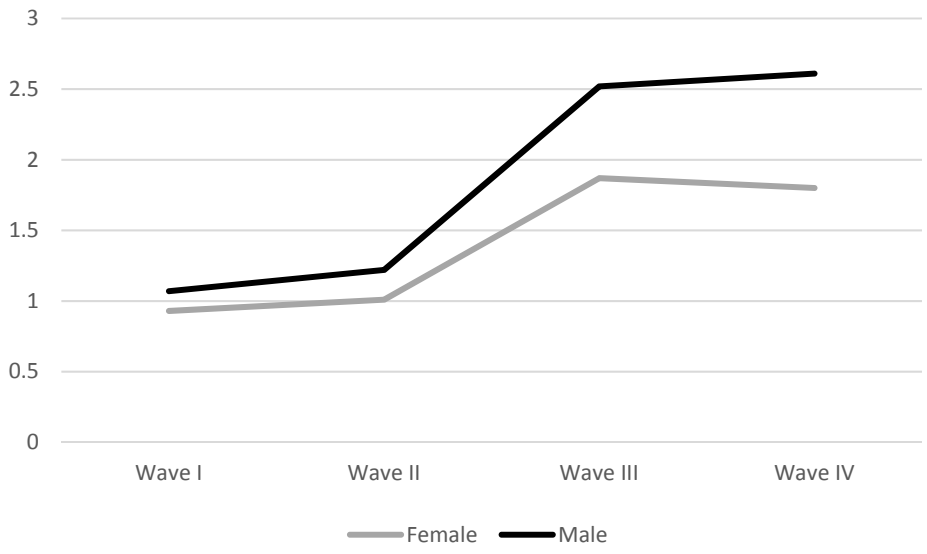

Figure 1: Alcohol Use Frequency by Wave and Sex

Table 14

Model Fit Indices for the Growth of Alcohol Use Frequency by Sex

	Males			Females		
	Wald Chi Square (change)	AIC (change)	BIC (change)	Wald Chi Square (change)	AIC (change)	BIC (change)
Linear	789.93	15847.65	15879.24	440.98	16872.52	16904.86
Quadratic	1116.95 (327.02)	15597.19 (-250.46)	15635.10 (-244.14)	682.59 (241.61)	16664.69 (-207.83)	16703.5 (-201.36)
Cubic	1117.00 (.05)	15599.02 (1.83)	15643.25 (8.15)	683.80 (1.21)	16665.44 (0.75)	16710.72 (7.22)

Note: All Wald Chi Square Statistics $p < .001$

Due to the nested nature of the data (i.e., observations within individuals and individuals within families), models of alcohol use frequency were estimated allowing individuals and families to have random intercepts. This allows the intercepts of individuals and families to vary about the overall fixed intercept of the sample. Similarly, random slopes for individual growth were estimated, allowing the trajectory of each individual to vary about the slope of the overall sample. Because the current dissertation is interested in the effects of distal and proximal stress, serotonergic polymorphisms, and their interactions, the current dissertation estimated only fixed effects of these covariates. The effect of all control variables were estimated as fixed effects as well. While these decisions were made for theoretical reasons, tests were conducted to establish whether

the random intercepts and random slopes of growth contributed to improving the growth model. A likelihood ratio test between fixed and random intercepts model suggested that the addition of the random intercepts was a better fit (male: LR Chi-Square = 414.75, $p < .001$; female: LR Chi-Square = 698.08, $p < .001$). A likelihood ratio test between fixed and random slope of growth also suggested that this addition was a better fit (male: LR Chi-Square = 52.09, $p < .001$; female: LR Chi-Square = 50.06, $p < .001$). Standard errors were estimated as robust standard errors to account for any heteroscedasticity of residual errors. All analyses were estimated with unstructured covariances to avoid default assumptions of independence of all variances and covariances. Multicollinearity diagnostics were analyzed with no variance inflation factor (VIF) over the suggested threshold of 10 (Hair, Black, Babin, Anderson, & Tatham, 2006). Age and age-squared terms, however, had high multicollinearity due to the nature of the terms. Due to overdispersion of the alcohol use variable (WI: mean = .99, variance = 2.00; WII: mean = 1.11, variance = 2.37; WIII: mean = 2.17, variance = 3.10; WIV: mean = 2.18, variance = 3.24), natural log transformation of the alcohol use variable was conducted resulting in a dependent variable that was not overdispersed (WI: mean = .48, variance = .36; WII: mean = .52, variance = .41; WIII: mean = .96, variance = .44; WIV: mean = .95, variance = .47).

Male analysis. Growth curve models for alcohol use frequency among males are presented in Table 15. Model 1 presents final model results for the stress sensitization hypothesis. In direct analyses (not presented in tables) of the influence of childhood abuse, early-onset, middle onset, and late-onset childhood abuse were not significantly associated with alcohol use frequency (early: gamma = -.03, $p = .36$; middle: gamma =

.05, p = .18; late: gamma = -.00, p = .99). Likewise, direct effect of proximal stress on alcohol use frequency was also non-significant (gamma = .04, p = .23). No significant distal environment by proximal environment interaction was observed (early: gamma = .07, p = .51; middle: gamma = -.12, p = .29; late: gamma = -.13, p = .19).

Model 2 presents the final model results of MAOA analyses. In direct analysis, MAOA was not significantly associated with alcohol use frequency (gamma = .00, p = .92). Two-way interactions between MAOA and childhood abuse were not significant (early: gamma = -.01, p = .81; middle: gamma = -.06, p = .37; late: gamma = -.02, p = .71). Two-way interaction between MAOA and proximal stress was found to be significant (gamma = .16, p = .04). In the presented three-way interaction (see Table 15, Model 2), a significant interaction was found between MAOA, late-onset childhood abuse, and proximal stress (gamma = -.58, p < .01).

Model 3 presents the final model results of 5-HTTLPR analyses. s/s and l/l carriers did not report significantly differing levels of alcohol use (s/s: gamma = -.00, p = .96; l/l: gamma = .04, p = .11). In two-way interactions, the effect of early childhood onset childhood abuse was significantly greater among those s/l carriers than among s/s heterozygotes (gamma = -.20, p < .01), a finding in the opposite than expected direction. Proximal stress did not significantly interact with the s/s genotype (gamma = .03, p = .77) or the l/l genotype (gamma = .06, p = .50). In three-way interactions presented in Model 3 of Table 15, no significant three-way interaction was found for the s/s genotype (early: gamma = .16, p = .50; middle: gamma = -.28, p = .41; late: gamma = .04, p = .87) or the l/l genotype (early: gamma = -.12, p = .55; middle: gamma = -.35, p = .18; late: gamma = .00, p = .99).

Table 15

Male Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.31***	.02	.31***	.02	.31***	.02
Age^2	-.01***	.00	-.01***	.00	-.01***	.00
Black	-.13***	.03	-.13***	.04	-.14***	.03
Hispanic	-.03	.03	-.03	.03	-.02	.03
Other	-.09*	.04	-.09*	.04	-.09*	.04
Parental Quality	-.03	.02	-.03	.02	-.03	.02
Depression	-.03	.05	-.03	.05	-.04	.05
Age of Alcohol Onset	-.05***	.00	-.05***	.00	-.05***	.00
Early Childhood Abuse (ECA)	-.03	.03	-.03	.04	.01	.04
Middle Childhood Abuse (MCA)	.06	.04	.08	.05	-.00	.06

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Late Childhood Abuse (LCA)	.01	.03	-.00	.04	-.00	.05
Proximal Stress (PS)	.07	.05	-.03	.06	.03	.07
MAOA-L	—	—	-.01	.03	—	—
s/s	—	—	—	—	.02	.04
l/l	—	—	—	—	.02	.03
ECA x PS	.07	.10	.05	.13	.06	.17
MCA x PS	-.12	.11	-.10	.16	.09	.22
LCA x PS	-.13	.10	.11**	.12	-.13	.15
MAOA-L x ECA	—	—	-.02	.06	—	—
MAOA-L x MCA	—	—	-.06	.07	—	—
MAOA-L x LCA	—	—	.04	.06	—	—
MAOA-L x PS	—	—	.25	.09	—	—
MAOA-L x ECA x PS	—	—	.04	.19	—	—
MAOA-L x MCA x PS	—	—	-.03	.22	—	—

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L x LCA x PS	—	—	-.58**	.20	—	—
s/s x ECA	—	—	—	—	-.22**	.07
l/l x ECA	—	—	—	—	.04	.07
s/s x MCA	—	—	—	—	.04	.09
l/l x MCA	—	—	—	—	.13	.09
s/s x LCA	—	—	—	—	.10	.07
l/l x LCA	—	—	—	—	-.02	.07
s/s x PS	—	—	—	—	.01	.11
l/l x PS	—	—	—	—	.11	.10
s/s x ECA x PS	—	—	—	—	.16	.24
l/l x ECA x PS	—	—	—	—	-.12	.20
s/s x MCA x PS	—	—	—	—	-.28	.34
l/l x MCA x PS	—	—	—	—	-.35	.26
s/s x LCA x PS	—	—	—	—	.04	.22

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
l/l x LCA x PS	—	—	—	—	.00	.25
Constant	-1.84***	.21	-1.82***	.21	-1.81***	.21
Random Effects						
Family						
Standard Deviation of Intercept	.17*	.02	.18*	.02	.18*	.02
Individual						
Standard Deviation of Intercept	.06*	.06	.06*	.06	.02*	.16
Standard Deviation of Slope	.55*	.01	.55*	.01	.55*	.01

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 1018; Model 2: n = 1018; Model 3: n = 1018.

Female analysis. Female alcohol use frequency models are presented in Table 16. Among females, similar to the results of male models, no significant direct effect was found for childhood abuse (early: gamma = -.03, p = .23; middle: gamma = -.01, p = .65; late: gamma = -.01, p = .65) or proximal stress (gamma = .05, p = .08). In the stress sensitization model, no significant interaction between childhood abuse and proximal stress on growth of alcohol use was found (early: gamma = .02, p = .72; middle: gamma = .18, p = .10; late: gamma = -.13, p = .06).

Model 2 presents the final analyses of the interaction between MAOA and distal and proximal stress on alcohol use. In direct effects models, MAOA was not significantly associated with alcohol use frequency (gamma = .04, p = .18). Two-way interactions between MAOA childhood abuse were not significant (early: gamma = -.03, p = .62; middle: gamma = -.06, p = .44; late: gamma = .01, p = .87). The two-way interaction between MAOA and proximal stress was not significant (gamma = .09, p = .28). Three-way interactions between MAOA, distal, and proximal stress can be seen in Model 2 of Table 16. No significant three-way interaction was found among females (early: gamma = -.29, p = .16; middle: gamma = .03, p = .91; late: gamma = .06, p = .75)

Model 3 presents the final results of 5-HTTLPR analyses. In direct effects analyses, the s/s genotype and the l/l genotype did not report significantly different levels of alcohol use frequency (s/s: gamma = .02, p = .52; l/l: gamma = -.01, p = .77). A significant two-way interaction was found between late-onset childhood abuse and the l/l genotype (gamma = .13, p < .01). Other two-way interactions between childhood abuse and the s/s genotype (early: gamma = -.03, p = .64; middle: gamma = -.08, p = .26; late: gamma = .09, p = .15) and l/l genotype (early: gamma = -.03, p = .56; middle: gamma = -

.03, p = .65) were not significant. Two-way interactions between proximal stress and the s/s genotype (gamma = .11, p = .22) and l/l genotype (gamma = .09, p = .18) were also not significant. In female alcohol use three-way interactions presented in Model 3 of Table 16, no significant three-way interaction was found for the s/s genotype (early: gamma = .13, p = .18; middle: gamma = -.22, p = .55; late: gamma = .30, p = .08) or the l/l genotype (early: gamma = -.02, p = .92; middle: gamma = -.15, p = .44; late: gamma = .12, p = .47).

Table 16

Female Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.25***	.02	.26***	.02	.25***	.02
Age^2	-.01***	.00	-.01***	.00	-.01***	.00
Black	-.09**	.03	-.07*	.03	-.09**	.03
Hispanic	-.04	.03	-.05	.04	-.04	.03
Other	-.11***	.03	-.09*	.04	-.12***	.03
Parental Quality	-.05**	.02	-.04	.02	-.05**	.02
Depression	.00	.03	-.02	.04	.00	.03
Age of Alcohol Onset	-.05***	.00	-.05***	.00	-.05***	.00
Early Childhood Abuse (ECA)	-.02	.02	-.05	.05	.01	.04
Middle Childhood Abuse (MCA)	-.05	.03	-.02	.05	-.04	.05
Late Childhood Abuse (LCA)	.00	.03	-.02	.04	-.05	.04

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Proximal Stress (PS)	.05	.04	.01	.07	.01	.06
MAOA-L	—	—	.04	.04	—	—
s/s	—	—	—	—	.01	.04
l/l	—	—	—	—	-.03	.03
ECA x PS	.02	.07	.16	.12	.01	.11
MCA x PS	.18	.10	.11	.16	.28	.15
LCA x PS	-.13	.07	-.18	.11	-.23*	.11
MAOA-L x ECA	—	—	.00	.07	—	—
MAOA-L x MCA	—	—	-.06	.08	—	—
MAOA-L x LCA	—	—	.00	.07	—	—
MAOA-L x PS	—	—	.13	.10	—	—
MAOA-L x ECA x PS	—	—	-.29	.20	—	—
MAOA-L x MCA x PS	—	—	.03	.27	—	—
MAOA-L x LCA x PS	—	—	.06	.20	—	—
s/s x ECA	—	—	—	—	-.05	.07

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
l/l x ECA	—	—	—	—	-.03	.05
s/s x MCA	—	—	—	—	-.05	.07
l/l x MCA	—	—	—	—	-.01	.07
s/s x LCA	—	—	—	—	.06	.06
l/l x LCA	—	—	—	—	.09*	.09
s/s x PS	—	—	—	—	.05	.10
l/l x PS	—	—	—	—	.09	.09
s/s x ECA x PS	—	—	—	—	.13	.18
l/l x ECA x PS	—	—	—	—	-.02	.15
s/s x MCA x PS	—	—	—	—	-.22	.37
l/l x MCA x PS	—	—	—	—	-.15	.20
s/s x LCA x PS	—	—	—	—	.30	.17
l/l x LCA x PS	—	—	—	—	.12	.16
Constant	-.96***	.19	-1.11***	.25	-.95***	.19

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Random Effects						
Family						
Standard Deviation of Intercept	.17*	.02	.16*	.02	.17*	.02
Individual						
Standard Deviation of Intercept	.08*	.03	.06*	.06	.07*	.04
Standard Deviation of Slope	.50*	.01	.50*	.01	.50*	.01

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 1179; Model 2: n = 643; Model 3: n = 1179.

