Predictors of off-diagonal binge drinking and marijuana use trajectory groups through the transition to adulthood

by

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Chapter 1

Introduction

From a developmental perspective, adolescence and the transition to adulthood are highly relevant to studying the etiology and epidemiology of substance use (Schulenberg et al., 2014; Schulenberg & Maggs, 2002). For the most commonly used substances among youth—binge drinking, typically defined as consuming five or more alcoholic beverages on a single occasion (National Institute on Alcohol Abuse and Alcoholism (NIAAA), 2015), and marijuana—rates of use tend to escalate through adolescence and then peak during the transition to adulthood (Johnston et al., 2015). Although relatively common, binge drinking and marijuana use can be problematic. At the individual level, substance use is associated with negative impacts on health and well-being, such as increased risk for psychiatric comorbidities and detriments to interpersonal relations (Grant et al., 2015; Hasin et al., 2007). In terms of public health, substance use contributes to economic burden and a considerable rate of morbidity and mortality (Centers for Disease Control and Prevention (CDC), 2014; Lozano et al., 2013). Compared to other drugs of abuse, alcohol and marijuana often have the highest rates of disordered use (Substance Abuse and Mental Health Services Administration (SAMHSA), 2015). Specifically, binge drinking is estimated to account for half of alcohol-related deaths and three-quarters of the economic burden attributable to excessive drinking (CDC, 2014). As with alcohol, heavy marijuana use may result in multiple negative consequences, such as deficits in learning, memory, and attention (Volkow et al., 2014; Volkow, et al., 2016). Marijuana use may also impair motor coordination while driving, which increases risk of injury to self and others

(Hartman & Huestis, 2013). Thus, identifying both risk and protective factors for these substances is a vital health concern.

Psychosocial, social context, and neural factors contribute to substance use during the transition to adulthood. Psychosocial and social context factors pertain to developmental transitions and tasks that occur from late adolescence through early adulthood. Developmental transitions and tasks are similar constructs, but transitions describe the *process* of change and tasks are characterized by *accomplishments* pertaining to those changes (Schulenberg et al., 2004). During late adolescence and through the transition to adulthood, parental monitoring decreases and peer socializing increases. These changes often coincide with developmental transitions, such as leaving the parental home and attending college. Related to the increasing importance of peers, substance use may be used to facilitate developmental tasks such as identify formation and social integration (Schulenberg et al., in press). In trying to find one's identify, experimental substance use may coincide with peer group membership. As such, substance use in social situations may encourage peer bonding and is relatively normative during the transition to adulthood (Schulenberg & Zarrett, 2006). For example, in college settings many youth no longer live at their parental home and there may be a greater number of opportunities for exposure to substances through peer socializing. For many youth, decreased substance use occurs after leaving college. For other youth, elevated substance use in college may set in motion a pattern of heavy use that continues through the transition to adulthood. Other social role transitions, such as marriage and parenthood, may decrease substance use through early adulthood (Bachman et al., 2002; Staff et al., 2010). A greater number of responsibilities and fewer opportunities for socializing often contribute to this decrease. In sum, the transition to adulthood, compared to all periods of time, is associated with formative developmental tasks and transitions that impact the course and extent of substance use.

In addition to psychological and social changes, there are also important neural changes underlying substance use during the transition to adulthood. Neural systems involved in cognitive control do not fully mature until the early 20s, whereas neural regions associated with reward responsivity reach maturity earlier in development during adolescence (Casey et al., 2008; Gogtay et al., 2004; Steinberg, 2008). Heightened reward sensitivity may contribute to risk behaviors, such as substance use, due to a decreased capacity for cognitive control. As stated previously, substance use during the transition to adulthood often occurs in the context of social bonding, which is an important developmental task during the transition to adulthood (Schulenberg et al., in press). Peer interactions tend to be highly rewarding on a neural level as well (e.g., Blakemore, 2008). In fact, the presence of peers may even elevate the perceived rewards of risk behaviors (Chein et al., 2011). Taken together, individual-level and social context factors during the transition to adulthood make this age period highly relevant to studying developmental patterns of substance use.

Developmental Trajectories of Off-Diagonal Substance Users

A key facet of identifying risk and protective factors of binge drinking and marijuana use is examining variability in patterns of use across development. Beyond group level means, there is often heterogeneity in onset and course. Existing evidence indicates varying degrees of increasing, decreasing, or consistent levels of either high or low binge drinking (e.g., Hill et al., 2007; Maggs & Schulenberg, 2004; Oesterle et al., 2004; Schulenberg et al., 1996a) and marijuana use (e.g., Epstein et al., 2015; Nelson et al., 2014; Schulenberg et al., 2005; Windle & Wiesner, 2004) through the transition to adulthood. Chronic high users tend to be the most problematic in terms of psychosocial and health outcomes later in development (e.g., Berg et al., 2013; Chassin et al., 2002; Chassin et al., 2004; Squeglia et al., 2009; Winward et al., 2014). Youth classified as chronic high substance users typically fall within the "Type 2" substance use disorder (SUD) subtype, characterized by externalizing behaviors and having a family history of SUDs. In comparison, the "Type 1" SUD subtype is more likely later onset and associated with negative affect (Babor et al., 1992; Cloninger et al., 1996; Zucker, 1987, 1994; Zucker et al., 2011). Chronic high users may be more likely to have a family history of SUDs (FH+) (Chassin et al., 2002; Jester et al., 2015), suggesting both environmental and biological susceptibilities for substance use. In many ways, chronic high users display continuity of problem behaviors from earlier in development and follow expected, albeit maladaptive, patterns of risk (Schulenberg et al., in press).

Following more unexpected patterns of risk are youth in off-diagonal substance use groups (Dever et al., 2012; Schulenberg & Maggs, 2002). The term "off-diagonal" describes unexpected patterns of behavior, which has been referred to as either "vulnerabilities despite what appear to be sufficient resources" or "resilience in the face of adversity" (Eccles, 2008, p. 2). In other words, unexpected outcomes among off-diagonal groups can either be negative, characterized by derailing from more adaptive prior functioning, or positive, in which certain youth "beat the odds" despite earlier adversity (Eccles, 2008; Schulenberg & Maggs, 2002). Off-diagonal substance use groups described in this dissertation were defined by two dimensions, which were level of substance use and level of risk. Figure 1 shows that late-onset substance users with low levels of use during adolescence but who then sharply increase use through the transition to adulthood comprised the first off-diagonal group assessed in this dissertation. Despite their elevated levels of substance use, this group had few prior indicators of vulnerability to substance use problems. Also shown in Figure 1, resilient FH+ youth with low substance use through the transition to adulthood were the second off-diagonal group examined. These youth were high on risk by having a family history of SUD but showed low levels of substance use through the transition to adulthood. Few studies have focused specifically on off-diagonal youth, due to these groups often being overshadowed by more expected risk groups, such as chronic high substance users. To address this deficit, the purpose of this dissertation was to identify characteristics and predictors of off-diagonal binge drinking and marijuana use among youth through innovative, multilevel methods.

Studying developmental factors underlying off-diagonal groups not only fills a gap in the literature, but also has important prevention and intervention implications (Dever et al., 2012; Eccles, 2008; Schulenberg et al., 2001). Among late-onset substance users, identifying predictors at the onset of their escalating use (i.e., late adolescence) and as their use continues to increase through the transition to adulthood may help target risk factors for this type of substance use behavior. Because they display low levels of substance use during adolescence, by the time late-onset youth enter the transition to adulthood, this population may be overlooked by typical intervention programs aimed at youth with earlier substance use problems. This is a concern, given the negative outcomes associated with late-onset, escalating substance use. Compared to low users, late-onset marijuana users show heightened substance use problems and sexual risk behaviors (Epstein et al., 2015), as well as mental and physical health problems (Caldeira et al., 2015). Late-onset heavy alcohol users are more likely to experience health detriments and economic disadvantage in young adulthood compared to low drinkers (Oesterle et al., 2004; Berg et al., 2013, respectively).

As with late-onset substance users, there are relatively few existing studies on resilient youth (e.g., low substance using FH+ youth). High substance using FH+ youth tend to receive the most empirical attention (e.g., DeVito et al., 2013; Heitzeg et al., 2015; Hussong et al., 2008; Iacono et al., 2008). Although studying vulnerable, high-risk groups is needed, it is also valuable to examine why certain youth do *not* follow more expected patterns of risk. This dissertation addresses this need by identifying protective factors among resilient youth. In turn, this information may be valuable to help inform prevention and intervention programs aimed at FH+ youth. Efforts to strengthen and maintain protective mechanisms, such as the capacity for self-regulation of thoughts and behaviors pertaining to alcohol and marijuana use, may reduce the likelihood of these youth developing later substance use problems. Self-regulation is involved with the behavioral undercontrol/disinhibition risk phenotype for SUDs (Zucker et al., 2011). This risk phenotype is closely related to the Type 2 SUD subtype characterized by externalizing behaviors of aggression and delinquency (Babor et al., 1992; Cloninger et al., 1996; Zucker, 1987, 1994). Behavioral undercontrol is defined by the inability, unwillingness, or failure to inhibit behaviors despite negative consequences associated with those behaviors (Hawkins et al., 1992; Zucker, 2006). Whereas behavioral undercontrol contributes to substance use risk at the behavioral level, disinhibition is involved with neural function. In other words, disinhibition is the neural mechanism underlying behavioral control. Thus, self-regulation is multidimensional, involving interrelated behavioral and neural constructs (Windle, in press). Although the majority of studies examining associations between the behavioral undercontrol/disinhibition phenotype and substance use have focused on risk, this pathway to substance use may also be important in relation to resilience. Self-regulated individuals may have a greater capacity for inhibiting impulsive responding to reward-driven stimuli, such as drugs of abuse. Yet, the interplay between behavioral and neural function related to substance use resilience has received little empirical attention.

To address this deficit in existing research, this dissertation examined both distal and proximal developmental characteristics and predictors of off-diagonal substance use groups during the transition to adulthood—late-onset substance users and resilient FH+ youth. Distal refers to risk factors from an earlier period, such as adolescence in relation to young adulthood. Proximal refers to factors closer to the outcome of substance use during the transition to adulthood (i.e., young adulthood). From a developmental perspective, both distal and proximal factors provide valuable information pertaining to substance use risk and resilience (Schulenberg et al., in press). Studying distal factors provides an indicator for continuity of earlier influences on more downstream outcomes (Caspi, 2000). In addition to exerting lasting effects, distal factors may produce a more delayed influence on substance use. Typically, however, proximal factors tend to be more powerful in comparison to distal factors (Schulenberg et al., in press). This power is likely due to the more direct temporal influence on a given outcome. Because late-onset substance users show discontinuity of substance use from adolescence through the transition to adulthood, proximal predictors may be especially important at the onset of and during this developmental shift. Distal predictors may be more pertinent to low substance using FH+ youth due to the continuity of their substance use through the transition to adulthood. Specifically, distal and proximal predictors centered on varying dimensions of developmental influences associated with substance use risk and resilience during the transition to adulthood. These influences included psychosocial factors, social context changes, and neural function underlying self-regulation (Table 1).

This dissertation utilized a multi-level, interdisciplinary approach to integrate the breadth and depth of two widely known, longitudinal studies on substance use to examine two off-diagonal substance use groups. Breadth allows for a better understanding of more generalizable characteristics, while depth gives particular attention to a unique population especially prone to substance use problems (i.e., FH+ youth). Providing breadth, Monitoring the Future (MTF) is a school-based, national survey study of American youth, focused particularly on attitudes, beliefs, and behaviors pertaining to drug use and abuse. Providing depth, the Michigan Longitudinal Study (MLS) is a prospective community-recruited study consisting primarily of families with parental SUD (2/3 of the sample). MLS includes extensive parent and child interviews and extensive target child assessments through early adulthood on topics such as substance use and psychosocial functioning. MLS also has a neuroimaging sub-sample of participants who have been studied longitudinally through functional magnetic resonance imaging (fMRI) assessments.

Theoretical Perspectives

Two theoretical perspectives provide the foundation for the studies included in this dissertation: 1) Developmental psychopathology and 2) Dual-systems models of risk-taking.

Developmental psychopathology. Developmental psychopathology, which describes a theoretical framework based on causal processes involved in continuity and discontinuity of normal development and pathology (Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000), is one theoretical perspective guiding this dissertation research. Developmental psychopathology offers a framework to study the complex, biopsychosocial mechanisms involved in the etiology and course of substance use from adolescence through the transition to adulthood (Cicchetti & Rogosch, 1999; Hussong et al., 2011; Schulenberg et al., in press; Zucker, 2006). Two specific principles of the developmental psychopathology perspective most strongly guide the following three chapters of this dissertation.

The first principle is risk versus resilience. Risk and protective factors among off-diagonal substance use groups may be either distal or more proximal, or a combination of these factors. Preexisting, distal factors occurring early in development may exert lasting influences through the transition to adulthood by setting in motion patterns of behaviors. Early risk factors prior to the onset of substance use may be predictive of greater risk for substance use problems later in development (Cicchetti & Rogosch, 1999; Dodge et al., 2009). Changes during the transition to adulthood associated with substance use risk, such as contextual shifts in increased peer influence, weaker parental monitoring, and greater availability of substances (Romer & Hennessy, 2007; Steinberg, 2008; Schulenberg et al., 2014), may exert more of a proximal influence on substance use outcomes. Yet, proximal factors can be influenced by prior, more distal influences (Schulenberg et al., 2004; Schulenberg et al., in press). Examining both distal and more proximal influences may help explain heterogeneity in substance use patterns through the transition to adulthood.

Not all youth with early risk factors, such as being the child of a parent with a SUD, are destined for negative downstream outcomes of experiencing substance use problems (i.e., off-diagonal resilient youth). Within a developmental psychopathology framework, adversity describes conditions associated with high risk for maladjustment (Luthar, 2006; Masten, 2001). Resilience describes successful adaptation despite adversity (Masten et al., 1990). Thus, positive adjustment is focused more on outcomes characterized by adaptive functioning and successfully completing developmental tasks (Masten & Tellegen, 2012). Attributes of resilience have yet to be fully identified (Hurd & Zimmerman, in press).

The second principle of developmental psychopathology relevant to this dissertation involves concepts of continuity and discontinuity. Examining developmental patterns of substance use through trajectory analysis can be used to identify youth at risk for, and resilient to, substance use problems. Given that studying cross-sectional samples of youth may not capture patterns of substance use among off-diagonal groups, longitudinal trajectory analysis allows for modeling increasing, decreasing, or consistent levels of substance use among particular subgroups. Additionally, investigating heterogeneity of substance use provides comparisons between normative and atypical patterns of use. For example, whole-sample averages for both binge drinking and marijuana use are important to show typical trends in substance use across a population. Group averages, however, may miss subgroups of youth who diverge from group means (Schulenberg et al., in press). Two terms relevant to continuity and discontinuity in this dissertation are multifinality and equifinality. Multifinality refers to different outcomes that emerge from a similar starting point, whereas equifinality describes similar outcomes despite dissimilar starting points (Cicchetti & Rogosch, 1999). Multifinality relates to comparisons between late-onset substance use and low substance use trajectory groups. These two groups start at similar levels of substance use earlier in development but diverge in levels of use through the transition to adulthood. Equifinality characterizes pathways of substance use among the late-onset and chronic high use trajectory groups. Levels of substance use in the late-onset group begin to converge with the chronic high use group through the transition to adulthood. Examining both distal and proximal factors related to multifinality and equifinality may uncover developmental factors underlying the course of these diverging and converging substance use patterns.

Dual-systems models of risk-taking. Dual-systems models of risk-taking provide another related and important theoretical foundation for this dissertation, particularly Chapter Four that examines neural predictors of resilient youth. More broadly, however, dual-systems models of risk-taking describe the underlying neural processes associated with self-regulation that are described in Chapters Two and Three. On average, a normative increase and peak in risk-taking behavior tends to occur during adolescence through early adulthood, following an inverted "U"-shaped pattern (Somerville et al., 2010; Steinberg et al., 2008). Dual-systems models of risk-taking posit that misaligned development of two neural systems influence this age-varying pattern of risk-taking behavior (Casey et al., 2008; Dahl, 2004; Luna et al., 2015; Steinberg, 2010). One system, the striatal limbic system, develops early in adolescence during the onset of puberty. This system includes subcortical brain regions, such as the ventral striatum (VS), which are involved in reward processing. The other system is comprised of cortical brain regions associated with inhibitory control involves the prefrontal cortex and anterior cingulate cortices. This system is involved with self-regulation and follows a more protracted development compared to the earlier developing limbic system. In other words, neural regions involved in reward responsivity are often referred to as "bottom up" or "hot" systems, while neural regions associated with behavioral control are more "top down" or "cool" (Casey, 2014). Neural regions involved in self-regulation continue maturing well into the early 20s, coinciding with the transition to adulthood (Casey et al., 2008; Gogtay et al., 2004; Steinberg, 2008). Changes to the brain's volume, structure, and connectivity occur during this maturation (Bava & Tapert, 2010). For example, the myelination of white matter tracts improves connectivity between cortical and subcortical brain regions (Luna et al., 2015). In contrast to increased myelination of white matter, grey matter volume decreases from adolescence through early adulthood. Synaptic pruning is associated with reductions in grey matter that contribute to more efficient neural processing (Giedd et al., 1999; Gogtay et al., 2004). Because grey matter reductions occur first in subcortical regions and then progress into cortical regions later in development, reward driven brain regions show greater efficiency earlier in development compared to control related regions. In turn, self-regulation over reward-driven impulses strengthens over the course of development. For example, an fMRI study of participants ranging in age from 7 to 29 found no difference in the nucleus accumbens's (NAcc) response to rewards between adolescents compared to adults. Yet, the orbitofrontal cortex activity of adolescents was more similar to children than that of adults (Galvan et al., 2006). More recent evidence from a meta-analysis using activation likelihood estimation (ALE), a technique used to determine commonly activated neural regions across studies, supports the notion of increased reward responsivity in relation to inhibitory control among adolescents compared to adults (Silverman et al., 2015). Findings indicated that, compared to adults, adolescents tend to show increased activation likelihood in limbic, frontolimbic, and striatal regions and decreased activation in executive control regions during reward processing tasks.

While there is little doubt that reward responsivity and inhibitory control contribute to risk behaviors, dual-systems models of risk-taking have been criticized for being overly simplistic (Pfeifer & Allen, 2012). While most dual-systems models focus on average risk-taking, they have less often been used to account for individual variation in extent of risk behaviors (Harden & Tucker-Drob, 2011; Pfeifer & Allen, 2012; Quinn & Harden, 2013). Even within the same age range and risk profile, there may be individual-level differences in capacities for self-regulation. For example, Heitzeg et al. (2008) examined differences in frontostriatal response to affective stimuli among youth with a family history of AUD who were either heavy drinkers or low drinkers. Low drinkers (i.e., resilient youth) showed a stronger capacity for self-regulation measured by affective responding. This study highlights the importance of looking within risk groups (e.g., FH+ youth) to examine variable among individuals that may contribute to resilience. Indeed, a substantial proportion of youth progress through adolescence and early adulthood without engaging in dangerous risk behaviors, such as substance use (Dahl, 2004). As in the case of this dissertation, low substance using youth may even include those at heightened risk for SUDs. Better understanding variability in brain function central to dual-systems models, in both subcortical and prefrontal regions, may help elucidate neural mechanisms involved in this resilience (Casey et al., 2014).

Chapter Two: Predictors of Late-Onset Substance Use: Results from National Panel Samples

The majority of studies examining longitudinal trajectories of substance use have used convenience or non-random samples. Additionally, these studies have not focused specifically on characteristics and predictors of late-onset binge drinking and marijuana use. This is problematic, since late-onset substances users may be a less expected risk-group compared to more obvious risk groups (i.e., chronic high users). Chapter Two addresses this gap by identifying binge drinking and marijuana use trajectories through the transition to adulthood using longitudinal panel samples from the MTF survey and then examining both distal and more proximal characteristics and predictors of off-diagonal, late-onset substance users compared to both low and high substance users. Furthermore, this study employed innovative methods to advance prior trajectory analyses using data from MTF samples (e.g., Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 1996b; Schulenberg et al., 2005). Group comparisons between late-onset youth were based on the developmental psychopathology concepts of multifinality and equifinality, respectively. For this chapter, predictors of late-onset binge drinking and marijuana use were examined separately. Although a relatively high degree of comorbidity exists between binge drinking and marijuana, there is a certain extent of variability among predictors of these substances (Jackson et al., 2008). Therefore, predictors of each substance were examined separately, but binge drinking was included as a covariate in the marijuana use model and marijuana use was included as a covariate in the binge drinking model. Trajectory analyses used in this study captured late-onset substance use from senior year of high school through age 26, which allowed for identifying distal psychosocial and contextual predictors during late adolescence and more proximal psychosocial and contextual predictors during early adulthood. More specifically, distal variables included high school risk factors (grades, college plans, truancy, evenings out with friends), internalizing and externalizing factors, and sensation seeking. These distal factors are robustly associated with greater levels of later substance use risk (Schulenberg et al., 2014; Schulenberg, 2005; Steinberg et al., 2008, respectively). Proximal factors include internalizing and externalizing factors and sensation seeking assessed later during the transition to adulthood at age 25/26. Distal and proximal measures of internalizing behaviors, externalizing behaviors, and sensation seeking pertain to self-regulation. Self-regulation assessed in these measures falls within the broader, multidimensional construct of behavioral control (Windle, in press). Internalizing behaviors are associated with the internalizing pathway to substance use, in which substances are used to regulate negative affect through self-medication (Hussong et al., 2011). Externalizing behaviors and sensation seeking are related more to the behavioral undercontrol pathway to substance use (Zucker et al. 2011). Additionally, this chapter examines social role changes occurring during the transition to adulthood known to influence substance use, such as college enrollment, college graduation, marriage, and becoming a parent

(Staff et al., 2010). This study contributes to the literature by identifying important psychosocial factors and social contexts pertaining to the development of late-onset substance use among national samples of youth.

Chapter Three: Predictors of Resilience Among Youth at Elevated Risk for Substance Use

Whereas MTF offers breadth due to its inclusion of national samples, the MLS provides depth by consisting predominately of youth with a family history of SUD (FH+). MLS also includes extensive measures associated with substance use risk and resilience. Existing studies among FH+ youth have focused predominately on heavy substance using youth rather than resilient, low using youth. Furthermore, predictors of heavy use are often compared to predictors of low use among FH+ youth. Often low use is not assessed across the entire timeframe of the transition to adulthood. The present study identified resilient FH+ youth through a comprehensive and innovative approach that combined results of developmental trajectory modeling and empirically-based cut off points for high levels of both binge drinking and marijuana use. This approach builds upon existing research by using more robust indicators of resilience.

The purpose of Chapter Three was to identify binge drinking and marijuana use trajectories from ages 17/18 through ages 25/26 using data from the MLS and then examine characteristics and predictors of resilient FH+ youth. Given that resilience describes successful adaptation despite adversity (Masten et al., 1990), resilient youth in this study were defined as having low levels of both binge drinking and marijuana use through the transition to adulthood. Resilient FH+ youth represent an off-diagonal substance use group by being high on risk for substance use problems but displaying low levels of substance use through the transition to adulthood. Thus, this group follows an unexpected path considering prior vulnerability. To identify developmental factors underlying resilience within the framework of family risk for SUD, this study examined protective factors among resilient FH+ youth compared to chronic high substance using FH+ youth.

To align with Chapter Two, trajectories of binge drinking and marijuana use were examined between approximately the same age ranges as used with MTF data. Compared to MTF, the MLS not only includes a sample enriched for family history of SUDs, but also provides greater depth with extensive longitudinal data on participants beginning during childhood. Thus, Chapter Three examined earlier, more developmentally distal predictors from early adolescence (ages 12-14) that coincide with the typical age of onset for substance use (SAMHSA, 2015) and more proximal late adolescent and young adult predictors coinciding with the beginning of the transition to adulthood (Johnston et al., 2015). Distal and proximal predictors included measures associated with self-regulation that are involved in substance use risk—resiliency, reactive control, internalizing and externalizing problems, and sensation seeking due to known associations between these factors and substance use risk (Wong et al., 2006; Windle, in press, respectively). As with Chapter Two, Chapter Three investigated social role changes occurring during the transition to adulthood that are associated with substance use—college enrollment, college graduation, marriage, and becoming a parent (Staff et al., 2010). This chapter makes a novel contribution to the literature by using a longitudinal approach to identify both distal and proximal predictors of resilient youth through the transition to adulthood.

Chapter Four: Neural function associated with substance use resilience among vulnerable youth

While Chapter Two used data from MTF to examine psychosocial and contextual predictors of late-onset youth and Chapter Three assessed data from MLS to investigate psychosocial and contextual predictors of resilient youth, Chapter Four included fMRI data from the neuroimaging sub-sample of MLS to examine both psychosocial and neural predictors of resilient youth. No studies to date have examined whether neural measure of inhibitory control and reward responsivity predict substance use resilience versus risk among FH+ youth over and above behavioral measures of these constructs. Chapter Four contributes to the literature by investigating the role of neural influences above and beyond distal and proximal psychosocial predictors of behavioral control identified in Chapter Three. Because of their association with inhibitory control, reward responsivity, and self-regulation (Zucker et al., 2011), psychosocial measures examined in Chapter Four include reactive control and externalizing problems. Behavioral undercontrol and disinhibition describe the same underlying construct pertaining to self-regulation; however, behavioral undercontrol describes its psychosocial attributes and disinhibition describes its underlying neural function (Zucker et al., 2011). Testing neural response during inhibitory control and reward tasks may uncover differences between resilient and risk groups through processes that behavioral self-report measures cannot capture. It is also possible, however, that self-report measures accurately identify their associated constructs independently from, or in addition to, neural measures. Thus, examining both psychosocial and neural risk factors for substance use may be used to identify youth vulnerable to developing substance use problems more accurately. Studying neural mechanisms associated with resilience provides valuable information on protective factors against substance use.

Thus, the primary focus of this study was to test neural function associated with inhibitory control and reward responsivity as predictors of resilience versus risk. Inhibitory control and reward responsivity are central to dual-systems models of risk-taking, and more specifically the behavioral undercontrol/disinhibition pathway to substance use (e.g., Zucker et al., 2011). Inhibitory control is a form of self-regulation characterized by cognitive control to inhibit a prepotent response (Ivanov et al., 2008; Whelan et al., 2012). Neural deficits in inhibitory control are associated with behavioral disinhibition, and thus, heightened risk for substance use problems (Heitzeg et al., 2015). Furthermore, youth with a family history of SUD have been found to show deficits in response inhibition (Hardee et al., 2014; Heitzeg et al., 2010). Yet, few studies have focused on *resilient* youth among this risk population, particularly resilience spanning the transition to adulthood when substance use risk is elevated. Defining resilience within a narrow age range may miss important developmental fluctuations in substance use through the transition to adulthood among this off-diagonal group.

In addition to inhibitory control, reward responsivity is a robust neural risk marker for substance use (Heitzeg et al., 2015). Reward responsivity is closely linked with both binge drinking and marijuana use, as these substances influence, and are influenced by, the brain's reward circuitry (Casey, 2014; Galvan, 2010). On average, adolescents and young adults may be more likely to display heightened reward sensitivity due to continued maturation of prefrontal neural systems involved in inhibitory control (Casey et al., 2008; Steinberg, 2008). Hyperactivity of striatal regions in response to rewarding stimuli, such as drugs of abuse, produces an influx of dopamine (Bava & Tapert, 2010). Increased dopamine, especially in the VS, may contribute to reward-seeking behavior and a greater risk for addiction (Volkow et al., 2002). As with inhibitory control, additional studies are needed to examine the influence of reward responsivity, not only on substance use risk, but also resilience. Chapter Four addresses this gap by examining differences in neural activation involved in inhibitory control and reward responsivity between resilient low substance using and chronic high using FH+ youth.

Chapter Five: Conclusion

In sum, this dissertation uses a multi-level approach to examine developmentally relevant risk and protective factors among two understudied, yet clinically important, off-diagonal substance use groups. Chapter Five concludes this dissertation by providing a unified discussion on risk and resilience among the off-diagonal groups examined in Chapters Two, Three, and Four. This concluding chapter expands developmental and theoretical perspectives relevant to each chapter. Furthermore, it includes a more thorough discussion on implications for future research, as well as prevention and intervention efforts.

Chapter 2

Predictors of late-onset substance use: Results from national panel samples

According to the U.S. National Survey on Drug Use and Health (Substance Abuse and Mental Health Services Administration (SAMHSA), 2015), alcohol and marijuana are the two most commonly used drugs of abuse among youth. Use of these substances often increases, peaks, and then declines through the transition to adulthood, the developmental period spanning late adolescence through early adulthood (Johnston et al., 2015). Survey data on national samples show that past two-week binge drinking, typically defined as consuming five or more alcoholic beverages on a single occasion (National Institute on Alcohol Abuse and Alcoholism (NIAAA), 2015), peaks between the ages of 21 and 22 with a prevalence rate of 38.4%, and thirty-day prevalence of marijuana use peaks between the ages of 19 and 20 at 24.3% (Johnston et al., 2015). However, population-level averages do not reflect the heterogeneity among certain subgroups of youth. Results of trajectory analyses indicate different developmental paths of substance use through the transition to adulthood (e.g., Epstein et al., 2015; Hill et al., 2007; Jackson et al., 2008; Oesterle et al., 2004; Schulenberg et al., 1996a; Schulenberg et al., 2005; Windle & Wiesner, 2004). For example, binge drinking and marijuana use trajectories during the transition to adulthood tend to include variations of chronic high-level users, low or non-users, decreasing users, and increasing users. Variability among these studies is also found in relation to ages when developmental upticks or downturns in use occur (e.g., Nelson et al., 2014). Emerging from prior work is evidence of off-diagonal substance users who follow relatively unexpected patterns of use. The term "off-diagonal" in the case of this dissertation, and described in previous substance use literature, describes two subgroups—individuals who are low risk yet display later problem behaviors and individuals who are high risk but display few problem behaviors later in development (Dever et al., 2012; Eccles, 2008; Schulenberg & Maggs, 2002). The focus of the present study was on the former group, defined as late-onset substance users.

Of particular clinical relevance is that late-onset substance use groups have been found to start out with low substance use during adolescence but then reach consumption levels similar to that of chronic high users by early adulthood (Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 2005). Thus, the transition to adulthood is a developmental period in which late-onset substance users are vulnerable to escalating substance use. Individual-level and social context factors likely contribute to this risk, given the developmental transitions and tasks occurring during the transition to adulthood (Schulenberg et al., in press). Although identity formation and social bonding gain momentum in adolescence, these developmental tasks continue through the transition to adulthood as young adults begin their professional lives, form more mature romantic relationships, and initiate family formation (Steinberg & Morris, 2001). Transitioning into these roles is developmentally normative, but there is also variation during the transition to adulthood in which some individuals delay social roles. This also delays responsibilities that coincide with reductions in substance use (e.g., marriage and parenthood). Additional research is needed to identify developmental social roles associated with late-onset substance use.

Identifying predictors of late-onset substance use is important given that late-onset substance are an off-diagonal substance use group that does not follow an expected pattern of substance use despite low prior risk. Although they have few early risk factors, elevated substance use among late-onset users is also associated with multiple negative outcomes

(Caldeira et al., 2012; Epstein et al., 2015; Oesterle et al., 2004). Yet, chronic heavy users tend to receive the majority of clinical and empirical attention (Berg et al., 2013; Chassin et al., 2002; Chassin et al., 2004; Squeglia et al., 2009; Winward et al., 2014). Predictors of late-onset binge drinking and marijuana use have not been fully identified both in late adolescence, when substance use more closely aligns with low/non-users, and in young adulthood, when substance use becomes more similar to chronic high users.

Thus, the aim of Chapter Two was to build upon on past research, use a more rigorous approach to trajectory analysis, and focus specifically on late-onset binge drinking and marijuana use among national panel samples from the Monitoring the Future (MTF) survey. Due to its breadth of measures and longitudinal study design, MTF samples are well suited for this purpose. Distal risk factors were assessed in late adolescence, when late-onset youth show no or low levels of use. Proximal risk factors were assessed during the transition to adulthood, when substance use steadily increases among these individuals. By examining early distal and later proximal risk factors among late-onset substance users, the present study aims both to fill a gap in the literature and inform existing prevention and intervention efforts that may overlook late-onset substance users.

Developmental Psychopathology Perspective

The present study used a developmental psychopathology perspective, giving attention to both risk and resilience and continuity and discontinuity across development. Developmental psychopathology describes an interdisciplinary, lifespan perspective to study patterns of adaptation and maladaptation involved in human development (Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000). A better understanding of normative development is a necessary baseline to then compare atypical development and is central a developmental psychopathology perspective. In the case of substance use trajectory research, average patterns of substance use among a whole population provide a useful comparison to study subgroups within that population, such as late-onset substance users. The present study takes advantage of large-scale, national survey data available through MTF that allowed for more accurate baseline measures of average substance use. The breadth of MTF has been useful in prior studies to identify small yet important subgroups of binge drinkers and marijuana users, such as late-onset trajectory groups (e.g., Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 2005).

It is difficult to assess risk versus resilience without considering both prior distal and more recent proximal functioning. On one hand, due to low levels of substance use in adolescence, youth categorized as late-onset binge drinkers or marijuana users may appear to be resilient to substance use problems early in development. On the other hand, these youth emerge as a relatively unexpected, off-diagonal risk group later in development, by displaying escalating substance use through the transition to adulthood. Thus, it may be important to examine both distal and proximal predictors corresponding with this escalating pattern of use in order to identify factors associated with off-diagonal substance use. The present study addresses this need by investigating the role of both distal risk factors occurring in late adolescence and risk factors more proximal to increasing substance use during the transition to adulthood. Comparisons were made between other substance use groups characterized by continuity, including low/non-users and chronic high level users who showed more continual patterns of either low or elevated substance use, respectively.

Discontinuity of substance use among late-onset youth reflects another set of processes central to developmental psychopathology theory—multifinality and equifinality. Multifinality describes a pathway to different outcomes that arise from a similar starting point, whereas equifinality describes two different starting points that result in similar outcomes later in development (Cicchetti & Rogosch, 1999). Late-onset binge drinking and marijuana use trajectory groups show similar levels of use as low/non-use groups during late adolescence but then diverge through the transition to adulthood. This pattern reflects multifinality. Conversely, late-onset binge drinking and marijuana use trajectory groups show different levels of use as chronic high users during late adolescence, but rates of use converge by young adulthood. This pattern describes equifinality. Thus, predictors of late-onset binge drinking and marijuana use in the present study were compared to both low/non-use (i.e., multifinality) and chronic high use (i.e., equifinality) trajectory groups. Focusing on these comparisons will allow for consideration of unique attributes of off-diagonal, late-onset substance use.

Late-Onset Binge Drinking and Marijuana Use Trajectories Through the Transition to Adulthood

In order to identify predictors of late-onset binge drinking and marijuana, the present study builds upon prior binge drinking and marijuana use trajectory research. Despite some variability by type of substance and age in which substance use increases, a number of different studies examining developmental trajectories of substance use have identified late-onset substance users (e.g., Nelson et al., 2014). Although not focused specifically on late-onset youth, these existing studies have identified various outcomes of late-onset use. These findings support the rationale of the present study that late-onset substance users are indeed an important risk group vulnerable to substance use problems despite low levels of prior use. For example, Oesterle et al. (2004) found that late-onset drinkers, compared to non-users, were more likely to engage in unsafe driving and to have been ill during young adulthood; likelihood of dangerous driving and illness did not differ between late-onset and chronic high binge drinkers. In other words, late-onset and chronic high drinkers showed similar health outcomes. These findings are striking, considering that analyses controlled for gender, race/ethnicity, socioeconomic status, and other drug use.

There are also negative consequences associated with late-onset marijuana use. In a large study following youth from ages 14 through 30, late-onset marijuana users had a greater extent of substance use problems and risky sexual behavior by early adulthood compared to non-users (Epstein et al., 2015). Among college students assessed over the course of six years following the first year of college, Caldeira et al. (2012) found that late-onset marijuana users had increased risk for anxiety and depression by year six of assessments compared to all other trajectory groups, including low/non-users and chronic high users.

Findings from the aforementioned studies highlight the importance of studying this off-diagonal group, yet they also indicate important gaps in the literature. Additional information is needed to identify risk factors of late-onset substance users, particularly using assessments among national samples. The present study extends existing work, both broadly and in relation to prior studies using MTF samples. In one existing study using MTF samples, Jackson et al. (2008) identified developmental trajectories of binge drinking, marijuana use, and cigarette use from ages 18 through 26 using growth mixture modeling (GMM). Findings from Jackson et al. (2008) showed a “cat’s cradle” pattern of substance use, including steady chronic high use, steady low/non-use, early high level but then decreasing use, and late-onset use groups that steadily increased use through the transition to adulthood. These patterns were found for all substances examined. Jackson et al. (2008) investigated sociodemographic and psychosocial risk factors of cross-substance comorbidity using least-squares analyses of variance (ANOVA) and binary logistic regression analyses. The present study advances prior work by Jackson et al. (2008) by focusing analyses specifically on late-onset versus chronic high and low/non-use rather than comorbidity groups. Furthermore, the present study extends GMM analyses used by Jackson et al. (2008). Through GMM, the R3STEP approach was used not only to identify trajectory groups but also to assess predictors of these groups. The primary advantage of using the R3STEP approach over other related analyses is that this method identifies predictors of latent trajectory class membership through multinomial logistic regression analyses while accounting for trajectory classification errors (Asparouhov & Muthén, 2014; Vermunt, 2010). Thus, the present study employs more innovative methods to examine a comprehensive set of risk factors for late-onset binge drinking and marijuana use.

The present study also advances findings from two of the first studies to examine substance use trajectories among MTF samples that identified late-onset binge drinking use groups. Schulenberg et al. (1996a) used a pattern-centered approach to examine intraindividual variability in binge drinking from ages 18 to 24. Using cluster analysis, Schulenberg et al. (1996a) found a cat's cradle pattern of substance use with the addition of a fling group showing an inverted "U" shape of developmentally limited use. Late adolescent sociodemographic factors and lifestyle characteristics were examined as predictors of binge drinking trajectory groups through logistic regression analyses. While work by Schulenberg et al. (1996a) was innovative at the time of its publication, more advanced methods (e.g., GMM and R3STEP) are needed to test predictors of late-onset trajectory group membership. Furthermore, Schulenberg et al. (1996a) focused solely on binge drinking trajectories. The present study builds upon work by Schulenberg et al. (1996a) by using more advanced methods, more recent cohorts of youth from MTF surveys, and an additional focus on predictors of late-onset marijuana use trajectories.

Based on findings from Schulenberg et al. (1996a), a set of follow-up analyses examined late adolescent personality characteristics and social contexts as predictors of binge drinking trajectory group membership (Schulenberg et al., 1996b). A major strength of methods used by Schulenberg et al. (1996b) was integrating variable- and pattern-centered approaches to identify predictors of developmental change in binge drinking. Comparisons, however, were made only between late-onset and occasional binge drinkers and between late-onset and fling binge drinkers. Furthermore, predictors of marijuana use trajectories were not examined. The present study extends results from Schulenberg et al. (1996b) by also examining comparisons between late-onset and chronic high level binge drinkers for both binge drinking and marijuana use. Comparisons between late-onset and chronic high level binge drinkers are important in order to examine factors associated with equifinality between these two groups. Furthermore, additional research is needed to assess predictors of late-onset marijuana use, due to recent increases in marijuana use among youth (Johnston et al., 2015).

Whereas Schulenberg et al. (1996a) and Schulenberg et al. (1996b) focused on predictors of binge drinking, Schulenberg et al. (2005) examined characteristics and predictors of marijuana use employing MTF data. Marijuana use trajectories through the transition to adulthood were compared in relation to sociodemographic and lifestyle characteristics, as well as behavioral, attitudinal, and socio-emotional correlates. Although Schulenberg et al. (2005) examined important group differences among these factors in late adolescence and young adulthood, this study did not make direct comparisons between marijuana use groups (e.g., late-onset versus chronic high users, late-onset versus low/non-users). The present study fills this gap by making needed comparisons to identify predictors of late-onset marijuana use, as well as late-onset binge drinking.

Distal and Proximal Predictors of Late-Onset Substance Use

The developmental etiology of substance use trajectories through the transition to adulthood, including late-onset use, involves early distal factors and more recent proximal factors in young adulthood (Schulenberg & Maggs, 2008; Schulenberg & Maslowsky, 2009; Schulenberg et al., in press; Zucker et al., 2008). Considering that late-onset substance users are a later emerging risk group, the present study examined risk factors both at the beginning of substance use onset and during the transition to adulthood when use tends to escalate.

For many health outcomes, including substance use, there is often an additive, cascading influence of both early distal and more recent proximal developmental mechanisms (Dodge et al., 2009). Whereas distal factors contribute to continuity of earlier influences on downstream outcomes (Caspi, 2000), proximal factors more temporally relevant to the transition to adulthood can also exert a powerful impact on functioning to increase, decrease, or even reverse effects of distal influences (Schulenberg & Zarrett, 2006; Schulenberg et al., in press). Therefore, the present study examined distal and proximal factors relevant to late-onset binge drinking and marijuana use. These factors centered not only on descriptive characteristics of trajectory groups, including sociodemographic characteristics, but also on high school risk factors, psychosocial factors, and social contexts particularly relevant to late-onset binge drinking and marijuana use (see Table 1). The rationale for included these measures is provided in the following sections.

Sociodemographic characteristics. Certain sociodemographic characteristics have been found to be indicators of substance use risk (Johnston et al., 2015). For example, heavy alcohol users are more likely to be male, White, and have higher parent education; heavy marijuana users are more likely to be male, Black (compared to White), and lower parent education (e.g., Haberstick et al., 2014). Although these sociodemographic factors are all robustly associated with substance use risk, less is known regarding how these factors may differentiate late-onset substance users between other trajectory groups. National samples, such as those in MTF, offer an advantage over datasets with less diverse samples of youth to uncover sociodemographic differences among late-onset substance users. In the present study, gender, race/ethnicity, parent education, and historical cohort were examined in relation to late-onset substance use.

High school risk factors. High school factors associated with substance use risk were also examined, including low grades, college plans, truancy, and evenings out with peers (e.g., Bachman et al., 2007; Patrick et al., 2013; Patrick & Schulenberg 2010; Schulenberg et al., 1996b; Schulenberg et al., 2005). These distal factors coincide with late adolescence, just prior to escalating substance use among late-onset youth. They also account for a certain extent of contextual influences, such as school and peer interactions that may contribute to late-onset substance use.

Psychosocial factors. Individual-level psychosocial factors associated with substance use risk were also examined, including self-esteem, sensation seeking, and interpersonal aggression. These psychosocial factors pertain to the broader concept of self-regulation, and more specifically to behavioral control that may contribute to substance use (Windle, in press). Self-regulation is important to examine in relation to late-onset substance use. Rationales for including constructs related to self-regulation are described below in the following sections.

The association between self-esteem and substance use risk is related to the internalizing pathway to substance use, in which deficits in emotional self-regulation contribute to substance use problems (Hussong et al., 2011). Negative affect is thought to influence substance use risk, in part, through low self-esteem (Shoal & Giancola, 2003; Tarter, 2002). Youth with low self-esteem may use substances to cope with deficits in self-regulation (Hussong et al., 2011). Late-onset substance users may be particularly vulnerable to using substances to cope with developmental tasks (e.g., peer bonding, identity formation) involved in the transition to adulthood (Schulenberg et al., 2005). Existing research, however, has produced equivocal findings regarding the connection between self-esteem and substance use risk (e.g., McGee & Williams, 2000; McKay et al., 2012; Patrick & Schulenberg, 2010; Schulenberg et al., 1996b; Swaim & Wayman, 2004; Windle & Weisner, 2004). Even less is known concerning self-esteem as a predictor of late-onset binge drinking and marijuana use. Thus, the present study examined the link between distal and proximal measures of self-esteem and late-onset substance use.

Sensation seeking, which describes a reward-driven personality trait associated with preference for novel, exciting experiences (Zuckerman, 1994) and behavioral undercontrol (Iacono et al., 2008; Windle, in press; Zucker, 2006), is a robust predictor of substance use (Crawford et al., 2003; Jackson & Sher, 2003; Malmberg et al., 2010; Pilgrim et al., 2006; Schulenberg et al., 2005). Although sensation seeking typically peaks between the ages of 14 and 16 (Harden & Tucker-Drob, 2011; Steinberg et al., 2008), individual variability exists. Individuals whose sensation seeking does not decline into later adolescence and early adulthood may be particularly susceptible to increased substance use through the transition to adulthood (Quinn & Harden, 2013). Thus, the present study tested the extent to which distal and proximal sensation seeking contribute to late-onset binge drinking and marijuana use.

The present study also examined interpersonal aggression, a measure of externalizing behavior, as a predictor of late-onset substance use. In addition to an internalizing pathway (Hussong et al., 2011), there is also an externalizing pathway to substance use problems associated with behavioral undercontrol (Zucker et al., 2011). Developmentally, the externalizing pathway to substance use problems often begins in childhood through displays of aggression and conduct problems; this pathway then tends to continue through adolescence into adulthood with antisocial behavior and heavy substance use (Dodge et al., 2009; Tarter et al., 1999; Zucker et al., 2006). Research examining developmental trajectories of substance use has most often identified chronic high users as having the highest levels of externalizing behaviors compared to the other trajectory groups (Brook et al., 2011; Chassin et al., 2002; Flory et al., 2004; Tucker et al., 2003). In relation to the developmental psychopathology concept of equifinality, however, late-onset substance users show similar levels of substance use with chronic high users by young adulthood. Thus, the present study tests associations between increasing substance use among late-onset users and heightened interpersonal aggression.

Young adult social roles. Increasing substance use among late-onset youth is likely due, at least in part, to individual by social context interactions during developmental turning points (Schulenberg & Maggs, 2002). For example, substance use during college may be normative to a certain extent and constructive for social purposes, but it may set in motion a pattern of heavy substance use (Schulenberg & Zarrett, 2006). Individuals with high rates of substance use have been shown to be less likely married (Hicks et al., 2010; Leonard & Rothbart, 1999; Schulenberg et al., 1996) or parents (Staff et al., 2010). Comparing social roles between late-onset and chronic high and low/non-users may reveal important predictors of discontinuity in substance use.

Research Questions and Hypotheses

The main purpose of the present study was to identify characteristics and predictors of off-diagonal, late-onset binge drinking and marijuana use trajectory groups. In line with developmental psychopathology processes of multifinality and equifinality (Cicchetti & Rogosch, 1999), predictors of late-onset binge drinking and marijuana trajectory groups were compared between chronic high (multifinality) and low/non-use groups (equifinality). Research questions guiding these analyses were the following: (1) Which sociodemographic, distal, and proximal psychosocial and social context factors differentiate late-onset binge drinkers from low/non-binge drinkers, as well as late-onset marijuana users and low/non-marijuana users?; (2) To what extent do these factors (i.e., sociodemographic, distal, and proximal) differentiate between late-onset binge drinkers and chronic high binge drinkers, as well as between late-onset marijuana users and chronic high marijuana users? Given that late-onset and low/non-using youth have similar levels of substance use at the beginning of the transition to adulthood, these two groups were hypothesized not to differ significantly on distal factors measured at age 18. Late-onset and chronic high using youth were hypothesized to show more dissimilar early predictors. As well, late-onset and chronic high using youth were hypothesized to share a greater number of later, more proximal predictors, due to their converging substance use through the transition to adulthood. Related to this shift in substance use, late-onset youth were hypothesized to differ from low/non-using youth in relation to proximal factors.

Predictors of binge drinking and marijuana use trajectory groups were examined separately in order to identify predictors of late-onset use unique to these substances. Although in some studies, binge drinking and marijuana trajectories share similar patterns (Flory et al., 2004; Nelson, 2014), a previous study using data from MTF found that only 8.3% of late-onset binge drinkers were also late-onset marijuana users (Jackson et al., 2008). Additionally, reasons for use have been found to differ between alcohol and marijuana, particularly during the transition to adulthood (Patrick et al., 2011). Predictors of binge drinking and marijuana use may vary, but there is still a high level of comorbidity between binge drinking and marijuana use (e.g., Schulenberg et al., 2005; Windle & Wiesner, 2004). To account for comorbidity, analytic models comparing late-onset binge drinking with both low/non-use and chronic high use included marijuana use as a covariate. Likewise, marijuana use models used the same group comparisons and included binge drinking as a covariate.

Methods

Participants and Procedures

MTF is an ongoing, epidemiological study of substance use among national samples of adolescents and young adults in the U.S. (Johnston et al., 2015). Every year since 1975, MTF has assessed approximately 16,000 high school seniors through self-administered questionnaires. Participants are selected through a three-stage sampling procedure, in which geographic areas, schools in each geographic area, and specific classes within each school are randomly selected. Less than 1% of students refuse to complete the questionnaire and non-response is predominately due to absenteeism on day of data collection. Each year beginning in 1976, approximately 2,400 participants from each senior-year cohort have been randomly selected for biennial follow-up assessments through mailed questionnaires. One half of the panel sample were randomly selected to receive surveys either 1 year or 2 years following senior year of high school, and every other year thereafter. All procedures are reviewed and approved on an annual basis by the University of Michigan's Institutional Review Board (IRB) for compliance with federal guidelines for the treatment of human subjects.

In the present study, participants were young adults from consecutive MTF high school senior cohorts spanning 1976—2006. Thus, the final follow-up assessment occurred in 2014 when participants were approximately 25 or 26 years of age. Five waves of data, including base year data, were used in the present study. On average, respondents were 18 years old at wave 1, ages 19 to 20 years old at wave 2, ages 21 to 22 at wave 3, ages 23 to 24 at wave 4, and ages 25 to 26 at wave 5. During senior year assessments and through panel questionnaires, respondents completed one of six different questionnaire forms distributed randomly at senior year (completing the same form for every assessment). All forms included demographic and key substance use variables. Questions pertaining to attitudes, beliefs, and behaviors on substance use, psychosocial factors, and the social environment vary by form. Data from forms 2 and 6 were used in the present study, given that the psychosocial factors of interest related to self-regulation, including self-esteem, sensation seeking, and interpersonal aggression, were only on these forms. The final weighted sample consisted of 19,730 respondents.

Measures

Substance use. Substance use measures were assessed at each wave. Binge drinking was measured by the following item: "During the last two weeks, how many times (if any) have you had five or more drinks in a row?" Response options were on a scale of 1 = None, 2 = Once, 3 = Twice, 4 = 3 to 5 times, 5 = 6 to 9 times, and 6 = 10 or more times. Marijuana use was measured by the following item, "On how many occasions have you used marijuana in the past 30 days?" Response options were on a scale of 1 = 0 occasions, 2 = 1-2 occasions, 3 = 3-5 occasions, 4 = 6-9 occasions, 5 = 10-19 occasions, 6 = 20-39 occasions, 7 = 40 or more occasions.

Sociodemographic characteristics. Sociodemographic measures were assessed at wave 1 and included: (1) Gender, coded as male (reference group) or female; (2) Race/ethnicity, coded as White (reference group), Black, Hispanic, Asian, or Other. The Other race/ethnicity group included adolescents who identified as Native American/Native Alaskan, Native Hawaiian/Pacific Islander, or multiple races/ethnicities; (3) Historical cohort, coded using known historical trends in both binge drinking and marijuana use among senior year cohorts (e.g., Jager et al., 2013; Johnston et al., 2015; Patrick et al., 2011). Binge drinking cohort groups were coded as 1976—1986, 1987—1993, and 1994—2006. Marijuana use cohort groups were coded as

1976—1991, 1992—1997, and 1998—2008. The earlier cohort groups for both binge drinking and marijuana use were used as the reference groups; and (4) Parent education, measured by the highest level of education obtained by at least one parent, coded as some college education or more (reference group) or high school degree or less.

High school risk factors. Items included the following assessed at wave 1: (1) High school grades, measured by a single item, "Which of the following best describes your average grade so far in high school?" Response options range from 1 = "D" to 9 = "A"; (2) College plans, measured by a single item, "How likely is it that you will graduate from college (four-year program)?" Response options range from 1 = "Definitely won't" to 4 = "Definitely will"; (3) Truancy, measured by a single item, "During the last four weeks, how many whole days of school have you missed because you skipped or "cut'?" Response options range from 1 = "None" to 7 = "11 or more"; (4) Evenings out with friends, measured by a single item, "During a typical week, on how many occasions do you go out for fun and recreation?" Response options range from 1 = "Less than one" to 6 = "Six or seven".

Psychosocial factors. Items included the following assessed at wave 1 and wave 5: (1) Self-esteem, measured by 4 items on a 5 point scale (1 = "Disagree" to 5 = "Agree", $\alpha = 0.83$). A sample item is "I take a positive attitude toward myself."; (2) Sensation seeking, measured by 2 items on a 5 point scale (1 = "Disagree" to 5 = "Agree", $\alpha = 0.83$). Items include "I get a real kick out of doing things that are a little dangerous" and "I like to test myself every now and then by doing something a little risky"; and (3) Interpersonal aggression measured by 5 items on a 5 point scale (1 = "Not at all" to 5 = "5 or more times", $\alpha = 0.78$). A sample item is "How often have you gotten into a serious fight at school or at work?"

Social roles. Social roles from waves 1 through 5 included ever enrolled in a four-year college, graduated from a four-year college, ever married, and ever had a child. College enrollment status was coded as (1) ever attended a four-year college or (0) never attended a four-year college. College graduation status was coded as (1) graduated from a four-year college or (0) did not graduate from a four-year college. Marital status was coded as (1) ever married or (0) never married. Child status was coded as (1) having at least one child or (0) having no children.

Analytic Plan

The analytic plan for the present study involved three steps: (1) Growth mixture modeling to estimate the best fitting number of trajectory classes for binge drinking and marijuana use through the transition to adulthood (waves 1-5); (2) Examination of the means and mean differences between late-onset versus chronic high users and late-onset versus low/non-users in relation to sociodemographic characteristics, distal late adolescent factors at wave 1, and proximal young adult factors; and (3) Use of bivariable and multivariable logistic regression[1] to identify sociodemographic, late adolescent, and young adult predictors of estimated trajectory groups. As with step 2, step 3 predictors of binge drinking and marijuana use trajectory classes involved two sets of comparisons—late-onset versus low/non-users and late-onset versus chronic high users.

Attrition and missing data. In prior work using longitudinal MTF samples, participants remaining in the panel study have been found to vary by substance use and certain respondent characteristics (Schulenberg et al., 2015). Thus, attrition weights were calculated as the inverse of the probability of participation at age 25/26 (the final time point used in the present study's

[1] Although often used interchangeably, the terms bivariate and bivariable, as well as multivariate and multivariable describe different analyses. Because bivariate and multivariate analyses refer to analyses with two or more dependent variables (Hidalgo & Goodman, 2013), the terms bivariable and multivariable were used in the present study.

trajectory analyses) based on the following covariates measured at age 18 and related to differential attrition: gender, race/ethnicity, college plans, high school grades, truancy, number of parents in the home, religiosity, parental education, alcohol use, cigarette use, marijuana use, other illicit drug use, region, cohort, and sampling weight correcting for over-sampling of age 18 substance users. All analyses were conducted through SAS version 9.4 (SAS Institute, Inc, Cary, NC) and Mplus software (version 7.4, Muthén & Muthén, 1998-2015). In Mplus, the estimator was robust maximum likelihood (MLR) with full information maximum likelihood (FIML). FIML accounts for missing data by using all available individuals who provide data for at least one time point and produces unbiased parameter estimates and standard errors. Mplus was used to conduct both LGM and GMM.

Step 1: Growth mixture modeling (GMM). GMM was conducted in Mplus to identify substance use trajectory groups. GMM extends beyond traditional, single group trajectory analysis by allowing for variability in intercept and growth parameters among unobserved subgroups (e.g., Jung & Wickrama, 2008; Muthén, 2004). Each subgroup is estimated as a discrete, latent trajectory class. The first step in GMM is to estimate the best fitting Latent Growth Model (LGM; Duncan & Duncan, 2004) to assess the mean trajectory for a particular outcome variable among the entire sample population. In the present study, the best fitting LGM was determined separately for binge drinking and marijuana use trajectories using data spanning waves 1 through wave 5. Three LGMs were tested: 1) linear slope model; 2) quadratic slope model; and 3) piecewise slope model (with piecewise components based on normative age trends for binge drinking and marijuana use through the transition to adulthood (Johnston et al., 2015). Model fit criteria were based on the following: 1) Root-mean-square error of approximation (RMSEA) ≤ 0.06; 2) Comparative fit index (CFI) $\geq .90$); 3) Tucker-Lewis index (TLI) $\geq .90$);

and 4) Chi-square difference test based on log-likelihood values and scaling correction factors from the MLR estimator.

Based on the best fitting LGM, GMM was conducted to identify homogenous, latent subgroups of binge drinking users and marijuana users through the transition to adulthood. As with LGM, GMM was conducted separately for binge drinking and marijuana use. GMMs were tested first with two latent classes and then subsequently with increasing numbers of classes until model fit declined. Given previous studies using data from MTF to perform trajectory analyses on binge drinking and marijuana use (e.g., Jackson et al., 2008), the four-class model was expected to provide the best fit with the data. Model fit criteria were based on the following: 1) Bayesian Information Criterion, (BIC: Schwarz, 1978), with lower numbers indicating better model fit; 2) Entropy closer to 1, which identifies better fitting classification of posterior probability class values (Jung & Wickrama, 2008); 3) Class estimates based on posterior probabilities consisting of no less than 5% of the total sample, which supports improved replicability (Jackson et al., 2008); 4) Lo-Mendell-Rubin (LMR) adjusted likelihood ratio test, which compares the fit of the k class model to the k-1 (e.g., 4 versus 3 class model) (Lo et al.,, 2001); and 5) Class interpretability (Jackson et al., 2008).

Step 2: Descriptive characteristics of late-onset binge drinking and marijuana users. Most likely trajectory class memberships, based on estimated posterior probabilities, were exported from Mplus to SAS. Frequencies and means for measures included in the present analyses were calculated and compared between the off-diagonal, late-onset versus low/non-users and late-onset versus chronic high users. Significant descriptive differences between these groups for categorical variables were examined with X^2 tests, and continuous variables were examined with independent samples *t*-tests.

Step 3: Predictors of late-onset binge drinking and marijuana use. To further compare late-onset with chronic high and low/non-use trajectory groups for both binge drinking and marijuana use, bivariable and multivariable logistic regression analyses were conducted using Mplus. Bivariable logistic regression models were used to examine the effect of each variable entered separately to predict late-onset trajectory group membership, comparing both chronic high and low/non-use groups. Multivariable logistic regression models were used to examine the combined influence of sociodemographic, late adolescent factors, and young adult factors predicting comparisons between the late-onset trajectory group with both chronic high and low/non-use trajectory groups. The R3STEP command in Mplus (Asparouhov & Muthén, 2014; Vermunt, 2010) was used to conduct both bivariable and multivariable logistic regression analyses. In the first step, the GMM was estimated using only latent class indicator variables. In the second step, most likely class probabilities were created using latent class posterior distribution. In the third step, trajectory classes were regressed on the predictor variables listed in the AUXILIARY statement through multinominal logistic regression, taking into account measurement error in the class variables. There are two main advantages of using the R3STEP approach: (1) it helps to stabilize the model by accounting for measurement error; and (2) multinomial logistic regression output shows predictors compared by trajectory class membership. The R3STEP approach does not, however, allow for hierarchical (i.e., stepwise) regression models due to model fit occurring only at the level of the GMM.

Results

Binge Drinking Trajectory Analyses

Growth mixture modeling (GMM). Results of LGM analyses indicated that the piecewise model fit the binge drinking data best (RMSEA = 0.01, CFI = 0.99, TLI = 0.99), compared to the linear (RMSEA = 0.04, CFI = 0.97, TLI = 0.96), and quadratic models (RMSEA = 0.02, CFI = 0.99, TLI = 0.99). Results from chi-square difference tests based on log-likelihood values and scaling correction factors confirmed the excellent fit of the piecewise model ($\chi^2(3) = 186.19$, $p < 0.001$) in relation to the baseline linear model. Thus, the piecewise LGM was used as the basis for all following GMM analyses. GMMs were then tested with two, three, four, and five classes (Table 2). To avoid solutions based on local maxima, increasing the number of random starts was used to replicate the best log-likelihood value (Jung & Wickrama, 2008). Increasing the number of random starts for the four-class model, however, produced an uninterpretable plot. The four-class model with the default number of random starts (20 initial stage starting values with 4 final stage optimizations) produced a trajectory plot supported by previous research using MTF binge drinking measures across the same time span (e.g., Jackson et al., 2008). The best fitting and most interpretable GMM estimated four trajectory classes (BIC = 182110.06, Entropy = 0.82, LMR = 5652.88, $p < 0.001$). The late-onset binge drinking group consisted of 11.83% of the sample, the low/non-use group consisted of 65.05% of the sample, the decreasing group consisted of 12.95% of the sample, and the chronic high group consisted of 10.17% of the sample (Figure 2).