Binge Drinking Frequency

Model specifications. To assess the shape of the growth curve of binge drinking across time, a visual inspection of the growth curve of binge drinking across sex was first conducted (see Figure 2). This curve suggested a non-linear growth of binge drinking. Linear, quadratic, and cubic functions of growth were assessed and fit indices are presented in Table 17. While each additional polynomial function increased model fit, the largest gains in improvement were seen with the addition of a quadratic term. Further, likelihood ratio tests suggested that while the quadratic model was a significant improvement over a linear model for both males and females (male: LR Chi-Square = 198.19, $p < .001$; female: LR Chi-Square = 73.24, $p < .001$), the cubic model was only significant among males and was a marginal improvement (male: LR Chi-Square = 6.32, $p < .05$; female LR Chi-Square = 3.81, $p > .05$). As such, binge drinking growth curve models are estimated using a quadratic growth curve model.

As in alcohol use frequency models, the appropriateness of inclusion of a random intercept and random slope for growth was assessed for binge drinking models. Analyses demonstrated a significant improvement in model fit with the inclusion of a random intercept (male: LR Chi-Square = 300.27, $p < .001$; female LR Chi-Square = 492.30, $p < .001$). Analyses also suggested an improvement in model fit with the inclusion of a random slope for growth (male: LR Chi-Square = 26.62, $p < .001$; female LR Chi-Square = 21.55, $p < .001$). Standard errors were estimated as robust standard errors to account for any heteroscedasticity of residual errors. All analyses were estimated with unstructured covariances to avoid default assumptions of independence of all variances and covariances. Multicollinearity diagnostics were analyzed with no variance inflation factor

(VIF) over the suggested threshold of 10 (Hair, Black, Babin, Anderson, & Tatham, 2006). Age and age-squared terms, however, had high multicollinearity due to the nature of the terms. Due to overdispersion of the binge drinking variable (WI: mean = .60, variance = 1.61; WII: mean = .76, variance = 2.03; WIII: mean = 1.19, variance = 2.47; WIV: mean = 1.11, variance = 2.23), natural log transformation of the binge drinking variable was conducted resulting in a dependent variable that was not overdispersed, with the exception of minor overdispersion in Wave I (WI: mean = .28, variance = .29; WII: mean = .35, variance = .35; WIII: mean = .56, variance = .42; WIV: mean = .53, variance = .40)

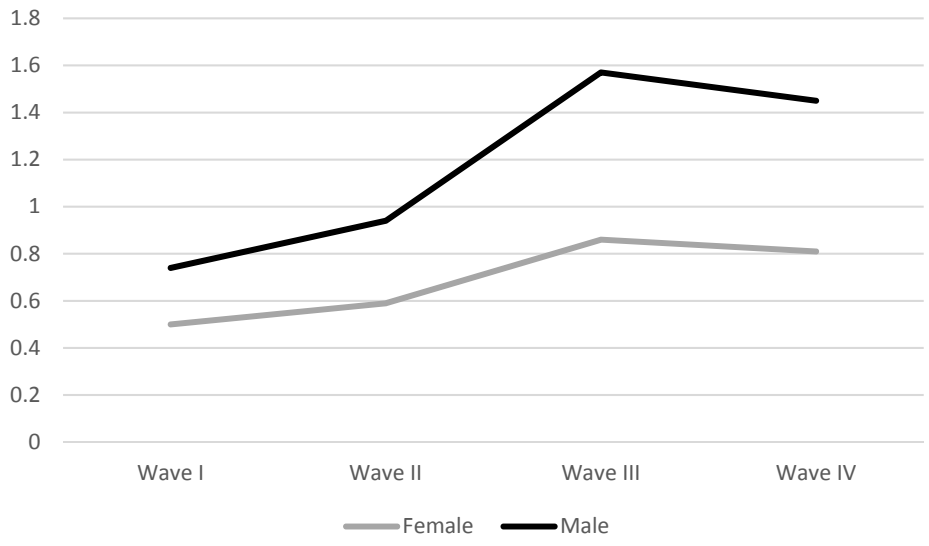

Figure 2: Binge Drinking Frequency by Wave and Sex

Table 17

Model Fit Indices for the Growth of Binge Drinking Frequency by Sex

	Males			Females		
	Wald Chi Square (change)	AIC (change)	BIC (change)	Wald Chi Square (change)	AIC (change)	BIC (change)
Linear	181.59	15262.78	15294.38	66.84	15175.33	15207.67
Quadratic	396.70	15066.59	15104.51	142.22	15104.09	15142.89
	(215.11)	(-196.19)	(-189.87)	(75.38)	(-71.24)	(-64.78)
Cubic	403.91	15062.27	15106.51	146.33	15102.28	15147.55
	(7.21)	(-4.32)	(2.00)	(4.11)	(-1.81)	(4.66)

Note: All Wald Chi Square Statistics $p < .001$

Male analysis. Final models for male binge drinking are presented in Table 18. Model 1 presents the final stress sensitization model. In direct effects analyses (not presented in tables), childhood abuse was not significantly associated with binge drinking (early: gamma = .04, p = .21; middle: gamma = .03, p = .39; late: gamma = .02, p = .56). Proximal stress was also not significantly associated with binge drinking (gamma = .04, p = .25). In the stress sensitization model (see Model 1, Table 18), no significant stress sensitization effect was found (early: gamma = -.03, p = .11; middle: gamma = -.05, p = .60; late: gamma = -.17, p = .08).

Model 2 presents the final model of the MAOA analyses. In models not presented in the table, MAOA did not exert a direct effect on binge drinking (gamma = .01, p = .74). Two-way interactions between MAOA and childhood abuse were not significant

(early: gamma = .07, p = .26; middle: gamma = -.12, p = .11; late: gamma = -.05, p = .46). The two-way interaction between MAOA and proximal stress was also non-significant (gamma = .15, p = .06). Three-way interactions presented in Model 2 of Table 18 show that no three-way interaction between MAOA, distal, and proximal stress was found for males (early: gamma = -.06, p = .75; middle: gamma = .01, p = .97; late: gamma = -.34, p = .10).

Model 3 of Table 18 presents the final analyses of 5-HTTLPR interactions on binge drinking among males. In direct effects models, no direct association was found between binge drinking and the s/s genotype (gamma = -.01, p = .75) or the l/l genotype (gamma = .03, p = .21). Two-way interactions between childhood abuse and the s/s genotype (early: gamma = -.13, p = .09; middle: gamma = .03, p = .73; late: gamma = .02, p = .75) and the l/l genotype (early: gamma = .11, p = .13; middle: gamma = .03, p = .76; late: gamma = -.09, p = .27) were not found to be significant. Proximal stress did not significantly interact with the s/s genotype (gamma = .01, p = .90) or the l/l genotype (gamma = .03, p = .72). Model 3 of Table 18 also presents the results of the three-way 5-HTTLPR analysis on binge drinking. As can be seen, no significant three-way interaction was found for the s/s genotype (early: gamma = .28, p = .26; middle: gamma = -.34, p = .27; late: gamma = .20, p = .37) or the l/l genotype (early: gamma = -.07, p = .80; middle: gamma = -.18, p = .38; late: gamma = .02, p = .93).

Table 18

Male Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.27***	.02	.27***	.02	.27***	.02
Age^2	-.01***	.00	-.01***	.00	-.01***	.00
Black	-.18***	.03	-.18***	.03	-.20***	.03
Hispanic	-.03	.04	-.03	.04	-.03	.04
Other	-.14**	.05	-.14**	.05	-.14**	.05
Parental Quality	-.03	.02	-.03	.02	-.03	.02
Depression	.04	.05	.04	.05	.04	.05
Age of Alcohol Onset	-.03***	.00	-.03***	.00	-.03***	.00
Early Childhood Abuse (ECA)	-.04	.03	-.07	.04	-.03	.05
Middle Childhood Abuse (MCA)	.04	.04	.08	.05	-.00	.07
Late Childhood Abuse (LCA)	.04	.03	.04	.05	.07	.05

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Proximal Stress (PS)	.07	.05	-.01	.05	.07	.07
MAOA-L	—	—	-.00	.03	—	—
s/s	—	—	—	—	.01	.04
l/l	—	—	—	—	.02	.03
ECA x PS	-.03	.11	-.01	.14	-.09	.19
MCA x PS	-.05	.10	-.06	.16	.11	.16
LCA x PS	-.17	.10	-.04	.12	-.21	.15
MAOA-L x ECA	—	—	.08	.07	—	—
MAOA-L x MCA	—	—	-.12	.08	—	—
MAOA-L x LCA	—	—	-.02	.06	—	—
MAOA-L x PS	—	—	.21*	.10	—	—
MAOA-L x ECA x PS	—	—	-.07	.21	—	—
MAOA-L x MCA x PS	—	—	.01	.20	—	—
MAOA-L x LCA x PS	—	—	-.34	.20	—	—
s/s x ECA	—	—	—	—	-.16*	.08

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
l/l x ECA	—	—	—	—	.12	.08
s/s x MCA	—	—	—	—	.07	.10
l/l x MCA	—	—	—	—	.05	.09
s/s x LCA	—	—	—	—	.00	.08
l/l x LCA	—	—	—	—	.05	.11
s/s x PS	—	—	—	—	-.03	.11
l/l x PS	—	—	—	—	.05	.11
s/s x ECA x PS	—	—	—	—	.28	.25
l/l x ECA x PS	—	—	—	—	-.07	.28
s/s x MCA x PS	—	—	—	—	-.34	.31
l/l x MCA x PS	—	—	—	—	-.18	.20
s/s x LCA x PS	—	—	—	—	.20	.22
l/l x LCA x PS	—	—	—	—	.02	.25
Constant	-1.72***	.22	-1.72***	.22	-1.70***	.22

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Random Effects						
Family						
Standard Deviation of Intercept	.19*	.02	.20*	.02	.19*	.02
Individual						
Standard Deviation of Intercept	.12*	.03	.11*	.04	.11*	.04
Standard Deviation of Slope	.54*	.01	.54*	.01	.54*	.01

Note: * $p < .05$; ** $p < .01$; *** $p < .001$; Model 1: n = 1018; Model 2: n = 1018; Model 3: n = 1018.

Female analysis. Among females, Model 1 of Table 19 presents the final model of the stress sensitization hypothesis. In direct effects models, childhood abuse was not found to be significantly associated with growth of binge drinking (early: gamma = -.02, p = .35; middle: gamma = -.01, p = .67; late: gamma = .02, p = .37). Proximal stress, however, was found to be significantly associated with a greater increase in growth of binge drinking (gamma = .09, p < .01). No significant stress sensitization effect was found between childhood abuse and growth of binge drinking (early: gamma = .02, p = .80; middle: gamma = .08, p = .39; late: gamma = -.13, p = .05).

Model 2 of Table 19 presents the final results of MAOA interaction analyses on binge drinking. In direct effects models, MAOA was not found to be directly related to binge drinking (gamma = -.00, p = .95). Two-way interactions between MAOA and childhood abuse were not found to be significant (early: gamma = .07, p = .24; middle: gamma = -.11, p = .12; late: gamma = .02, p = .80) nor was the two-way interaction between MAOA and proximal stress (gamma = .01, p = .88). Three-way interactions between MAOA, distal, and proximal stress are presented in Model 2 of Table 19. No significant three-way interaction was found for female binge drinking (early: gamma = -.22, p = .23; middle: gamma = .12, p = .65; late: gamma = .26, p = .20).

Model 3 of Table 19 presents the final results of 5-HTTLPR interactions of female binge drinking. In direct effects analyses, no direct effect of the s/s genotype (gamma = .01, p = .78) or l/l genotype (gamma = .00, p = .91) was found. Two-way interaction analyses found a significant interaction between the s/s genotype and middle childhood onset abuse (gamma = -.23, p < .01) although no significant interaction between s/s genotype and early or late-onset childhood abuse (early: gamma = -.03, p =

.61; late: gamma = -.02, p = .68). No significant two-way interaction was found between childhood abuse and the l/l genotype (early: gamma = .00, p = .99; middle: gamma = -.08, p = .23; late: gamma = .06, p = .24). Proximal stress did not significantly interact with the s/s genotype (gamma = .16, p = .07) or the l/l genotype (gamma = .07, p = .24). Three-way interactions between 5-HTTLPR and distal and proximal stress on female binge drinking are presented in Model 3 of Table 19. No significant three-way interaction was found for the s/s genotype (early: gamma = .26, p = .19; middle: gamma = -.28, p = .40; late: gamma = .22, p = .26). A significant three-way interaction between middle-onset childhood abuse, proximal stress, and l/l genotype was found (gamma = -.41, $p < .05$) but not for early- or late-onset childhood abuse (early: gamma = -.16, p = .23; late: gamma = -.12, p = .43).

Table 19

Female Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.12***	.01	.13***	.02	.12***	.01
Age^2	-.00***	.00	-.00***	.00	-.00***	.00
Black	-.12***	.02	-.12***	.03	-.13***	.02
Hispanic	-.04	.03	-.03	.04	-.04	.03
Other	-.11**	.04	-.03	.05	-.10**	.03
Parental Quality	-.06***	.02	-.05*	.02	-.06***	.02
Depression	.01	.04	-.01	.05	.01	.04
Age of Alcohol Onset	-.03***	.00	-.03***	.00	-.03***	.00
Early Childhood Abuse (ECA)	-.02	.02	-.09*	.04	-.02	.04
Middle Childhood Abuse (MCA)	-.02	.03	.01	.05	.03	.05
Late Childhood Abuse (LCA)	.04	.03	.04	.04	.02	.04

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Proximal Stress (PS)	.10**	.04	.06	.06	.01	.05
MAOA-L	—	—	-.00	.04	—	—
s/s	—	—	—	—	.04	.03
l/l	—	—	—	—	-.01	.03
ECA x PS	.02	.07	.14	.11	.03	.10
MCA x PS	.08	.10	.02	.14	.27	.14
LCA x PS	-.13	.07	-.22*	.10	-.14	.09
MAOA-L x ECA	—	—	.10	.06	—	—
MAOA-L x MCA	—	—	-.13	.07	—	—
MAOA-L x LCA	—	—	-.01	.06	—	—
MAOA-L x PS	—	—	-.01	.10	—	—
MAOA-L x ECA x PS	—	—	-.22	.18	—	—
MAOA-L x MCA x PS	—	—	.12	.27	—	—
MAOA-L x LCA x PS	—	—	.26	.20	—	—

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
s/s x ECA	—	—	—	—	-.06	.06
l/l x ECA	—	—	—	—	.01	.05
s/s x MCA	—	—	—	—	-.20**	.07
l/l x MCA	—	—	—	—	-.04	.07
s/s x LCA	—	—	—	—	-.05	.06
l/l x LCA	—	—	—	—	.07	.05
s/s x PS	—	—	—	—	.10	.10
l/l x PS	—	—	—	—	.18*	.08
s/s x ECA x PS	—	—	—	—	.26	.19
l/l x ECA x PS	—	—	—	—	-.16	.13
s/s x MCA x PS	—	—	—	—	-.28	.33
l/l x MCA x PS	—	—	—	—	-.41*	.19
s/s x LCA x PS	—	—	—	—	.22	.20
l/l x LCA x PS	—	—	—	—	-.12	.15

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Constant	-.17	.16	-.21	.21	-.18	.16
Random Effects						
Family						
Standard Deviation of Intercept	.18*	.02	.19*	.02	.18*	.02
Individual						
Standard Deviation of Intercept	.12*	.02	.07*	.05	.12*	.03
Standard Deviation of Slope	.45*	.01	.45*	.01	.45*	.01

Note: * $p < .05$; ** $p < .01$; *** $p < .001$; Model 1: n = 1179; Model 2: n = 643; Model 3: n = 1179.