Descriptive characteristics of late-onset binge drinkers. Table 3 shows correlations between all variables included in analyses, and Table 4 shows descriptive comparisons and significant differences between late-onset binge drinkers and non/low binge drinkers. Table 5 shows descriptive comparisons and significant differences between late-onset and chronic high binge drinkers. Descriptive information is also shown for the total sample.

Predictors of late-onset binge drinking. Table 6 shows bivariable and multivariable multinomial logistic regression results for comparisons between the late-onset and low/non binge drinking groups in relation to sociodemographic characteristics, late adolescent factors, and young adult factors. Bivariable analyses modeled each variable independently, whereas multivariable analyses included the combined influence of all variables. Results of bivariable analyses for sociodemographic predictors showed that, compared to low/non binge drinkers, late-onset binge drinkers were significantly more likely to identify as male and have high parent education. Compared to White participants, late-onset binge drinkers were less likely to be Black, Hispanic, or Asian. There were no significant differences by cohort. Among late adolescent factors, late-onset binge drinkers were more likely to have college plans, cut class, spend evenings out with friends, have greater marijuana use, and higher sensation seeking. Among young adult factors, late-onset binge drinkers had higher marijuana use, higher self-esteem, higher sensation seeking, and were more likely college graduates. Late-onset binge drinkers had lower odds of being married and a parent. Multivariable results indicate that late-onset binge drinkers had higher odds of being male but lower odds of being Asian (compared to White participants). Among late-adolescent factors, late-onset binge drinkers were more likely to spend evenings out with friends and have greater marijuana use compared to low/non-users. In relation to young adult factors, late-onset binge drinkers had higher odds of greater marijuana use and lower odds of being married and a parent.

Table 7 shows bivariable and multivariable multinomial logistic regression results for comparisons between the late-onset and chronic high binge drinking groups in relation to sociodemographic characteristics, late adolescent factors, and young adult factors. Results of bivariable analyses for sociodemographic predictors showed that late-onset binge drinkers were significantly less likely to be male and more likely to report high parent education. Among late adolescent factors, late-onset binge drinkers were more likely to have college plans but less likely to have lower grades, cut class, and use marijuana. Late-onset binge drinkers also had lower sensation seeking and interpersonal aggression. Bivariable results for young adult factors showed that late-onset binge drinkers were more likely to have lower self-esteem and sensation seeking. However, late-onset binge drinkers were more likely to have been enrolled in college, graduated college, been married, or a parent. Multivariable results indicated that, compared to chronic high users, late-onset binge drinkers had higher odds of being Black (compared to White participants) and were in the most recent cohort. However, due to the low number of Black youth in the late-onset binge drinking group, these results should be interpreted with caution. During late adolescence, late-onset binge drinkers had higher interpersonal aggression and were less likely to cut class and use marijuana. No significant differences were found among young adult factors.

Marijuana Use Trajectory Analyses

Growth mixture modeling (GMM). Results of LGM analyses indicate that the quadratic model fit the marijuana use data best (RMSEA = 0.01, CFI = 0.99, TLI = 0.99), compared to the linear (RMSEA = 0.03, CFI = 0.96, TLI = 0.96) and piecewise models (RMSEA = 0.01, CFI = 0.99, TLI = 0.99). Results from the chi-square difference test based on log-likelihood values and scaling correction factors confirmed the excellent fit of the quadratic model ($\chi^2(3) = 548.61$, $p < 0.001$) compared to the baseline linear model. Thus, the quadratic LGM was used as the basis for GMM analyses. As with the binge drinking models, GMMs for marijuana use were fit with two, three, four, and five classes. Increasing the number of random starts to 100 initial stage starting values and 25 final stage optimizations was used to replicate the best log-likelihood value (Jung & Wickrama, 2008). As expected given previous research using MTF marijuana use data (e.g., Jackson et al., 2008), the best fitting quadratic GMM estimated four trajectory classes (BIC =

167066.20, Entropy = 0.95, LMR = 8770.33, $p < 0.001$). Results of the Lo-Mendell-Rubin adjusted likelihood ratio test indicated that the model did not improve significantly by adding an additional class to the four-class model, as was found when testing the five-class model. In addition, the fifth trajectory class followed a similar pattern as the decreasing marijuana use group, with a slightly lower initial intercept but nearly identical slope into young adulthood. Due to the similarities between the fifth trajectory class and the decreasing trajectory class, the four-class marijuana use model collapsed these two similar groups. Collapsing these two groups provides improved validity for the decreasing trajectory class. As shown in Figure 3, the four-class marijuana use model consisted of 5.72% of the sample categorized in the late-onset group, 82.19% of the sample in the low/non-use group, 7.56% of the sample in the decreasing group, and 4.53% of the sample in the chronic high group.

Descriptive characteristics of late-onset marijuana users. Table 8 shows descriptive comparisons and significant differences between late-onset and low/non-users, whereas Table 9 chronic high marijuana users. Descriptive information is also shown for the total sample.

Predictors of late-onset marijuana use. Table 10 shows both bivariable and multivariable multinomial logistic regression results for comparisons between the late-onset and low/non marijuana use groups in relation to sociodemographic characteristics, late adolescent factors, and young adult factors. Bivariable logistic regression results for sociodemographic predictors indicate that late-onset marijuana users were significantly less likely to be male but significantly more likely to have high parent education and be in the most recent cohort. Among late adolescent factors, late-onset marijuana users were more likely to have lower grades, cut class, spend evenings out with friends and have higher rates of binge drinking, sensation seeking, and interpersonal aggression. Among young adult factors, late-onset marijuana users were less likely enrolled in college and married. Late-onset marijuana users were more likely to have greater rates of binge drinking, higher sensation seeking, and higher interpersonal aggression. Multivariable logistic regression analyses showed no significant differences between late-onset and low/non marijuana users in terms of sociodemographic characteristics. Among late adolescent factors, findings indicate that late-onset marijuana users had higher odds of late-adolescent binge drinking and self-esteem compared to low/non-users. In regard to young adult factors, late-onset marijuana users had higher self-esteem and lower odds of being married. Late-onset marijuana users had higher odds of both young adult binge drinking and sensation seeking.

Bivariable results in Table 11 show that late-onset marijuana users were significantly less likely to be male, Other race/ethnicity (compared to White participants), and high parent education. Late-onset marijuana users were more likely to be Black, compared to White participants. There were no significant differences by cohort. Due to the small sample size of Asian late-onset and chronic high binge drinkers (0.82%, 0.84%, respectively), multivariable logistic regression results for these groups were uninterpretable. Among late adolescent factors, late-onset marijuana users were less likely to have lower grades, cut class, spend evenings out with friends, have greater marijuana use, higher sensation seeking, and higher interpersonal aggression. Late-onset marijuana users were more likely to have college plans. Among bivariable young adult factors, late-onset marijuana users were more likely to have been enrolled in college and graduated college. They were less likely, however, to have been married. Multivariable logistic regression results showed no significant differences between late-onset and chronic high marijuana in relation to sociodemographic characteristics. Among late adolescent factors, late-onset marijuana users were more likely to have college plans and have higher self-esteem. Late-onset marijuana users were also less likely to cut class. No significant differences were found between late-onset and chronic high marijuana users for young adult factors.

Overlap in Binge Drinking and Marijuana Use Classes

As expected, and supported by prior work (Jackson et al., 2008), individuals in both late-onset binge drinking and marijuana use groups comprised a low number of the total sample (0.88%). This finding supports separate analyses for binge drinking and marijuana use conducted in the present study. Among late-onset binge drinkers, 10.63% were also in the late-onset marijuana use group. In the late-onset marijuana use group, 19.42% of individuals were also classified as late-onset binge drinkers. The majority of late-onset binge drinkers were low/non using marijuana users (79.01%). Also among late-onset binge drinkers, 5.82% were in the decreasing marijuana use class and 4.54% were in the chronic high marijuana use class. Late-onset marijuana users tended to be most likely in the low/non-binge group (47.46%), while 19.32% were in the decreasing binge group and 13.80% were in the chronic high binge group.

Discussion

The overall purpose of the present study was to extend prior substance use trajectory research, both more broadly and in relation to previous studies using national MTF samples (e.g., Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 1996b; Schulenberg et al., 2005). The present study advances previous work by identifying distal and proximal predictors of late-onset binge drinking and marijuana use among national samples of youth. Focusing specifically on this pattern of substance use is important given that late-onset users represent an off-diagonal substance use group characterized by low levels of early risk in late adolescence but then elevated substance use by young adulthood, more closely aligned with chronic heavy users. Developmental trajectory methods were used to examine distal indicators of risk in late adolescence, prior to escalating use, and proximal risk factors in young adulthood, coinciding with increased heavy use among late-onset binge drinkers and marijuana users. Findings from the present study highlight the complexities of studying late-onset substance use, since results of multivariable analyses indicate few differences on distal factors between low/non-use groups (for both substances examined). However, stronger support was found for hypotheses pertaining to late-onset compared to chronic high substance users. Interpretations of results in relation to developmental psychopathology theory, prevention and intervention implications, and future directions are expanded upon in the following sections.

Evidence for Multifinality: Comparisons Between Late-Onset and Low/Non-Use Groups

As described previously, analyses between late-onset and low/non-using binge drinkers and marijuana users reflect the developmental psychopathology concept of multifinality. Multifinality describes different outcomes that arise from a similar starting point (Cicchetti & Rogosch, 1999). Thus, the present study examined distal and proximal predictors of multifinality between late-onset and low/non-use substance use groups. Also pertaining to developmental psychopathology theory, evidence from the present study supports the notion that understanding normative development (i.e., low/non-use) is important as a baseline comparison to atypical development (late-onset use). Major findings from comparisons between late-onset and low/non-use binge drinking and marijuana use groups are presented below.

By examining sociodemographic characteristics, late adolescent factors, and young adult factors between late-onset and low/non-use binge drinking and marijuana use groups, findings from the present study provide a better understanding of distal and proximal factors that contribute to the emergence of atypical substance use among late-onset substance users. Late-onset substance use in this sense is described as atypical because these youth are off-diagonal, showing low early risk but high levels of later substance use through the transition to adulthood.

Although there were a certain extent of differences among sociodemographic characteristics examined in descriptive and bivariable analyses, late-onset substance users did not differ greatly from low/non-users when also accounting for late adolescent factors and young adult factors. Late-onset users tended to be more likely male, White, and of higher parent education, as shown in previous research among MTF samples (e.g., Johnston et al., 2015; Patrick et al., 2013). Taken together, these findings suggest that it may be difficult to distinguish between late-onset and low/non-marijuana users by sociodemographic differences.

Late adolescent and young adult factors may provide better indicators of differences between late-onset and low/non-use binge substance use groups. For example, late-onset binge drinkers appear to be succeeding academically (in terms of GPA and college plans) in late adolescence, but are also more likely to spend evenings out with friends and have higher rates of marijuana use. These results suggest a greater extent of socializing and using substances in the context of social bonding. Indeed, substance use among adolescents and young adults often coincides with peer socializing (e.g., Schulenberg, in press; Schulenberg & Zarrett, 2006). Social reasons for both alcohol and marijuana use are common through the transition to adulthood (Patrick et al., 2011), supporting the notion that substance use may be an integral part of forming new peer relationships and meeting social goals (Schulenberg & Maggs, 2002). However, social bonding associated with substance use may also involve affiliations with deviant peers (e.g., Dodge et al., 2009). Thus, specific types of social interactions are important to assess. It is possible that late-onset substance use may coincide with changes in social contexts that increase exposure to substance-using peers. Indeed, late-onset binge drinkers were more likely to have college plans compared to low/non-users. In college settings, binge drinking may be used to enhance social situations and facilitate new relationships. In turn, associating substance use with social enhancement may contribute to increased use through the transition to adulthood. Additional research is needed to more directly test how changing social contexts through development are associated with late-onset substance use.

Comparisons between late-onset and low/non-use binge drinking and marijuana use also indicate differences among certain adolescent psychosocial factors associated with externalizing behaviors. Late-onset marijuana users had a greater likelihood of cutting class, evenings out with friends, binge drinking, sensation seeking, and interpersonal aggression in late adolescence compared to low/non-users. Similar factors also differentiated late-onset and low/non-using binge drinkers, although to a slightly lesser extent. Taken together, late-onset binge drinkers and marijuana users appear to show a greater extent of externalizing behaviors and propensity for risk-taking compared to low/non-users prior to onset of increasing use. Whereas chronic heavy substance users may be at heightened risk to follow a Type 2, antisocial pathway to substance use, late-onset users may be more likely to follow the Type 1 pathway to substance use associated with negative affect (Babor et al., 1992; Cloninger et al., 1996; Zucker, 1987, 1994). However, results of the present study suggest that late-onset youth may share certain externalizing characteristics of the Type 2 substance use pathway. This finding is supported by research showing high comorbidity between internalizing and externalizing problems (e.g., Colder et al., 2013). It is also supported by recent work demonstrating inconsistencies in age of onset as a distinguishing factor between Type 1 and Type 2 substance use pathways (Hussong et al., 2011). Taken together, late-onset substance users may more actually describe a moderate externalizing pathway, or even combined internalizing/externalizing developmental pathway to substance use. Additional research is needed to test this possibility and examine the extent to which moderate levels of externalizing behaviors influence late-onset substance use.

One particularly interesting finding emerged in relation to distal and proximal predictors examined in multivariable analyses. Whereas late-onset marijuana users reported higher self-esteem during late adolescence compared to low/non-users, the late-onset group reported significantly lower levels of self-esteem by young adulthood. Supporting these results, prior research examining marijuana use trajectories through the transition to adulthood found that early-onset heavy users had the lowest self-esteem and non-users had the highest self-esteem compared to all other trajectory groups (Flory et al., 2004). In the present study, the late-onset group had a greater likelihood of high self-esteem compared to low/non-users when rates of marijuana use between these groups were comparable (i.e., late adolescence). However, late-onset users' self-esteem decreased as marijuana use increased during early adulthood. Although it was not possible in the present study to examine the variables underlying these changes in self-esteem, declines in self-esteem may be associated with coinciding increases in substance use. This possibility pertains to research showing a link between negative affect, internalizing problems, and substance use risk (e.g., Hussong et al., 2011). Given recent increases in marijuana use among young adults, coupled with decreasing perceptions of harm (Johnston et al., 2015), additional research is needed to more closely examine effects of marijuana use on internalizing symptoms, such as self-esteem. Conversely, it is possible low self-esteem may contribute to increased marijuana use. These possible bidirectional influences highlight the need for future studies to test bidirectional influences of marijuana use and internalizing behaviors.

Related to social roles, both late-onset binge drinkers and marijuana users showed a lower likelihood of marriage compared to low/non-users. Late-onset binge drinkers, but not marijuana users, also showed a lower likelihood of parenthood. These results are generally consistent with studies documenting the associations between declines in substance use and marriage and becoming a parent (e.g., Leonard & Rothbard, 1999; Staff et al., 2010). It was found that often marriage and becoming a parent coincided with maturing out of heavy substance use. Late-onset youth who delay social roles of marriage and parenthood may continue to incorporate substance use into social situations that encourage mate selection and that are not affected by the time constraints associated with becoming a parent. While a low level of substance use during late adolescence may have certain constructive social benefits (Schulenberg & Zarrett, 2006), continuing to use substances in social contexts may result in escalating levels of substance use through the transition to adulthood. Relying on substances as a social lubricant for an extended period of time may set in motion a more destructive pattern of elevated substance use later in development.

Evidence for Equifinality: Comparisons Between Late-Onset and Chronic High Use Groups

Equifinality describes similar outcomes arising from two different starting points (Cicchetti & Rogosch, 1999). In other words, equifinality describes a process opposite of multifinality. Because levels of substance use between late-onset and chronic high users differ during late adolescence but converge later in development, this pattern represents equifinality. Pertaining to equifinality, it was expected that these two substance use groups would differ to a greater extent on distal, late adolescence factors compared to proximal, young adult factors. Indeed, findings from the present study indicate that distal factors in late-adolescence, including high school risk factors and psychosocial factors, were most significantly associated with late-onset versus chronic high substance use. Proximal factors, therefore, may be just as, if not more, powerful than distal factors in predicting problematic substance use (Cicchetti & Rogosch, 1999; Lewis, 1999; Schulenberg et al., in press).

Among late adolescent factors, late-onset binge drinkers had fewer externalizing behaviors (i.e., cutting class, lower likelihood of marijuana use, sensation seeking, and interpersonal aggression) compared to chronic high binge drinkers. Lower externalizing behaviors are not entirely surprising, since late-onset substance users are not as likely to follow the externalizing pathway to SUDs (Babor et al., 1992; Cloninger, 1987; Zucker, 1987, 1994). Yet, it is interesting that late-onset substance users showed greater levels of externalizing behaviors compared to low/non-users. Both of these findings lend support to the possibility of a moderate-level externalizing pathway to substance use problems. In other words, dichotomizing substance use pathways as externalizing (e.g, Zucker et al., 2011) or internalizing (e.g., Hussong et al., 2011) may not fully capture late-onset patterns of substance use. This is problematic, since late-onset substance users reach high levels of use by young adulthood. Future studies are needed to investigate predictors and outcomes of youth following a more moderate externalizing pathway to substance use problems.

As with binge drinking, multivariable comparisons between late-onset and chronic high marijuana users showed no significant differences between young adult factors over and above the influence of sociodemographic characteristics and late adolescent factors. Findings on marijuana use align with the concept of equifinality (Cicchetti & Rogosch, 1999), in that the late-onset and chronic high groups were characterized not only by differences in substance use at wave 1 but also by certain distal psychosocial factors. For example, late-onset marijuana users were significantly more likely to have college plans, less likely to be truant, and more likely to have higher self-esteem. Into young adulthood and by ages 25 to 26, however, late-onset and chronic high marijuana users were more similar both in terms of marijuana use and all young adult factors included in the multivariable model. It is important to note that findings pertaining to self-esteem align with comparisons between late-onset and low/non-marijuana users. Late-onset marijuana users showed higher self-esteem in late adolescence and lower self-esteem in young adulthood compared to low/non-users. Compared to chronic high users, late-onset marijuana users showed higher self-esteem in late adolescence but no differences between this group by young adulthood. Additional research is needed to uncover developmental factors underlying associations between self-esteem and marijuana use among late-onset youth. For example, it is possible that marijuana may be used as a coping mechanism to self-medicate in response to negative affect.

It is worth noting that very few late-onset binge drinkers were also late-onset marijuana users. A still small, but greater number of individuals in the late-onset marijuana use group were also classified as late-onset binge drinkers. Although beyond the scope of the present study, future research is needed to give specific attention to individuals who are late-onset substance users across multiple substances. It may be informative to assess the extent to which predictors and outcomes among these individuals compare or differ in relation to individuals who show late-onset use for a single substance. Late-onset users of multiple substances may represent a unique risk group.

Strengths and Limitations

A major strength of the present study was the breadth of national panel samples of youth reporting data from 1976 through 2014. Because off-diagonal groups, such as late-onset binge drinkers and marijuana users, follow unexpected patterns in relation to group averages and continuity of earlier behaviors, these groups are often fairly small in number. Thus, using population-level survey data to study characteristics and predictors of developmental trajectories of binge drinking and marijuana use provides an important way to examine off-diagonal substance use from a big picture perspective that is often unavailable in smaller datasets.

Another strength of the present study was its use of national longitudinal data. Cross-sectional studies that do not account for developmental shifts in substance use may group both late-onset and chronic high users into the same group based solely on level of use. As shown in the present study, examining characteristics and predictors at a single point in time, such as between the ages of 25 and 26, may not accurately differentiate late-onset versus chronic high users. While such high levels of use may be problematic for both groups, using a developmental perspective to examine the multiple, varying paths toward heavy substance use may help to identify distal and proximal predictors of these groups. In turn, information from the present study may inform substance use prevention and intervention efforts. Furthermore, differentiating between late-onset versus chronic high use may be beneficial to compare health and well-being outcomes of long-term use compared to more acute high use.

In light of these strengths, limitations should also be noted. One important limitation of this study was that it did not test reciprocal associations between distal and proximal factors in relation to binge drinking and marijuana use trajectory group membership. Issues of endogeneity and selection effects present challenges to developmental research (Schulenberg et al., in press). Thus, future research using cross-lagged models is needed to assess causal ordering of measures included in the present study. This information may be useful to differentiate developmental factors contributing to and resulting from late-onset substance use. Another limitation is that data in the present study were only available beginning during senior year of high school (wave 1) and did not include high school dropouts. Thus, prior binge drinking and marijuana use data were not available to assess earlier patterns of use. Additional studies are needed to assess predictors of late-onset substance use in early adolescence and even childhood that may provide possible indicators of escalating use later during the transition to adulthood. More downstream outcomes may also be useful to examine in future studies. Because they have late-onset substance use, these youth may experience more delayed negative outcomes. Another limitation of MTF data is the limited depth of questionnaire items. Although MTF questionnaires do provide some measure of psychosocial factors, such as self-esteem, sensation seeking, and interpersonal aggression, these are self-report and scales were created from a limited number of items. Despite this limitation, self-esteem (e.g., Bachman et al., 2011), sensation seeking (Keyes et al., 2015), and interpersonal aggression (e.g., Schulenberg et al., 2005) have been used widely in publications using data from MTF.

Conclusions

The present study gives due attention to late-onset substance users and highlights the need to focus additional research on this understudied, yet clinically relevant, off-diagonal group. Late-onset binge drinking and marijuana use is problematic, given that youth in this trajectory group escalate use through the transition to adulthood to levels similar to that of chronic substance users. Thus, they may be at heightened risk for later onset, negative affect SUDs (Babor et al., 1992; Cloninger, 1987; Zucker, 1987;1994). Results of the present study build upon existing literature on developmental trajectories of substance use by giving due attention to late-onset substance users. By examining distal and more proximal risk factors of late-onset binge drinking and marijuana use, the present study uncovers potential developmental mechanisms driving this pattern of substance use behavior—both in comparison to low/non-use and chronic high use trajectory groups. Findings of the present study may help to identify youth vulnerable to emerging substance use problems and provide valuable information for substance use prevention and intervention efforts. Such efforts may be beneficial to curtail increasing substance use among late-onset substance users. In sum, late-onset binge drinkers and marijuana users comprise relatively small groups of the population, but they are an important off-diagonal risk group as indicated by their escalating use over a relatively short period of time. Results of the present study suggest that late-onset substance users represent an off-diagonal risk group that warrants additional research and clinical attention.

Chapter 3

Predictors of resilience among youth at elevated risk for substance use

Developmentally, substance use tends to begin in adolescence and then increase, peak, and decline through early adulthood (Johnston et al., 2015). However, there is often variability in patterns of use through this developmental period, referred to as the transition to adulthood. Existing research indicates heterogeneity in trajectories of substance use, including the most commonly used licit and illicit drugs in the U.S.—alcohol and marijuana, respectively (e.g., Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 2005). Chronic heavy substance users are often most vulnerable to detrimental outcomes, because they start substance use early and persist with elevated use through adulthood (Berg et al., 2013; Chassin et al., 2002; Squeglia et al., 2009; Winward et al., 2014). One particularly strong risk factor for chronic heavy substance use is having a family history of substance use disorder (FH+; SUD; e. g., Chassin et al., 2004; Kendler et al., 2008; King et al., 2009; Zucker, 2014). Despite this vulnerability, a resilient, off-diagonal subgroup of FH+ youth displays persistently low levels of substance use (e.g., Chassin et al., 2002). Resilience, as it applies broadly to this subgroup, is defined broadly as the ability to avoid a pathological outcome, or achieve a successful one, despite the experience of adversity (e.g., Masten et al., 1990; Rutter, 1987; Windle & Zucker, 2010). This group is referred to as off-diagonal because they have low levels of substance use through the transition to adulthood despite being at elevated risk for substance use problems. Existing studies, however, have focused predominately on heavy substance users, often overshadowing facets of resilience among low substance using at-risk youth. This is problematic, since identifying protective factors among this off-diagonal group may benefit efforts to prevent problematic substance use among this vulnerable population.

Thus, the overall purpose of the present study was to identify predictors of resilience (i.e., low substance use) among FH+ youth through the transition to adulthood. Predictors included in the present study are shown in Table 1. Within the field of addiction research and developmental psychopathology, earlier experiences often have downstream effects on functioning later in adulthood (Dodge et al., 2009; Schulenberg & Maggs, 2008; Schulenberg & Maslowsky, 2009). Analyses centered on the additive influence of key developmental predictors of substance use, which included early and late adolescent psychosocial factors and young adult social roles. Developmental psychopathology theory posits that a longitudinal, multidimensional approach is useful to examine the complex factors involved in both resilience and risk (Drabick & Steinberg, 2011; Rutter & Sroufe, 2000).

Psychosocial predictors examined in the present study focused on self-regulation. This was due to evidence indicating that FH+ youth are more likely to follow a pathway to substance use problems characterized by deficits in self-regulation (Zucker et al., 2011). Low substance use among FH+ youth is associated with a better regulatory capacity (Wong et al., 2006). Because low levels of substance use among resilient youth are relatively stable through the transition to adulthood, distal predictors were measured during early adolescence when substance use tends to initiate among FH+ youth (e.g., Wong et al., 2006). Predictors at this age were examined to test the influence of early psychosocial factors on later patterns of substance use when the risk for elevated use is greatest. In addition, these same predictors were examined more proximally to the transition to adulthood (i.e., during late adolescence). Late adolescence coincides the emergence of elevated substance use and when SUDs are most likely to emerge (Johnston et al., 2015;

Substance Abuse and Mental Health Services Administration (SAMHSA), 2015, respectively). Distal and proximal predictors examined in the present study focus on self-regulation, considering that deficits in self-regulation are positively associated with substance use risk (e.g., Windle, in press) and negatively associated with resilience (e.g., Sameroff & Rosenblum, 2006). Because of the relation between social contexts and substance use during the transition to adulthood (e.g., Staff et al., 2010), college enrollment and graduation, marriage, and parenthood were also examined. The importance of studying psychosocial factors and social roles among resilient FH+ youth is expanded upon in the following sections. Identifying predictors of resilience among FH+ youth is valuable for substance use prevention and intervention efforts in order to target important protective factors involved with positive development (Hurd & Zimmerman, in press). The present study sets the stage for a comprehensive focus on predictors of resilience among vulnerable populations.

Developmental Pathways of Substance Use

Existing research has identified different trajectories of substance use through the transition to adulthood (e.g., Epstein et al., 2015; Hill et al., 2007; Jackson et al., 2008; Nelson et al., 2014; Oesterle et al., 2004; Schulenberg et al., 1996a; Schulenberg et al., 2005; Windle & Wiesner, 2004). The majority of youth progress through the transition to adulthood with relatively low levels of substance use, only engaging in occasional experimental or social use (Brown et al., 2008). Some youth have earlier, heavier use during adolescence but then decrease use over time. Often, this decrease is related to increased responsibilities associated with certain social roles, such as marriage or parenthood (e.g., Staff et al., 2010). Late-onset youth show an opposite pattern of substance use (i.e., off-diagonal), with low levels during adolescence but then increase use through the transition to adulthood. Perhaps the most concerning substance use group, are heavy substance users. For example, chronic heavy marijuana users are more likely to have lower educational attainment and greater risk for marijuana use disorder in young adulthood compared to other trajectory groups (Windle & Wiesner, 2004). Frequent binge drinkers are more likely to engage in risky sexual behavior (Wu et al., 2010), have poor health (Berg et al., 2013), and as with chronic heavy marijuana use, develop substance use problems in young adulthood (Chassin et al., 2002; Flory et al., 2004; Hill et al., 2007). The majority of research on FH+ youth has focused on individuals in the chronic heavy use trajectory group (e.g., Zucker et al., 2008). Examining risk factors for chronic, high levels of substance use among FH+ youth is crucial to inform prevention and intervention programs aimed at youth most vulnerable to developing SUDs. Yet, identifying protective factors associated with low use among off-diagonal youth is beneficial to understand the underlying mechanisms of this resilience (Schulenberg & Maggs, 2002). In the present study, protective factors against substance use take center stage.

Distal and Proximal Predictors of Substance Use Resilience

From a developmental psychopathology perspective, the interplay between continuity and discontinuity of distal and proximal factors through development contributes to psychopathology, including substance use (Drabick & Steinberg, 2011; Rutter & Sroufe, 2000; Schulenberg et al., in press). The relation between psychosocial and contextual factors contributes, in part, to substance use vulnerability among FH+ youth (Zucker, 2014). It is likely that these factors also contribute to substance use resilience. In the present study, distal factors measured in early adolescence and proximal psychosocial factors measured in late adolescence can be described broadly within the concept of self-regulation, and more specifically behavioral control. Aspects of self-regulation, such as the balance between impulsive responding and behavioral control of those impulses, may contribute not only to substance use risk but also to resilience. Although deficits in behavioral control are robustly associated with substance use risk (Windle, in press), the extent to which they are involved in substance use resilience remains unclear.

Associations between self-regulation and substance use pertain to dual-systems models of risk-taking. Dual-systems models of risk-taking describe the developmental mismatch between subcortical, “bottom-up” brain regions involved in reward responsivity and cortical brain regions related to “top down” cognitive control (Casey, 2014). Reward driven regions mature at the onset of puberty during early adolescence, whereas regions associated with cognitive control have a more protracted development into the early 20s (Casey et al., 2008; Gogtay et al., 2004; Raznahan et al., 2014; Steinberg, 2010). As a conceptual model, dual-systems models of risk-taking are useful to describe mechanisms involved in heightened risk-taking among adolescents and young adults, such as elevated substance use during this time. However, they do not account for individual differences in risk-taking among certain subgroups of youth (Harden & Tucker-Drob, 2011; Pfeifer & Allen, 2012; Quinn & Harden, 2013). This last point is particularly relevant to the present study. The present study extends prior work related to dual-systems models of risk-taking by testing differences in self-regulation between resilient and risk groups

Measures of self-regulation examined in the present study related to substance use resilience versus risk were resiliency, reactive control, sensation seeking, internalizing behaviors, and externalizing behaviors. A developmental psychopathology perspective accounts for risk in relation to resilience, just as it accounts for typical versus atypical development and continuity versus discontinuity (Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000). In other words, this perspective focuses on continuums of function and dysfunction. Thus, factors examined in the present study have been shown to contribute both to risk and resilience. For example, a greater number of externalizing problems have been shown to predict substance use risk, whereas a lesser extent of externalizing problems is protective against substance use (e.g., Colder et al., 2013). Since self-regulation is multidimensional, psychosocial predictors in the present study can be categorized within three specific dimensions. Resiliency and reactive control pertain to temperament, sensation relates to personality, and externalizing and internalizing behaviors describe behavioral functioning. Examining factors within these dimensions may uncover important promotive factors of resilience among FH+ youth.

In terms of temperament, resiliency and reactive control are based on concepts developed by Eisenberg et al. (2003) and Block and Block (1980). Resiliency describes flexible adaptation to contextual demands, particularly stressful interactions (Eisenberg et al., 2003). It is important to note that resiliency differs from resilience, which refers to experiencing a successful outcome despite adversity (Masten et al., 1990). Resiliency examined in the present study is based on the construct of ego resiliency developed by Block and Block (1980). Ego resiliency describes the ability to regulate impulsive responding in relation to varying environments. In other words, ego-resilient individuals are adaptive and behave appropriately depending on the context. Reactive control, on the other hand, describes a more automatic response to impulsive, reward-driven behaviors (Eisenberg et al., 2003). Reactive control is based on the construct of ego control conceptualized by Block and Block (1980) that describes self-regulation over emotional, impulsive responses. Ego undercontrol is characterized by deficits in impulse regulation and the inability to delay gratification (Block & Block, 1980). Thus, reactive undercontrol is associated with heightened risk for substance use problems (Wong et al., 2006). Pertaining to bottom-up reward responsivity involved with dual-systems models of risk-taking, reactive control is predominately involuntary (Eisenberg et al., 2003). Therefore, a greater capacity to regulate impulsive responding through reactive control and adapt appropriately to stressful situations through resiliency may contribute to lower substance use among FH+ youth.

Sensation seeking was included in the present study as a personality measure of self-regulation related to substance use resilience and risk. Youth who score high on measures of sensation seeking show a preference for novel, exciting, and arousing experiences (Zuckerman, 1994). Sensation seeking has been described as a lower-level factor within the overarching construct of behavioral undercontrol (Bogg & Finn, 2010). As such, sensation seeking is driven by more immediate rewards despite the potential for negative consequences. In line with dual-systems models of risk-taking, sensation seeking is associated with bottom-up, reward responsivity. Although individuals high on sensation seeking may partake in non-drug related, high intensity activities (e.g., bungee jumping, sky diving) the highly rewarding experience of substance use is also common among these individuals. Indeed, sensation seeking is a strong predictor of chronic heavy substance use (Brook et al., 2011; Flory et al., 2004; Malmburg et al., 2010; Schulenberg et al., 1996b). Because high sensation seeking is related to substance use, it is also likely that low levels of sensation seeking are associated with substance use resilience. Although sensation seeking tends to decrease into late adolescence (Steinberg et al., 2008), a smaller developmental decline is related to greater increases in substance use (Quinn & Harden, 2013). Thus, the present study tested the extent to which sensation seeking, both measured in early adolescence and late adolescence, predicts substance use resilience.

Internalizing and externalizing problems fall within the behavioral dimension of self-regulation related to substance use risk and resilience. Youth with a family history of SUD are at elevated risk for both internalizing and externalizing problems in addition to early onset substance use (Hussong et al., 2011; Zucker, 2014). Whereas externalizing behaviors are related to the “Type 2” pathway to SUDs characterized by earlier onset use and antisocial behaviors, internalizing behaviors are associated with “Type 1” SUDs that are later onset and characterized by negative affect (Babor et al., 1992; Cloninger et al., 1996; Zucker, 1987, 1994). Although externalizing behaviors typically describe delinquency and aggression, the externalizing pathway to SUD is more broadly characterized by behavioral undercontrol. Behavioral undercontrol is a risk phenotype for SUD often first evident in early childhood as a temperamental trait (Kendler et al., 2008). This risk phenotype describes the inability, unwillingness, or failure to inhibit behaviors despite negative consequences associated with those behaviors (Hawkins et al., 1992; Kandel, 1978; Zucker, 2006; Zucker et al., 2011). Examining externalizing behaviors in early and late adolescence as predictors of substance use during the transition to adulthood may provide important information on distal and proximal indicators of substance use risk versus resilience.

As with the externalizing pathway to SUDs, the internalizing pathway involves behavioral deficits in self-regulation. Despite both constructs being associated with self-regulation, the link between internalizing behaviors and substance use is often weaker compared to that of externalizing behaviors (Hussong et al., 2011; Zucker, 2008). Perhaps the most consistent finding is that individuals high on internalizing problems may use substances as a coping mechanism (e.g., Carpenter & Hassin, 1999). Some studies, however, have shown that internalizing behaviors may actually be protective against substance use (e.g., Colder et al., 2013). Not only may individuals with anxiety avoid social situations in which substance use is involved, but they also may fear the negative consequences of substance use (Colder et al., 2013). Due to these mixed findings, additional research is needed to test the longitudinal influence of internalizing behaviors on substance use through the transition to adulthood.

In addition to self-regulation, social contexts associated with substance use risk and resilience were also examined. These measures were included due to their associations with substance use risk during the transition to adulthood (e.g., Staff et al., 2010). A number of major social role changes occur during the transition to adulthood (Shanahan, 2000), and how youth navigate these shifting contexts may impact substance use risk and resilience (Schulenberg & Zarrett, 2006). Therefore, these factors may also contribute to substance use resilience among FH+ youth. Developmental tasks during the transition to adulthood center on certain domains, such as family, school, and work roles (Staff et al., 2010). Norms and expectations associated with family roles, including marriage and parenthood, tend to discourage substance use (Staff et al., 2010). College settings, however, are often less discouraging of substance use (Jager et al., 2013). Mismatches in person-context fit may result in difficulties adapting to social role changes, such as attending college (Schulenberg & Zarrett, 2006). For example, a youth who engaged in low levels of substance use during high school, due to high parental monitoring and involvement with low substance using peers, may then begin using substances in college due to greater independence and exposure to social contexts more encouraging of substance use. Many individuals, however, decrease substance use upon leaving college. For others, college drinking sets in motion a pattern of escalating consumption that becomes a developmental turning point to continued heavy use (Schulenberg et al., 2014). Other developmental turning points, such as marriage and parenthood, may actually decrease substance use (Leonard & Rothbard, 1999; Staff et al., 2010). Resilient youth may be more likely to successfully negotiate social role changes during the transition to adulthood. Thus, social roles were examined in relation to substance use resilience versus risk.

Research Questions and Hypotheses

Distal and proximal psychosocial measures related to self-regulation and young adult social roles were examined as predictors of resilience versus risk among FH+ youth. In line with developmental psychopathology concepts of resilience and risk, the comparison group was comprised of FH+ youth with high levels of binge drinking and marijuana use through the transition to adulthood. Resilient and risk groups examined in the present study had a shared vulnerability related to both genetic and environmental factors (e.g., Lieb et al., 2002; Zucker et al., 2014). Because of this shared vulnerability, predictors associated with resilience could be more directly isolated.

To align with trajectory models computed in Chapter 2, the present study used the same age groupings as used for analyses of Monitoring the Future data. These included binge drinking and marijuana use at ages 17-18, 19-20, 21-22, 23-24, and 25-26 years old. Research questions guiding these analyses were: (1) Which distal factors during early adolescence are associated with differing patterns of substance use through the transition to adulthood among resilient versus risk groups?; (2) Which more proximal factors during late adolescence differentiate resilient and risk groups?; (3) Which young adult social roles, which coincide with trajectories of substance use through the transition to adulthood, are associated with substance use resilience versus risk?; and (4) To what extent does the additive influence of early adolescent, late adolescent, and young adult factors predict resilience compared to risk? For both distal and proximal factors examined in the present study, resilient youth were hypothesized to have greater resiliency and reactive control compared to risk youth. Resilient youth were also hypothesized to have lower distal and proximal levels of sensation seeking, internalizing behaviors, and externalizing behaviors. Proximal measures of the same factors were expected to have a stronger impact on resilience versus risk during the transition to adulthood compared to distal measures (i.e., reactive control measured in late adolescence versus in early adolescence). Among young adult social roles, resilient youth were hypothesized to be more likely to be enrolled in and graduate from college, be married, and be parents.

Methods

Participants and Procedures

The present sample consisted of 235 participants (75.32% male; 96.60% White; 85.53% parents with at least some college education; 46.38% with one parent with SUD; and 53.63% with two parents with SUD) from the Michigan Longitudinal Study (MLS), an ongoing, prospective study of community-recruited youth from families at high risk for SUD (Zucker, 2000). Initial recruitment included men across a four-county area in central Michigan who were convicted of a drunk driving offense (as indicated by court records) and had at least one preschool-age male child. Partners were also recruited, although their substance use status was free to vary. Initial recruitment included only male children and White families, however female siblings and non-White families were included later. A control set of families with identical family structure but low levels of alcohol use were selected through door-to-door canvasing from the same neighborhoods as the court-recruited families. Through this canvasing, an additional sample of non-court involved sample of men with alcohol use disorders (AUD) and their families were recruited. Assessments occurred at baseline (between the ages of 3 and 5) and every 3 years (T-waves) with psychosocial, behavioral, and drug use measures appropriate for developmental age. Annual assessments (A) were also conducted beginning at age 11, the typical age for substance use onset (Wong et al., 2006). MLS has low rates of attrition. The MLS has maintained contact with approximately 90% of all still-living participants, both parents and offspring.

Due to the focus of the present study on youth at high risk for substance use problems, the current study consisted only of FH+ youth (i.e., a family history of SUD). Family history of SUD, defined as having a biological father and/or mother with a diagnosis of any alcohol or drug use disorder, was ascertained by a clinical psychologist using the Diagnostic Interview Schedule—Version 4 (DIS-IV) (Robins et al., 2000). Children who exhibited signs of fetal alcohol syndrome (FAS) were excluded from study enrollment (Loukas et al., 2001; Sokol & Clarren, 1989). Additional exclusion criteria included neurologic, acute, uncorrected, or chronic medical illness; treatment with psychoactive medication within the past 6 months; history of psychosis or schizophrenia in a first degree relative; and presence of Axis I psychiatric or developmental disorders, except for conduct and attention-deficit/hyperactivity disorders (ADHD) or prior SUD, as excluding these participants with these latter three disorders would eliminate part of the phenomena of interest. The DIS-IV was used to determine diagnosis. All participants provided informed consent approved by the University of Michigan Medical School Institutional Review Board.

Measures

Substance use. Binge drinking was measured by the Drinking and Drug History Form (Zucker et al., 1990) by the number of days in the past year participants reported consuming five or more standard drinks of beer, wine, or liquor. Marijuana use was measured by the Drinking and Drug History Form through a single item, "On how many occasions (if any) have you used marijuana (grass, pot, weed, ganga) or hashish (hash, hash oil) during the past year?" Response options were on a scale of 0 = Never, 1 = 1 to 2 occasions, 2 = 3 to 5 occasions, 3 = 6 to 9 occasions, 4 = 10 to 19 occasions, 5 = 20 to 39 occasions, 6 = 40 to 99 occasions, 7 = 100 to 249 occasions, 8 = 250 to 499 occasions, or 9 = 500 or more occasions.

Sociodemographic measures. Sociodemographic measures were gender, parent education (a proxy for socioeconomic status (SES)), and number of parents diagnosed with a SUD. Given that initial recruitment only included families who identified as White and that 96.60% of the present sample were White, race/ethnicity was not included in the present study. Gender was coded as 1= male or 0 = female. Parent education was measured by the highest level of education obtained by at least one parent. Participants reported the highest level of education their father and mother completed. Response options included number of years completed in elementary, high school, college, graduate school, or vocational-tech school and the type of college, graduate, or vocational-tech certificate received. In the present study, parent education was coded as 1 = some college education or more (high parent education) or 0 = high school degree or less (low parent education. Number of parents diagnosed with a SUD was coded as 0, 1, or 2 biological parents diagnosed with a SUD based on DIS-IV lifetime criteria for alcohol or drug use disorder.

Resiliency. Resiliency was measured by modified versions of the clinician-administered California Child Q-Sort (CCQ; Block, 1980) when participants were 12 to 14 years old (early adolescence) and the Revised Adult California Q-Sort (CAQ; Block, 1980) when participants were 17 to 18 years old (late adolescence). Both the CCQ and CAQ are based on the California Q-Sort, which included 100 statements of various behavioral adaptations sorted by a clinician on a scale from 1 = "extremely uncharacteristic" to 9 = "extremely characteristic" of the participant. Resiliency scores are means of item totals, and higher scores signify a greater extent of resiliency. Eisenberg et al. (1996) adapted the CCQ to include 23 items that measured resiliency and later created a more refined version that included 11 items most reflective of resiliency (Eisenberg et al., 2003). The resiliency scale developed by Eisenberg et al. (2003) was used in the present study and showed high reliability (α = 0.82). Sample items measured during early adolescence were “Uses and responds to reason” and “Can recoup or recover after stressful experiences.” Resiliency in late adolescence was measured by the CAQ through 11 items adapted from Eisenberg’s (1996; 2003) resiliency scale, α = 0.84. Sample items include “Is productive; gets things done” and “Values own independence and autonomy”.

Reactive control. As with resiliency, reactive control was measured by Q-sort items modified by Eisenberg and colleagues (1996; 2003). In early adolescence, 14 items (α = 0.81) were selected based on the Eisenberg et al. (2003) scale. Sample items measured during early adolescence were “Is inhibited and constricted” and “Is reflective; deliberates before speaking or acting.” In late adolescence, 12 items (α = 0.81) were selected to measure reactive control. Example items include “Unable to delay gratification” and “Is self-indulgent”. The scale for items measuring reactive control ranged from 1 = “extremely uncharacteristic” to 9 = “extremely characteristic” of the participant.

Sensation seeking. The sensation seeking subscale of the Multiple Affect Adjective Check List (MAACL-R/6; Zuckerman & Lubin, 1965, revised in 1985) was used to measure sensation seeking during both early and late adolescence. Sensation seeking was assessed by the sum of 10 self-reported items (α = 0.70). Respondents were instructed to mark an “x” (“x” = 1 or no marking = 0) beside the words that describe how they generally feel. Sample words include “Adventurous”, “Daring”, and “Wild”.

Internalizing problems. The Youth Self-Report (YSR; Achenbach, 1991) was used to measure internalizing problems in early adolescence. The sum of 32 items from three internalizing subscales—social withdrawal, somatic complaints, and anxiety and depression problems—formed the total internalizing problems scale. Self-reported behaviors were based on rating the accuracy of statements on a 3-point scale where 0 = “not at all true”, 1 = “somewhat true”, and 2 = “very true” ($\alpha = 0.80$). Sample items include “I keep from getting involved with others” (social withdrawal), “I feel dizzy” (somatic complaints), “I am too fearful or anxious” (anxiety), and “There is very little that I enjoy” (depression). The Adult Self-Report (ASR; Achenbach, 1991) was used to measure internalizing problems during late adolescence. Self-reported behaviors are based on rating the accuracy of statements on a 3-point scale where 0 = “not at all true”, 1 = “somewhat true”, and 2 = “very true” ($\alpha = 0.85$). The internalizing subscales used on the YSR during early adolescence (social withdrawal, somatic complaints, and anxiety and depression problems) were used on the ASR during late adolescence, with modifications made for certain questions to be more age appropriate. Sample items include “I keep from getting involved with others” (social withdrawal), “I feel dizzy or lightheaded” (somatic complaints), “I am too fearful or anxious” (anxiety), and “There is very little that I enjoy” (depression).

Externalizing problems. In early adolescence, self-reported externalizing behaviors were assessed by the YSR (Achenbach, 1991). Externalizing behaviors were measured by the sum of 30 items from two externalizing subscales—aggressive behavior and delinquency. Self-reported behaviors were based on rating the accuracy of statements on a 3-point scale where 0 = “not at all true”, 1 = “somewhat true”, and 2 = “very true” ($\alpha = 0.85$). Sample items include “I disobey at school” (aggressive behavior) and “I hang around with kids who get in trouble” (delinquency). In late adolescence, externalizing behaviors were measured by the sum of three externalizing subscales—aggressive behavior, rule breaking, and intrusiveness. These subscales consisted of 35 items with responses on a 3 point scale where 0 = “not true”, 1 = “somewhat or sometimes true”, and 2 = “very true or often true” ($\alpha = 0.80$). Sample items include “I blame others for my problems” (aggressive behavior), “I break rules at work or elsewhere” (rule breaking) and “I tease others a lot” (intrusiveness). As with internalizing measures, externalizing subscales used on the YSR during early adolescence were used on the ASR during late adolescence, with age-appropriate modifications. Due to trajectory class groupings formed on the basis of binge drinking and marijuana use, items on the YSR and ASR pertaining to substance use were removed from the delinquency subscale (items 105 on the YSR and 90 on the ASR “I use alcohol or drugs for non-medical purposes” and “I drink too much or get drunk”, respectively).

Young adult social roles. Social roles were dichotomized as ever enrolled in college, graduated from college, married, and became a parent. To assess college enrollment and graduation status, participants were asked, “What is your current grade level in school?” Response options included number of years completed in elementary, high school, college, graduate school, or vocational-tech school and the type of college, graduate, or vocational-tech certificate received. College enrollment status was coded as (1) ever attended college or (0) never attended college. College graduation status was coded as (1) graduated from college or (0) did not graduate from college. To assess marital status, participants were asked, “Which answer best fits your current marital situation?” Response options included married (living with a partner), divorced, separated, or single (never married). Marital status was coded as (1) ever reported being married or (0) never reported being married. To assess child status, participants were asked, “Please list all of the children you have fathered or that have been born to you.” Child status was coded as (1) ever reporting having at least one child or (0) never reporting having a child.

Analytic Plan

The analytic plan for the present study involved four steps: (1) Use growth mixture modeling (GMM) to estimate the best fitting number of trajectory classes for binge drinking and marijuana use, examined separately, from late adolescence through the transition to adulthood; (2) Identify resilient and risk groups using GMM results and more conservative groupings based on existing criteria for high levels of binge drinking and marijuana use (Schulenberg et al., 1996a; Schulenberg et al., 2005, respectively); (3) Examine descriptive differences between resilient and risk groups in relation to sociodemographic characteristics, early adolescent factors (ages 12-14), late adolescent factors (ages 17-18), and adult social roles (18-26); and (4) Identify predictors of membership in the resilient versus risk groups using hierarchical multivariable logistic regression to test the additive influence of sociodemographic characteristics, early adolescent factors, late adolescent factors, and young adult social roles.

Steps 1 and 2 involved analyses conducted through Mplus software (version 7.4, Muthén & Muthén, 1998-2015). The robust maximum likelihood (MLR) estimator with full information maximum likelihood (FIML) was used in Mplus analyses. An advantage of using FIML is that it accounts for missing data by using all available data from at least 1 time point and produces unbiased parameter estimates and standard errors. Mplus was used to conduct both LGM and GMM. Analyses in steps 2 (assessing high levels of binge drinking and marijuana use through cutoffs established in the literature), 3, and 4 were performed using IBM SPSS Statistics 22.

Step 1: Growth mixture modeling (GMM). GMM was conducted in Mplus to identify substance use trajectory groups. GMM is a person-centered trajectory group modeling approach that allows for variability in intercept and growth parameters among latent subgroups (e.g., Jung & Wickrama, 2008; Muthén, 2004). Determining the best fitting Latent Growth Model (LGM; Duncan & Duncan, 2004) is the first step in GMM. LGM is used to assess the mean trajectory for a particular outcome variable among the entire sample population. In the present study, the best fitting LGM was determined separately for binge drinking and marijuana use trajectories using data spanning the transition to adulthood. Four LGMs were run and then compared for model fit: 1) the intercept only model; 2) the intercept and linear slope model; 3) the interception, linear, and quadratic slope model; and 4) the intercept, linear, and piecewise slope model. Cut offs for the piecewise model was based on normative age trends for binge drinking and marijuana use through the transition to adulthood (Johnston et al., 2015). Model fit criteria were based on the following: 1) Root-mean-square error of approximation (RMSEA) ≤ 0.06; 2) Comparative fit index (CFI) $\geq .90$); 3) Tucker-Lewis index (TLI) $\geq .90$); and 4) chi-square difference test based on log-likelihood values and scaling correction factors from the MLR estimator.

Using the best fitting LGM, GMM was performed to determine the most likely number of latent subgroups for binge drinking users and marijuana users. As with LGM analyses, GMM analyses were conducted separately for binge drinking and marijuana use. First, the two class GMM was tested, followed by an increasing number of classes until model fit declined. Model fit was based on the following criteria: 1) Bayesian Information Criterion, (BIC: Schwarz, 1978), with lower numbers indicating better model fit; 2) Entropy closer to 1, which identifies better fitting classification of posterior probability class values (Jung & Wickrama, 2008); 3) Class estimates based on posterior probabilities consisting of no less than 5% of the total sample, which supports improved replicability (Jackson et al., 2008); 4) Lo-Mendell-Rubin (LMR) adjusted likelihood ratio test, which compares the fit of the k class model to the k-1 (i.e., 4 versus 3 class model) (Lo et al., 2001); and 5) Class interpretability (Jackson et al., 2008).

Step 2: Identify resilient and risk groups. GMM estimates most likely trajectory class probabilities (i.e., latent subgroups among the full sample). Once the best fitting number of classes were determined through GMM, the estimated class for each subject was outputted to SPSS. Although GMM is beneficial for identifying developmental trajectories among subgroups of individuals and FIML offers a useful way for dealing with missing data in GMM analyses, additional criteria were used to improve the face validity of low/non-use and high use trajectory class groupings among the FH+ MLS sample. Based on previously established indicators of high-level binge drinking and marijuana use (Schulenberg et al., 1996a; Schulenberg et al., 2005, respectively), frequent binge drinking was determined by reporting weekly binge drinking occasions during the past year, and frequent marijuana use was determined by instances of 20 or more occasions during the past year.

These additional criteria were used because MLS consists primarily of FH+ youth. Having a family history of SUD is robustly associated with substance use risk among offspring (e. g., Chassin et al., 2004; Kendler et al., 2008; King et al., 2009; Zucker, 2014). Thus, youth classified as low binge drinkers and low marijuana users reported higher rates of use compared to national samples (Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 2005). Additionally, youth in the present study were categorized as at risk or resilient based on low levels of binge drinking and marijuana use. However, GMM was performed separately for binge drinking and marijuana use. Indicators of low use on both of these substances were necessary to form resilient versus risk groups.

For classification into the resilient group, participants were selected if they were FH+ and reported no frequent binge drinking as well as no frequent marijuana use occasions across the five waves of data collection. For classification into the risk group, participants qualified as heavy substance users if they were FH+ and reported frequent binge drinking and/or frequent marijuana use on at least two occasions over the five time points assessed. Either heavy binge drinking or marijuana use qualified as risky substance use. These classification criteria were selected to account for a more consistent and less developmentally limited extent of heavy substance use. In relation to normative peaks in substance use through the transition to adulthood (Johnston et al., 2015), heavy use measured at one time point may not be a strong indicator of high risk. Because comparisons between resilient and risk groups were the focal point of the present study, only these groups were included in all following analyses.

***Step 3: Descriptive characteristics of resilient and risk groups*.** After assigning resilient versus risk groups, frequencies and means for sociodemographic characteristics, early adolescent factors (ages 12-14), late adolescent factors (ages 17-18), and adult social roles (18-26) among these groups were identified and compared with the risk group. Significant descriptive differences between resilient and risk groups for categorical variables were examined with X^2 tests, and continuous variables were examined with independent samples *t*-tests.

Step 4: Predictors of resilient versus risk substance use groups. The present study categorized resilient and risk trajectory groups according to separate binge drinking and marijuana use models in order to assess substance use risk among the two most commonly used drugs of abuse (SAMHSA, 2015). Because these models were examined separately, logistic regression models could not be performed directly in Mplus through the R3STEP command. Although there are several advantages of the R3STEP approach (Asparouhov & Muthén, 2014; Vermunt, 2010), a shortcoming is that it cannot be used for hierarchical multivariable logistic regression models. In the present study, predictors of resilient versus risk substance use groups were examined in SPSS using a series of three hierarchical multivariable logistic regression models[2]. The outcome variable was substance use group (resilient versus risk). In these models, predictors of substance use groups were examined in temporal order. Model 1 consisted of early adolescent factors (resiliency, reactive control, sensation seeking, internalizing and externalizing behaviors) controlling for sociodemographic characteristics, model 2 added late adolescent factors (resiliency, reactive control, sensation seeking, internalizing and externalizing behaviors), and model 3 added adult social roles (college enrollment, college graduate status, marriage, and parent status). Nagelkerke R^2 and the change in likelihood ratio test, as indicated by the model χ^2 test, were used to assess model fit at each step.

Results

Growth Mixture Modeling

Binge drinking. Results of LGM analyses indicate that the linear model fit the binge drinking data best (RMSEA = 0.07, CFI = 0.90, TLI = 0.85), compared to the piecewise (RMSEA = 0.00, CFI = 1.00, TLI = 1.00) and quadratic (RMSEA = 0.00, CFI = 1.0, TLI = 1.0) models. Although results of the chi-square difference test based on log-likelihood indicated that quadratic (χ^2 (3) = 17.44, p <0.001) and piecewise (χ^2 (3) = 17.43, p <0.001) models had improved model fit over the linear model, both the quadratic and piecewise models showed non-positive error messages for the latent variable covariance matrix. No errors were indicated with the linear LGM and this model showed good model fit. Thus, the linear LGM was used to conduct GMM. The best fitting piecewise GMM estimated three trajectory classes (BIC = 15242.77, Entropy = 0.96, LMR = 155.28, p < 0.001), as shown in Table 12. This model consisted of 11.21% of the sample in the late-onset group, 85.28% of the sample in the low/non-

[2] Although often used interchangeably, the terms multivariate and multivariable describe different analyses. Because multivariate analyses refer to analyses with two or more dependent variables (Hidalgo & Goodman, 2013), the term multivariable was used in the present study.

use binge group, and 3.52% of the sample in the chronic high binge group. Figure 4 shows developmental trajectories of binge drinking for the three identified groups.

Marijuana use. As with the binge drinking trajectory model, the linear LGM was the best fitting model for marijuana use data (RMSEA = 0.06, CFI = 0.97, TLI = 0.96) compared to the quadratic (RMSEA = 0.00, CFI = 1.00, TLI = 1.00) and piecewise (RMSEA = 0.00, CFI = 1.00, TLI = 1.00) models. Although the quadratic (χ^2 (3) = 12.14, p <0.01) and piecewise (χ^2 (3) = 11.92, p <0.01) models showed improved model fit over the linear (null) model, testing the quadratic and piecewise models in GMM resulted in non-positive error messages for the latent variable covariance matrix. Thus, the linear model, which still showed excellent fit statistics RMSEA = 0.058, CFI = 0.97, and TLI = 0.96 was selected for GMM analyses. The best fitting linear GMM estimated three trajectory classes (BIC = 5691.71, Entropy = 0.95, LMR = 158.41, p < 0.001), as shown in Table 12. Displayed in Figure 5, the chronic high marijuana use group consisted of 18.15% of the sample, the moderate marijuana use group consisted of 10.89% of the sample, and the low marijuana use group consisted of 70.90% of the sample.

Descriptive Characteristics of Resilient and Risk Groups

Using both GMM and cut-offs used in previous studies (Schulenberg et al., 1996a; Schulenberg et al., 2005), resilient and risk groups were identified. Results indicated that 84 participants were categorized as resilient youth—FH+, membership in both low binge drinking and low marijuana use trajectory groups, and no instances of frequent binge drinking or marijuana use occasions across the five waves of data collection. One-hundred and fifty-one participants were categorized as risk youth—FH+, membership in either high binge drinking or high marijuana use trajectory groups, and at least two occasions of weekly binge drinking or monthly marijuana use occasions across the five waves of data collection. Correlations among all variables included in analyses are shown in Table 13. Table 14 shows descriptive comparisons and significant differences between resilient and risk groups.

Predictors of Resilient Versus Risk Substance Use Groups

Among sociodemographic characteristics, resilient youth were significantly less likely to be male. In relation to early adolescent factors, resilient youth were more likely to have higher levels of reactive control and lower levels of externalizing behaviors. During late adolescence, resilient youth were more likely to have higher levels of resiliency and reactive control during late adolescence but lower levels of externalizing behaviors. Among young adult social roles, resilient youth were more likely to be married.

Hierarchical multivariable logistic regression analyses were used to examine predictors of being in the resilient group compared to risk group. Table 15 displays the stepwise approach used to compare Model 1 (sociodemographic and early adolescent factors), Model 2 (sociodemographic, early adolescent factors, and late adolescent factors), and Model 3 (sociodemographic, early adolescent factors, late adolescent factors, and young adult social roles). Results of Model 1 indicate that resilient youth were less likely to be male compared to the risk group. No other predictors were significant. In Model 2, the addition of late adolescent factors showed that resilient youth were more likely to have higher reactive control and lower externalizing behaviors compared to the risk group. The effect of gender remained significant. Adding late adolescent factors resulted in a statistically significant improvement in model fit and increased the Nagelkerke R^2 from 0.17 in Model 1 to 0.34 in Model 2. In Model 3, resilient youth continued to show a lower likelihood of being male, having higher reactive control, and lower externalizing behaviors compared to youth in the risk group. Resilient youth were also more likely to report being married during young adulthood. Model 3 showed improved model fit over Model 2, both in relation to statistically significant model χ^2 and a higher Nagelkerke R^2.

Discussion

Developmental research indicates that substance use during the transition to adulthood is associated with a constellation of both distal and proximal predictors related to psychosocial functioning and social contexts (e.g., Dodge et al., 2009; Schulenberg & Maslowsky, 2009; Schulenberg et al., in press). However, the extent to which these factors differentiate between resilient and risk groups is less well known. The present study contributes to the literature by identifying predictors of low binge drinking and marijuana use through the transition to adulthood among off-diagonal FH+ youth (i.e., resilient youth). Examining predictors of resilience is useful in order to focus on strengths of at-risk youth (Hurd & Zimmerman, in press).