Alcohol Use Onset

Model specifications. To estimate the effects of the genetically moderated stress sensitization hypothesis on alcohol use onset, Cox Proportional Hazards models were employed. Multicollinearity diagnostics were analyzed with no variance inflation factor (VIF) over the suggested threshold of 10 (Hair, Black, Babin, Anderson, & Tatham, 2006). Proportional hazards assumptions were assessed for each model presented in tables and in text via a chi-square test of proportional hazards and no model exceeded the $p < .05$ threshold.

Male analysis. Survival analyses results for male onset of alcohol use are presented in Table 20. Model 1 presents the results of the final stress sensitization hypothesis. In direct effects models, late-onset childhood abuse was significantly associated with a decrease in alcohol use age of onset (H.R. = .82, $p < .01$). Early- and middle-onset childhood abuse were not significantly associated with age of onset (early: H.R. = 1.08, $p = .35$; middle: H.R. = 1.17, $p = .15$). Proximal stress was also not significantly associated with alcohol use onset (H.R. = 1.00, $p = .98$). In the stress sensitization model (see Model 1, Table 20), no significant interaction was found between childhood abuse and proximal stress among males (early: H.R. = .81, $p = .44$; middle: H.R. = 1.21, $p = .58$; late: H.R. = 1.28, $p = .13$).

Model 2 presents the final results of MAOA interactions. In direct effects models, MAOA was not significantly associated with alcohol use onset (H.R. = 1.02, $p = .75$). No significant two-way interaction was found between MAOA and childhood abuse (early: H.R. = 1.04, $p = .81$; middle: H.R. = 1.16, $p = .47$; late: H.R. = .93 $p = .59$) or proximal stress (H.R. = 1.28, $p = .14$). Three-way interactions for MAOA, distal and proximal

stress, as presented in Model 2, were not significant (early: H.R. = 1.78, p = .27; middle: H.R. = .45, p = .22; late: H.R. = .77, p = .42).

Model 3 presents the final results of 5-HTTLPR interactions with distal and proximal stress on male alcohol use onset. No direct effect of the s/s genotype (H.R. = .98, p = .84) or l/l genotype (H.R. = .99, p = .88) was found. A significant two-way interaction between middle-onset childhood abuse and the s/s genotype was found (H.R. = 2.05, p < .001). Other two-way interactions between childhood abuse and the s/s genotype (early: H.R. = 1.09, p = .65; late: H.R. = .99, p = .97) and l/l genotype (early: H.R. = 1.30, p = .16; middle: H.R. = 1.52, p = .10; late: H.R. = .92, p = .59) were not significant. Two-way interactions between proximal stress and the s/s genotype (H.R. = 1.38, p = .09) and l/l genotype (H.R. = 1.18, p = .48) were not significant. No significant three-way interactions were found between the s/s genotype, proximal stress, and childhood abuse (early: H.R. = 1.40, p = .54; middle: H.R. = 1.84, p = .35; late: H.R. = .69, p = .26). Three-way interactions for the l/l genotype were not significant (early: H.R. = 4.92, p = .20; middle: H.R. = .61, p = .48; late: H.R. = .89, p = .74).

Table 20

Male Cox Regression Models of Alcohol Use Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	-.11	.90	.08	-.11	.90	.08	-.13	.88	.08
Hispanic	-.20	.82*	.07	-.21	.81*	.07	-.19	.82*	.07
Other	-.05	.95	.09	-.04	.96	.10	-.05	.96	.10
Parental Quality	-.09	.92	.05	-.09	.92	.05	-.10	.91	.05
Depression	-.34	.71	.12	-.21	.73	.13	-.28	.75	.13
Early Childhood Abuse (ECA)	.09	1.09	.09	.10	1.10	.12	.02	1.02	.11
Middle Childhood Abuse (MCA)	.14	1.16	.12	.05	1.05	.14	-.13	.88	.13
Late Childhood Abuse (LCA)	-.22	.80**	.05	-.20	.82*	.07	-.21	.81*	.07
Proximal Stress (PS)	-.02	.98	.11	-.15	.86	.12	-.15	.86	.13
MAOA-L	—	—	—	-.02	.98	.08	—	—	—
s/s	—	—	—	—	—	—	-.12	.89	.09
l/l	—	—	—	—	—	—	-.08	.93	.08

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
ECA x PS	-.21	.81	.22	-.41	.66	.22	-.40	.67	.31
MCA x PS	.19	1.21	.41	.53	1.70	.61	.22	1.25	.70
LCA x PS	.25	1.28	.22	.38	1.46	.32	.37	1.44	.37
MAOA-L x ECA	—	—	—	.01	1.01	.16	—	—	—
MAOA-L x MCA	—	—	—	.21	1.24	.26	—	—	—
MAOA-L x LCA	—	—	—	-.05	.95	.13	—	—	—
MAOA-L x PS	—	—	—	.31	1.36	.29	—	—	—
MAOA-L x ECA x PS	—	—	—	.58	1.78	.94	—	—	—
MAOA-L x MCA x PS	—	—	—	-.80	.45	.29	—	—	—
MAOA-L x LCA x PS	—	—	—	-.26	.77	.25	—	—	—
s/s x ECA	—	—	—	—	—	—	.08	1.08	.23
l/l x ECA	—	—	—	—	—	—	.22	1.25	.23
s/s x MCA	—	—	—	—	—	—	.63	1.87**	.36
l/l x MCA	—	—	—	—	—	—	.44	1.55	.40
s/s x LCA	—	—	—	—	—	—	.03	1.03	.17

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
l/l x LCA	—	—	—	—	—	—	-.06	.94	.16
s/s x PS	—	—	—	—	—	—	.28	1.33	.33
l/l x PS	—	—	—	—	—	—	.17	1.18	.32
s/s x ECA x PS	—	—	—	—	—	—	.34	1.40	.77
l/l x ECA x PS	—	—	—	—	—	—	1.59	4.92	6.06
s/s x MCA x PS	—	—	—	—	—	—	.61	1.84	1.20
l/l x MCA x PS	—	—	—	—	—	—	-.49	.61	.43
s/s x LCA x PS	—	—	—	—	—	—	-.37	.69	.23
l/l x LCA x PS	—	—	—	—	—	—	-.12	.89	.32

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 982; Model 2: n = 982; Model 3: n = 982.

Female analysis. Among females, results of the stress sensitization analyses are presented in Model 1 of Table 21. In direct effects models, late-onset childhood abuse was associated with alcohol use onset (H.R. = .80, $p < .001$). Early and middle-onset childhood abuse were not significantly associated with alcohol use onset (early: H.R. = 1.00, p = .96; middle: H.R. = 1.14, p = .10). Proximal stress was not significantly associated with alcohol use onset (H.R. = 1.01, p = .84). The stress sensitization model presented in Model 1 of Table 21 found no significant two-way interaction between childhood abuse and proximal stress (early: H.R. = 1.43, p = .09; middle: H.R. = 1.19, p = .48; late: H.R. = 1.38, p = .15).

Model 2 of Table 21 displays results for the final MAOA moderated stress sensitization hypothesis. MAOA was not significantly associated with alcohol use onset (H.R. = .88 p = .12). MAOA did not significantly interact with childhood abuse (early: H.R. = .89, p = .55; middle: H.R. = .94, p = .80; late: H.R. = 1.22, p = .22) or proximal stress (H.R. = .88, p = .69). As presented in Model 2, no significant three-way interaction was found between MAOA, childhood abuse, and proximal stress (early: H.R. = 1.21, p = .76; middle: H.R. = 1.26, p = .78; late: H.R. = 2.62, p = .18).

Model 3 of Table 21 presents results for 5-HTTLPR interactions with distal and proximal stress on female alcohol use onset. Direct effects of the s/s genotype (H.R. = .89, p = .09) and l/l genotype (H.R. = .96, p = .54) were not significant. A significant two-way interaction was found between the s/s genotype and late-onset childhood abuse (H.R. = 1.48, $p < .05$). No other significant interaction between childhood abuse and the s/s genotype (early: H.R. = .83, p = .32; middle: H.R. = .91, p = .65) or l/l genotype (early: H.R. = 1.02, p = .90; middle: H.R. = 1.13, p = .52; late: H.R. = 1.28, p = .08) was found.

Proximal stress did not significantly interact with the s/s genotype (H.R. = .95, p = .84) or l/l genotype (H.R. = 1.06, p = .79). No significant three-way interaction was found between childhood abuse, proximal stress, and the s/s genotype (H.R. = .97, p = .96; middle: H.R. = .2.44, p = .09; late: H.R. = 2.00, p = .23) or the l/l genotype (early: H.R. = .64, p = .36; middle: H.R. = .50, p = .18; late: H.R. = 1.79, p = .21).

Table 21

Female Cox Regression Models of Alcohol Use Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	-.10	.90	.07	-.04	.96	.11	-.12	.89	.07
Hispanic	-.18	.84*	.07	-.13	.88	.11	-.18	.83*	.07
Other	-.24	.78*	.08	-.20	.82	.11	-.22	.80*	.09
Parental Quality	-.08	.93	.04	-.14	.87*	.05	-.08	.93	.04
Depression	-.34	.71**	.08	-.18	.84	.11	-.34	.71**	.09
Early Childhood Abuse (ECA)	-.40	.96	.07	.01	1.01	.14	-.02	.98	.11
Middle Childhood Abuse (MCA)	.12	1.13	.10	.07	1.07	.16	.10	1.10	.12
Late Childhood Abuse (LCA)	-.24	.79***	.05	-.31	.73***	.08	-.38	.68***	.07
Proximal Stress (PS)	-.19	.83	.13	-.18	.83	.19	-.31	.74	.18

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
MAOA-L	—	—	—	-.14	.87	.10	—	—	—
s/s	—	—	—	—	—	—	-.15	.86*	.09
l/l	—	—	—	—	—	—	.12	.89	.07
ECA x PS	.35	1.43	.30	.41	1.51	.50	.64	1.90	.60
MCA x PS	.18	1.19	.30	.45	1.56	.44	.43	1.54	.46
LCA x PS	.32	1.38	.31	.45	1.56	.46	-.08	.92	.24
MAOA-L x ECA	—	—	—	-.10	.90	.19	—	—	—
MAOA-L x MCA	—	—	—	-.03	.97	.23	—	—	—
MAOA-L x LCA	—	—	—	.20	1.22	.21	—	—	—
MAOA-L x PS	—	—	—	-.20	.81	.41	—	—	—
MAOA-L x ECA x PS	—	—	—	.19	1.21	.77	—	—	—
MAOA-L x MCA x PS	—	—	—	.23	1.26	1.04	—	—	—
MAOA-L x LCA x PS	—	—	—	.96	2.62	1.88	—	—	—
s/s x ECA	—	—	—	—	—	—	-.15	.86	.16

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
l/l x ECA	—	—	—	—	—	—	.07	1.07	.18
s/s x MCA	—	—	—	—	—	—	-.11	.90	.20
l/l x MCA	—	—	—	—	—	—	.18	1.19	.23
s/s x LCA	—	—	—	—	—	—	.37	1.45*	.23
l/l x LCA	—	—	—	—	—	—	.21	1.23	.17
s/s x PS	—	—	—	—	—	—	-.14	.87	.41
l/l x PS	—	—	—	—	—	—	.23	1.26	.42
s/s x ECA x PS	—	—	—	—	—	—	-.03	.97	.54
l/l x ECA x PS	—	—	—	—	—	—	-.44	.64	.31
s/s x MCA x PS	—	—	—	—	—	—	.89	2.44	1.29
l/l x MCA x PS	—	—	—	—	—	—	-.70	.50	.26
s/s x LCA x PS	—	—	—	—	—	—	.69	2.00	1.16
l/l x LCA x PS	—	—	—	—	—	—	.58	1.79	.82

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 1135; Model 2: n = 611; Model 3: n = 1135.

Preliminary Analyses

The following analyses involving alcohol dependence and sex roles are to be regarded as preliminary. Alcohol dependence models are considered preliminary due to unknown time ordering of variables. Specifically, because alcohol dependence was measured as a lifetime prevalence and proximal stress was measured in the past year, it is not possible to determine whether life stress contributed to alcohol dependence or whether the opposite temporal ordering occurred. Models of samples stratified by sex roles are also considered preliminary due to low sample numbers. In an effort to increase power, some parameters were collapsed as compared to previous sex-stratified models. Specifically, 5-HTTLPR was coded as the number of s-alleles as opposed to comparison of s/s and l/l genotypes to s/l genotype. Further, childhood abuse was collapsed into experience of abuse, by wave, at any time rather than by distinct time period categorization. After these parameters were removed, alcohol use and binge drinking presented in Models 1 estimated 12 parameters and Models 2 and 3 estimated 16 parameters each. Alcohol use onset Model 1 estimated 9 parameters and Models 2 and 3 estimated 13 parameters. Given that the range of participants for models that ranged from 62 to 183, many of these models are underpowered to adequately avoid type I and type II errors. Here, only parameters of interest from Models 1, 2, and 3 (presented in Appendices A through D) will be discussed and future research is needed to replicate these models.

Alcohol dependence. Models of male alcohol dependence are presented in Table A1 (see Appendix A). The stress sensitization model (Model 1) did not find a significant interaction between childhood abuse and proximal stress ($b = -.29$, $p = .61$). MAOA did

not significantly interact with proximal, and distal stress (b = 1.15, p = .34). Neither the three-way interactions between childhood abuse and distal stress with the s/s genotype (b = -.82, p = .59) nor the l/l genotype (b = 2.79, p = .07) was found to be significant.