By using hierarchical multivariable logistic regression models, the present study took examining predictors of resilience versus risk one step further than most prior studies. In other words, this method provided a useful approach to examine key differences between resilient and risk groups pertaining to psychosocial functioning and social roles. Mean level analyses provided a more narrow perspective on predictors of resilience versus risk examined in the present study. However, hierarchical multivariable logistic regression models assessed the additive influence of distal and proximal predictors in relation to resilience versus risk. There are important benefits of examining the additive influence of distal and proximal factors, given theoretical support from developmental psychopathology concepts of continuity and discontinuity (e.g., Schulenberg et al., in press). Prior functioning may contribute to more downstream effects on substance use during the transition to adulthood, but more recent influences also exert strong influences. Indeed, evidence from the present study suggests that, as expected, proximal factors had a stronger influence predicting substance use resilience compared to more distal factors. Proximal factors related to self-regulation and involved in the behavioral undercontrol pathway to substance use problems (e.g., Zucker et al., 2011)—reactive control and externalizing behaviors—showed particularly strong associations with substance use resilience versus risk. Marriage also appeared to be strongly associated with resilience. Although results from the present study provide the strongest support for proximal influences on substance use resilience during the transition to adulthood among FH+ youth, examining early predictors is also important. Examining psychosocial predictors between the ages of 12-14 years old, around the average age of onset for drinking and drug use (Wong et al., 2006), may help identify early risk and protective factors. Because they occur prior to heavy substance use, these factors are potentially the most malleable to prevention efforts aimed at reducing the risk for later substance use problems. In sum, identifying both distal and proximal predictors of substance use resilience may help inform prevention and intervention programs to reduce the risk for the development of problematic substance use among this vulnerable population.

Identification of Resilient and Risk Groups

The present study used an innovative approach to define resilient and risk groups, through advanced trajectory analysis and cut-off points for high levels of use derived from previous studies on binge drinking (Schulenberg et al., 1996a) and marijuana use (Schulenberg et al., 2005). Although approximately 80% of youth in the present study were classified as low binge drinkers and approximately 70% classified as low marijuana users, more stringent classification criteria having a family history of SUDs, no occasions of weekly binge drinking, and no monthly marijuana use resulted in a final sample of 84 participants identified as resilient. This is compared to 151 participants in the risk group. It may appear that low binge drinking and marijuana use groups identified in the present study comprised a larger percentage than comparable groups identified in the national MTF sample discussed in Chapter 2, and described in previous studies using MTF data (Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 2005). However, participants in the present study reported an overall greater level of use—approximately 50 days a year—compared to the MTF low binge group—approximately 13 days a year. Likewise, the high binge drinking group in the MLS sample was smaller than the MTF sample but showed a much higher rate of use. These differences are likely due to the MLS sample being initially recruited in relation to parental AUD. Low and high marijuana use trajectories were more similar to national rates among participants in the MTF survey. In the MLS sample, approximately 71% of youth were in the low use group, reporting around 1-2 occasions during the past year, and 11% were in the moderate use group, reporting around 6-19 occasions during the past year. Use trajectories among MLS participants did not follow the same developmental pattern as found among MTF participants. However, combining the low and moderate groups from the MLS sample produced a similar percentage of low to moderate users as found in the MTF sample (approximately 82% low marijuana users). Occasions of marijuana use were more similar between MTF and MLS samples for high use groups, although there were a greater number of high users among MLS participants. Resilient and risk group categorizations developed in the present study set the stage for future studies to focus on more comprehensive approaches to identify and study off-diagonal substance users.

Comparisons Between Resilient and Risk Groups

In relation to concepts of resilience and risk within a developmental psychopathology perspective, distal and proximal influences contribute the etiology and course of substance use (Dodge et al., 2009; Schulenberg et al., in press). Although having a family history of SUD is a strong risk factor for developing substance use problems, not all FH+ youth experience this risk outcome. Multiple, often complex, processes contribute to whether or not offspring go on to have SUDs themselves. Furthermore, resilience and risk processes may act individually or additively in their influence on developing SUDs (Cicchetti & Rogosch, 1999). The present study addressed these complexities both through mean level analyses and hierarchical multivariable logistic regression models that accounted for the influence of functioning in early adolescence, late adolescence, and young adulthood.

Major findings from mean level analyses were that the resilient group showed significantly greater reactive control and lower levels of externalizing behaviors in early adolescence compared to the risk group. Examining reactive control and externalizing behaviors through hierarchical multivariable logistic regression analyses revealed, however, that only reactive control and externalizing behaviors during late adolescence significantly distinguished between resilient and risk groups. Thus, the hypothesis that these resilient youth would have a greater extent of reactive control and lower level of externalizing behaviors compared to high substance using FH+ youth was supported. These findings suggest that higher reactive control and lower externalizing problems more proximal to the transition to adulthood may be stronger indicators of substance use resilience among vulnerable youth. Both reactive control and externalizing behaviors are involved in self-regulation pertaining to impulsive responding (Wong et al., 2006). Results from the present study lend support to the notion that dual-systems models of risk-taking may not fully account for individual differences in inhibitory control and reward responsivity among youth (e.g., Harden & Tucker-Drob, 2011; Pfeifer & Allen, 2012; Quinn & Harden, 2013). Higher levels of inhibitory control may be protective among youth with a family history of SUD. Considering that family history of SUD is associated with greater likelihood for externalizing problems (Zucker et al., 2011), both resilient and risk FH+ groups may have elevated levels of externalizing problems in relation to FH- youth. Inhibitory control may be the key differentiator between these vulnerable groups. Thus, strengthening inhibitory control, and self-regulation more broadly, among FH+ may be a beneficial approach to reduce substance use risk.

Another noteworthy finding pertains to resiliency. Unlike in early adolescence, resilient youth had significantly greater mean levels of resiliency in late adolescence compared to risk youth. This relationship was not found in multivariable results, however. As stated previously, the term "resilience" describes the low drinking trajectory group in the present study that is also characterized as FH+ for SUDs. This form of resilience relates to the notion of positive adaptation to adversity through the theoretical framework of developmental psychopathology (e.g., Luthar et al., 2006; Masten, 2001). Resiliency, however, is defined as the ability to adapt self-control flexibly in response to different environmental contexts (e.g., Eisenberg et al., 2003; Wong et al., 2006). Interestingly, resilient youth had lower mean levels of resiliency than risk youth in early adolescence, although this difference was not statistically significant. Then in late adolescence, differences in resiliency between resilient and risk groups reached statistical significance, with higher mean levels in the resilient group. Although resiliency did not maintain significance in hierarchical multivariable logistic regression analyses accounting for other factors in the model, resilient youth appear to increase resiliency into late adolescence compared to risk youth. Since substance use also tends to increase during adolescence, due to factors such as a greater extent of peer socializing and identify exploration (Schulenberg et al., 2014), a heightened capacity for resiliency may help resilient FH+ youth regulate impulsive responding in contexts involving opportunities for substance use. This is valuable information for substance use prevention and intervention efforts, considering the important role of social contexts in which substance use is more prevalent during the transition to adulthood (e.g., college; Schulenberg & Zarrett, 2006).

Despite the positive association between sensation seeking and substance use problems (e.g., Brook et al., 2011; Flory et al., 2004; Malmburg et al., 2010; Schulenberg et al., 1996b), sensation seeking did not differ significantly between resilient and risk groups during early or late adolescence in neither mean level analyses nor multivariable analyses. Although mean levels of sensation seeking were lower among resilient youth, they did not significantly differ from the risk group in relation to mean differences or in hierarchical multivariable logistic regression models. Resilient and risk youth may have a similar propensity for risk-taking behavior due to the fact that both groups share a family history of SUD. While greater sensation seeking may be shared vulnerability among resilient and risk groups, greater reactive control and lower externalizing behavior may be a unique characteristic of resilient youth. It is possible, then, that resilient youth may not express risk-taking through substance use but through more prosocial outlets. Additional research is needed to examine differences in positive versus negative risk-taking behaviors between resilient and risk youth.

Internalizing behaviors, during both early and late adolescence, were also non-significant between resilient and risk groups in all regression models. Support for the internalizing pathway to SUDs, in comparison to the externalizing pathway, has been mixed (e.g., Hussong et al., 2011; King et al., 2004; O'Niell et al., 2011). One possible reason for the stronger influence of externalizing behaviors on substance use is that processes involved in externalizing and internalizing pathways to SUDs may overlap (Colder et al., 2013). There is often high comorbidity between internalizing and externalizing behaviors among substance using youth, and it has been suggested that the effects of internalizing behaviors on substance use may be more difficult to identify in relation to more robustly associated externalizing behaviors (Hussong et al., 2011). Indeed, results from the present study show that correlations between internalizing and externalizing behaviors during early and late adolescence were relatively high. Externalizing problems may even moderate or mediate the relation between internalizing symptoms and substance use (Scalco et al., 2014). Thus, additional research is needed to test how interactions between internalizing and externalizing symptoms may contribute to substance use resilience.

Building upon prior research linking substance use risk with social roles (e.g., Staff et al., 2010), marriage appears to exert a strong effect on substance use resilience. This finding is supported by previous literature showing "the marriage effect" to decrease substance use (e.g., Leonard & Rothbard, 1999). Interestingly, the present study did not find significant differences between resilient and risk groups in terms of college enrollment and graduation or parenthood. In some ways, however, this is not entirely unexpected. For example, college students are more likely to engage in binge drinking and report only somewhat lower levels of marijuana use compared to non-college attending peers (Johnston et al., 2015). In relation to parenthood, non-significant differences between resilient and risk groups may pertain to the relatively high number of males in the MLS sample. Parenthood is not associated with the same declines in substance use for men as compared to women (Staff et al., 2010). The relation between parenthood and substance use risk may also depend on whether or not the parent is residing with their child (Staff et al., 2010). These factors should be considered in future analyses linking social roles, such as parenthood, with substance use resilience and risk.

Strengths and Limitations

Major strengths of the present study include its depth in measures used to assess resilience, the sample being enriched for family history of SUDs, and longitudinal design. An additional strength was combing a trajectory modeling approach (i.e., GMM) and a data-driven approach (i.e., high-use cut offs established in prior literature) to provide more comprehensive and accurate groupings of resilient and risk groups. Limitations of this study, however, are its small sample size and limited generalizability due to the sample consisting primarily of white males. Yet, in many ways this sample is appropriate, given that white males and FH+ youth are at heightened risk for substance use problems (Johnston et al., 2015; Zucker, 2014, respectively). An additional limitation is that using family history of FH+ alone as a marker for substance use vulnerability contributes to a narrow definition of resilience versus risk. Studies are needed to test more comprehensive characteristics of resilience. For example, resilient youth in the present study may express other risk behaviors that were not measured, such as risky sexual behavior and risky driving. Another important limitation pertains to endogeneity, in that causal relations among variables were not assessed. Therefore, it is difficult to determine if the predictors examined in this study contributed to resilience or if resilient youth may have been more likely to express certain characteristics through a potential third variable confound. Future research is needed, perhaps through cross-lagged modeling, to test these possibilities. Additionally, the present study did not focus specifically on promotive factors of resilience. In line with developmental psychopathology theory positing that resilience should be assessed in relation to risk (e.g., Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000), measures included in the present study were factors associated with both low and high substance use. For example, a greater extent of sensation seeking is positively associated with chronic high levels of substance use and negatively associated with persistently lower levels substance use (e.g., Brook et al., 2011; Flory et al., 2004; Malmburg et al., 2010; Schulenberg et al., 1996b). Other factors more directly involved with resilience should be assessed by future studies in order to identify specific mechanisms of low substance use among FH+ youth.

Conclusions

In sum, the present study gives due attention to an understudied yet clinically important off-diagonal substance use group—youth with a family history of SUD who remained resilient to heavy substance use through the transition to adulthood. Findings indicate important distal and proximal factors that may uncover mechanisms underlying this resilience, including those related to self-regulation and contextual changes occurring during the transition to adulthood. Specifically, higher levels of reactive control and lower levels of externalizing behaviors during late adolescence, which were more proximal to substance use during the transition to adulthood, appeared to most strongly distinguish resilient and risk groups. Furthermore, marriage was a strong predictor of substance use resilience during the transition to adulthood. Taken together, examining predictors of resilience may be useful for strategies to promote adaptive functioning among vulnerable youth. In particular, strategies resilient youth used earlier in development to maintain low substance use through the transition to adulthood may be strengthened in order to promote continued resilience.

Chapter 4

Neural function associated with substance use resilience among vulnerable youth

The transition to adulthood is an important developmental period in relation to substance use risk (Schulenberg & Maggs, 2002; Schulenberg et al., 2004). On average, rates of use for alcohol and marijuana—the most commonly used drugs in the U.S.—peak during this time (Johnston et al., 2015). The transition to adulthood also coincides with the onset of substance use disorders (SUDs) among some youth (Substance Abuse and Mental Health Services Administration, (SAMHSA), 2015). Due in part to genetic factors and environmental context, a strong risk factor for substance use problems is having a family history of SUD (FH+; e.g., Lieb et al., 2002; Zucker et al., 2014). Yet, a proportion of FH+ youth do not go on to experience substance use problems (e.g., Carle & Chassin, 2004; Heitzeg et al., 2008). In other words, these off-diagonal youth are resilient. Broadly, resilience describes the ability to avoid a pathological outcome, or achieve a successful one, despite experiencing adversity (Masten et al., 1990; Rutter, 1987). Although studying risk factors for substance use problems is valuable to target individuals who may benefit most from prevention and intervention programs, factors pertaining to resilience may be equally beneficial by identifying important protective mechanisms (Hurd & Zimmerman, in press; Schulenberg & Maggs, 2002). However, the majority of studies within the field of substance use research focus on risk groups. An additional gap in the literature is that few studies have examined multi-level processes involved in both risk and resilience, particularly among vulnerable youth (i.e., FH+ youth). Developmental psychopathology theory posits that examining multiple domains and levels of analysis is vital to study mechanisms involved in resilience and risk (Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000). Indeed, multiple biopsychosocial factors are involved in the etiology and course of substance use through the transition to adulthood (Cicchetti & Rogosch, 1999; Hussong et al., 2011; Schulenberg et al., in press; Zucker, 2014). To address this deficit, the overall purpose of the present study was to examine both psychosocial and neural function associated with resilience versus risk among FH+ youth.

Neural Processes of Inhibitory Control and Reward Responsivity Involved in Substance Use Resilience and Risk

The present study focused on psychosocial and neural processes related to the behavioral undercontrol/disinhibition pathway to substance use problems (Zucker et al., 2011), and more specifically, dual-systems models of risk-taking (Casey et al., 2008; Dahl, 2004; Luna et al., 2015; Somerville et al., 2010; Steinberg, 2010), described in greater detail below. The behavioral undercontrol/disinhibition pathway has also been referred to as an externalizing risk phenotype for SUDs, characterized by impulsive and antisocial behaviors (Babor et al., 1992; Cloninger et al., 1996; Zucker, 1987, 1994). Behavioral undercontrol describes the inability, unwillingness, or failure to inhibit behaviors despite negative consequences associated with those behaviors (Hawkins et al., 1992; Kandel, 1978; Zucker, 2006). Whereas behavioral undercontrol describes psychosocial deficits in self-regulation pertaining to substance use, disinhibition refers to underlying neural processes involved in behavioral control.

Neural processes associated with disinhibition pertain to dual-systems models of risk-taking. Dual-systems models of risk-taking posit that heightened risk behaviors during adolescence and early adulthood are attributable to a developmental mismatch between two brain systems—later maturing cortical brain regions involved in cognitive control and earlier developed subcortical brain systems associated with reward responsivity (Casey et al., 2008; Dahl, 2004; Luna et al., 2015; Shulman et al., 2015; Somerville et al., 2010; Steinberg, 2010).

Cortical brain regions associated with self-regulatory processes refer primarily to areas within the prefrontal cortex (PFC). Multiple developmental changes occur in the PFC pertaining to dual-systems models of risk-taking. One of those changes involves synaptic pruning. Synaptic pruning describes a neurodevelopmental processes in which unnecessary synapses are eliminated (Chambers et al., 2003; Huttenlocher & Dabholkar, 1997). Synaptic pruning is evident by decreases in grey matter density in the PFC from adolescence through early adulthood (Giedd, 2004; Gogtay et al., 2004; Sowell et al., 2004). However, grey matter reductions in subcortical brain regions occur earlier in development. By improving the efficiency of PFC function, synaptic pruning is associated with age-related gains in cognitive control (Steinberg, 2008). This differential progression of synaptic pruning indicates delayed maturation in the PFC, and thus, a lower capacity for cognitive control in relation to reward related processing. Whereas synaptic pruning contributes to decreases in grey matter, myelination is associated with linear increases in white matter through early adulthood (Gogtay et al., 2004). By insulating nerve fibers in a fatty white sheath, myelination improves connectivity between cortical and subcortical brain regions (Luna et al., 2015). Therefore, neural regions involved in cognitive control can better regulate reward driven behaviors deriving from subcortical brain activity.

Remodeling of the dopaminergic system involved in reward responsivity is also relevant to dual-systems models of risk-taking. Dopamine plays a key role in learning and prediction of rewards (Casey, 2014), including the reinforcing attributes of drugs of abuse (Robinson & Berridge, 2001). In early adolescence, the density of dopamine receptors peaks in the ventral striatum (VS). Not until early adulthood, however, does dopamine receptor density reach similar levels in the PFC (Spear, 2000). Dopaminergic projections between the VS and the PFC thereby influence cortical regions' capacity for self-regulation in response to rewarding stimuli (Grace et al., 2007). The nucleus accumbens (NAcc), which is located in the VS, is particularly sensitive to rewarding stimuli. From a developmental perspective, adolescents have been found to show heightened NAcc response to rewarding outcomes compared to both children and adults (Galvan et al., 2006; Heitzeg et al., 2014).

While a useful heuristic to understanding why adolescents and young adults are often disproportionately susceptible to risk behaviors compared to other age groups, dual-systems models of risk-taking tend to focus on whole population averages (e.g., Casey et al., 2008; Steinberg, 2010). By doing so, they often fail to account for individual differences in neural function and risk taking among youth (Harden & Tucker-Drob, 2011; Pfeifer & Allen, 2012; Quinn & Harden, 2013). This may be particularly relevant to youth who share the same vulnerability but different developmental outcomes (i.e., FH+ resilient and risk groups). Thus, the first aim of the present study was to examine differences in neural function associated with inhibitory control and reward responsivity between these resilient and risk groups. This study expands upon developmental trajectory analyses conducted in Chapter Three that identified a subgroup of off-diagonal, resilient FH+ youth and a more expected risk group of high substance using FH+ youth. To conduct these analyses, two neuroimaging tasks were used to test brain function associated with inhibitory control and reward, respectively—the Go/No-Go task and the Monetary Incentive Delay Task (MIDT).

The Go/No-Go task is a widely used, well-validated measure used to assess inhibitory control through response inhibition (Durston et al., 2002). As discussed previously, PFC function is particularly relevant to inhibitory control. Inhibitory control describes the ability to inhibit a prepotent response (Ivanov et al., 2008; Whelan et al., 2012). Existing research using response inhibition tasks, such as the Go/No Go task used in the present study, indicates improved performance with age and positive associations between task performance and PFC activation (e.g., Cragg & Nation, 2008; Durston et al., 2006). Even among individuals of the same age range, however, there may be variability in PFC function. An example of this individual variability pertains to deficits in inhibitory control that contribute to substance use risk among some individuals (Heitzeg et al., 2015). For example, Norman et al. (2011) found blunted neural activation in brain regions involved in inhibitory control, including the PFC, during a Go/No-Go task among substance naïve early adolescents who became heavy drinkers four years later. Mahmood et al. (2013) found similar results among a sample of late adolescent substance users by identifying an association between decreased ventromedial PFC activation during a Go/No-Go task and a greater number of SUD symptoms 18 months later at follow-up.

Youth with a family history of SUD may be particularly vulnerable to deficits in PFC function related to inhibitory control. Using a longitudinal study design, Hardee et al. (2014) compared neural activation during a Go/No-Go task between FH+ youth and matched controls without a family history of SUD (FH- youth). One particularly striking finding was that although inhibitory control improved with age for both groups, FH+ youth showed no significant developmental changes in middle frontal gyrus (MFG) and caudate activation compared to FH- youth. The present study goes beyond intergroup comparisons between FH+ and FH- groups by assessing the extent to which inhibitory control may differ between resilient and risk groups of FH+ youth. In doing so, neural markers of resilience among this vulnerable population may be identified.

In addition to the Go/No-Go task, the MIDT was used in the present study to measure reward responsivity. The MIDT is a well-validated task designed to measure neural response to monetary incentives (Knutson et al., 2001). This task measures neural activation in response to the anticipation of rewards or losses, as well as to the receipt of rewards or losses. Activation in the VS, including the NAcc, is robustly associated with the anticipation of monetary rewards during the MIDT (Knutson et al., 2001). For example, Heitzeg et al. (2014) found heightened NAcc activation to reward anticipation during the MIDT among adolescents compared to both children and young adults. Furthermore, this study revealed an association between greater NAcc activation and later alcohol problems, even after accounting for lifetime drinking. In a study examining VS functioning among FH+ youth compared to matched controls, the FH+ group showed blunted NAcc activation during reward anticipation trials of the MIDT (Yau et al., 2012). FH+ youth in this sample were also found to have a greater extent of externalizing problems, suggesting a link between reward responsivity and aggressive and delinquent behaviors. Interestingly, this study also included a resilient group of FH+ youth categorized as light drinkers. FH+ light drinkers showed reduced NAcc response to reward anticipation trials of the MIDT and fewer externalizing behaviors compared to both heavier drinking FH+ youth and controls. The present study, however, provides an even more comprehensive classification of resilience, by including family history of both alcohol and drug use disorders and using developmental trajectory analyses of binge drinking and marijuana use to form resilient and risk groups.

Reactive Control and Externalizing Behaviors Associated with Substance Use Risk and Resilience

A deficit in existing literature is the extent to which neural measures involved in inhibitory control and reward responsivity predict substance use resilience versus risk over and above psychosocial measures. Failing to account for multi-level predictors of substance use resilience is problematic, considering the multiple domains associated both with substance use risk more broadly (Schulenberg et al., in press) and resilience among vulnerable youth (Hurd & Zimmerman, in press). Furthermore, a developmental psychopathology perspective stresses the importance of accounting for multiple levels of analysis when studying processes involved with risk and resilience (Drabick & Steinberg, 2011). To provide a more comprehensive analysis of multiple domains of functioning and levels of analysis related to substance use during the transition to adulthood among FH+ youth, the second aim of the present study builds upon Chapter Three. The central focus of this aim was to examine neural predictors of resilience versus risk, accounting also for distal and proximal psychosocial measures of behavioral undercontrol.

As with neural processes of inhibitory control and reward responsivity, psychosocial predictors of reactive control and externalizing behaviors are associated with the behavioral undercontrol/disinhibition pathway to SUDs (Zucker et al., 2011). Behavioral undercontrol is associated with two related yet distinct psychosocial constructs—reactive control and externalizing behaviors. Reactive control describes impulsive responding to immediate rewards (Eisenberg et al., 2003), and is based on Block and Block's (1980) construct of ego control. Ego control measures self-regulation of emotional, impulsive responding. Thus, reactive control is a relatively automatic, involuntary action. Individuals characterized by low reactive control (i.e., reactive undercontrol) are sensitive to immediate gratification and rewarding stimuli and therefore at heightened risk for substance use problems (e.g., Wong et al., 2006). Due to this characteristic, reactive undercontrol is associated with subcortical neural regions involved in “bottom-up” processing (Heitzeg et al., 2008). A greater capacity for reactive control reflects cortical “top-down” processing to suppress impulsive responding.

In addition to reactive control, externalizing problems, which include acting out through aggressive behavior or delinquency, were also included in the present study. Due to the influence of earlier externalizing problems on later substance use (e.g., Zucker et al., 2011), both distal and proximal measures were used in the present study. Existing literature has shown a robust association between externalizing behaviors and substance use (e.g., Krueger et al., 2007). This is likely due in part to youth with externalizing behavior problems having an increased likelihood of associating with more deviant peers who endorse greater social acceptance of substance use (Brook et al., 2011; Dodge et al., 2009).

Although reactive control and externalizing behaviors are related to self-regulation, these factors are distinct predictors of substance use risk. For example, Wong et al. (2006) found a significant association between low behavioral control and heightened substance use among a sample of youth with parental alcohol use disorder, even after controlling for externalizing behaviors. Therefore, the present study measured both reactive control and externalizing problems to examine the contribution of each of these mechanisms underlying substance use risk versus resilience. Because of their associations with neural processing involved in inhibitory control and reward responsivity, examining reactive control and externalizing behaviors advances existing work related to dual-systems models of risk-taking. Assessing both psychosocial and neural mechanisms related to these models may be particularly beneficial to studying off-diagonal subgroups who may not show expected patterns of risk (i.e., resilient youth). In other words, multidimensional measures are important to identify predictors of off-diagonal substance use.

Research Questions and Hypotheses

The main purpose of the present study involved two main aims: 1) Compare neural function involved in inhibitory control and reward responsivity between a resilient, off-diagonal group of low substance using FH+ youth and a risk group of high substance using FH+ youth; and 2) Use a multi-level approach integrating psychosocial and neural measures to examine the extent to which neural function involved in inhibitory control and reward responsivity predict resilient or risk over and above the influence of psychosocial measures of reactive control and externalizing behaviors. To achieve these aims, psychosocial predictors were assessed both distally when substance use often begins among FH+ youth (Wong et al., 2006) and more proximally at the beginning of the transition to adulthood when substance use peaks (Johnston et al., 2015) and disordered use tends to emerge (Windle & Zucker, 2010). Thus, distal measures were from early adolescence, assessed between the ages of 12 and 14, and proximal measures were from late adolescence, assessed between the ages of 17 and 18. Due to relatively consistent and stable patterns of substance use among resilient and risk groups, neuroimaging data was assessed in late adolescence, coinciding with the beginning of the transition to adulthood. Measures included in the present study are shown in Table 1.

Research questions guiding these analyses were: (1) Do youth categorized as resilient versus risk differ in relation to neural function associated with inhibitory control?; (2) Do youth categorized as resilient versus risk differ in relation to neural function associated with reward responsivity?; (3) Do neural mechanisms involved in inhibitory control predict substance use resilience versus risk over and above distal and proximal psychosocial measures of reactive control and externalizing behaviors? Because having a family history of SUD is a risk factor for disinhibition related to substance use risk (Zucker et al., 2011) and greater cognitive control helps regulate reward responsivity (Casey, 2014), resilient and risk groups were hypothesized to differ in terms of neural function associated with inhibitory control and reward responsivity. Thus, compared to the risk group, resilient youth were hypothesized to have greater neural activation in cortical brain regions involved in inhibitory control and lower neural activation in subcortical brain regions involved in reward responsivity. Relatedly, when adding neural function to psychosocial measures of reactive control and externalizing behaviors, neural activation related to inhibitory control and reward responsivity were expected to differ in the same direction between resilient and risk groups.

Methods

Participants and Procedures

Participants were 57 youth (71.93% male; 96.49% White; 50.88% with one parent with SUD; and 49.12% with two parents with SUDs) from the Michigan Longitudinal Study (MLS), an ongoing, prospective study of community-recruited youth from families at high risk for SUD and a contrast sample of families without SUD (Zucker, 2000). Family history of SUD was defined as having a biological father and/or mother with a diagnosis of any alcohol or drug use disorder assessed by a clinical psychologist using the Diagnostic Interview Schedule—Version 4 (DIS-IV) (Robins et al., 2000). The MLS has maintained contact with approximately 90% of all still-living participants, both parents and offspring.

The 57 participants included in the present study were selected as resilient and risk groups from Chapter Three and who participated in the neuroimaging component of the MLS. Children who exhibited signs of fetal alcohol syndrome (FAS) were excluded from study enrollment (Loukas et al., 2001; Sokol & Clarren, 1989). Additional exclusion criteria included being left-handed or ambidextrous, determined by the Edinburgh Handedness Inventory

(Oldfield, 1971); neurologic, acute, uncorrected, or chronic medical illness; treatment with psychoactive medication within the past 6 months; history of psychosis or schizophrenia in a first degree relative; and presence of Axis I psychiatric or developmental disorders, except for conduct and attention-deficit/hyperactivity disorders (ADHD) or prior SUD, as these disorders would eliminate participants at high risk for SUD. The DIS-IV was used to determine diagnosis.

All female participants underwent a urine pregnancy test immediately prior to the scan; pregnancy was exclusionary. All participants were instructed to abstain from alcohol and illicit substances and, if applicable, stop taking medication for ADHD at least 48 hours prior to scanning. Participants were given a multi-drug 5-panel urine screen before scanning. Due to THC metabolites being detectable in urine for a week or longer, participants who tested positive for marijuana but self-reported abstinence within 48 hours prior to the scan were not excluded from the study. Self-reported marijuana use within this timeframe and/or a positive test for alcohol and other drugs not including marijuana were exclusionary. All participants provided informed consent approved by the University of Michigan Medical School Institutional Review Board.

Measures

Substance use. Binge drinking was measured by the Drinking and Drug History questionnaire (Zucker et al., 1990) by the number of days in the past year participants reported consumed five or more standard drinks of beer, wine, or liquor. Marijuana use was measured by the Drinking and Drug History questionnaire through a single item, “On how many occasions (if any) have you used marijuana (grass, pot, weed, ganga) or hashish (hash, hash oil) during the past year?” Response options were on a scale of 0 = Never, 1 = 1 to 2 occasions, 2 = 3 to 5 occasions, 3 = 6 to 9 occasions, 4 = 10 to 19 occasions, 5 = 20 to 39 occasions, 6 = 40 to 99 occasions, 7 = 100 to 249 occasions, 8 = 250 to 499 occasions, or 9 = 500 or more occasions.

Sociodemographic characteristics. Sociodemographic measures were gender and number of parents diagnosed with a SUD. Gender was coded as 1= male or 0 = female. Number of parents diagnosed with a SUD was coded as whether one or two biological parents were diagnosed with a SUD based on DIS-IV lifetime criteria for alcohol or drug use disorder.

Reactive control. Reactive control was measured by modified versions of the clinician-administered California Child Q-Sort (CCQ; Block, 1980) when participants were 12 to 14 years old (early adolescence) and the Revised Adult California Q-Sort (CAQ; Block, 1980) when participants were 17 to 18 years old (late adolescence). Both the CCQ and CAQ are based on the California Q-Sort, which included 100 statements of various behavioral adaptations sorted by a clinician on a scale from 1 = "extremely uncharacteristic" to 9 = "extremely characteristic" of the participant. Reactive control scores are means of item totals. Higher scores signified a greater extent of reactive control. Reactive control was measured by Q-sort items modified by Eisenberg and colleagues (1996; 2003). In early adolescence, 14 items ($\alpha = 0.81$) were selected based on Eisenberg et al. (2003)'s scale. Sample items included "Is inhibited and constricted" and "Is reflective; deliberates before speaking or acting." In late adolescence, 12 items ($\alpha = 0.81$) were selected to measure reactive control. Example items include "Unable to delay gratification" and "Is self-indulgent".