Models of female alcohol dependence are presented in Table A2 (see Appendix A). The interaction between childhood abuse and proximal stress was not found to be significant (b = -.67, p = .67). The three-way interaction between MAOA, proximal, and distal stress was not able to be estimated. Childhood abuse and proximal stress did not significantly interact with the s/s genotype (b = -.67, p = .69) or the l/l genotype (b = -2.27, p = .21).

Alcohol use. Growth curve models of alcohol use among the masculine subsample are presented in Table B1 (see Appendix B). The stress sensitization hypothesis was not supported in Model 1 (b = -.13, p = .50). MAOA three-way interactions were not significantly associated with growth of alcohol use (b = -.31, p = .51). No significant three-way interaction was found for 5-HTTLPR (b = -.13; p = .56).

Models of the feminine subsample are presented in Table B2 (see Appendix B). No significant stress sensitization effect was found (b = -.19, p = .48). The three-way interaction with MAOA was not significant (b = .37, p = .49). The three-way interaction with 5-HTTLPR with childhood abuse and proximal stress was not found to be significant (b = .08, p = .76).

Models of the androgynous subsample are presented in Table B3 (see Appendix B). The interaction between childhood abuse and proximal stress was not found to be significant (b = -.20, p = .25). Three-way MAOA interaction with childhood abuse and proximal stress was not found to be significant. (b = .32, p = .40). A significant

interaction between 5-HTTLPR, childhood abuse, and proximal stress was found to be associated with growth of alcohol use ($b = .42$, $p < .05$).

Models of the undifferentiated subsample are presented in Table B4 (see Appendix B). Among those undifferentiated participants, the experience of childhood abuse significantly decreased the effect of proximal stress on the growth of alcohol use ($b = -.30$, $p < .05$). In three-way interactions, MAOA was not found to be significantly associated with alcohol use ($b = -.14$, $p = .69$) and 5-HTTLPR was not found to be significant ($b = .15$, $p = .44$).

Binge drinking. Masculine subsample growth curve models are presented in Table C1 (see Appendix C). Models of stress sensitization did not find a significant interaction between childhood abuse and proximal life stress ($b = -.06$, $p = .78$). In three-way interactions with MAOA, no significant three-way interaction was found ($b = -.02$, $p = .97$). In three-way interactions with 5-HTTLPR, no significant three-way interaction was found ($b = .08$, $p = .76$).

Feminine subsample binge drinking models are presented in Table C2 (see Appendix C). The two-way interaction between childhood abuse and proximal stress was found to be significant ($b = -.38$, $p < .05$). MAOA interaction with childhood abuse and proximal stress was not found to be significant ($b = -.38$, $p = .43$). The number of 5-HTTLPR s-alleles did not significantly interact with childhood abuse and proximal stress to explain growth of binge drinking ($b = .06$, $p = .76$).

Androgynous subsample binge drinking models are presented in Table C3 (see Appendix C). The stress sensitization hypothesis was not supported in Model 1 ($b = -.24$, $p = .59$). In Model 2, three-way interaction with MAOA was not significant ($b = .17$, $p =$

.69). In Model 3, no significant three-way interaction with 5-HTTLPR was found (b = .30, p = .12).

Undifferentiated subsample binge drinking models are presented in Table C4 (see Appendix C). The two-way interaction between childhood abuse and proximal stress was not found to be significant (b = -.21, p = .18). Three-way interaction with MAOA was not found to be significant (b = -.06, p = .87). Three-way interaction with 5-HTTLPR was not found to be significant (b = .10, p = .66)

Alcohol use onset. Cox proportional hazard models of the masculine subsample are presented in Table D1 (see Appendix D). Childhood abuse and proximal stress did not significantly interact to explain alcohol use onset (H.R. = .99, p = .80). A significant three-way interaction with MAOA was found (H.R. = .01, p < .001). No significant three-way interaction with 5-HTTLPR was found (H.R. = 1.01, p = .99).

Table D2 (see Appendix D) presents the feminine subsample models of alcohol use onset. Model 1 did not find a significant stress sensitization effect (H.R. = .66, p = .65). Model 2's three-way interaction with MAOA was not significant (H.R. = 2.51, p = .40). Model 3's three-way interaction with 5-HTTLPR was not found to be significant (H.R. = .98, p = .98).

Table D3 (see Appendix D) presents the androgynous subsample models of alcohol use onset. The two-way interaction between childhood abuse and proximal stress was not found to be significant (H.R. = 1.38, p = .72). MAOA interaction with childhood abuse and proximal stress was found to be significant (H.R. = .00, p < .001). The significance of the three-way interaction with the number of 5-HTTLPR s-alleles was not able to be estimated.

Table D4 (see Appendix D) presents the undifferentiated subsample models of alcohol use onset. The stress sensitization hypothesis was not supported in Model 1 (H.R. = 1.10, p = .81). Model 2 did found a significant three-way interaction with MAOA (H.R. = 4.02, p < .05). Model 3 did not find a significant three-way interaction with 5-HTTLPR (H.R. = 1.06, p = .93).

Summary of Findings

Collectively, little support for the genetically moderated stress sensitization hypothesis for alcohol use, binge drinking, and alcohol use onset was found. A summary table of findings can be seen in Table 22. Generally, models suggest that while late-onset childhood abuse directly increased alcohol age of onset in males and females, these effects were moderated when assessing impact of this environmental exposure on other alcohol use behaviors.

Among males, a significant negative three-way interaction between MAOA, late-onset childhood abuse, and proximal stress was found for alcohol use frequency. As depicted in Figure 3, while proximal stress and abuse increase alcohol use frequency in isolation, as compared to MAOA-H carriers, MAOA-L carriers display an increased effect of proximal stress for those males that had experienced late-onset childhood abuse rather than had not experienced late-childhood onset childhood abuse. This interaction withstood correction for multiple comparisons, calculated as original p-value multiplied by three for comparisons of three dependent variables (adjusted p-value = .012). The interaction found between MAOA and proximal stress did not withstand corrections for multiple comparisons (adjusted p-value = .117).

In 5-HTTLPR models, a significant negative two-way interactions was found for the s/s genotype and early-onset childhood abuse on alcohol use frequency. This coefficient withstood corrections for multiple comparisons (adjusted p-values = .009). Contrary to predictions, the effects of early-onset childhood abuse were greater for individuals with the s/l genotype than those with the s/s genotype. Consistent with predictions, the impact of middle-onset childhood abuse on alcohol use age of onset was greater among those with the s/s genotype than those with the s/l genotype (adjusted p value < .001).

Table 22

Summary of Findings

	Male Models			Female Models		
	Alcohol Use	Binge Drinking	Alcohol Onset	Alcohol Use	Binge Drinking	Alcohol Onset
Stress Sensitization						
Proximal Stress x Early Abuse	X	X	X	X	X	X
Proximal Stress x Middle Abuse	X	X	X	X	X	X
Proximal Stress x Late Abuse	X	X	X	X	X	X
MAOA						
MAOA x Early Abuse	X	X	X	X	X	X
MAOA x Middle Abuse	X	X	X	X	X	X
MAOA x Late Abuse	X	X	X	X	X	X
MAOA x Proximal Stress	* (positive)	X	X	X	X	X
MAOA x Proximal Stress x Early Abuse	X	X	X	X	X	X

	Male Models			Female Models		
	Alcohol Use	Binge Drinking	Alcohol Onset	Alcohol Use	Binge Drinking	Alcohol Onset
MAOA x Proximal Stress x Middle Abuse	X	X	X	X	X	X
MAOA x Proximal Stress x Late Abuse	** (negative)	X	X	X	X	X
5-HTTLPR						
s/s x Early Abuse	** (negative)	X	X	X	X	X
s/s x Middle Abuse	X	X	*** (positive)	X	** (negative)	X
s/s x Late Abuse	X	X	X	X	X	* (positive)
l/l x Early Abuse	X	X	X	X	X	X
l/l x Middle Abuse	X	X	X	X	X	X
l/l x Late Abuse	X	X	X	** (positive)	X	X
s/s x Proximal Stress	X	X	X	X	X	X
l/l x Proximal Stress	X	X	X	X	X	X
s/s x Proximal Stress x Early Abuse	X	X	X	X	X	X
s/s x Proximal Stress x Middle Abuse	X	X	X	X	X	X
s/s x Proximal Stress x Late Abuse	X	X	X	X	X	X
l/l x Proximal Stress x Early Abuse	X	X	X	X	X	X
l/l x Proximal Stress x Middle Abuse	X	X	X	X	* (negative)	X
l/l x Proximal Stress x Late Abuse	X	X	X	X	X	X

Note: X = not significant; * p < .05; ** p < .01; *** p < .001.

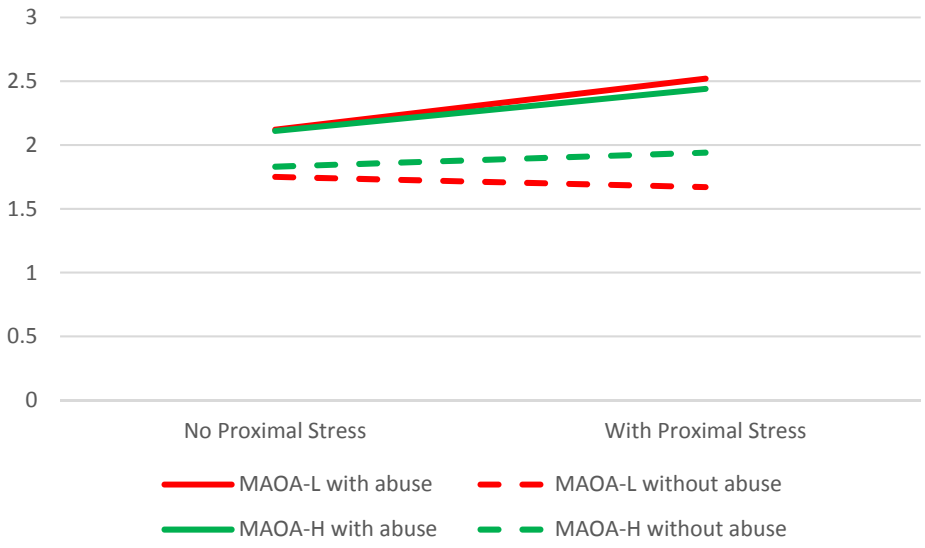

Figure 3: Male MAOA x Late-Onset Childhood Abuse x Proximal Stress on Alcohol Use Frequency

Among females, no stress sensitization effect was found. No two-way or three-way interactions for MAOA were found. A significant, positive two-way interaction between 5-HTTLPR l/l genotype and late onset childhood abuse for alcohol use and a significant negative two-way interaction between 5-HTTLPR s/s genotype and middle-onset childhood abuse was found for binge drinking. The effect of late onset childhood abuse on growth of alcohol use was greater for l/l carriers as compared to s/l carriers. The effect of middle-onset childhood abuse on binge drinking was greater for s/l genotype carriers than s/s carriers. A significant positive two-way interaction between the s/s genotype and late-onset childhood abuse was found for alcohol use age of onset. The impact of late-onset childhood abuse was greater for those with the s/s genotype than those with the s/l genotype. After corrections for multiple comparisons, these two two-way interactions remained significant (adjusted p values = .024, .006, .039, respectively). A significant three-way interaction between the l/l genotype, middle-onset childhood

abuse, and proximal stress was found to be significant but did not withstand corrections for multiple comparisons (adjusted p value = .087).

CHAPTER V

Discussion

The current dissertation contributes to a small body of literature testing a genetically moderated stress sensitization hypothesis. This is the first study to test whether this model explains variation in alcohol use frequency, binge drinking frequency, age of onset of alcohol use, and alcohol dependence. Specifically, MAOA and 5-HTTLPR were hypothesized to interact with distal and proximal stress to explain these behaviors among males and females with a preliminary examination of alcohol dependence. Further, these hypotheses were tested in preliminary models across sex-role identification (i.e., masculine, feminine, androgynous, and undifferentiated). This chapter will summarize and place the current findings in context of the current literature. The limitations of the current dissertation along with a discussion of future research needs will be highlighted.

Gender Variation in Alcohol Use and Risk Exposure

Previous literature has consistently found that alcohol use is greater among males than females (Brady & Randall, 1999; Cotto, Davis, Dowling, Elcano, Staton, & Weiss, 2010). Consistent with this, males were found in the current dissertation to consume alcohol and binge drink more frequently than females. The majority of previous literature suggests that males tend to begin drinking at an earlier age than females (Casswell et al., 2002) or that there are no gender differences in the age of onset (Flory et al., 2004; Pitkanen, Lyyra, & Pulkkinen, 2005). Similarly, in the current study, females began drinking at a significantly older age; the average male began alcohol use at the age of 16.46 while the average female began alcohol use at the age of 17.25 ($p < .001$). Recent

meta-analytic evidence, however, finds that recent trends suggest that females are beginning to surpass males in early alcohol use onset (Cheng & Anthony, 2017). Given evidence suggesting that earlier alcohol use is associated with more deleterious alcohol use patterns (DeWit, Adlaf, Offord, & OGborne, 2000; Grant & Dawson, 1997; Grant et al., 2006; Labouvie et al., 1997), this general shift in earlier onset of female use may have lasting effects on male and female alcohol use across the life course that may deviate from current findings.

Previous research suggests that females are more likely to be exposed to childhood abuse (Dube, Anda, Whitfield, Brown, Felitti, Dong, & Giles, 2005; Friedman, Marshal, Guadamuz, Wei, Wong, Saewyc, & Stall, 2011; Lake, 1995; McClellan, Farabee, & Crouch, 1997) and proximal stress (Hankin, Mermelstein, & Roesch, 2007). In the current study, females were found to be significantly more likely to experience early-, middle-, and late-onset childhood abuse as compared to males. Contrary to previous research, however, no gender differences in exposure to proximal stress were found. This variation from previous literature may be due to the limited scope of the proximal stress measure. Whereas previous literature finding gender differences in proximal stress have captured a wide array of stressful life experiences, the reliance in the current study on severe victimization and vicarious victimization experience may have contributed to this deviation from previous findings.