Externalizing behaviors. In early adolescence, self-reported externalizing behaviors were assessed by the YSR (Achenbach, 1991). Externalizing behaviors were measured by the sum of 30 items from two externalizing subscales—aggressive behavior and delinquency. Self-reported behaviors were based on rating the accuracy of statements on a 3-point scale where 0 = "not at all true", 1 = "somewhat true", and 2 = "very true" (α = 0.85). Sample items include "I disobey at school" (aggressive behavior) and "I hang around with kids who get in trouble" (delinquency). In late adolescence, externalizing behaviors were measured by the sum of three externalizing subscales—aggressive behavior, rule breaking, and intrusiveness. These subscales consisted of 35 items with responses on a 3 point scale where 0 = "not true", 1 = "somewhat or sometimes true", and 2 = "very true or often true" (α = 0.80). Sample items include "I blame others for my problems" (aggressive behavior), "I break rules at work or elsewhere" (rule breaking) and "I tease others a lot" (intrusiveness). The externalizing subscales used on the YSR during early adolescence were used on the ASR during late adolescence, with age-appropriate modifications. Due to trajectory class groupings formed on the basis of binge drinking and marijuana use, items on the YSR and ASR pertaining to substance use were removed from the delinquency subscale items 105 on the YSR and 90 on the ASR ("I use alcohol or drugs for non-medical purposes" and "I drink too much or get drunk", respectively).

fMRI Paradigms

Go/No-Go task. An event-related fMRI Go/No-Go task (Durston et al., 2002; Hardee et al., 2014; Heitzeg et al., 2014) was used to measure BOLD (blood oxygen level dependent) response associated with inhibitory control. A schematic illustration of the Go/No-Go task is shown in Figure 6. Participants were instructed to respond as quickly and accurately as possible to target stimuli (letters other than "X") by pressing a button but not to press a button during infrequent non-target stimuli ("X"). Target stimuli were categorized as Go trials and non-target stimuli were categorized as No-Go trials. Stimulus duration lasted 500 ms, followed by 3500 ms of a fixation cross. There were a total of 5 runs of 49 trials, each lasting 3.5 minutes and containing 11, 12, or 13 No-Go trials for a total of 60 No-Go trials out of 245 total trials. No-Go trials were preceded by 1, 3, or 5 Go trials. The distribution of parametric manipulation was split evenly among No-Go trials (20 trails for each condition). Behavioral performance measures included false alarm rates (incorrect response during a No-Go trial), hit accuracy (correct response to targets), and hit reaction times to targets. Prior to scanning, participants completed a practice session of 49 trials on a desktop computer. In order to focus on inhibitory control, analyses in the present study were conducted using the contrast for correct inhibition (correct No-Go trials) versus baseline trials. Data from scan 1 or 2 of the Go/No-Go task were used depending on the age at time of scan that most closely aligned with the first age used in trajectory analyses to determine resilient and risk groups (ages 17–18).

Monetary Incentive Delay Task (MIDT). To assess neural response during anticipation of monetary reward, participants performed a modified version of the MIDT (Heitzeg et al., 2014; Knutson et al., 2001; Yau et al., 2012). A schematic illustration of the MIDT is shown in Figure 7. For each trial, participants first saw an incentive cue for 2000 milliseconds (ms), indicating whether on that trial they could win \$5.00 (large reward), lose \$5.00 (large loss), win \$0.20 (small reward), or lose \$0.20 (small loss), or no money was at stake (neutral condition). They then saw a white fixation cross for 2000 ms (*fixation*), followed by a variable-duration target (*target*), during which they were instructed to press a button as quickly as possible. Pressing the button while the target was on the screen signified a correct response. Finally, participants were shown feedback indicating whether they won money, failed to win money, lost money, avoided losing money, or no money was at stake (*feedback*). Participants received any money won during the MIDT in addition to fixed participation rates. Data from scan 1 or scan 2 of the MIDT were used depending on the age at time of scan that most closely aligned with the first age used in trajectory analyses to determine resilient and risk groups (ages 17 – 18).

The duration of the target screen was determined for each participant during a brief training session immediately preceding the scan. At the conclusion of training sessions, mean reaction time was recorded. Target duration ranged from 200–300 ms and was adjusted so that each participant would achieve approximately 60% accuracy (“hit accuracy”). Simulations were conducted using AFNI’s 3Deconvolve to examine the covariance between anticipation and receipt. These simulations showed colinearity between anticipation and receipt ranged between $r = 0.10$ and $r = 0.24$, which is within acceptable levels ($r < 0.30$). In order to focus on reward responsivity, analyses in the present study were conducted using the contrast for 1) reward anticipation–combined large and small reward cue anticipation (reward anticipation) > neutral cue anticipation (neutral anticipation) trials; and 2) receipt of reward—combined large and small reward positive feedback (CRPF) > combined large and small reward negative feedback (CRNF) trials. Positive reward feedback occurred if participants won money, whereas negative reward feedback occurred if participants failed to win money.

fMRI Acquisition

Participants were scanned using a 3.0 Tesla GE Signa scanner (GE Healthcare). Whole-brain blood oxygen level-dependent (BOLD) images were acquired using a T2*-weighted single-shot combined spiral in/out sequence (Glover and Law, 2001; repetition time [TR] = 2000 ms; echo time [TE] = 30 ms; flip angle = 90°; field of view [FOV] = 200 mm; 64 × 64 matrix; in plane resolution = 3.12 × 3.12 mm^2; slice thickness = 4 mm). For spatial normalization, a high-resolution anatomical T1-weighted scan was obtained (TR = 25 ms; minimum TE; FOV = 25 cm; 256 × 256 matrix; slice thickness = 1.4 mm). Foam padding around the head secured with a forehead strap minimized participant motion. During the informed consent process and prior to scanner entry, participants were instructed to remain still during scanning. Participant head motion was corrected using the FSL 5.0.2.2 analysis tools library (Analysis Group, FMRIB, Oxford, UK); slice-acquisition timing was corrected using SPM8 (Wellcome Institute of Cognitive Neurology, London, UK). Each volume was compared to the previous volume for motion. Runs were excluded if they exceeded 3 mm translation, 3° rotation in any direction (movement 3mm in directions x, y, z or pitch, roll, or yaw), or two volumes showed a shift greater than 3mm. All remaining image processing was completed using SPM8. Functional images were spatially normalized to a standard stereotactic space as defined by the Montreal Neurological Institute (MNI). A 6 mm full-width at half-maximum Gaussian spatial smoothing kernel was applied to improve signal-to-noise ratio and account for individual anatomic differences.

Analytic Plan

The analytic plan for the present study involved four steps: (1) Identify resilient and risk groups based on developmental trajectory analyses, using both growth mixture modeling (GMM) and high versus low use classifications from existing binge drinking and marijuana use literature (Schulenberg et al., 1996a; Schulenberg et al., 2005); (2) Examine descriptive differences between off-diagonal, resilient youth and risk youth among the neuroimaging subsample of the MLS. Measures included sociodemographic characteristics, early adolescent factors (ages 12-14), late adolescent factors (ages 17-18), and task performance during the Go/No-Go task (inhibitory control versus baseline contrast) and MIDT (reward anticipation versus neutral contrast; positive versus negative reward feedback contrast); (3) Examine whole-brain task activation during the Go/No-Go task and MIDT among both resilient and risk groups in order to select ROIs for hierarchical multivariable logistic regression analyses[3]; (4) Examine between-group (resilient versus risk) differences in task activation in SPM during the Go/No-Go task and the MIDT tasks; (5) Conduct hierarchical multivariable logistic regression to examine the extent to which neural mechanisms of inhibitory control and reward responsivity predict resilient versus risk group membership over and above distal and proximal behavioral measures of reactive control and externalizing behaviors.

Step 1: Resilient versus risk group classifications. Resilient and risk groups were identified based on developmental trajectory analyses performed in Chapter Three. First, Latent Growth Modeling (LGM; Duncan & Duncan, 2004) was used to assess mean trajectories for both binge drinking and marijuana use among the entire sample population. Based on model fit criteria described in Chapter Three, the linear model provided the best fit for both binge drinking and marijuana use. GMM was performed to determine the most likely number of latent subgroups for binge drinking and marijuana use, examined separately. A three-class model fit the data best for both binge drinking and marijuana use GMM analyses. In addition to trajectory group membership estimates from GMM, additional criteria were used to provide more conservative trajectory class groupings. Frequent binge drinking was defined as consuming five or more drinks in a row at least once during the past week (Schulenberg et al., 1996a). Frequent marijuana use was defined as more than 20 occasions during the past year (Schulenberg et al., 2005). The risk group was classified as FH+ youth who reported frequent binge drinking and/or frequent marijuana use on at least two occasions over the five time points assessed. The presence of heavy binge drinking or marijuana use qualified as risky substance use. In relation to normative peaks in substance use through the transition to adulthood (Johnston et al., 2015),

[3] Although often used interchangeably, the terms multivariate and multivariable describe different analyses. Because multivariate analyses refer to analyses with two or more dependent variables (Hidalgo & Goodman, 2013), the term multivariable was used in the present study.

heavy use measured at one time point may not be a strong indicator of high risk. This classification criteria accounts for a more consistent and less developmentally limited extent of heavy substance use. In line with the aims of the present study, participants were included who met the following criteria: 1) categorized as FH+ risk or resilient groups based on the aforementioned criteria; and 2) participated in the neuroimaging subsample of MLS.

Step 2: Descriptive characteristics of resilient and risk groups. Frequencies and means for sociodemographic characteristics (gender and number of parents with SUDs), mean age at the time of the Go/No-Go task, mean age at the time of the MIDT, binge drinking, marijuana use, early adolescent (ages 12-14) reactive control and externalizing problems, late adolescent (ages 17-18) reactive control and externalizing problems, and fMRI task performance for the Go/No-Go task and MIDT were identified and compared between resilient and risk groups. Descriptive analyses were conducted using IBM SPSS Statistics 22.

Step 3: Between-group differences in task activation. To conduct fMRI whole-brain group analyses between the resilient and risk groups, two-sample *t*-tests were conducted in SPM for each Go/No-Go task and MIDT contrast of interest. For both the Go/No-Go task and MIDT, Type I error was controlled at $\alpha = 0.05$ by a statistical significance threshold of $p < 0.005$ (uncorrected for multiple comparisons) with a 77 voxel extent. This threshold was established based on simulation results generated by AlphaSim in AFNI (Cox, 1996). Extracted between-group differences in task activation were imported into SPSS for additional analyses.

Step 4: Whole-brain task activation. One-sample *t*-tests were completed in SPM to examine whole-brain activation associated with the contrasts of interest for the Go/No-Go task and MIDT. For the Go/No-Go task, three regressors of interest were convolved with the canonical hemodynamic response function. These included correct No-Go trials, failed No-Go trials, and Go trials. Remaining data not modeled into these three events was classified as the implicit baseline, as in DeVito et al. (2013) and Heitzeg et al. (2014). To examine neural function associated with inhibitory control, the main contrast of interest—correct inhibition versus baseline—was modeled. For the MIDT, regressors of interest for all events (cues: large reward, large loss, small reward, small loss, neutral; anticipation delay for each cue; positive outcomes for cue; negative outcomes for each cue) were convolved with the canonical hemodynamic response function. To examine neural function associated with reward responsivity, reward versus neutral anticipation and CRPF versus CRNF were modeled. For both the Go/No-Go task and MIDT, motion parameters and white matter signal intensity were modeled as nuisance regressors to remove residual motion artifacts and capture non–task-related noise, respectively. Clusters in areas of activation during contrasts of interests were considered significant if they reached a minimum family-wise error (FWE) corrected threshold of $p < 0.05$ with a voxel extent of 25. Beta values for significant areas of activation were extracted using MarsBaR (Brett et al., 2002) and then imported into SPSS for further analysis in hierarchical multivariable logistic regression models.

Step 5: Hierarchical multivariable logistic regression. Reactive control and externalizing behaviors, in addition to neural activation in ROIs identified through whole-brain task activation predicting substance use trajectory group (resilient versus risk) were examined using a series of hierarchical multivariable logistic regression models. Predictors of substance use groups were examined in temporal order, with step 1 of each model consisting of reactive control and externalizing behaviors from ages 12-14, controlling for sociodemographic characteristics, step 2 adding reactive control and externalizing behaviors during late adolescence, and step 3 adding neural activation involved in each contrasts examined in the Go/No-Go task and MIDT. Gender and number of parents with SUD were included. These variables are robustly associated with substance use risk (e.g., Johnston et al., 2015; Heitzeg et al., 2008, respectively). ROIs included in step 3 were determined by whole-brain task activation. To examine top-down processes involved in inhibitory control, hierarchical multivariable logistic regression models were tested with data from the correct inhibition versus baseline contrast during the Go/No-Go task. Due to the relatively small sample size included in the present study and to isolate the influence of each contrast of interest, each ROI was included individually in separate models. In the case of bilateral areas (i.e., left and right) of the same brain region, both left and right ROIs were included together in the model. Nagelkerke R^2 and the change in likelihood ratio test, as indicated by the model χ^2 test, were used to assess model fit at each step.

Results

Descriptive Characteristics of Resilient and Risk Groups

Comparisons between sociodemographic characteristics, substance use, early adolescent factors, and late adolescent factors between resilient and risk groups are shown in Table 16. Resilient and risk groups did not differ significantly on gender, number of parents with SUDs, mean age at the time of the Go/No-Go task, and mean age at the time of the MIDT. As expected, due to resilient and risk groups formed based on patterns of substance use, the resilient group showed significantly lower levels of both binge drinking and marijuana use from age 17 through 26 compared to the risk group. Among early adolescent factors, the resilient group showed significantly higher mean levels of reactive control and significantly lower mean levels of externalizing behaviors compared to the risk group. Among late adolescent factors, the resilient and risk groups did not differ significantly on reactive control, although the resilient group had a higher mean level compared to the risk group. The resilient group showed significantly lower mean levels of externalizing behaviors during late adolescence.

Go/No-Go Task Results

Task performance. Mean task performance for the Go/No-Go task is shown in Table 17. Results from independent samples *t*-tests showed no significant differences between resilient and risk groups in relation to hit accuracy, hit reaction time, and correct inhibition rate.

Between-group differences in task activation. Differences in brain activation during the Go/No-Go task between resilient and risk groups were examined through two-sample *t*-tests in SPM. Between-group analyses showed significant differences in activation between resilient and risk groups in four, frontal brain regions (Figure 8). Compared to the risk group, the resilient group showed significantly greater activation in the left middle orbitofrontal gyrus (midOFG), left superior frontal gyrus (SFG), right medial orbitofrontal cortex (mOFC), and left inferior frontal cortex (iFC).

Whole-brain task activation. Whole-brain task effects for the Go/No-Go task are provided in Table 18. Neural activation during the correct inhibition versus baseline contrast occurred in the right dorsolateral prefrontal cortex (DLPFC), right inferior orbitofrontal gyrus (iOFG), left MFG. Neural activation in each of these regions were then imported into SPSS to test in hierarchical multivariable logistic regression analyses predicting resilient versus risk group membership.

Hierarchical multivariable logistic regression. Correlations between all variables examined in hierarchical multivariable logistic regression models are shown in Table 19. Hierarchical logistic regression analyses were computed using three additive models (Table 20). Model 1 included reactive control and externalizing behaviors during early adolescence, with covariates of gender and number of parents with SUDs. No variables included in Model 1 were significant predictors of resilient versus risk group membership. Model 2 included all variables in Model 1 with the addition of late adolescent reactive control and externalizing behaviors. Results indicated that resilient youth were significantly less likely than the risk group to report externalizing behaviors in late adolescence. Nagelkerke R^2 indicated improved model fit over Model 1 and the model χ^2 was significant. Model 3, which added neural activation in the right DLPFC during the correct inhibition versus baseline contrast, showed that resilient youth were significantly more likely to report higher reactive control during adolescence, lower externalizing behaviors during late adolescence, and greater activation in the right DLPFC during the correct inhibition versus baseline contrasts. Nagelkerke R^2 indicated improved model fit over Model 2 and the model χ^2 was significant.

Two additional hierarchical multivariable logistic regression analyses were conducted with the same sociodemographic characteristics, early adolescent factors, and late adolescent factors included in Table 21 for Model 1, 2, and 3. In these additional analyses, however, Model 3 was revised to include, separately, the other ROIs found through whole-brain task activation during the correct inhibition versus baseline contrast of the Go/No-Go task. In analyses with activation in the right iOFG, Nagelkerke R^2 was 0.46 and model was significant (χ^2 = 15.88(7), $p < 0.05$). Results for Model 1 and Model 2 remained the same. In Model 3, the only significant predictor of substance use group was late adolescent externalizing behaviors. Resilient youth showed significantly lower levels of externalizing behaviors compared to the risk group (OR = 0.77, $p < 0.05$). There were no significant differences by substance use group in right iOFG activation (OR = 1.28, $p = 0.15$). In analyses that added activation in the left MFG to Model 3, Nagelkerke R^2 was 0.52 and model was significant (χ^2 = 18.39(7), $p < 0.05$). The only significant predictor of substance use group was late adolescent externalizing behaviors, with the resilient group reporting lower externalizing behaviors compared to the risk group (OR = 0.70, $p < 0.05$). Left MFG activation trended toward significance (OR = 1.48, $p = 0.06$) but did not reach a significant threshold of $p < 0.05$ to predict differences by substance use group.

MIDT results

Task performance. Mean task performance for the MIDT task is shown in Table 17. There were no significant differences between resilient and risk groups in relation to hit accuracy and hit reaction time for all trial types (reward, loss, neutral).

Between-group differences in task activation. Differences in brain activation during the MIDT reward anticipation and feedback contrasts between resilient and risk groups were then examined through two-sample *t*-tests in SPM. Correcting for multiple comparisons, between-group analyses indicated a significant difference in activation between resilient and risk groups during the reward anticipation versus neutral anticipation contrast (Figure 9). Relative to the risk group, the resilient group showed significantly lower activation in the left SFG. For the feedback contrast, the resilient group showed significantly lower activation in the left inferior parietal lobe (IPL) (Figure 10).

Whole-brain task activation. Whole-brain task effects for the MIDT, during contrasts focused on both reward anticipation and receipt, are shown in Table 18. Neural activation during the reward anticipation versus neutral contrast was found in left and right VS. The VS, specifically the NAcc, has been found to show robust activations in response to reward anticipation (Heitzeg et al., 2008). Left and right regions of the VS did not become differentiated until a family-wise error (FWE) corrected threshold of $p < 0.00005$ with a minimum voxel extent of 25 (Figure 11). During the feedback contrast, neural activation occurred in left and right VS.

Neural activations in each of these regions were then imported into SPSS to test in hierarchical multivariable logistic regression analyses.

Hierarchical multivariable logistic regression. Correlations between all variables examined in hierarchical multivariable logistic regression models are shown in Table 19. As with hierarchical multivariable logistic regression analyses using data from the Go/No-Go task, significant whole-brain activation during the MIDT was assessed as a predictor of substance use group membership over and above sociodemographic characteristics, early adolescent reactive control and externalizing behaviors, late adolescent reactive control and externalizing behaviors. As shown in Table 21, the addition of left and right VS activation during reward anticipation in Model 3 did not result in any significant predictors of substance use group membership. Nagelkerke R^2 = 0.36, which indicates decreased model fit compared to Model 2. In addition, model χ^2 was non-significant. Table 22 shows significant VS ROIs during feedback included in Model 3. Thus, neural activation in the left and right VS were added to Model 3. Neural activation in these regions did not significantly predict substance use group membership over and above sociodemographic characteristics, reactive control, and externalizing behaviors during early and late adolescence. Furthermore, no variables in Model 3 were significant predictors of resilience versus risk group. Nagelkerke R^2 indicated no improvement in model fit over Model 2 and the model χ^2 was non-significant.

Discussion

Through an innovative and integrative approach, findings from the present study highlight the importance of using multi-level methods to identify predictors of resilience among vulnerable youth. First, neural activation associated with inhibitory control and reward responsivity were compared between resilient versus risk groups. By doing so, individual differences pertaining to dual-systems models of risk-taking could be assessed. Second, in addition to examining between-group differences among resilient versus risk groups in terms of inhibitory control and reward responsivity, whole-brain task activation for both resilient and risk groups was extracted and included in a series of hierarchical multivariable logistic regression models. Hierarchical multivariable logistic regression models were then used to determine the extent to which neural response involved in inhibitory control and reward responsivity predicted substance use resilience versus risk over and above both distal and proximal psychosocial measures of reactive control and externalizing behaviors. One key finding from this work is that resilient youth, compared to risk youth, had heightened neural activation associated with inhibitory control and blunted activation associated with reward responsivity. Because these differences centered in cortical brain regions, findings suggest that resilient youth may show a greater extent of self-regulation compared to risk youth. An additional significant finding was that heightened inhibitory control in the DLPFC differentiated between resilient and risk groups in hierarchical multivariable logistic regression models that included distal and proximal measures of reactive control and externalizing behaviors. This latter finding provides further support for the role of self-regulation as an indicator of resilience among FH+ youth.

Taken together, this work advances prior studies that focus on group level development of inhibitory control in relation to reward responsivity. By identifying differences between two groups of vulnerable youth, results from the present study provide support for individual differences in self-regulation. This information indicates the importance of inhibitory control as a protective mechanism. In turn, prevention and intervention programs may benefit from improved regulatory control among vulnerable populations (i.e., FH+ youth).

Between-Group Differences in Inhibitory Control and Reward Responsivity

Findings from the Go/No-Go task measuring inhibitory control indicated differences between resilient and risk groups in four brain regions, all within the frontal cortex. Considering that dual-systems models of risk-taking posit that deficits in inhibitory control associated with prefrontal brain regions contribute to risk taking behaviors such as a substance use (e.g., Shulman et al., 2015), it was expected that the resilient group would show greater neural activation in frontal regions involved in inhibitory control. Indeed, the resilient group showed significantly greater activation in the left midOFG, left SFG, right mOFC and left iFC compared to the risk group.

Both the left midOFG and right mOFC are orbitofrontal brain regions central to inhibitory control over rewarding stimuli (Casey et al., 1997; Elliott et al., 2000; Szatkowska et al., 2007). Subtle differences exist between these two regions in relation to neural function. The midOFG is involved more with negative feedback evaluation and the mOFC is related to neural processing of reinforcement-based learning (Kringlebach & Rolls, 2004; Walton et al., 2010). In a recent animal study examining differences in impulsivity and dopamine transporter function in rats using a cued Go/No-Go task, decreased activation in orbitofrontal regions was associated with increased impulsive behavior as measured by greater responding during the No-Go condition of the task (Yates et al., 2016). These findings suggest that orbitofrontal functioning may contribute to individual differences involved in discriminate learning to withhold prepotent responses (i.e., inhibitory control). A different animal study that used a stop-signal task supports and extends the link between orbitofrontal activity and inhibitory control, by finding that a more accurate description of orbitofrontal function is cognitive control required to suppress conflict-induced behavioral responding (Bryden & Roesch, 2015). In other words, rats in this study that successfully stopped and redirected their behavior were found to have increased activity in orbitofrontal regions. Legion studies in humans corroborate these results, showing that individuals with orbitofrontal damage show deficits in impulse regulation and inappropriate behavior (Berlin et al., 2004). Neural projections from orbitofrontal regions to the VS contribute to processing rewarding stimuli and modifying behaviors in response to rewards involved in adaptive learning (Knutson et al., 2001). Thus, the top-down function of the OFC related to decision-making involved in inhibiting and regulating behavioral responses contributes to its role in addiction susceptibility (Feil et al., 2010; Schoenbaum et al., 2006; Volkow et al., 2002). Orbitofrontal regions may also be affected by continued substance use. For example, individuals with AUDs may have decreased neural and glial densities (Miguel-Hidalgo et al., 2006). Additional research is needed to differentiate between prior susceptibility in the OFC and OFG function that may contribute to substance use risk and effects of continued substance use on inhibitory control.

The present study also showed between-group activation differences in the left SFG, with the resilient group showing significantly greater activation associated with inhibitory control compared to the risk group. Greater activation in the left SFG in particular is related to efficiency of response inhibition (Li et al., 2006). In a study of participants with frontal lobe lesions, those with damage to the SFG displayed deficits in response inhibition during a Go/No-Go task (Picton et al., 2007). Structural imaging studies have also demonstrated a link between the left SFG and impulsivity. In one study of healthy adolescents who participated in the IMAGEN Study, a European multi-site longitudinal imaging study, less cortical thickness of the left SFG was associated with greater trait impulsivity (Schilling et al., 2013). Associations between SFG volume and impulsivity have also been found among substance using populations. Adolescents who were heavy marijuana users had decreased cortical thickness in bilateral SFG regions

(Lopez-Larson et al., 2011). In a study on differences in prefrontal and subcortical brain volumes underlying substance use risk among neuroimaging participants in the MLS, young adults with smaller left SFG volumes were found to be vulnerable to substance use (Weiland et al., 2014). While structural studies cannot definitively link cortical thickness and brain volume to brain function associated with inhibitory control, these results suggest abnormal brain structure in the left SFG is linked to impulsive responding. Future studies are needed to disentangle the influence of both brain structure and function in the SFG related to inhibitory control.

The resilient group also showed greater neural activation in another prefrontal region compared to the risk group—the left iFC. Existing research has identified the iFC as important brain region involved in attentional processes involved in inhibitory control (Duann et al., 2009). Thus, greater activation in the iFC is associated with improved performance during No-Go trials (i.e., correct inhibition). Some studies suggest that the right iFC is primarily involved in inhibitory control (e.g., Aron, 2011; Duann et al., 2009). However, other studies also support the role of the left iFC in relation to inhibitory control (Hirose et al., 2012; Swick et al., 2008). For example, compared to matched controls, individuals with legions in the left iFC had a greater difficulty with response inhibition during a Go/No-Go task and committed a greater number of false alarm errors (Swick et al., 2008). Because of its role in inhibitory control, the left iFC may be associated with greater substance use risk, which is supported by the findings in the present study. In a structural study using data from IMAGEN, Whalen et al. (2014) found that current binge drinkers had decreased left IFG volume compared to controls. Furthermore, continued substance use may alter functional brain connectivity within the left executive control network that includes the left iFC (Weiland et al., 2014). Future studies that disentangle preexisting susceptibilities versus effects of continued use may help identify important risk factors among vulnerable youth.

For the MIDT, there were two between-group differences in neural activation. For the reward versus neutral anticipation contrast, resilient youth had decreased activation in the left SFG compared to the risk group. Weiland et al. (2014), using anatomic MRI with participants from the MLS, found that young adults who reported early high levels of substance use had smaller left SFG volumes. The authors suggest this structural difference may indicate an underlying risk factor for substance use problems and later maturing top-down cortical control systems among youth who engage in risk behaviors, such as substance use. In this study, youth with a family history of SUD were included as a single group and the control group included youth without a family history of SUD. There was not a comparison group *within* the family history positive group. It is possible then, that results from the present study on neural function to reward responsivity may have captured differences in brain activation unique to resilient youth. In another study that examined both brain structure and function during the MIDT, (Whelan et al., 2014) found that youth with greater activation in the left SFG during reward outcome were more likely to binge drink two years later. Although this finding pertains to reward outcome rather than anticipation, it suggests that increased neural activity in reward networks may be a risk factor for substance use risk.

During the reward feedback contrasts of the MIDT, the resilient group showed decreased activation in the IPL compared to the risk group. The parietal cortex underlies task-reward and behavior-outcome associations (Wisniewski et al., 2015). The left IPL has been shown to have greater activation in response to reward anticipation rather than outcome (Liu et al., 2011). Interestingly, the risk group in the present study showed greater activation in this brain region to the receipt of rewards compared to the resilient group. Although activation in the left IPL was not compared in the risk group across reward anticipation and reward feedback contrasts, greater activation during feedback may indicate that the risk group shows a heightened sensitivity to obtaining rewards. In turn, this reward sensitivity may translate into increased substance use behavior.

Neural Activation and Psychosocial Measures of Inhibitory Control

Using a developmental psychopathology approach, the present study examined multiple levels of analysis—psychosocial and neural—related to the behavioral control/disinhibition pathway to substance use problems (Zucker et al., 2011). Thus, extracted ROIs from whole-brain task activation were added to a series of hierarchical logistic regression models that included psychosocial factors of reactive control and externalizing behaviors. These additive models were used to test if neural activation associated with inhibitory control and reward responsivity predicted substance use group membership (resilient versus risk) over and above distal and proximal psychosocial measures of behavioral control.

No significant predictors of substance use trajectory group were found in Model 1, which included sex, number of parents with SUD, early adolescent reactive control, and early adolescent externalizing behaviors. In Model 2, which added late adolescent reactive control and externalizing behaviors, results showed that resilient youth had significantly lower odds of having late adolescent externalizing behaviors. This finding is consistent with literature that shows a connection between a greater extent of externalizing problems and higher levels of substance use (e.g., Zucker et al., 2011).

Activation in the right iOFG and the left MFG during inhibitory control did not significantly improve prediction in Model 3. Although these are brain regions involved in inhibitory control (e.g., Giedd, 2008), they do not appear to predict substance use group membership above and beyond the influence of sociodemographic and behavioral measures. The only significant predictor in Model 3 was late adolescent externalizing behaviors, suggesting the particular strength of externalizing behaviors to differentiate resilient and risk groups.

In Model 3, however, DLPFC activation associated with inhibitory control was a significant predictor of being in the resilient group versus risk. Related to dual-systems models of risk-taking, functioning of the DLPFC is involved in top-down cognitive control processes, including inhibitory control (MacDonald et al., 2000) and response inhibition (Blasi et al., 2006; Garavan et al., 2002; Kelly et al., 2004). Not only is the DLPFC involved in top-down cognitive processes, but it also shares connections with brain regions associated with reward responsivity, including the OFC, amygdala, and hippocampus (Fiel et al., 2010). Due to its association with both cognitive control and reward processing, the DLPFC is involved in risk for addiction (Goldstein & Volkow, 2011). Deficits in DLPFC function may contribute to inappropriate responding to goal-directed behaviors, such as engaging in substance use, that does not weigh negative consequences in relation to positive outcomes (Feil et al., 2010). In the present study, resilient youth were found to have a stronger neural response in the DLPFC while engaging in an inhibitory control task compared to the risk group. Furthermore, this was reflected in psychosocial measures of high early reactive control during the age when substance use tends to initiate among FH+ youth (Wong et al., 2006) and low externalizing behaviors when substance use tends to escalate in late adolescence (Johnston et al., 2015). It is possible that a greater extent of early reactive control provided a foundation for effective self-regulation prior to the onset of substance use. In turn, this may have led to less engagement in externalizing behaviors and substance use. Additional research is needed to test this possibility and explore other related explanations.