Direct and Interactive Effects of Distal and Proximal Stress on Alcohol Use Behaviors

Proximal stress has been consistently found in previous literature to be associated with increased levels of alcohol related behaviors (Boden, Fergusson, & Horwood, 2014;

Carney, Armeli, Tennen, Affleck, & O'Neil, 2000; Cole, Tucker, & Friedman, 1990; King, Bernardy, & Hauner, 2003; Magrys & Olmstead, 2015). The current study examined the effect of proximal stress specifically on the rate of growth of alcohol use and binge drinking and the age at which individuals began drinking. Among males, no evidence of an association between proximal stress with these three behaviors were found. Among females, however, proximal stress increased the rate of growth of binge drinking behavior. While a large proportion of the study sample engaged in alcohol use and binge drinking, findings suggesting that proximal stress increases the frequency of binge drinking above that of normal behavior suggests that the salience of proximal stress is greater among females. These findings suggest that models examining the effects of proximal stress on alcohol use behaviors may be misspecified without concentration on gender differences in these effects.

Distal stressors such as childhood abuse have also been found to increase alcohol use behaviors (Afifi, Mota, Dasiewicz, MacMillan, & Sareen, 2012; Hamburger, Leeb, & Swahn, 2008; Kilpatrick, Acierno, Saunders, Resnick, Best, & Schnurr, 2000; Rothman, Edwards, Heeren, & Hingson, 2008; Sartor, Lynskey, Bucholz, McCutcheon, Nelson, Waldron, & Heath, 2007). The current study found this direct effect among both males and females. Contrary to the findings of Andersen et al. (2008), however, the effects of childhood abuse varied across age of abuse onset with late-childhood onset abuse being the most likely to reduce age of alcohol use onset. Previous literature suggests that earlier age of onset is highly problematic (DeWit, Adlaf, Offord, & OGborne, 2000; Grant & Dawson, 1997; Grant et al., 2006; Labouvie et al., 1997). The current study supports that body of literature, with alcohol use age of onset being a fairly consistent predictor of

greater growth of alcohol use and binge drinking patterns in males and females. Thus, individuals that experience childhood abuse during this critical developmental period may have increased alcohol-use behavior risk stemming from earlier alcohol use onset.

The emergence of the stress sensitization hypothesis has provided an avenue through which the effects of stress on individual behavior may be understood as a developmental phenomenon. Proposing that early life stress enhances the effects of later life stress suggests that individuals may vary in their response to stress due to distal developmental factors. In the current study, no stress sensitization effect was found for males or females in regard to alcohol use, binge drinking, or alcohol use age of onset.

This finding and the overall lack of stress sensitization, particularly among females, stands in contrast to previous literature suggesting that the effects of stress among females is more salient than among males (Boden, Fergusson, & Horwood, 2014; King et al., 2003. Rospenda et al., 2008). For example, a recent longitudinal study assessing the impact of stressful life events on alcohol abuse and dependence symptoms found a greater impact for females than for males (Boden, Fergusson, & Horwood, 2014). Further, strain theorists have proposed that males and females cope with stress through differing behaviors. Broidy and Agnew (1997) proposed that gender differences in responses to strain can explain why males react to stress and strain with increased serious criminal behavior while females may cope with strains through more introverted mechanisms such as substance use. The current lack of findings of stress sensitization among women suggests that, at least in regard to alcohol use within this subsample of females, coping with proximal stress through alcohol use is not increased by exposure to childhood abuse.

Although only preliminary results could be presented in the current dissertation, the effects of stress on alcohol use behaviors may not only fluctuate across biological sex, but may vary by identification with the social expectations of each gender. Preliminary analyses of the effects of stress across sex-role identification found that childhood abuse actually lessens the effect of proximal stress on the growth or alcohol use and binge drinking among individuals that do not identify with masculine sex-roles (undifferentiated and feminine, respectively). These findings suggest that while childhood abuse may increase feelings of stress, coping with proximal stress via alcohol use behaviors may be more likely when social norms support alcohol use such as those that accompany masculinity (Landrine, Bardwell, & Dean, 1988). Further, like primary analyses of males, the three-way interaction between MAOA, distal, and proximal stress was in the opposite than expected direction for those that identified with masculine sex roles (masculine and androgynous). That is, MAOA-L carriers displayed a reduced stress sensitization process in explanation of alcohol use onset. The current finding suggests that expectations of prosocial coping mechanisms for those that identify as masculine or feminine may influence coping following distal and environmental stress exposure, especially when coupled with sensitivity to those environments conferred by genetic factors. Further research is needed to replicate these results with adequate statistical power.

Genetically Moderated Stress Sensitization Hypothesis

The current dissertation sought not only to examine the stress sensitization hypothesis but also to test a genetically moderated stress sensitization hypothesis, arguing that the effects of distal stress on the effects of proximal stress on alcohol use should be

mediated by the serotonin polymorphisms MAOA and 5-HTTLPR. Currently, the body of literature examining the effect of genetic polymorphisms on stress sensitization is very limited. The majority of previous genetically moderated stress sensitivity research has examined the role of serotonergic polymorphisms on depression (Grabe et al., 2012; Starr, Hammen, Conway, Raposa, & Brennan, 2014). Only one study has tested genetic moderation of stress sensitization in relation to a criminogenic outcome (Wells et al., forthcoming). This dissertation expands this body of research by examining MAOA and 5-HTTLPR moderation of stress sensitization as it related to alcohol use, binge drinking, and alcohol use age of onset.

Theoretically, increased serotonin availability conferred by the low expressing MAOA and the short 5-HTTLPR alleles are thought to increase the effect of environmental risk exposure and thus increase risk for deleterious outcomes following exposure. The interaction between MAOA and 5-HTTLPR with distal and proximal stress on alcohol use behaviors have to date been limited to two-way interactions. As previously discussed, this body of literature has found significant heterogeneity of risk with some studies finding that the effects of distal and proximal stress vary across MAOA and 5-HTTLPR genotype (Covault et al., 2007; Daw et al., 2013; Ducci et al., 2008; Kaufman et al., 2012; Kim et al., 2015; Kranzler et al., 2012; Olsson et al., 2005; Laucht et al., 2009; Nilsson et al., 2005, 2008) while others find null effects (Daw et al., 2013; Kim et al., 2015; Kranzler et al., 2012; Laucht et al., 2009; Nilsson et al., 2008) or opposite than anticipated risk alleles (Nilsson et al., 2005, 2008; Laucht et al., 2009). As such, it is difficult to determine to what extent MAOA and 5-HTTLPR increase the salience of distal and proximal stress exposure.

Based upon previous literature, the current study anticipated finding two-way interactions between MAOA and 5-HTTLPR with distal and proximal stress to explain alcohol use, binge drinking, and alcohol use age of onset. Current findings of two-way interactions of MAOA or 5-HTTLPR with distal or proximal were limited and mixed in regard to hypothesized directions. Based upon previous literature, the low expressing alleles of MAOA and the number of the s-alleles of 5-HTTLPR should increase sensitivity to distal and proximal environmental stressors. Findings of the current study were consistent with the hypothesized direction in an MAOA interaction with proximal stress on alcohol use among males. Not unlike previous literature, the interactive effects of MAOA among females were not found (Schmidt et al., 2000).

Two-way interactions with 5-HTTLPR, however, were mixed in regard to their hypothesized directions. Among males, as compared to those carriers of the s/l genotypes, s/s carriers displayed a decreased effect of early-onset childhood on alcohol use. Similarly, among females, s/s carriers had a decreased impact of middle-onset childhood abuse on binge drinking as compared to s/l heterozygotes. These findings were contrary to that anticipated, however, are in line with Nilsson et al.'s (2005) finding of increased risk of intoxication frequency following poor family relations by males carrying the s/l genotype. Both male and female alcohol use age of onset was more greatly affected by middle- and late- onset childhood abuse, respectively, for s/s carriers than s/l carriers. This finding was anticipated due to previous research and theoretical guidance suggesting increased risk following environmental risk exposure for each additional s-allele.

These mixed findings highlight a need for consistent replication of GxE studies. Mixed findings across GxE studies have led some to question the efficacy of GxE research, suggesting that non-replicability of studies is evidence not only of publication bias but of data-mining as well, an unethical practice of searching for significant associations for publication (Duncan & Keller, 2011; Eaves, 2006; Munafo & Flint, 2009). A body of research based upon data mining violates a number of statistical assumptions and thus may lead to incorrect conclusions based on chance alone, otherwise referred to as false positive results (Duncan & Keller, 2011). Indeed, if data mining were prevalent within GxE research, this practice could undermine the current state of knowledge regarding how genes and environments infer risk and resilience for a variety of behaviors and disorders. The current dissertation took steps toward correcting for multiple comparisons; however, the current null findings stand in contrast with the majority of published studies. These effects can be assessed with meta-analytic approaches to summarizing the current literature and testing publication bias. Although previous research was mixed, the current study anticipated finding two-way interaction between MAOA and 5-HTTLPR with distal and proximal stress wherein consistent "risk" alleles would increase the impact of distal and proximal stress on alcohol use behaviors.

Three-way interactions tested the moderation of stress sensitization by MAOA and 5-HTTLPR polymorphisms. It was hypothesized that MAOA-L and 5-HTTLPR s/s homozygotes would have an increased risk for stress sensitization leading to alcohol use behaviors. After adjusting for multiple comparisons, only one significant three-way interaction was found. In the model of alcohol use growth among males, sensitization of

proximal stress by late onset childhood abuse was greatest for those carriers of low expressing MAOA alleles. After replication of this effect omitting those 5-repeat allele carriers (n = 15) due to mixed evidence concerning functionality of this allele (Deckert et al., 1999; Denny, Koch, & Craig, 1999; Sabol, Hu, & Hamer, 1998), this effect remained. As such, research examining two-way interactions between MAOA and distal or proximal stress may be reporting such mixed findings due to a failure to account for participant exposure to stress at other time periods. If, as suggested by this finding, proximal stress exposure increases the risk of deleterious behavioral outcomes among MAOA-L carriers but this effect depends in part on exposure to childhood abuse, failure to account for either early abuse exposure or later proximal stress exposure may underlie apparent null findings for males.

Despite this significant finding, it is noteworthy that the vast majority of GxExE tests were not found to be significant. The lack of findings could be due to the relatively low seriousness of the dependent variables of interest. That is, alcohol use and, to some extent, binge drinking are normative behaviors. It could be that patterns of alcohol related behaviors are not dependent on a GxExE effect. Additionally, the lack of findings could be due to a number of methodological limitations that are reviewed below.

Limitations and Future Research

While the current research contributes to the current body of studies examining the genetically moderated stress sensitization hypothesis and is the only study to examine alcohol use behaviors, there are several limitations of the current study that warrant caution in drawing conclusions from the current research and highlight the need for future research. First, the measures of childhood abuse in the current study are somewhat

limited by the use of retrospective accounts of timing of onset. Previous literature have found mixed results regarding the reliability of retrospective accounts of childhood abuse with some suggesting adequate reliability (Dube, Williamson, Thompson, Felitti, & Anda, 2004) and others finding the contrary (Henry, Moffitt, Caspi, Langley, & Silva, 1994; Widom & Morris, 1997). While debate exists about the validity of retrospective abuse measures, scholars have supported the use of retrospective abuse measures due to more severe abuse histories of those that recall childhood abuse at later life stages (Kendall-Tackett & Becker-Blease, 2004) and findings that suggests that retrospective accounts of abuse are predictive of adult psychological outcomes (Shaffer, Huston, & Egeland, 2008). The current dissertation assumes reliable information concerning both the presence and timing of physical, sexual, and emotional childhood abuse. This limitation is somewhat tempered due to the use of prevalence of abuse rather than frequency of abuse and thus less recall bias may have influenced results. Future research should obtain more timely estimates of abuse onset and duration.

Second, while categorization of abuse timing into early, middle, and late onset childhood abuse was guided by previous research (Andersen et al., 2008; Hart & Rubia, 2012; Sowell, Peterson, Thompson, Welcome, Henkenuius, & Toga, 2003), the effect of timing of abuse may be more fluid than that suggested by the current categorization. Categorization was employed in a first step toward assessing the varying impacts of timing of childhood abuse that have been suggested to be curvilinear, with effects of abuse peaking in middle childhood and supported by the current research among the female subsample. Future research should further clarify whether these effects are fluid

or categorical by comparison of the current findings with those that examine continuous age of abuse onset variables, including polynomial functions if deemed appropriate.

Third, the current dissertation analyzed the effects of any physical, sexual, or emotional abuse in childhood. There may be stark differences between the effects of childhood abuse and alcohol use behaviors that vary by type and severity of abuse, particularly by sex that were not examined in the current dissertation. Future research should model the approach of Shin, Miller, and Teicher (2013) and examine the effects of each type of abuse independently. Further, poly-victimization (i.e., victimization by more than one type of abuse) may also have a greater impact on alcohol use behaviors than single abuse type experiences (Bensley, Spieker, van Eenwyk, & Schoder, 1999; Ford, Elhai, Connor, Frueh, 2010). As such, there remains a need to examine the current research questions for both individual types of abuse as well as the number of types of abuse experienced in childhood. While the current study employed age categorization and collapsed abuse categories in an effort to avoid potential recall biases in abuse measures, data that addresses the first limitation by collecting more timely abuse measures would be well suited to address these limitations.

Fourth, the measure of proximal stress included in this study is somewhat limited. The current proximal stress measure included both experiencing victimization and witnessing the victimization of others. While this measure was ideal for the purposes of the current study, as these events may be viewed as equally stressful across participant ages from adolescence to adulthood, there remains many unmeasured stressors that were not captured in the current study. For example, previous research suggests that financial strain such as unemployment and low socioeconomic status may increase stress and vary

in effects across gender (Boden, Fergusson, & Horwood, 2014; Carney, Armeli, Tennen, Affleck, & O'Neil, 2000; Cole, Tucker, & Friedman, 1990; King, Bernardy, & Hauner, 2003; Magrys & Olmstead, 2015). While these variables were available in the Add Health data at Waves III and IV, they were not included in the current analysis due to fluctuation in their meaning across the life course. For example, financial strain should not equally affect early adolescents and emerging adults. To achieve consistent measurement across waves, these stressors were not included. Future research, however, should employ more comprehensive proximal stress measures. While this may be problematic across the life course, age- and wave- specific proximal stress measures may better capture subjective stressful experiences.

Limitations of the current study also include measurement and inclusion of control variables. The current measure of parental quality is somewhat limited as it is captured only at Wave I following the guidance of previous research (Shin, Miller, & Teicher, 2013). Further, previous literature suggests that peer drinking behaviors influences individuals' alcohol use behaviors (Bray, Adams, Getz, & McQueen, 2003; Mason & Windle, 2001). Due to data constraints (no measurement in Wave IV), the current dissertation was unable to control for these effects. Future research should analyze datasets that include parental quality and peer behaviors more regularly across time. Models from the current study controlled for the effects of depression on alcohol use, binge drinking, and age of onset of alcohol use based upon the modeling strategy of previous research (Shin, Miller, & Teacher, 2013). Given research suggesting increased alcohol use of those affected by PTSD, anxiety disorders, and other mental health issues (Jacobsen, Southwick, & Kosten, 2001; Jane-Llopis & Matytsina, 2006), future research

should control for more extensive mental health factors. Finally, although it was possible to account for censorship in models focused upon alcohol use onset, in models where alcohol use onset was used as a control variable, it was not possible to detect the true age of onset for individuals who had not yet begun alcohol use. To increase statistical power, these individuals were coded to onset at their greatest reported age although this is a likely deviation from what will be the true age of onset of these individuals.

Dependent variable limitations may have also influenced the current study. First, the response categories for alcohol use frequency and binge drinking frequency were measured on an extensive ordinal scale. Although these response categories were of a range wide enough to treat the measure as continuous for the purposes of the current study, the measures are not truly continuous. As such, some variability in the alcohol use and binge drinking frequency was lost, and important differences may exist within the captured ranges. The current study found a peak of alcohol use at Wave III for females and Wave IV for males. Regarding male alcohol use, it is yet unknown whether this is a true peak or whether males will continue to escalate alcohol use into later stages of adulthood. For females, due to extended time lapse in data collection from Wave III (age range 18-26) and Wave IV (24-32), it is unknown whether this is a true peak of alcohol use or whether it simply falls within this time range. As such, the results of the current study may be specific to this period of alcohol use behaviors and may fluctuate as general alcohol use behavior patterns vary into later adulthood. Future research should consider raw number measurements of alcohol use and binge drinking frequency as well as collect data more frequently during the critical time period of transition from late adolescence to early adulthood, allowing for more salient conclusions to be drawn.

Preliminary models presented for alcohol dependence and sex-role adherence are fraught with issues that render these findings a first step in the direction toward consideration. In regard to alcohol dependence, temporal ordering cannot be established and thus it is unclear whether stress in the past year influences the likelihood of alcohol dependence diagnosis or whether diagnosis of alcohol dependence increases past year stress. This lifetime prevalence measure of alcohol dependence diagnosis renders this ordering impossible to parse. Future research should include alcohol dependence diagnosis in the past year across all waves of data collection. Sex-role models are also constrained due to small sample sizes. Because a large number of predictor variables are included in the models, these findings should be regarded with caution. Future research should employ samples with greater sample sizes that measure both genetic polymorphisms as well as BSRI scores to better measure potential fluctuation in GxExE effects across sex-role identification.

Limitations of the current modeling technique should also be explored in the future. As estimated, the models employed in the current dissertation assumed constant influence of predictor variables across time. Meta-analytic evidence suggests that there may be some fluctuation in the influence of genes and environments across the life course with environmental risk factors playing a larger role in childhood and adolescence and genetic factors having a larger impact in adulthood (Bergen, Gardner, & Kendler, 2007; Hansell et al., 2008; Kendler, Schmitt, Aggen, & Prescott, 2008). Analysis of the fluctuation in these effects could be garnered by extending models to incorporate random slopes for these key variables but is beyond the scope of the current dissertation. As the goal of the current dissertation was to assess consistent effects of the hypothesized

developmental processes, future research should reexamine how the effect of each source of stress may fluctuate across the life course.

Finally, GxE and ExE estimates assume no correlation between the two interactive variables. Consistent with previous research (Enoch, 2010; Gomez, 2011; Turner, Finkelhor, & Ormrod, 2010), the current study found some significant but weak associations between MAOA and 5-HTTLPR with distal and proximal stress. Although these associations were found to be weak and analyses proceeded, this minor correlation could have somewhat influenced the presented results. Future research is needed to replicate these results in data with no gene-environment or distal-proximal environment correlations.

Implications

The complex interplay between genes and environments has not been fully understood. To the academic community, the current dissertation suggests that understanding of human behavior requires both consideration of biological and environmental risk factors as well as consideration of developmental processes as they relate to environmental risk exposure throughout the life course. Although the GxExE hypothesis was largely unsupported by the current findings, two-way interactions between distal stress and 5-HTTLPR and one important MAOA, abuse, proximal stress interaction suggest that understanding of alcohol related behaviors may require consideration of all three avenues of influence. Given recent evidence suggesting varying gene and environmental contributions to minor and severe criminal offending, wherein the effect of serotonergic polymorphisms is greater in more serious offending patterns (Armstrong et al., 2014), more research is needed to detect whether these patterns

generalize to alcohol use behaviors. While temporal ordering could not be established in alcohol dependence models in the current research, future research examining more serious alcohol use outcomes are likely better explained by the genetically moderated stress sensitivity hypothesis.

Practically, the importance of late-onset childhood abuse among males and females should be underscored. Here, childhood abuse was found to have many lasting effects both directly and through interaction with 5-HTTLPR and MAOA. While female alcohol use is generally lower than that of males, here and in previous research, females exposed to proximal stress are more likely than their male counterparts to use alcohol as a coping mechanism (Brady & Randall, 1999; Cotto, Davis, Dowling, Elcano, Staton, & Weiss, 2010). Understanding of this, and interactions with serotonergic suggests that some victims may have an increased need to develop positive coping strategies for stress.

If alcohol use behaviors are to be reduced, particularly those following exposure to childhood abuse, effective programming must take underlying developmental processes into consideration. To accomplish this goal, programs must either prevent exposure to the initial risk factor of childhood abuse or, if delivered after abuse exposure, address underlying trauma-related issues. Effective programming designed to reduce childhood abuse among high-risk populations have been shown to reduce later alcohol use behaviors (Connell, Dishion, Yasui, & Kavanagh, 2007; Olds et al., 1998). The Nurse-Family Partnership program developed by David Olds targets high-risk families, delivering parenting information to expectant mothers and periodically following the development of the child. This program has been shown to both reduce childhood abuse and to reduce adolescent alcohol use in the riskiest households (Olds et al., 1998). With a

similar goal, the Positive Family Support program targets high-risk households in an effort to increase constructive family relations as an alternative to abuse. This program has also been shown to reduce adolescent alcohol use (Connell, Dishion, Yasui, & Kavanagh, 2007).

Despite these efforts at abuse prevention, many individuals are still victimized by childhood abuse, putting them at risk for later problematic behaviors, including alcohol use and abuse. Although unsupported by the current findings, as suggested by previous literature highlighted throughout this dissertation, the experience of this traumatic environment may have long lasting direct effects as well as long lasting effects on coping with later life stress. Trauma-informed and trauma-specific approaches to solving underlying problems may be best suited to reduce alcohol use in victims of childhood abuse. Trauma-Focused Cognitive Behavior Therapy has been shown to be effective at reducing trauma-related symptoms, child behavior problems, and childhood depression (Cohen et al., 2004). While this program presents some promise at reducing later alcohol use behaviors, to date substance use has not been evaluated as an outcome of interest following program completion.

Further, the current dissertation has also highlighted variation in response to childhood abuse and life stress by MAOA genotype and childhood abuse timing across gender. As such, trauma-informed care should incorporate these gender differences in programming. The Trauma Recovery and Empowerment Model (TREM) shows promise in reducing alcohol and other substance use following abuse exposure by incorporating not only effective coping strategies but also by being gender-specific wherein TREM was designed for treatment of female trauma victims while Men's TREM (M-TREM) was

designed for treatment of male trauma victims. These services, typically delivered in mental health or correctional settings, have been shown to reduce both alcohol use and stressful life events (Fallot, McHugo, Harris, & Xie, 2011; but see Fallot & Harris, 2002 for a variant of treatment delivery method and null results for alcohol use reduction). Given the weight of the evidence concerning the role of childhood abuse on direct and developmental risk for alcohol use, programs such as TREM/M-TREM may currently be most effective at reducing problematic alcohol use behaviors.

Although programs designed to aid participants in coping with traumatic events in the past are currently effective in reducing alcohol use, future programming should incorporate previous evidence of stress sensitization by extending these coping mechanisms to coping with non-trauma associated stressors. Results from TREM/M-TREM may not have only been a result of effective coping with past trauma, but may have operated through reducing life stress. Because those who have been victimized by childhood abuse may experience life stress to a greater extent, reducing this stress or developing methods for which to effectively cope with life stress may increase treatment efficacy.

Conclusion

In conclusion, previous research suggests that alcohol related behaviors cannot be fully understood without consideration of genetic and distal and proximal environmental influences. The current study contributes some evidence suggesting that specific environmental stressors interact with serotonergic polymorphisms to explain certain alcohol use behaviors. Developmental processes wherein the effects of life stress are potentiated by exposure to childhood abuse must be examined, taking into account

genetic variation, if deleterious coping mechanisms for stress are to be explained. The effects of childhood abuse on alcohol related vary across timing of abuse. Victims of childhood abuse that begins between after the age of 13 were found to be at greatest risk both for alcohol use behaviors generally and for coping with life stress through alcohol use. While scholars have begun to assess interactions between genetic factors and environmental risk exposure, it is important to consider not only the presence or absence of environmental risk but the general (distal or proximal) and specific (age at exposure) timing of the exposure. Through thorough consideration of timing, the plethora of mixed GxE findings may become clearer. Finally, future research is needed to examine the influence of socialized norms, such as those imparted in sex-role identification, surrounding alcohol use and to examine more serious alcohol use patterns such as those leading to alcohol dependence.

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APPENDIX A

Alcohol Dependence Supplemental Tables

Table A1

Male Logistic Regression Models of Alcohol Dependence

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	-.10	.06	-.10	.06	-.09	.06
Black	-.87	.43	-.84*	.43	-.78	.44
Hispanic	-.26	.35	-.28	.35	-.26	.35
Other	-.62	.55	-.61	.55	-.69	.56
Parental Quality	-.23	.20	-.22	.20	-.24	.20
Depression	.84**	.30	.88**	.31	.92**	.31
Age of Alcohol Onset	-.20***	.03	-.20***	.03	-.20***	.03
Any Childhood Abuse (CA)	.76**	.25	1.14***	.32	.95**	.35
Proximal Stress (PS)	.01	.41	.10	.52	.31	.53

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.38	.36	—	—
s/s	—	—	—	—	-.33	.58
l/l	—	—	—	—	.21	.38
CA x PS	-.29	.59	-.83	.79	-.88	.89
MAOA-L x CA	—	—	-.93	.50	—	—
MAOA-L x PS	—	—	-.18	.85	—	—
MAOA-L x CA x PS	—	—	1.15	1.20	—	—
s/s x CA	—	—	—	—	.40	.70
l/l x CA	—	—	—	—	-.93	.57
s/s x PS	—	—	—	—	.51	1.08
l/l x PS	—	—	—	—	-1.65	1.20
s/s x CA x PS	—	—	—	—	-.82	1.55
l/l x CS x PS	—	—	—	—	2.79	1.56

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 1009; Model 2: n = 1009; Model 3: n = 1009.

Table A2

Female Logistic Regression Models of Alcohol Dependence

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	-.09	.08	-.15	.11	-.09	.08
Black	-.03	.45	-.04	.63	.07	.46
Hispanic	-.50	.47	-.05	.67	-.44	.48
Other	.19	.57	.37	.84	.16	.59
Parental Quality	-.15	.23	-.03	.32	-.15	.23
Depression	.98**	.30	1.31	.40	.98**	.30
Age of Alcohol Onset	-.27***	.05	-.24**	.06	-.27***	.05
Any Childhood Abuse (CA)	.72	.36	.36***	.58	.24	.46
Proximal Stress (PS)	1.11*	.49	.93	.90	.45	.71
MAOA-L	—	—	-.75	1.13	—	—
s/s	—	—	—	—	-.35	.81

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
l/l	—	—	—	—	-1.82	1.07
CA x PS	-.67	.67	-.21	1.11	.02	.99
MAOA-L x CA	—	—	1.55	1.23	—	—
MAOA-L x PS	—	—	.98	1.57	—	—
MAOA-L x CA x PS	—	—	+	+	—	—
s/s x CA	—	—	—	—	.14	.96
l/l x CA	—	—	—	—	2.11	1.14
s/s x PS	—	—	—	—	1.44	1.22
l/l x PS	—	—	—	—	1.70	1.45
s/s x CA x PS	—	—	—	—	-.67	1.68
l/l x CS x PS	—	—	—	—	-2.27	1.81

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 1171; Model 2: n = 620; Model 3: n = 1171; + = parameter predicts failure perfectly

APPENDIX B

Alcohol Use Frequency Sex Role Models

Table B1

Masculine Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.20**	.06	.18**	.06	.19**	.06
Age^2	-.00**	.00	-.00*	.00	-.00**	.00
Black	-.14	.10	-.17	.12	-.17	.11
Hispanic	-.07	.11	-.12	.12	-.07	.11
Other	-.02	.07	-.02	.08	-.02	.08
Male	.09	.08	.12	.11	.09	.08
Parental Quality	-.09	.08	-.05	.08	-.09	.08
Depression	-.08	.13	-.04	.15	-.09	.13

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Age of Alcohol Onset	-.05***	.01	-.05***	.01	-.05***	.01
Any Childhood Abuse (CA)	-.04	.08	.10	.13	-.01	.10
Proximal Stress (PS)	.10	.14	-.05	.17	-.10	.18
MAOA-L	—	—	.04	.10	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	-.03	.08
CA x PS	-.13	.19	.02	.25	-.00	.23
MAOA-L x CA	—	—	-.19	.17	—	—
MAOA-L x PS	—	—	.42	.25	—	—
MAOA-L x CA x PS	—	—	-.31	.48	—	—
5-HTTLPR x CA	—	—	—	—	-.05	.09
5-HTTLPR x PS	—	—	—	—	.24	.13
5-HTTLPR x CA x PS	—	—	—	—	-.13	.23
Constant	-.39	.68	-.45	.77	-.32	.67

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Random Effects						
Family						
Standard Deviation of Intercept	.22*	.05	.00	+	.22*	.05
Individual						
Standard Deviation of Intercept	.00*	.00	.20*	.07	.00*	.01
Standard Deviation of Slope	.53*	.02	.54*	.03	.53*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 108; Model 2: n = 83; Model 3: n = 108.