Neural Activation and Behavioral Measures of Reward Responsivity

To examine neural activation involved in reward responsivity, hierarchical multivariable logistic regression models were tested with data from anticipation of rewards and the feedback contrasts during the MIDT. Results indicated that adding VS activation during the reward anticipation contrast did not significantly predict substance use trajectory group. The only significant predictor differentiating resilient and risk groups was the measure of late adolescent externalizing behaviors in Model 2, without the addition of neural function. Among measures of neural activation added to hierarchical multivariable logistic regression models, inhibitory control rather than reward responsivity appears to differentiate resilient and risk groups. Due to both resilient and risk groups having a family history of SUD, it is possible that both groups may be susceptible to greater reward responsivity. For example, youth with a family history of SUD have been found to have heightened NAcc responsivity during reward anticipation in comparison to youth without this vulnerability (Andrews et al., 2011). In an fMRI study of adolescents with a family history of SUDs and matched controls without a family history of SUDs, no differences were found between groups in relation to NAcc activation to the anticipation of rewards during the MIDT (Bjork et al., 2008). Both groups, however, excluded youth with behavioral or mood disorders. Thus, the authors suggest that youth with a family history of SUDs without such disorders may be resilient. This position is supported by results from the present study showing that late adolescent externalizing behaviors alone (Model 2) were the only significant predictor of substance use trajectory group when examining only sociodemographic characteristics and psychosocial factors.

As with VS activation during reward anticipation, adding VS activation during reward feedback did not significantly predict substance use trajectory group membership. Although the VS, which encompasses the NAcc, is associated with reward evaluation, (e.g., Diekhof et al., 2008), VS activation during reward feedback in the present study did not significantly predict substance use trajectory group over and above sociodemographic characteristics, and early and late adolescent measures of reactive control and externalizing behaviors. Results from other studies have shown similar findings. In a study comparing youth with a family history of SUDs and matched controls without family history of SUDs who completed a modified MIDT through the IMAGEN study, both groups showed activation of the VS to both reward anticipation and win feedback trials but did not show significant between-group differences (Müller et al., 2014). The authors suggest these findings may have been due to the younger age of their sample (ages 13-15) and delayed effects of family history of SUD on reward circuitry, which is not supported by our findings using an older sample. In a novel approach to studying reward responsivity, Telzer et al. (2013) tested whether prosocial rewards would be associated with heightened VS activation and lower risk taking among adolescents. These results suggested that not all forms of reward-driven behaviors are negative, such as charitable giving and academic achievement. Furthermore, reward sensitivity to such prosocial activities may reduce the likelihood of detrimental rewards such as a substance use. In the case of the present study, it is possible that reward responsivity to the receipt of prosocial rewards may be associated with resilience. Future research with prosocial reward tasks is needed to test this hypothesis. There may be yet another explanation for lack of differences in relation to reward responsivity, but not inhibitory control, between resilient versus risk groups. Findings from prior work indicate that individuals with weak self-control and heightened reward seeking may be more likely to experience early progression into heavy substance use, whereas individuals with higher reward seeking but also higher self-control may be more likely to engage in only occasional substance use (Khurana et al., 2015). Thus, self-regulatory capacity may be an indicator for resilience to substance use even among those who are more likely to engage in risk behaviors, such as FH+ youth.

Strengths and Limitations

Major strengths of the present study are its focus on off-diagonal, resilient youth and its innovative approach to examine both psychosocial and neural mechanisms involved in substance use resilience versus risk. The present study adds to existing literature by providing evidence for individual differences in inhibitory control and reward responsivity among vulnerable populations. This information may help inform substance use prevention and intervention programs by identifying important protective mechanisms. For example, training youth on skills related to self-regulation may strengthen capabilities in cognitive control. Despite limited generalizability due to being a relatively homogenous sample in terms of race/ethnicity and family history of SUDs, the MLS is one of only a few longitudinal studies that also includes a neuroimaging component. This allows for more comprehensive analyses of complex psychosocial and neural processes involved in substance use resilience and risk, such as those related to dual-systems models of risk-taking,

Despite its strengths, there were limitations of the present study. Youth categorized in the risk group either had chronic high levels of binge drinking, marijuana use, or both binge drinking and marijuana use. Thus, it is possible that differences in risk may depend on the specific substance or in relation to having both heavy alcohol use and marijuana use. Further analyses should examine how these subgroups may represent different levels of risk and how these different groups compare to resilient youth. In addition, differences in neural function between resilient and risk groups may have been attributable to long-term effects of substance use rather than preexisting factors. Indeed, substance use has toxic effects on neurodevelopment, which may impact self-regulation (Windle, in press). Continued substance use, a characteristic of the risk group examined in the present study, may alter neural function. For example, a recent study examining cross-lagged associations between marijuana use and reward responsivity during early adulthood found that, over time, marijuana use contributed to blunted response to the anticipation of monetary rewards (Martz et al., in press). Additional research is needed to test preexisting differences in neural function between resilient and risk groups, and should also include more specific drug-related cues. Another limitation of the present study was that neural regions involved in inhibitory control and reward responsivity were examined separately. The present study used fMRI techniques pertaining to neural faction, rather than structure or connectivity. Thus, the interconnectedness between these two neural systems was not assessed. It is possible that greater neural connectivity between inhibitory control and reward processing regions may be a characteristic of resilient youth, although this association needs to be tested.

Conclusions

In sum, examining neural activation involved in inhibitory control and reward responsivity may help identify brain function unique to resilient FH+ youth. Indeed, significant differences pertaining to these neural functions were found between resilient and risk FH+ youth. Importantly, results of the present study suggest that greater activation in the DLPFC associated with inhibitory control may be a protective factor among resilient youth, over and above psychosocial measures of early adolescent reactive control and late adolescent externalizing behaviors. Through an innovative study design using multi-level methods, findings provide evidence of individual-level variability in neural systems underlying dual-systems models of risk-taking. Examining the link between developmental trajectories of substance use and neural correlates of resilience may provide a more comprehensive understanding of neurodevelopmental processes protective against substance use.

Chapter 5

Conclusion

The overall purpose of this dissertation was to advance existing developmental theory, inform prevention and intervention efforts, and set the stage for continued work focused specifically on off-diagonal substance use groups. Using a multi-level approach, this dissertation aimed to identify distal and proximal predictors of off-diagonal binge drinking and marijuana use through the transition to adulthood. Studying substance use during the transition to adulthood is often a complex endeavor. On one hand, a certain extent of substance use is developmentally normative. Results from national samples indicate peak rates of binge drinking and marijuana use occur during the transition to adulthood. For example, approximately 40% of youth ages 21 and 22 report binge drinking within the last two weeks and nearly a quarter of youth ages 19 and 20 report marijuana use within the past month (Johnston et al., 2015). Yet, upon closer inquiry, there is often heterogeneity in patterns of substance use through this developmental period. Chronic high level substance use groups tend to receive the greatest empirical and clinical attention due to their association with multiple negative outcomes (e.g. Berg et al., 2013; Chassin et al., 2002; Squeglia et al., 2009; Winward et al., 2014). From a developmental psychopathology perspective, however, off-diagonal substance use groups merit equal consideration. The three studies in this dissertation give due attention to off-diagonal substance use groups that represent low prior risk but high levels of substance use through the transition to adulthood (i.e., late onset youth) and high prior risk but low levels of substance use through the transition to adulthood (i.e., resilient FH+ youth). In the case of late-onset substance users, what may appear to be normative substance use in adolescence then shifts over the course of the development as evident by linear increases in use through the transition to adulthood. Youth with a family history of SUD (FH+) comprise another off-diagonal pattern of substance use. Despite genetic and environmental vulnerabilities to elevated substance use (e.g., Lieb et al., 2002; Zucker et al., 2014), resilient FH+ youth defy the odds and show consistently low levels of substance use during the transition to adulthood when risk for use is greatest. Although off-diagonal substance use trajectory groups have been identified in literature (e.g., Chassin et al., 2002; Schulenberg et al., 1996a; Schulenberg et al., 2005), existing work has not fully identified the complex distal and proximal developmental factors underlying these unique populations.

To address this deficit, this dissertation focused on identifying key developmental factors involved in off-diagonal substance use. Two long-standing and internationally recognized studies with breadth (MTF) and depth (MLS) were utilized. MTF is a large scale, national survey study well suited to examine the relatively small group of youth categorized as late-onset substance users. MLS is a longitudinal study consisting primarily of youth vulnerable to SUDs, which allowed for studying characteristics and predictors of resilience among FH+ youth. An additional advantage of MLS is its inclusion of a subsample of youth who have completed longitudinal neuroimaging assessments. In sum, this dissertation provides both a big picture perspective and more in-depth analysis on predictors of off-diagonal substance use.

Novel Contributions

Through an innovative, multi-level approach, the three chapters included in this dissertation built upon existing literature on developmental trajectories of substance use. The primary contribution of this work is its specific focus on both distal and proximal predictors of two understudied, off-diagonal binge drinking and marijuana use groups—late-onset using youth and resilient FH+ youth. Chapter Two used national survey data from the MTF survey to provide a big picture perspective on factors during late adolescence and early adulthood that contribute to late-onset binge drinking and marijuana use. Even though a minority of youth are classified as late-onset substance users, they are an important risk group due to their steep escalation of substance use through the transition to adulthood. This escalation is problematic due to its association with later negative outcomes (e.g., Caldeira et al., 2012; Epstein et al., 2015; Oesterle et al., 2004). The breadth of such large, diverse samples within MTF allowed for analyses of this small, yet clinically important risk group. Chapter Two built upon previous studies that identified predictors of late-onset substance use (e.g., Jackson et al., 2008; Schulenberg et al., 1996a; Schulenberg et al., 1996b; Schulenberg et al., 2005) through its equal focus on the two most commonly used substances among youth (i.e., alcohol and marijuana use) and its inclusion of both distal and proximal predictors examined through Growth Mixture Modeling (GMM) and multivariable logistic regression analyses.

In Chapter Two, examining separate substance use models for binge drinking and marijuana use (while controlling for marijuana use in the binge drinking model and controlling for binge drinking in the marijuana use model) allowed for a specific focus on predictors of trajectory membership unique to each of these substances. Yet, by including the same distal and proximal measures in binge drinking and marijuana use models, predictors relevant to both of these substances could also be examined. Because it is unlikely that either type of substance use was done in complete isolation of other drugs of abuse, binge drinking models controlled for distal and proximal marijuana use. Likewise, marijuana use models controlled for distal and proximal measures of binge drinking. A noteworthy finding from both binge drinking and marijuana use models was that late-onset and chronic high use groups showed no differences in terms of proximal predictors. In line with the developmental psychopathology term of equifinality (described in more detail below), late-onset and chronic high groups shared both similar levels of substance use in addition to psychosocial and social context predictors in early adulthood. These results contrast to comparisons between late-onset and low/non-use groups who showed more variability in terms of late adolescent predictors when levels of substance use were relatively comparable between these two groups (i.e., multifinality). In other words, it may be difficult to identify early “red flags” of off-diagonal, late-onset substance use.

An additional contribution of Chapter Two was its use of multivariable logistic regression models. Specifically, this study used the R3STEP method in Mplus to examine distal and proximal predictors of late-onset binge drinking and marijuana use. An advantage of the R3STEP method is that it stabilizes the analytic model by accounting for missing data and measurement error involved in identifying trajectory groups (Asparouhov & Muthén, 2014; Vermunt, 2010). While results examining sociodemographic characteristics, late adolescent factors, and young adult factors in descriptive and bivariable predictive models are useful to isolate associations with substance use trajectory membership, multivariable logistic regression models account for the combined influence of these factors. In other words, they reflect combined developmental influences on substance use trajectory outcomes. This is important, considering that a combination of factors representing different levels of functioning (e.g., psychosocial and contextual) and at different points in development (e.g., distal and proximal) contribute to substance use risk and resilience (Hurd & Zimmerman, in press; Schulenberg et al., in press). For example, comparisons between late-onset with low/non-marijuana users indicated that late-onset youth had greater self-esteem in late adolescence but lower self-esteem more proximally in early adulthood. Because of corresponding increases in substance use during the transition to adulthood, it is possible that declines in self-esteem may be a function of increases in substance use, although this possibility needs to be tested in future research.

In contrast to the breadth provided by MTF, the MLS provided depth by the sample consisting predominately of youth with a family history of SUD (FH+) and by including a greater extent of measures associated with substance use risk and resilience. This is important, considering that studies involving FH+ youth tend to focus on risk factors rather than resilience. Predictors of resilience among low substance using FH+ youth are important in order to uncover protective factors among this vulnerable population. To fill this gap in the literature, Chapter Three used hierarchical multivariable logistic regression analyses to examine the additive influence of distal and proximal predictors of resilience among FH+ youth in comparison to high substance using FH+ youth.

Compared to the breadth of measures available in MTF surveys, the depth of measures available in the MLS allowed for the inclusion of even more distal predictors during early adolescence. Considering these earlier factors was important because both resilient and risk groups showed consistent levels of either low or high substance use, respectively, through the transition to adulthood. In addition to examining late adolescent and young adult factors coinciding with substance use patterns through the transition to adulthood, distal factors in early adolescence may set in motion psychosocial functioning associated with later patterns of substance use during the transition to adulthood. Interestingly, however, early adolescent factors did not distinguish between resilient and risk groups. The most significant results from Chapter Three center instead on the strong role of late adolescent factors of reactive control and externalizing behaviors predicting membership in the resilient versus risk group. While existing evidence clearly points to the important role of early factors predicting later substance use

(Schulenberg et al., in press; Zucker, 2006), findings from Chapter Three suggest that more proximal factors seem to be stronger indicators for substance use resilience versus risk during the transition to adulthood. Building upon evidence for the disinhibition pathway to substance use problems (Zucker et al., 2011), a greater extent of reactive control and lower level of externalizing behaviors may be particularly influential to promote resilience among FH+ youth. This information may be useful for prevention and intervention efforts targeting this population.

Chapter Four extended Chapter Three analyses by examining both psychosocial and neural predictors of substance use resilience versus risk. Due to their relevance to the disinhibition pathway to substance use problems (Zucker et al., 2011), psychosocial and neural factors in Chapter Four focused specifically on inhibitory control and reward responsivity. These measures also pertain to neural processes underlying behavioral disinhibition, and more broadly, dual-systems models of risk taking described to a greater extent in the following section. There are two key contributions from results of Chapter Four. First, Chapter Four built upon previous research comparing resilient and risk FH+ groups on neural function (Heitzeg et al., 2008), by focusing on differences in inhibitory control and reward responsivity between these groups. Thus, measures assessed in Chapter Four pertained to processes involved in dual-systems models of risk-taking (e.g., Casey et al., 2008; Gogtay et al., 2004; Raznahan et al., 2014; Steinberg, 2010). Dual-systems models of risk-taking have been criticized for being overly simplistic due to their failure to account for individual differences in neural function (Harden & Tucker-Drob, 2011; Pfeifer & Allen, 2012; Quinn & Harden, 2013). Chapter Four addressed this concern by examining differences in neural function underlying inhibitory control and reward responsivity between resilient and risk groups. Both resilient and risk groups were approximately the same age, which according to dual-systems models of risk-taking would suggest similar levels of inhibitory control and reward responsivity between these two groups. However, this was not fully supported by Chapter Four findings. Results indicated that in cortical brain regions, resilient youth appeared to show heightened neural activation associated with inhibitory control and blunted activation associated with reward responsivity. Thus, resilient youth show a greater extent of self-regulation, which may reduce substance use risk.

Second, neural function associated with inhibitory control and reward responsivity were examined in hierarchical multivariable logistic regression analyses. By doing this, the additive influence of neural function could be examined in relation to psychosocial measures. This was a novel, multi-level methodological approach that tested the extent to which neural function could predict resilience versus risk among FH+ youth, over and above psychosocial factors measuring related constructs. Results of Chapter Four did not find a significant influence of neural function involved in reward responsivity added to hierarchical multivariable logistic regression models. Of particular interest, however, neural function in the right DLPFC associated with inhibitory control was a significant predictor of resilience versus risk among FH+ over and above both distal and proximal psychosocial measures. Taken together, these results provide a better understanding of neural function differentiating resilient and risk groups.

Theoretical Implications

In line with the hallmarks of a developmental psychopathology perspective, which center on an interdisciplinary, lifespan approach, this dissertation used multiple modalities to examine predictors of off-diagonal substance use risk and resilience. These included a large-scale national survey (MTF), a community based sample of youth with a family history of SUDs (MLS), and a neuroimaging subsample of MLS participants who completed fMRI assessments. Furthermore, studying off-diagonal substance use fits well within the purpose of a developmental psychopathology framework that posits that adaptation and maladaptation must both be considered when studying developmental phenomena (Cicchetti & Rogosch, 1999; Rutter & Sroufe, 2000). The term "off-diagonal" implies that a certain behavior does not follow an expected (i.e., diagonal) pattern. In Chapter Two, predictors of off-diagonal late-onset binge drinking and marijuana use were compared to predictors of low/non-use and chronic high use. These latter two groups showed more expected and continuous patterns of substance use in relation to prior levels of functioning. In Chapters Three and Four, the resilient off-diagonal group was unexpected in that these youth had a family history of SUDs but showed consistently low levels of substance use through the transition to adulthood, when risk for heavy use is greatest (Johnston et al., 2015). Predictors of this off-diagonal substance use group were compared to the more expected FH+ risk group with chronic high levels of substance use. Thus, in Chapters Two, Three, and Four, off-diagonal groups were identified based on maladaptation or adaptation and then compared to the diagonal group. In doing so, findings indicated predictors of risk (i.e., late-onset binge drinking and marijuana use) and resilience (i.e., low substance use among FH+ youth) that took into account vulnerabilities and developmental patterns of substance use.

The studies included in this dissertation also provide support for developmental psychopathology concepts of continuity and discontinuity, as well as resilience and risk. Specifically related to continuity and discontinuity, findings from Chapter Two have theoretical implications for multifinality and equifinality. Analyses were conducted to compare late-onset binge drinkers and marijuana users to low/non-users. This comparison represents multifinality, in which these two groups started with similar levels of substance use in late adolescence but then diverged on levels of use by young adulthood. Chapter Two analyses also compared late-onset binge drinkers and marijuana users to chronic high users, which represents equifinality. In other words, these two groups started at dissimilar starting points in terms of levels of use in late adolescence but then converged on levels of use by young adulthood. The present study also examined distal predictors at the beginning of increasing use and later, more proximal predictors once use had escalated through the transition to adulthood. One key finding from Chapter Two was that there appeared to be greater support for equifinality between late-onset and chronic high use groups in comparison to multifinality between late-onset and low/non-use groups. For both binge drinking and marijuana use models, the late-onset and chronic high use groups did not differ on predictor variables measured in young adulthood. This finding suggests that not only did these two groups appear to converge on substance use, but that other areas of their life shifted as well, such as changes in self-esteem, sensation seeking, and interpersonal aggression.

Chapters Three and Four were particularly relevant to developmental psychopathology concepts of risk and resilience. A robust risk factor for substance use problems is having a family history of SUD, which occurs through both environmental and genetic influences (Lieb et al., 2002; Zucker et al., 2014). Despite this vulnerability, some FH+ individuals do not experience substance use problems. Whereas Chapter Three focused on psychosocial and contextual predictors of this resilience, Chapter Four focused on psychosocial and neural factors. Both of these studies found that a greater level of reactive control and a lower level of externalizing behaviors predicted substance use resilience through the transition to adulthood. Chapter Four took these analyses one step further by examining the extent to which neural function associated with reactive control and externalizing behaviors may predict resilience over an above behavioral measures of these constructs. Findings from these analyses indicate that greater activation in the right DLPFC predicted resilience even after accounting for reactive control and externalizing behaviors. These results lend support to criticism that dual-systems models of risk-taking may be overly simplistic (e.g., Pfeifer & Allen, 2012). This position argues that dual-systems models of risk-taking do not account for individual differences in risk behaviors, such as substance use, among youth of a similar age range. Despite adolescents and young adults generally having greater levels of risk behaviors compared to younger and older age groups, due in part to less mature prefrontal brain regions involved in cognitive control compared to more mature reward driven brain regions (Casey et al., 2008; Dahl, 2004; Luna et al., 2015; Steinberg, 2010), not all youth are prone to these behaviors. Indeed, resilient FH+ youth appear to have a greater level of inhibitory control compared to heavy substance using FH+ youth. These two groups appear to have few differences in relation to neural correlates of reward responsivity, suggesting the importance of self-regulation as a neural marker of resilience among this population.

Clinical Implications

One piece of the puzzle to better understand off-diagonal substance users is to identify predictors of these groups, as done in this dissertation. How predictors of these groups translate to clinical applications is another essential piece of that puzzle. Doing so may reduce problematic substance use among late-onset youth and promote continuity of low use displayed by resilient FH+ youth. Although the studies in this dissertation did not test causal associations between predictor variables and off-diagonal substance use binge drinking and marijuana use groups, results of these studies may be useful to information clinical efforts. For example, results of Chapter Two indicate that it may be possible to identify certain early risk factors prior to escalating substance use. Yet, these factors are often nuanced. School-based substance use prevention programs may overlook late-onset substance users because of their low substance use and few deviant behaviors. Thus, late-onset youth may benefit more from prevention programs during the transition to adulthood, when substance use begins to escalate. College-based prevention programs may be especially useful for late-onset substance users. Because late-onset users have few prior experiences with substance use, prevention efforts aimed at harm-reduction may be most effective for these youth. For example, University of Michigan has developed a harm-reduction program called "Stay in the Blue" that provides approaches for students to moderate their substance use. Programs such as this may be useful to promote strategies in substance use moderation that could be carried forward beyond college into other contexts in which drug use may be present. Although non-college populations may be more difficult to assess with targeted prevention efforts, promoting harm-reduction techniques would also likely be useful to prevent late-onset substance use among this population.

Results from Chapters Three and Four also have applied clinical applications. Examining predictors of resilience may uncover protective mechanisms among vulnerable populations, such as FH+ youth. These mechanisms may be of high value to prevention and intervention efforts, due to the robust association between family history of SUD and later substance use problems among offspring (e.g., Chassin et al., 2002; Zucker, 2014). One important finding from Chapter Three was that greater reactive control and lower externalizing behaviors were both significant predictors of substance use resilience during the transition to adulthood. Thus, strategies to improve self-regulation may be important predictors of resilience among vulnerable youth. Furthermore, these factors may be especially important just prior to the transition to adulthood when the risk for heightened substance use is greatest (Johnston et al., 2015). Techniques such as cognitive behavioral therapy (CBT) may help improve self-regulation by linking thoughts and behaviors related to substance use. For example, the National Institute on Drug Abuse (NIDA,

2012) reports that enhanced self-monitoring of drug cravings and identifying contexts in which substance use may occur are particularly beneficial to reduce substance use.

Results from Chapter Four support the role of reactive control and externalizing behaviors as promotive factors for resilience. Furthermore, Chapter Four findings indicate that neural response involved in inhibitory control is also associated with greater substance use resilience among FH+ youth. One possible clinical implication from these findings is that neuroimaging techniques, such as fMRI, may be useful in pre-test/post-test interventions aimed at improving self-regulation. Neural assessments may be useful to acquire a baseline measure of inhibitory control that could be tested again after interventions aimed at boosting self-regulation. Neuroimaging data may provide an advantage over behavioral self-reports. For example, the Go/No-Go task measures relatively automatic top-down processing to inhibit a prepotent response. Unlike behavioral assessments, neuroimaging analyses measure both response time and neural processing involved in inhibitory control. Thus, neuroimaging results may uncover changes involving neural recruitment of certain regions or changes in neural activation associated with improved self-regulation.

Future Directions

While findings from this dissertation provide evidence for psychosocial, contextual, and neural predictors of off-diagonal substance use that contribute to existing literature, additional research is needed to extend this work. In relation to Chapter Two, a limitation of survey research is the minimal depth of response items. Although MTF samples were large enough to identify the relatively small proportion late-onset substance users, available items to measure psychosocial predictors of this trajectory group were limited. Furthermore, closer attention is needed to assess interactions between the individual-level factors analyzed in Chapter Two (e.g., sensation seeking) and changing social contexts during the transition to adulthood. Certain protective factors in place during late adolescence, such as high parental monitoring, may be protective against substance use among youth with deficits in self-regulation. Yet, when external mechanisms of control are removed, these youth may be vulnerable to late-onset substance use. For example, moving out of the parental home and attending college may contribute to this vulnerability. Taken together, future research should take a more comprehensive approach to analyze individual- and contextual-level interactions that may contribute to late-onset substance use.

Additional research is also needed to study outcomes of off-diagonal substance use groups, including late-onset users and resilient FH+ youth. While some existing work has indicated certain outcomes of late-onset substance use (e.g., Epstein et al., 2015; Flory et al., 2004), future studies should take a more nuanced approach by examining the extent to which late-onset substance use outcomes may differ by certain subgroups. For example, results from Chapter Two found that females had a significantly greater frequency of being in the late-onset substance use group compared to the chronic high use group for both binge drinking and marijuana use. Males tend to be more likely to be heavy drinkers than females (Johnston et al., 2015), yet females in the late-onset group reach elevated levels of substance similar to the chronic high use group by early adulthood. Just because they reach a similar level of substance use by early adolescence, it is unknown whether outcomes may differ not only between substance use classes but also within classes. Thus, additional research using larger, more population-based samples is needed to examine how substance use outcomes among late-onset youth differ by subgroups of individuals. Further subgrouping may also be useful to examine, including interactions between gender and race. This information may identify different levels of functioning among subgroups within late-onset substance users.

Future studies should also develop more comprehensive classifications of resilience among FH+ youth. In the present study, resilience was only by level of substance use through the transition to adulthood. Although other measures of psychosocial functioning were assessed in early adolescence and late adolescence, such as internalizing and externalizing behaviors, these measures were not examined through the transition to adulthood. It is possible that resilient youth defined in Chapters Three and Four may have experienced other deficits in functioning that were not accounted for by defining resilience only in terms of substance use. For instance, due to their low levels of substance use through the transition to adulthood, these youth may experience more social exclusion. Forming social bonds in adolescence and young adulthood is an important developmental task. Social exclusion may occur because a certain extent of substance use, especially during this developmental period, plays a role in social bonding (Schulenberg & Zarrett, 2006). Yet, at the same time, social bonding associated with substance use may involve affiliations with deviant peers (e.g., Dodge et al., 2009). How substance use pertains to social bonding may then depend on the type of social group and the level of substance use involved in social situations. Taken together, there are multiple ways to categorize resilience within the broad definition of successful functioning despite adversity (Masten et al., 1990). Therefore, future studies should provide a more comprehensive definition of resilience as it pertains to substance use.

Future studies examining neural function in relation to substance use risk and resilience, as was done in Chapter Four, would benefit from recent advancements in neuroimaging methods. Joint independent components analysis (jICA) may be a particularly useful technique to uncover the complex processes underlying substance use behaviors. jICA is an approach used to jointly analyze multiple modalities of structural, resting state, and task-related neural activations in the same set of subjects (Calhoun et al., 2009). Integrating these neuroimaging methods may be useful to provide a more complete picture of brain networks involved in substance use risk and resilience. Pertaining specifically to Chapter Four, methodological innovations may help to refine heuristic models of neurodevelopment, including dual-systems models of risk-taking (Dahl, 2015). More advanced methods, such as jICA, could provide a more comprehensive analysis to uncover individual differences in neural response associated with inhibitory control and reward responsivity.

In conclusion, each of the studies presented in this dissertation reveal important developmental factors contributing to off-diagonal substance use. Whether those factors contribute to risk (i.e., late-onset users) or resilience (low substance using FH+ youth) is equally valuable to advance developmental theory, build upon existing research, and inform prevention and intervention efforts. Risk factors may provide early indicators of problem use, whereas resilience factors may target protective factors for positive functioning. As indicated by each of the three studies in this dissertation, the contribution of risk and protective factors may vary across development, as demonstrated by the different extent of influences measured distally and also more proximally to patterns of substance use through the transition to adulthood. Utilizing multi-level methods provides a comprehensive approach to uncover nuanced indicators of risk and resilience among off-diagonal substance use groups. Because off-diagonal substance users are a less apparent population, such comprehensive methods are crucial to identify these individuals.

Tables

Table 1

List of Variables Included in Chapters Two, Three, and Four

	Sociodemographic characteristics	Substance use	High school factors	Psychosocial factors of self-regulation	Social roles	Neural function
Chapter 2	Sex Race/ethnicity Parent education Historical cohort	Binge drinking Marijuana	GPA College plans Cut class Evenings out	Sensation seeking[a] Self-esteem[b] Interpersonal agg.[b]	College enrollment College graduation Marriage Parenthood	
Chapter 3	Sex Parent education Num. parents with SUD	Binge drinking Marijuana		Sensation seeking[a] Resiliency[c] Reactive control[c] Internalizing behavior[b] Externalizing behavior[b]	College enrollment College graduation Marriage Parenthood	
Chapter 4	Sex Num. parents with SUD	Binge drinking Marijuana		Reactive control[c] Externalizing behavior[b]		Inhibitory control Reward responsivity

Note. [a]Personality dimension of self-regulation; [b]Behavioral dimension of self-regulation; [c]Temperamental dimension of self-regulation; GPA = grade point average; num. = number; agg. = aggression.

Table 2

Growth Mixture Model Fit for Binge Drinking and Marijuana Use, Chapter Two

	BIC	Entropy	Class proportions	L-M-R test	L-M-R *p*-value
Binge drinking models					
2 classes	188337.21	0.94	23.22, 76.78	11742.69	< 0.001
3 classes	181046.90	0.98	5.01, 18.62, 76.36,	7149.96	< 0.001
4 classes	**182110.06**	**0.82**	**11.83, 12.95, 10.17, 65.05**	**5652.88**	**< 0.001**
5 classes	176639.16	0.86	4.37, 11.40, 11.90, 8.24, 64.89	-1702.73	1.000
Marijuana use models					
2 classes	185214.03	0.99	11.99, 88.01	22786.82	< 0.001
3 classes	176017.44	0.99	6.50, 84.30, 9.20	9909.65	< 0.001
4 classes	**167066.20**	**0.95**	**82.19, 7.56, 5.72, 4.53**	**8770.33**	**< 0.001**
5 classes	160830.93	0.96	5.03, 5.22, 4.23, 79.67, 5.85	4751.14	0.06

Note. Model fit is shown for the piecewise binge drinking model and quadratic marijuana use model; BIC = Bayesian Information Criteria; class proportions for the latent class patterns based on estimated posterior probabilities; L-M-R Test = Lo-Mendell-Rubin adjusted likelihood ratio value; L-M-R *p*-value = *p* value associated with Lo-Mendell Rubin adjusted likelihood ratio value.