Table B2

Feminine Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.23***	.04	.23***	.05	.23***	.04
Age^2	-.00***	.00	-.00***	.00	-.00***	.00
Black	-.34**	.10	-.48***	.08	-.34**	.10
Hispanic	-.30	.09	-.29*	.15	-.14	.08
Other	.18**	.07	-.40**	.15	-.26**	.09
Male	.18**	.07	.13	.09	.17**	.06
Parental Quality	-.10	.06	-.13	.11	-.09	.06
Depression	-.09	.09	-.11	.11	-.09	.09
Age of Alcohol Onset	-.06***	.00	-.06***	.01	-.06***	.00
Any Childhood Abuse (CA)	.05	.06	.13	.10	.01	.08
Proximal Stress (PS)	.02	.19	.05	.16	.06	.27

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.25	.15	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	-.07	.05
CA x PS	-.19	.26	-.59	.36	-.22	.37
MAOA-L x CA	—	—	-.27	.17	—	—
MAOA-L x PS	—	—	.05	.36	—	—
MAOA-L x CA x PS	—	—	.37	.54	—	—
5-HTTLPR x CA	—	—	—	—	.07	.07
5-HTTLPR x PS	—	—	—	—	-.08	.20
5-HTTLPR x CA x PS	—	—	—	—	.08	.27
Constant	-.55	.60	-.43	.79	-.51	.60
Random Effects						
Family						
Standard Deviation of Intercept	.12*	.02	.11*	.04	.01*	.16

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.09*	.06	.11*	.04	.14*	.07
Standard Deviation of Slope	.48*	.02	.45*	.03	.48*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 106; Model 2: n = 65; Model 3: n = 106; + = parameter predicts failure perfectly.

Table B3

Androgynous Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.25***	.04	.30***	.04	.25***	.04
Age^2	-.00***	.00	-.01***	.00	-.00***	.00
Black	-.04	.06	-.10	.06	-.03	.06
Hispanic	.07	.06	.05	.08	.07	.06
Other	-.16	.10	-.06	.09	-.17	.09
Male	.06	.05	.03	.05	.07	.05
Parental Quality	.03	.04	.08	.04	.03	.04
Depression	.09	.09	.19	.11	.10	.08
Age of Alcohol Onset	-.06***	.00	-.05***	.01	-.06***	.00
Any Childhood Abuse (CA)	.01	.05	.00	.09	-.02	.08
Proximal Stress (PS)	.17	.12	.15	.16	.41	.22

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.09	.08	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	.01	.04
CA x PS	-.20	.17	-.29	.24	-.57*	.27
MAOA-L x CA	—	—	-.09	.13	—	—
MAOA-L x PS	—	—	.14	.29	—	—
MAOA-L x CA x PS	—	—	.32	.38	—	—
5-HTTLPR x CA	—	—	—	—	.03*	.06
5-HTTLPR x PS	—	—	—	—	-.27	.17
5-HTTLPR x CA x PS	—	—	—	—	.42	.21
Constant	-1.38**	.43	-2.17***	.50	-1.40**	.44
Random Effects						
Family						
Standard Deviation of Intercept	.18*	.03	.15*	.04	.18*	.03

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.00*	.00	.00*	.00	.00*	.00
Standard Deviation of Slope	.51*	.02	.51*	.02	.51*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 183; Model 2: n = 126; Model 3: n = 183; + = parameter predicts failure perfectly.

Table B4

Undifferentiated Growth Curve Models of Alcohol Use Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.24***	.05	.25***	.05	.23***	.05
Age^2	-.00***	.00	-.01***	.00	-.00***	.00
Black	-.21**	.06	-.21**	.07	-.22**	.06
Hispanic	-.10	.08	-.08	.10	-.11	.08
Other	-.24**	.08	-.33**	.10	-.24**	.08
Male	.04	.06	.09	.07	.04	.06
Parental Quality	-.03	.04	-.04	.05	-.03	.04
Depression	-.05	.10	-.04	.12	-.05	.10
Age of Alcohol Onset	-.05***	.00	-.04***	.01	-.05***	.00
Any Childhood Abuse (CA)	.03	.06	-.01	.09	.05	.09
Proximal Stress (PS)	.25*	.10	.25	.15	.24	.19

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.06	.10	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	.00	.05
CA x PS	-.30*	.15	-.25	.20	-.45*	.22
MAOA-L x CA	—	—	.10	.14	—	—
MAOA-L x PS	—	—	.18	.26	—	—
MAOA-L x CA x PS	—	—	-.14	.35	—	—
5-HTTLPR x CA	—	—	—	—	-.03	.07
5-HTTLPR x PS	—	—	—	—	.01	.16
5-HTTLPR x CA x PS	—	—	—	—	.15	.19
Constant	-.89	.57	-1.17	.68	-.88	.58
Random Effects						
Family						
Standard Deviation of Intercept	.18*	.04	.18*	.04	.18*	.04

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.00*	.00	.00*	.00	.00*	.00
Standard Deviation of Slope	.54*	.02	.56*	.02	.54*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 167; Model 2: n = 129; Model 3: n = 167.

APPENDIX C

Binge Drinking Frequency Sex Role Models

Table C1

Masculine Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.17**	.06	.18**	.07	.17**	.06
Age^2	-.00*	.00	-.00*	.00	-.00*	.00
Black	-.26**	.08	-.36***	.08	-.30**	.09
Hispanic	-.09	.13	-.11	.14	-.08	.12
Other	-.05	.15	-.08	.14	-.03	.16
Male	.12	.09	.09	.12	.11	.08
Parental Quality	-.13	.09	-.07	.09	-.14	.09
Depression	.03	.20	.00	.24	.03	.19

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Age of Alcohol Onset	-.03***	.01	-.04***	.01	-.03***	.01
Any Childhood Abuse (CA)	-.01	.08	.20	.14	-.01	.10
Proximal Stress (PS)	.13	.12	.03	.16	-.04	.14
MAOA-L	—	—	.20	.10	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	-.06	.08
CA x PS	-.06	.20	-.08	.30	-.09	.21
MAOA-L x CA	—	—	-.35*	.17	—	—
MAOA-L x PS	—	—	.29	.22	—	—
MAOA-L x CA x PS	—	—	-.02	.50	—	—
5-HTTLPR x CA	—	—	—	—	-.03	.09
5-HTTLPR x PS	—	—	—	—	.19	.15
5-HTTLPR x CA x PS	—	—	—	—	.08	.26
Constant	-.42	.71	-.82	.79	-.25	.72

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Random Effects						
Family						
Standard Deviation of Intercept	.27*	.04	.24*	.05	.26*	.04
Individual						
Standard Deviation of Intercept	.00*	.00	.00*	.03	.00*	.00
Standard Deviation of Slope	.52*	.02	.55*	.03	.52*	.02

Note: * $p < .05$; ** $p < .01$; *** $p < .001$; Model 1: n = 108; Model 2: n = 83; Model 3: n = 108.

Table C2

Feminine Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.19***	.05	.15**	.05	.19***	.05
Age^2	-.00***	.00	-.00**	.00	-.00***	.00
Black	-.28**	.08	-.42**	.14	-.27***	.08
Hispanic	-.04	.09	.09	.13	-.04	.09
Other	-.24*	.09	-.18	.14	-.19*	.10
Male	.12	.08	.10	.10	.11	.08
Parental Quality	-.08	.07	.11	.14	-.07	.07
Depression	-.02	.10	-.01	.12	-.02	.09
Age of Alcohol Onset	-.04***	.00	-.04***	.01	-.04***	.00
Any Childhood Abuse (CA)	.06	.07	.11	.13	-.03	.11
Proximal Stress (PS)	.20	.15	.04	.13	.30	.20

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	-.03	.13	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	-.05	.05
CA x PS	-.38*	.18	-.37	.25	-.34	.26
MAOA-L x CA	—	—	.11	.19	—	—
MAOA-L x PS	—	—	.58	.40	—	—
MAOA-L x CA x PS	—	—	-.38	.49	—	—
5-HTTLPR x CA	—	—	—	—	.11	.09
5-HTTLPR x PS	—	—	—	—	-.21	.15
5-HTTLPR x CA x PS	—	—	—	—	.06	.19
Constant	-.66	.64	-1.15	.84	-.57	.63
Random Effects						
Family						
Standard Deviation of Intercept	.23*	.04	.17*	.04	.23*	.04

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.00*	.00	.17*	.03	.00*	.00
Standard Deviation of Slope	.43*	.03	.43*	.03	.43*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 106; Model 2: n = 65; Model 3: n = 106; + = parameter predicts failure perfectly.

Table C3

Androgynous Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.10**	.04	.14**	.04	.10**	.04
Age^2	-.00*	.00	-.00**	.00	-.00*	.00
Black	-.22***	.04	-.27***	.06	-.21***	.05
Hispanic	-.04	.07	-.00	.09	-.04	.07
Other	-.13	.11	-.11	.18	-.11	.11
Male	.15**	.05	.08	.06	.15**	.05
Parental Quality	-.01	.04	.01	.05	-.01	.04
Depression	.21*	.09	.29*	.12	.21*	.09
Age of Alcohol Onset	-.03***	.00	-.03***	.00	-.03***	.00
Any Childhood Abuse (CA)	-.06	.05	-.05	.08	-.00	.07
Proximal Stress (PS)	.21	.11	.12	.12	.50**	.18

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.12	.08	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	.04	.04
CA x PS	-.28	.14	-.27	.16	-.55*	.25
MAOA-L x CA	—	—	-.12	.11	—	—
MAOA-L x PS	—	—	.44	.29	—	—
MAOA-L x CA x PS	—	—	.17	.43	—	—
5-HTTLPR x CA	—	—	—	—	-.07	.06
5-HTTLPR x PS	—	—	—	—	-.32*	.14
5-HTTLPR x CA x PS	—	—	—	—	.30	.19
Constant	-.24	.45	-.73	.50	-.27	.45
Random Effects						
Family						
Standard Deviation of Intercept	.15*	.14	.16*	.15	.13*	.16

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.12*	.17	.08*	.30	.13*	.16
Standard Deviation of Slope	.48*	.02	.48*	.02	.48*	.02

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 183; Model 2: n = 126; Model 3: n = 183; + = parameter predicts failure perfectly.

Table C4

Undifferentiated Growth Curve Models of Binge Drinking Frequency

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Fixed Effects						
Age	.16**	.05	.18**	.05	.15**	.05
Age^2	-.00**	.00	-.00**	.00	-.00**	.00
Black	-.16*	.07	-.16*	.08	-.17*	.07
Hispanic	.03	.09	.03	.10	.02	.09
Other	-.16	.09	-.20	.11	-.16	.10
Male	.09	.06	.13	.07	.08	.06
Parental Quality	-.03	.04	-.01	.05	-.03	.04
Depression	.01	.14	.03	.18	.02	.14
Age of Alcohol Onset	-.03***	.01	-.02***	.01	-.03***	.01
Any Childhood Abuse (CA)	.03	.06	-.01	.09	.07	.10
Proximal Stress (PS)	.19	.11	.24	.16	.07	.21

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
MAOA-L	—	—	.05	.09	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	.00	.05
CA x PS	-.21	.16	-.23	.22	-.31	.24
MAOA-L x CA	—	—	.13	.15	—	—
MAOA-L x PS	—	—	.00	.29	—	—
MAOA-L x CA x PS	—	—	-.06	.36	—	—
5-HTTLPR x CA	—	—	—	—	-.04	.07
5-HTTLPR x PS	—	—	—	—	.13	.18
5-HTTLPR x CA x PS	—	—	—	—	.10	.23
Constant	-.62	.52	-1.12	.61	-.60	.52
Random Effects						
Family						
Standard Deviation of Intercept	.00*	.00	.00*	.00	.00*	.00

	Model 1 DE x PE		Model 2 MAOA x DE x PE		Model 3 5-HTTLPR x DE x PE	
	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE	Coefficient (Estimate)	Robust SE
Individual						
Standard Deviation of Intercept	.23*	.03	.22*	.09	.23*	.16
Standard Deviation of Slope	.54*	.02	.56*	.12	.54*	.04

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 167; Model 2: n = 129; Model 3: n = 167; + = parameter predicts failure perfectly

APPENDIX D

Alcohol Use Age of Onset Sex Role Models

Table D1

Masculine Cox Regression Models of Alcohol Use Age of Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	-.24	.78	.19	-.51	.60	.21	-.26	.77	.20
Hispanic	.14	1.15	.31	-.06	.94	.31	.15	1.16	.33
Other	-.22	.80	.30	-.18	.84	.34	-.21	.81	.30
Male	.24	1.27	.21	.45	1.56	.36	.24	1.28	.23
Parental Quality	-.24	.79	.11	-.15	.86	.13	-.23	.79	.13
Depression	-.64	.53**	.11	-.65	.52*	.15	-.61	.54**	.10
Any Childhood Abuse (CA)	-.14	.87	.14	-.24	.79	.21	.15	1.16	.33
Proximal Stress (PS)	-.01	.99	.79	-.54	.58	.59	.19	1.21	1.42

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
MAOA-L	—	—	—	-.15	.86	.28	—	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	—	—	.11	1.12	.22
CA x PS	.68	1.98	1.69	2.21	9.15*	9.48	.96	2.61	3.28
MAOA-L x CA	—	—	—	.66	1.93	.84	—	—	—
MAOA-L x PS	—	—	—	2.62	13.80*	14.30	—	—	—
MAOA-L x CA x PS	—	—	—	-4.68	.01***	.01	—	—	—
5-HTTLPR x CA	—	—	—	—	—	—	-.39	.68	.15
5-HTTLPR x PS	—	—	—	—	—	—	-.27	.76	1.19
5-HTTLPR x CA x PS	—	—	—	—	—	—	.01	1.01	1.69

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 100; Model 2: n = 77; Model 3: n = 100.

Table D2

Feminine Cox Regression Models of Alcohol Use Age of Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	-.71	.49*	.17	-1.01	.36	.26	-.75	.47	.19
Hispanic	-.44	.65*	.14	-.31	.74	.23	-.42	.66	.14
Other	-.43	.48	.19	-.67	.51	.29	-.67	.51	.20
Male	.15	1.16	.23	.03	1.03	.25	.12	1.13	.23
Parental Quality	-.34	.71	.20	-.08	.92	.38	-.30	.74	.22
Depression	-.34	.64	.16	-.58	.56	.19	-.51	.60	.17
Any Childhood Abuse (CA)	.03	1.03	.18	-.16	.85	.23	.08	1.08	.35
Proximal Stress (PS)	.53	1.70	1.42	1.36	3.89	3.54	.44	1.55	1.49
MAOA-L	—	—	—	.20	1.22	.35	—-	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	—	—	-.12	.89	.14

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
CA x PS	-.41	.66	.60	-1.19	.31	.30	-.40	.67	.69
MAOA-L x CA	—	—	—	.06	1.07	.49	—	—	—
MAOA-L x PS	—	—	—	.22	1.25	1.30	—	—	—
MAOA-L x CA x PS	—	—	—	.92	2.51	2.76	—	—	—
5-HTTLPR x CA	—	—	—	—	—	—	-.02	.98	.28
5-HTTLPR x PS	—	—	—	—	—	—	.11	1.12	.79
5-HTTLPR x CA x PS	—	—	—	—	—	—	-.02	.98	.72

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 103; Model 2: n = 62; Model 3: n = 103; + = parameter predicts failure perfectly.

Table D3

Androgynous Cox Regression Models of Alcohol Use Age of Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	-.08	.92	.16	-.6	.94	.20	-.06	.94	.17
Hispanic	-.32	.73	.13	-.47	.62*	.14	-.32	.73	.13
Other	.24	1.27	.31	.39	1.47	.34	.19	1.21	.33
Male	.06	1.06	.14	.07	1.07	.17	.08	1.08	.15
Parental Quality	-.02	.98	.11	-.10	.91	.11	-.02	.98	.11
Depression	-.36	.70	.21	-.05	.95	.31	-.40	.67	.21
Any Childhood Abuse (CA)	.09	1.10	.14	-.15	.86	.16	.04	1.04	.21
Proximal Stress (PS)	-.30	.74	.18	-.41	.66	.31	-.32	.72	.23
MAOA-L	—	—	—	.11	1.11	.29	—	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	—	—	.02	1.01	.13

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
CA x PS	.33	1.38	.72	1.54	4.69	3.82	-18.60	.00***	.00
MAOA-L x CA	—	—	—	.01	1.01	.35	—	—	—
MAOA-L x PS	—	—	—	.11	1.12	.63	—	—	—
MAOA-L x CA x PS	—	—	—	-32.28	.00***	.00	—	—	—
5-HTTLPR x CA	—	—	—	—	—	—	.06	1.07	.17
5-HTTLPR x PS	—	—	—	—	—	—	.03	1.04	.28
5-HTTLPR x CA x PS	—	—	—	—	—	—	19.10	.00	+

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 176; Model 2: n = 121; Model 3: n = 176; + = parameter predicts failure perfectly.

Table D4

Undifferentiated Cox Regression Models of Alcohol Use Age of Onset

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
Black	.06	1.07	.23	.13	1.14	.27	.13	1.14	.24
Hispanic	-.36	.70	.16	-.35	.71	.21	-.41	.66	.15
Other	-.35	.70	.16	.03	1.03	.25	-.51	.60*	.15
Male	-.16	.85	.13	-.15	.86	.16	-.19	.83	.13
Parental Quality	-.17	.84	.10	-.18	.84	.16	-.18	.83	.10
Depression	.12	1.13	.26	-.02	.98	.21	.07	1.07	.27
Any Childhood Abuse (CA)	-.26	.77	.11	-.03	.97	.22	-.35	.71	.18
Proximal Stress (PS)	.23	1.26	.30	.75	2.11*	.62	.09	1.10	.39
MAOA-L	—	—	—	.02	1.02	.24	—	—	—
5-HTTLPR s-alleles (5-HTTLPR)	—	—	—	—	—	—	.08	1.09	.19

	Model 1 DE x PE			Model 2 MAOA x DE x PE			Model 3 5-HTTLPR x DE x PE		
	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE	Coefficient	Haz.	Robust SE
CA x PS	.10	1.10	.44	-.71	.49	.26	-.09	.91	.82
MAOA-L x CA	—	—	—	-.36	.70	.24	—	—	—
MAOA-L x PS	—	—	—	-1.08	.34*	.16	—	—	—
MAOA-L x CA x PS	—	—	—	1.39	4.02*	2.80	—	—	—
5-HTTLPR x CA	—	—	—	—	—	—	.08	1.08	.23
5-HTTLPR x PS	—	—	—	—	—	—	.18	1.20	.46
5-HTTLPR x CA x PS	—	—	—	—	—	—	.06	1.06	.65

Note: * p < .05; ** p < .01; *** p < .001; Model 1: n = 160; Model 2: n = 122; Model 3: n = 16

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EDUCATION

Doctor of Philosophy, doctoral candidate in Criminal Justice and Criminology, Sam Houston State University, Huntsville, Texas. Dissertation title: "Individual Differences in the Impact of Stress on Alcohol use, Binge Drinking, and Alcohol Use Onset: The Role of Developmental and Biological Variation." Chair: Dr. Danielle Boisvert. Anticipated Graduation May, 2017

Masters of Arts (May, 2013) in Criminal Justice and Criminology, Sam Houston State University, Huntsville, Texas. Thesis title: "Molecular Genetic Underpinnings of Self-Control: 5-HTTLPR and Environmental Risk Factors." Chair: Dr. Todd Armstrong

Bachelor of Arts (May, 2011) in Criminology & Criminal Justice and English, Southern Illinois University, Carbondale, Illinois.

PUBLICATIONS

Peer Reviewed Publications

Wells, J., Armstrong, T., Boisvert, D., Lewis, R., Gangitano, D., & Hughes-Stamm, S. "Stress, genes, and generalizability across gender: Effects of MAOA and stress sensitivity on crime and delinquency." Accepted at *Criminology*.

Boisvert, D., **Wells, J.,** Armstrong, T., Lewis, R., & Woeckner, M. "Low resting heart rate and stalking." *Accepted at Journal of Interpersonal Violence.*

Wells, J., Armstrong, T., Boutwell, B., Boisvert, D., Flores, S., Symonds, M., & Gangitano, D. (2015). Molecular genetic underpinnings of self-control: 5-HTTLPR and self-control in a sample of inmates. *Journal of Criminal Justice, 43*(5), 386-396.

Armstrong, G. S., Atkin-Plunk, C. A., & **Wells, J.** (2015). The relationship between work–family conflict, correctional officer job stress, and job satisfaction. *Criminal Justice and Behavior, 42*(10), 1066-1082.

Articles Under Review

Armstrong, T., Boisvert, D., **Wells, J**., Lewis, R., Woeckner, M., & Cooke, E. "Self-control, psychopathy, sensation seeking and crime." *Under review at Criminology.*

Technical Reports

Armstrong, G. S., **Wells, J.,** & Atkin-Plunk, C. A. (2013). *"The "silent killer" of correctional officers: Examining job stress among TDCJ correctional officers* (Correction Management Institute of Texas Report 2013-No. 1). Huntsville, TX: Correctional Management Institute of Texas.

Works in Progress

Wells, J., Armstrong, T., & Boisvert, D. "Empathy and aggression: The mediating role of psychopathy."

Wells, J., Armstrong, T., Cooke, E., & Boisvert, D. "Psychopathy, reactive, & proactive aggression: A gendered approach."

Boisvert, D., **Wells, J.,** Woeckener, M., & Armstrong, T. "TPH polymorphism and violent and nonviolent criminal offending in a sample of male inmates"

Armstrong, T., Boisvert, D., **Wells, J.,** Boutwell, B., Nobles, M., Motl, J., . . . Gangitano, D. "Dopamine beta hydroxylase and aggression."

Woeckener, M., Boisvert, D., Armstrong, T., **Wells, J.** "Parental criminality and offspring stalking perpetration."

Randa, R., & **Wells, J. "**BMI and bullying victimization: An evolutionary perspective of extremes."

SELECTED PRESENTATIONS

Wells, J., (November, 2016). "Individual differences in the impact of stress on substance use: The role of developmental and biological variation" American Society of Criminology, New Orleans, LA.

Wells, J., Armstrong, T., Simmons, S. (March, 2016). "It depends: A spatial environmental approach to heartrate-environment interation." Academy of Criminal Justice Sciences, Denver, CO.

Wells, J., Randa, R., & Simmons, S. (March, 2016). "BMI and bullying victimization: An evolutionary perspective of extremes." Academy of Criminal Justice Sciences, Denver, CO.

Wells, J., Armstrong, T., Boisvert, D., Lewis, R. (November, 2015). "Stress, genes, and generalizability across gender: Direct and interactive effects of candidate genes and life stress on antisocial behavior." American Society of Criminology, Washington, D.C. (also presented at Graduate Research Symposium, Sam Houston State University).

Wells, J., Cooke, E., Armstrong, T., Boisvert, D. (March, 2015). "The Association between Psychopathy, Reactive, and Proactive Aggression: A Gendered Approach." Academy of Criminal Justice Sciences. Orlando, FL.

Wells, J. (February, 2015). "Serotonin Transporter Gene Polymorphism in Interaction with Monoamine Oxidase SNPs in the Explanation of Sensation Seeking via Reward Processing." Graduate Research Exchange. Sam Houston State University.

Wells, J. (November, 2014). "Aggression, psychopathy, & empathy." American Society of Criminology. San Francisco, CA.

Wells, J. (November, 2013). "The association between the serotonin transporter gene and self-control." American Society of Criminology. Atlanta, GA.

Wells, J., Armstrong, G., & Atkin, C. (March 2013). "The impact of work-family conflict on correctional officer job stress and job satisfaction." Academy of Criminal Justice Sciences. Dallas, TX.

ACADEMIC AWARDS

Doctoral Research Fellowship, College of Criminal Justice, Sam Houston State University, 2016–present.

Excellence in Writing Award, Academic Success Center, Sam Houston State University, Spring, 2015.

Rolando V. del Carmen Student Endowed Criminal Justice Scholarship, College of Criminal Justice, Sam Houston State University, 2015–2016.

Graduate Research Summer Fellowship, College of Criminal Justice, Sam Houston State University, Summer, 2014, 2015, 2016.

Graduate Research Assistantship, College of Criminal Justice, Sam Houston State University, 2011 – present.

Outstanding Leadership Award, College of Criminal Justice, Sam Houston State University, 2013

Summer Tuition Scholarship, Office of Graduate Studies, Sam Houston State University, 2013.

ACADEMIC EMPLOYMENT

2015 — present: Doctoral Teaching Fellow for the Department of Criminal Justice and Criminology, College of Criminal Justice, Sam Houston State University.

2012 — present: Graduate Research Assistant for the College of Criminal Justice, Department of Criminal Justice and Criminology Sam Houston State University. Research focuses on individual differences in correlates of antisocial behavior. Under: Dr. Todd Armstrong & Dr. Danielle Boisvert

2011 — 2011: Graduate Research Assistant for the Correctional Management Insisutue of Texas, College of Criminal Justice, Sam Houston State University. Research focused on the relationship between corrctional officer work-family conflict and job stress and job satisfaction. Under: Dr. Gaylene Armstrong

2012 — 2015	Graduate Teaching Assistant, College of Criminal Justice, Sam Houston State University CRIJ 3361 – Comparative Criminal Justice Systems CRIJ3340 – Gender and Crime CRIJ 2362 – Criminology

RELEVANT RESEARCH EXPERIENCE

2016 — present	The Relationship between Biological Factors, Criminal Behavior, Psychopathologies, and Risk of Victimization Department of Criminal Justice and Criminology, College of Criminal Justice, Sam Houston State University Under: Dr. Danielle Boisvert Duties: project development, survey creation, budget formation, graduate student coordination, data collection (e.g., survey, DNA, saliva sampling, heart rate, and skin conductance)
2013 — present	Biosocial Underpinnings of Stalking Wave 2 Enhancement Research Grant funded, $10,000

Department of Criminal Justice and Criminology, College of Criminal Justice, Sam Houston State University
Under: Dr. Todd Armstrong
Duties: creation of codebook and database, data collection coordination, data collection (e.g., survey, DNA, and heart rate), data entry, DNA extraction, DNA quantification, DNA VNTR and SNP genotyping

2012 — present Biosocial Underpinnings of Stalking Wave 1
Department of Criminal Justice and Criminology, College of Criminal Justice, Sam Houston State University
Under: Dr. Todd Armstrong
Duties: data entry and data management

2015 — present The LoneStar Project: Study of Offender Trajectories, Associations, and Reentry (National Institute of Justice funded)
Department of Criminal Justice and Criminology, College of Criminal Justice, Sam Houston State University
University of Colorado, Bolder
Arizona State University
Under: Drs. Gaylene Armstrong, David Pyrooz, Scott Decker
Duties: conducted interviews including additional segregation interviews; certified trained in Blaise computer assisted personal interviewing

2011 — 2012 Correctional Officer Work-Family Stress
Correctional Management Institute of Texas (CMIT)
Under: Dr. Gaylene Armstrong
Duties: data collection coordination, data collection, data entry

Journal Reviewer

Journal of Qualitative Criminology
Journal of School Violence
Criminal Justice and Behavior

GRANTS SUBMITTED

Thomas, S., Drawve, G., & **Wells, J. (2015). "**Examining the influence of incident, police organizational, and community level characteristics on the clearance by arrest for violent and non-violent offenses." National Institute of Justice, $39,349, *not funded*.

TEACHING AND RELATED EXPERIENCE

Undergraduate Courses Taught

Department of Criminology and Criminal Justice, Sam Houston State University

Introduction to Methods of Research (Writing Enhanced). Spring, 2017.

Introduction to Methods of Research (Writing Enhanced). Fall, 2016.

Gender and Crime. Spring, 2016.

Criminology (**A**cademic **C**ommunity **E**ngagement). Fall, 2015.
Honors Contract Supervisor

COLLEGE AND UNIVERSITY-LEVEL COMMITTEE MEMBERSHIP

2014 – present Sexual Assault Awareness Month Planning Committee, SHSU

2012 – 2013 Advisor, Dean's Student Advisement Committee, College of Criminal Justice, SHSU

ORGANIZATIONAL MEMBERSHIP

2015 – 2016 Fierce Focus Writing Group, College of Criminal Justice, SHSU; Organizer

2014 – present Criminal Justice Graduate Student Organization, College of Criminal Justice, SHSU; Technology Liaison.

2014 – present Criminal Justice Graduate Student Organization, College of Criminal Justice, SHSU; Service Committee Member

2013 – 2014 Criminal Justice Graduate Student Organization, College of Criminal Justice, SHSU; Chair of Service Committee

2012 – present Criminal Justice Graduate Student Organization, College of Criminal Justice, SHSU; Member

2012 – present Graduate Student Mentor, College of Criminal Justice, SHSU;

PROFESSIONAL DEVELOPMENT

2017 SHSU Teaching Assistant Certification Series
2016 SHSU Teaching Conference

2016 ACJS Doctoral Student Summit
2015 SHSU Teaching Conference
2015 ICPSR SEM in STATA Workshop
2015 SHSU DELTA Blackboard Training Certification Series
2015 SHSU Science Writing Workshop
2015 SHSU Online Teaching Conference
2015 SHSU CJ GSO Stata Workshop
2015 SHSU IDEA Workshop
2014 SHSU Teaching Conference
2012 SHSU Child Abuse Mandate, Reporting in Texas
2012 SHSU Statistics Workshop
2012 SHSU Professional Writing Workshop

PROFESSIONAL MEMBERSHIP

Academy of Criminal Justice Sciences

American Society of Criminology, Division on Developmental/Life-Course Criminology; Division on Women & Crime

Biosocial Criminology Association