Table 3

Correlations Between Predictor Variables Examined in Logistic Regression Models Predicting Late-Onset Binge Drinking and Marijuana Use

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Male	1														
2. White	0.00	1													
3. Black	-0.01	0.62***	1												
4. Hispanic	0.00	-0.47***	-0.17***	1											
5. Asian	0.01	0.12***	-0.08***	-0.06***	1										
6. Other race/ethnicity	0.01	-0.31***	-0.11***	-0.08***	-0.06***	1									
7. High parent education	0.02**	0.14***	-0.05***	-0.16***	0.04***	-0.00	1								
8. Binge cohort 1976-1986	-0.02**	0.08***	-0.01	-0.10***	-0.03***	-0.00	-0.12***	1							
9. Binge cohort 1987-1993	0.01*	0.02*	-0.01	-0.00	-0.02*	-0.01	-0.03***	-0.27***	1						
10. Binge cohort 1994-2006	0.00	-0.08***	0.01*	0.08***	0.03***	0.02*	0.12***	-0.53***	-0.68***	1					
11. Marijuana cohort 1976-1991	-0.01	0.09***	-0.02**	-0.08***	-0.04***	-0.02**	-0.12***	0.64***	0.39***	-0.83***	1				
12. Marijuana cohort 1992-1997	0.00	-0.02**	0.01	0.01	0.01	0.00	0.03***	-0.26***	0.12***	0.10***	-0.41***	1			
13. Marijuana cohort 1998-2006	0.00	-0.07***	0.01	0.07***	0.03***	0.02*	0.09***	-0.38***	-0.28***	0.72***	-0.60***	-0.48***	1		
14. C+ or lower	0.12***	-0.14***	0.11***	0.06***	-0.05***	0.02**	-0.11***	0.04***	0.04***	-0.06***	0.05***	0.00	-0.05***	1	
15. College plans	-0.06***	0.01	0.01	-0.01	0.08***	-0.03***	0.26***	-0.16***	-0.02*	0.14***	-0.15***	0.05***	0.11***	-0.25***	1
16. Cut ≥1 class/week	0.05***	-0.00	-0.05***	0.05***	0.01	0.02**	0.00	-0.02***	0.01	0.01	-0.01*	0.01	0.00	0.17***	-0.07***
17. 3+ evenings out/week	0.10***	0.10***	-0.08***	-0.03***	-0.06***	-0.02**	0.02**	0.00	0.01	-0.01	0.01	0.01	-0.02	0.07***	-0.03***
18. Wave 1 binge drinking	0.18***	0.11***	-0.14***	-0.00	-0.07***	0.00	-0.00	0.07***	0.01	-0.07***	0.09***	-0.03***	-0.06***	0.13***	-0.10***
19. Wave 1 marijuana use	0.12***	0.02***	-0.03***	-0.01*	-0.05***	0.01	0.00	0.08***	-0.09***	0.02**	0.01	-0.02**	0.01	0.13***	-0.11***
20. Wave 1 self-esteem	0.03***	-0.04***	0.10***	-0.02	-0.02**	-0.05***	0.03***	0.01	-0.00	-0.00	0.00	0.02	-0.01	-0.12***	0.13***
21. Wave 1 sensation seeking	0.25***	0.11***	-0.17***	0.02***	0.00	0.01	0.04***	-0.12***	0.02**	0.08***	-0.10***	0.04***	0.06***	0.06***	-0.02*
22. Wave 1 interpersonal aggression	0.20***	-0.09***	0.03***	0.04***	-0.01	0.06***	-0.02*	-0.05***	0.03***	0.01	-0.03**	0.03***	0.00	0.12***	-0.09***
23. Enrolled in college (W2-W5)	0.00	0.01	0.03**	-0.03*	0.07***	-0.03**	0.32***	-0.22***	0.00	0.17***	-0.17***	0.04***	0.14***	-0.29***	0.66***
24. College grad (W2-5)	0.01	0.11***	-0.08***	-0.06***	0.09***	-0.04***	0.30***	-0.18***	-0.04***	0.19***	-0.17***	0.04***	0.15***	-0.28***	0.48***
25. Married (W2-5)	-0.05***	0.02	-0.06***	0.03**	-0.07***	0.02*	-0.14***	0.06***	0.03***	-0.08***	0.07***	0.01	-0.08***	0.08***	-0.21***
26. Parent (W2-5)	-0.06***	-0.24***	0.19***	0.09***	-0.08***	0.05***	-0.22***	-0.03**	0.04***	-0.01	-0.01	0.02	-0.00	0.20***	-0.27***
27. Wave 5 binge drinking	0.24***	0.07***	-0.06***	-0.02*	-0.04***	-0.01	0.03**	-0.01	-0.01**	0.03**	-0.02*	-0.01	0.02**	0.08***	-0.02
28. Wave 5 marijuana use	0.11***	-0.00	0.02*	-0.03***	-0.03**	0.00	0.03**	0.01	-0.05***	0.03***	-0.02**	-0.00	0.03***	0.11***	-0.04***
29. Wave 5 self-esteem	0.06***	-0.04***	0.05***	0.01	-0.01	-0.01	0.05***	-0.02*	0.02*	-0.00	-0.01	0.02*	-0.01	-0.07***	0.07***
30. Wave 5 sensation seeking	0.27***	0.07***	-0.12***	0.02*	0.03**	0.01	0.07***	-0.10***	0.01	0.08***	-0.10***	0.02*	0.08***	0.04***	0.01
31. Wave 5 interpersonal aggression	0.10***	-0.05***	0.04***	0.01	-0.01	0.02*	-0.04***	0.00	-0.00	-0.00	0.00	-0.01	0.00	0.06***	-0.06***

$*p < 0.05$ $**p < 0.01$ $***p < 0.001$; W1 = wave 1; W2 = wave 2; W5 = wave 5.

Table 3 (continued)

Correlations Between Predictor Variables Examined in Logistic Regression Models Predicting Late-Onset Binge Drinking and Marijuana Use

	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31
1. Male																
2. White																
3. Black																
4. Hispanic																
5. Asian																
6. Other race/ethnicity																
7. High parent education																
8. Binge cohort 1976-1986																
9. Binge cohort 1987-1993																
10. Binge cohort 1994-2006																
11. Marijuana cohort 1976-1991																
12. Marijuana cohort 1992-1997																
13. Marijuana cohort 1998-2006																
14. C+ or lower																
15. College plans																
16. Cut ≥1 class/week	1															
17. 3+ evenings out/week	0.15***	1														
18. Wave 1 binge drinking	0.23***	0.27***	1													
19. Wave 1 marijuana use	0.22***	0.22***	0.42***	1												
20. Wave 1 self-esteem	-0.08***	0.04***	-0.05***	-0.06***	1											
21. Wave 1 sensation seeking	0.17***	0.17***	0.23***	0.16***	0.08***	1										
22. Wave 1 interpersonal aggression	0.16***	0.13***	0.30***	0.23***	-0.09***	0.18***	1									
23. Enrolled in college (W2-W5)	-0.05***	-0.06***	-0.11***	-0.12***	0.09***	0.00	-0.07***	1								
24. College grad (W2-5)	-0.06***	-0.07***	-0.09***	-0.11***	0.10***	-0.00	-0.07***	0.71***	1							
25. Married (W2-5)	0.05***	0.02	0.02	-0.02	0.02	-0.00	0.03**	-0.17***	-0.11***	1						
26. Parent (W2-5)	0.08***	0.01	0.05***	0.05***	-0.01	0.01	0.11***	-0.35***	-0.29***	0.56***	1					
27. Wave 5 binge drinking	0.12***	0.16***	0.34***	0.20***	-0.01	0.17***	0.14***	0.01	0.02*	-0.16***	-0.10***	1				
28. Wave 5 marijuana use	0.13***	0.13***	0.20***	0.41***	-0.02*	0.14***	0.13***	-0.08***	-0.07***	-0.10***	-0.01	0.24***	1			
29. Wave 5 self-esteem	-0.02	0.04***	0.02	-0.02*	0.36***	0.03**	-0.01	0.11***	0.10***	0.02*	-0.04***	0.01	-0.04	1		
30. Wave 5 sensation seeking	0.09***	0.08***	0.14***	0.09***	-0.01	0.42***	0.14***	0.05***	0.04***	-0.12***	-0.09***	0.23***	0.15***	0.03**	1	
31. Wave 5 interpersonal aggression	0.06***	0.04***	0.07***	0.04***	-0.05***	0.03**	0.22***	-0.05***	-0.05***	-0.01	0.06***	0.10***	0.09***	-0.07***	0.09***	1

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$; W1 = wave 1; W2 = wave 2; W5 = wave 5.

Table 4

Participants' Characteristics by Binge Drinking Trajectory Classes – Late-Onset Versus Low/Non-Use

	Total sample	Binge drinking trajectory class		X^2 *or t*-value
		Late-onset	Low/non-use	
Sociodemographic characteristics				
Male	55.03%	64.38%	48.34%	245.61***
White	62.82%	72.64%	59.55%	172.00***
Black	18.58%	11.35%	21.84%	160.04***
Hispanic	11.39%	9.24%	11.47%	11.91**
Asian	2.69%	2.16%	3.36%	10.69*
Other race/ethnicity	5.28%	4.65%	5.18%	1.35
High parent education	63.03%	68.86%	62.55%	39.19***
1976-1986 alcohol use cohort	17.29%	17.22%	15.92%	2.99
1987-1993 alcohol use cohort	25.18%	23.40%	25.39%	5.03
1994-2006 alcohol use cohort	57.52%	59.39%	58.69%	0.47
Other substance use				
Wave 1 marijuana use	1.70 (1.94)	1.55 (1.70)	1.35 (1.44)	6.42***
Wave 2 marijuana use	1.59 (1.75)	1.80 (1.97)	1.33 (1.34)	14.06***
Wave 3 marijuana use	1.59 (1.74)	1.94 (2.12)	1.34 (1.37)	17.15***
Wave 4 marijuana use	1.53 (1.69)	1.85 (2.06)	1.32 (1.35)	15.14***
Wave 5 marijuana use	1.48 (1.61)	1.82 (2.01)	1.25 (1.24)	16.98***
Late adolescent factors (W1)				
C+ or lower	29.27%	23.75%	26.19%	7.42**
College plans	70.29%	76.62%	72.45%	19.87***
Cut ≥1 class/week	33.57%	31.10%	27.56%	14.91***
3+ evenings with friends	49.16%	51.54%	41.24%	99.21***
Self-esteem	4.10 (1.12)	4.13 (1.11)	4.13 (1.12)	0.08
Sensation seeking	2.96 (1.54)	3.31 (1.45)	3.01 (1.59)	9.29***
Interpersonal aggression	1.21 (0.60)	1.15 (0.44)	1.14 (0.47)	1.20
Young adult factors				
Self-esteem (W5)	4.32 (0.85)	4.36 (0.85)	4.31 (0.88)	2.23*
Sensation seeking (W5)	2.65 (1.48)	3.04 (1.52)	2.48 (1.48)	15.70***
Interpersonal aggression (W5)	1.04 (0.22)	1.04 (0.22)	1.03 (0.19)	4.02***
Enrolled in college (W2-W5)	83.72%	86.47%	85.31%	1.41
Graduated college (W2-5)	56.04%	62.74%	56.97%	19.09***
Married (W2-5)	53.38%	32.63%	56.21%	300.76***
Parent (W2-5)	45.89%	30.40%	47.02%	155.44***

Note. Total weighted N = 19,730; Analyses included only participants who completed forms 2 or 6; Mean differences between categorical variables are shown by X^2 tests; W1 = wave 1; W2 = wave 2; W5 = wave 5.

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

Table 5

Participants' Characteristics by Binge Drinking Trajectory Classes – Late-Onset Versus Chronic High Use

	Total sample	Binge drinking trajectory class		X^2 or *t*-value
		Late-onset	Chronic high	
Sociodemographic characteristics				
Male	55.03%	64.38%	73.58%	58.04***
White	62.82%	72.64%	74.34%	2.14
Black	18.58%	11.35%	9.70%	4.20*
Hispanic	11.39%	9.24%	10.59%	2.96
Asian	2.69%	2.16%	1.10%	10.43**
Other race/ethnicity	5.28%	4.65%	4.23%	0.61
High parent education	63.03%	68.86%	63.31%	19.24***
1976-1986 alcohol use cohort	17.29%	17.22%	21.22%	14.88***
1987-1993 alcohol use cohort	25.18%	23.40%	23.86%	0.17
1994-2006 alcohol use cohort	57.52%	59.39%	54.92%	11.81***
Other substance use				
Wave 1 marijuana use	1.70 (1.94)	1.55 (1.70)	2.60 (2.39)	-18.60***
Wave 2 marijuana use	1.59 (1.75)	1.80 (1.97)	2.51 (2.37)	-10.39***
Wave 3 marijuana use	1.59 (1.74)	1.94 (2.12)	2.48 (2.28)	-7.80***
Wave 4 marijuana use	1.53 (1.69)	1.85 (2.06)	2.30 (2.25)	-6.29***
Wave 5 marijuana use	1.48 (1.61)	1.82 (2.01)	2.23 (2.14)	-5.84***
Late Adolescent Factors (W1)				
C+ or lower	29.29%	23.75%	38.55%	146.84***
College plans	70.29%	76.62%	65.90%	76.60***
Cut ≥1 class/week	33.57%	31.10%	52.54%	272.94***
3+ evenings with friends	49.16%	51.54%	69.64%	192.53***
Self-esteem	4.10 (1.12)	4.13 (1.11)	4.06 (1.11)	2.17*
Sensation seeking	2.96 (1.54)	3.31 (1.45)	3.59 (1.32)	-7.46***
Interpersonal aggression	1.21 (0.60)	1.15 (0.44)	1.36 (0.68)	-11.94***
Young Adult Factors				
Self-esteem (W5)	4.32 (0.85)	4.36 (0.85)	4.33 (0.78)	1.05
Sensation seeking (W5)	2.65 (1.48)	3.04 (1.52)	3.02 (1.32)	3.34***
Interpersonal aggression (W5)	1.04 (0.22)	1.04 (0.22)	1.08 (0.31)	-4.38***
Enrolled in college (W2-W5)	83.72%	86.47%	79.87%	20.62***
Graduated college (W2-5)	56.04%	62.74%	54.12%	21.40***
Married (W2-5)	53.38%	32.63%	42.04%	25.80***
Parent (W2-5)	45.89%	30.40%	40.98%	35.06***

Note. Total weighted N = 19,730; Analyses included only participants who completed forms 2 or 6; Mean differences between categorical variables are shown by X^2 tests; W1 = wave 1; W2 = wave 2; W5 = wave 5.

*$p < 0.05$ **$p < 0.01$ ***$p < 0.001$

Table 6

Logistic Regression Models Predicting Binge Drinking Class Membership – Late-Onset Versus Low/Non-Use

	Bivariable logistic regression		Multivariable logistic regression	
	OR	95% CI	OR	95% CI
Sociodemographic characteristics				
Male	2.16***	(1.88, 2.48)	2.14***	(1.50, 3.04)
Female	--		--	
White	--		--	
Black	0.39***	(0.29, 0.52)	0.34	(0.09, 1.27)
Hispanic	0.75*	(0.57, 0.98)	0.92	(0.37, 2.27)
Asian	0.59*	(0.38, 0.92)	0.18**	(0.06, 0.56)
Other race/ethnicity	0.88	(0.61, 1.27)	0.96	(0.33, 2.82)
High parent education	1.40***	(1.20, 1.64)	0.84	(0.56, 1.27)
Low parent education	--		--	
1976-1986 alcohol use cohort	--		--	
1987-1993 alcohol use cohort	1.04	(0.91, 1.19)	0.90	(0.53, 1.54)
1994-2006 alcohol use cohort	0.88	(0.75, 1.03)	1.15	(0.69, 1.91)
Late adolescent factors (W1)				
C+ or lower	0.84	(0.71, 1.01)	0.84	(0.48, 1.49)
College plans	1.31**	(1.10, 1.56)	0.68	(0.37, 1.26)
Cut ≥1 class/week	1.21*	(1.03, 1.41)	1.34	(0.89, 2.02)
3+ evenings out/week	1.62***	(1.41, 1.85)	1.75**	(1.25, 2.44)
Marijuana use	1.23***	(1.16, 1.31)	1.57*	(1.10, 2.23)
Self-esteem	1.01	(0.92, 1.11)	0.92	(0.73, 1.17)
Sensation seeking	1.28***	(1.21, 1.36)	1.13	(0.96, 1.32)
Interpersonal agg.	1.20	(0.79, 1.81)	1.70	(0.56, 5.19)
Young adult factors				
Marijuana use (W5)	3.49***	(1.90, 6.41)	4.44*	(1.37, 14.38)
Self-esteem (W5)	1.60***	(1.48, 1.73)	1.28	(0.94, 1.76)
Sensation seeking (W5)	5.93*	(1.45, 24.32)	1.12	(0.95, 1.76)
Interpersonal aggression (W5)	1.13	(1.00, 1.27)	2.25	(0.34, 15.05)
Enrolled in college (W2-W5)	1.13	(0.86, 1.48)	0.95	(0.49, 1.85)
Graduated college (W2-5)	1.34**	(1.12, 1.59)	1.15	(0.70, 1.88)
Married (W2-5)	0.31***	(0.26, 0.38)	0.45***	(0.31, 0.66)
Parent (W2-5)	0.43***	(0.35, 0.54)	0.43**	(0.24, 0.76)

Note. OR = odds ratio; 95% confidence interval in parentheses; – reference group; agg. = aggression; W1 = wave 1; W2 = wave 2; W5 = wave 5.

*p < 0.05 **p < 0.01 ***p < 0.001

Table 7

Logistic Regression Models Predicting Binge Drinking Class Membership – Late-Onset Versus Chronic High Use

	Bivariable logistic regression		Multivariable logistic regression	
	OR	95% CI	OR	95% CI
Sociodemographic characteristics				
Male	0.62***	(0.51, 0.75)	0.57	(0.32, 1.00)
Female	--		--	
White	--		--	
Black	1.09	(0.72, 1.65)	23.34[a]	(1.72, 316.33)
Hispanic	0.84	(0.58, 1.21)	1.14	(0.26, 5.05)
Asian	1.92	(0.87, 4.20)	0.48	(0.11, 2.06)
Other race	1.17	(0.70, 1.95)	6.82	(0.14, 324.15)
High parent education	1.34**	(1.10, 1.63)	1.11	(0.62, 1.95)
Low parent education	--		--	
1976-1986 alcohol use cohort	--		--	
1987-1993 alcohol use cohort	0.99	(0.80, 1.23)	1.40	(0.71, 2.79)
1994-2006 alcohol use cohort	1.19	(0.99, 1.41)	2.34*	(1.16, 4.74)
Late adolescent factors (W1)				
C+ or lower	0.50***	(0.38, 0.56)	0.54	(0.24, 1.21)
College plans	1.73***	(1.40, 2.15)	1.97	(0.80, 4.86)
Cut ≥1 class/week	0.38***	(0.31, 0.47)	0.49**	(0.29, 0.81)
3+ evenings out/week	0.46	(0.38, 0.56)	0.61	(0.38, 1.00)
Marijuana use	0.72***	(0.68, 0.76)	0.74***	(0.63, 0.87)
Self-esteem	1.11	(0.96, 1.27)	0.84	(0.56, 1.24)
Sensation seeking	0.81***	(0.75, 0.88)	0.73*	(0.53, 0.99)
Interpersonal agg.	0.38***	(0.26, 0.55)	0.20***	(0.09, 0.44)
Young adult factors				
Marijuana use (W5)	0.95	(0.90, 1.01)	0.93	(0.80, 1.09)
Self-esteem (W5)	0.85**	(0.77, 0.94)	0.90	(0.53, 1.52)
Sensation seeking (W5)	0.64*	(0.41, 0.98)	0.91	(0.72, 1.16)
Interpersonal aggression (W5)	1.08	(0.91, 1.29)	0.78	(0.05, 12.11)
Enrolled in college (W2-W5)	1.58**	(1.14, 2.21)	0.80	(0.29, 2.22)
Graduated college (W2-5)	1.40**	(1.11, 1.78)	0.76	(0.36, 1.61)
Married (W2-5)	0.71*	(0.54, 0.94)	1.90	(0.85, 4.24)
Parent (W2-5)	0.65**	(0.48, 0.87)	0.77	(0.33, 1.79)

Note. OR = odds ratio; 95% confidence interval in parentheses; [a]uninterpretable due to small sample size; – reference group; agg. = aggression; W1 = wave 1; W2 = wave 2; W5 = wave 5.

**p* < 0.05 ***p* < 0.01 ****p* < 0.001

Table 8

Participants' Characteristics by Marijuana use Trajectory Classes – Late-Onset Versus Low/Non-Use

		Marijuana use trajectory class		
	Total sample	Late-onset	Low/non use	X^2 *or t*-value
Sociodemographic characteristics				
Male	46.59%	65.83%	52.04%	123.91***
White	76.00%	61.84%	63.01%	0.95
Black	10.12%	20.56%	18.40%	5.01*
Hispanic	7.52%	9.58%	11.74%	7.36**
Asian	2.60%	0.82%	3.08%	27.98***
Other race/ethnicity	3.75%	4.34%	5.18%	2.38
High parent education	67.46%	68.78%	62.64%	25.20***
1976-1991 marijuana use cohort	39.12%	27.30%	34.20%	34.50***
1992-1997 marijuana use cohort	36.26%	26.14%	25.20%	0.75
1998-2006 marijuana use cohort	24.61%	46.56%	40.60%	23.85***
Other substance use				
Wave 1 binge drinking	1.82 (1.67)	2.20 (1.88)	1.62 (1.51)	14.99***
Wave 2 binge drinking	1.85 (1.58)	2.43 (1.87)	1.70 (1.50)	15.48***
Wave 3 binge drinking	1.95 (1.62)	2.73 (2.03)	1.81 (1.56)	17.93***
Wave 4 binge drinking	1.87 (1.53)	2.55 (1.91)	1.75 (1.48)	15.69***
Wave 5 binge drinking	1.76 (1.44)	2.55 (1.89)	1.65 (1.39)	17.82***
Late adolescent factors (W1)				
C+ or lower	29.27%	35.79%	26.53%	70.53***
College plans	70.29%	70.64%	72.08%	1.57
Cut ≥1 class/week	33.57%	43.73%	29.38%	158.78***
3+ evenings out/week	49.16%	60.94%	44.58%	166.74***
Self-esteem	4.10 (1.12)	4.10 (1.21)	4.12 (1.14)	-0.56
Sensation seeking	2.96 (1.54)	3.55 (1.49)	3.09 (1.60)	11.15***
Interpersonal aggression	1.21 (0.60)	1.33 (0.76)	1.17 (0.51)	10.72***
Young adult factors				
Self-esteem (W5)	4.32 (0.85)	4.26 (0.96)	4.33 (0.87)	-2.33*
Sensation seeking (W5)	2.65 (1.48)	3.13 (1.56)	2.59 (1.52)	10.03***
Interpersonal aggression (W5)	1.04 (0.22)	1.09 (0.45)	1.03 (0.19)	7.53***
Enrolled in college (W2-W5)	83.72%	81.74%	84.94%	4.72*
Graduated college (W2-5)	56.04%	51.78%	57.72%	8.33**
Married (W2-5)	53.38%	36.48%	54.52%	76.68***
Parent (W2-5)	45.89%	46.25%	45.11%	0.34

Note. Total weighted *N* = 19,730; Analyses included only participants who completed forms 2 or 6; Mean differences between categorical variables are shown by X^2 tests; W1 = wave 1; W2 = wave 2; W5 = wave 5.

**p* < 0.05 ***p* < 0.01 ****p* < 0.001

Table 9

Participants' Characteristics by Marijuana Use Trajectory Classes – Late-Onset Versus Chronic High Use

	Total sample	Marijuana use trajectory class		X^2 *or t*-value
		Late-onset	Chronic high	
Sociodemographic characteristics				
Male	46.59%	65.83%	75.63%	38.15***
White	76.00%	61.84%	65.75%	5.45*
Black	10.12%	20.56%	14.86%	18.26***
Hispanic	7.52%	9.58%	9.15%	0.18
Asian	2.60%	0.82%	0.84%	0.00
Other race/ethnicity	3.75%	4.34%	7.27%	13.13***
High parent education	67.46%	68.78%	63.62%	9.45**
1976-1991 marijuana use cohort	39.12%	27.30%	31.05%	5.63*
1992-1997 marijuana use cohort	36.26%	26.14%	23.95%	2.10
1998-2006 marijuana use cohort	24.61%	46.56%	44.99%	0.82
Other substance use				
Wave 1 binge drinking	1.82 (1.67)	2.20 (1.88)	3.20 (1.57)	-16.21***
Wave 2 binge drinking	1.85 (1.58)	2.43 (1.87)	3.00 (1.44)	-7.20***
Wave 3 binge drinking	1.95 (1.62)	2.73 (2.03)	2.97 (1.49)	-2.90**
Wave 4 binge drinking	1.87 (1.53)	2.55 (1.91)	2.77 (1.46)	-2.63**
Wave 5 binge drinking	1.76 (1.44)	2.55 (1.89)	2.61 (1.40)	-0.68
Late adolescent factors (W1)				
C+ or lower	29.27%	35.79%	45.42%	31.81***
College plans	70.29%	70.64%	57.53%	57.73***
Cut ≥1 class/week	33.57%	43.73%	60.48%	92.29***
3+ evenings out/week	49.16%	60.94%	76.94%	92.69***
Self-esteem	4.10 (1.12)	4.10 (1.21)	3.96 (0.95)	3.45***
Sensation seeking	2.96 (1.54)	3.55 (1.49)	3.71 (1.05)	-3.70***
Interpersonal aggression	1.21 (0.60)	1.33 (0.76)	1.49 (0.70)	-5.65***
Young adult factors				
Self-esteem (W5)	4.32 (0.85)	4.26 (0.96)	4.24 (0.68)	0.40
Sensation seeking (W5)	2.65 (1.48)	3.13 (1.56)	3.17 (1.14)	-0.48
Interpersonal aggression (W5)	1.04 (0.22)	1.09 (0.45)	1.06 (0.22)	1.25
Enrolled in college (W2-W5)	83.72%	81.74%	67.72%	24.37***
Graduated college (W2-5)	56.04%	51.78%	38.49%	17.25***
Married (W2-5)	53.38%	36.48%	45.03%	7.83**
Parent (W2-5)	45.89%	46.25%	49.24%	1.02

Note. Total weighted N = 19,730; Analyses included only participants who completed forms 2 or 6; Mean differences between categorical variables are shown by X^2 tests; W1 = wave 1; W2 = wave 2; W5 = wave 5.

$^*p < 0.05$ $^{**}p < 0.01$ $^{***}p < 0.001$

Table 10

Logistic Regression Models Predicting Marijuana Class Membership – Late-Onset Versus Low/Non-Use

	Bivariable logistic regression		Multivariable logistic regression	
	OR	95% CI	OR	95% CI
Sociodemographic characteristics				
Male	1.64***	(1.59, 2.26)	1.28	(0.70, 2.36)
Female	--		--	
White	--		--	
Black	1.17	(0.89, 1.54)	1.88	(0.60, 5.85)
Hispanic	0.78	(0.55, 1.22)	0.17	(0.01, 1.95)
Asian	0.19	(0.06, 0.56)	0.79	(0.17, 3.81)
Other race	0.81	(0.53, 1.25)	0.17	(0.00, 4500.75)
High parent education	1.36**	(1.12, 1.66)	1.39	(0.52, 1.97)
Low parent education	--		--	
1976-1991 marijuana use cohort	--		--	
1992-1997 marijuana use cohort	1.06	(0.87, 1.29)	1.01	(0.52, 1.97)
1998-2006 marijuana use cohort	1.31**	(1.10, 1.56)	1.88	(0.91, 3.88)
Late adolescent factors (W1)				
C+ or lower	2.36***	(2.06, 2.71)	0.67	(0.26, 1.72)
College plans	0.93	(0.77, 1.13)	2.80	(0.93, 8.29)
Cut ≥1 class/week	1.99***	(1.67, 2.38)	1.30	(0.72, 2.33)
3+ evenings out/week	2.08***	(1.71, 2.52)	0.65	(0.35, 1.22)
Binge drinking	1.46***	(1.38, 1.55)	1.65***	(1.30, 2.09)
Self-esteem	0.97	(0.85, 1.11)	1.62*	(1.01, 2.59)
Sensation seeking	1.45***	(1.31, 1.60)	1.05	(0.78, 1.41)
Interpersonal agg.	2.18***	(1.94, 2.45)	0.67	(0.29, 1.56)
Young adult factors				
Binge drinking (W5)	1.75***	(1.62, 1.89)	1.65***	(1.33, 2.05)
Self-esteem (W5)	0.85	(0.73, 1.00)	0.57**	(0.38, 0.84)
Sensation seeking (W5)	1.51***	(1.37, 1.66)	1.58*	(1.11, 2.25)
Interpersonal aggression (W5)	3.16***	(1.79, 5.58)	0.04	(0.00, 1.07)
Enrolled in college (W2-W5)	0.78***	(0.59, 1.02)	0.42	(0.17, 1.08)
Graduated college (W2-5)	0.76	(0.58, 1.00)	0.76	(0.36, 1.59)
Married (W2-5)	0.43***	(0.32, 0.57)	0.41*	(0.20, 0.86)
Parent (W2-5)	1.05	(0.78, 1.41)	1.70	(0.72, 4.02)

Note. OR = odds ratio; 95% confidence interval in parentheses; – reference group; agg. = aggression; W1 = wave 1; W2 = wave 2; W5 = wave 5.

**p* < 0.05 ***p* < 0.01 ****p* < 0.001

Table 11

Logistic Regression Models Predicting Marijuana Class Membership – Late-Onset Versus Chronic High Use

	Bivariable logistic regression		Multivariable logistic regression	
	OR	95% CI	OR	95% CI
Sociodemographic characteristics				
Male	0.63***	(0.51, 0.78)	0.76	(0.30, 1.90)
Female	--		--	
White	--		--	
Black	1.52*	(1.09, 2.12)	0.87	(0.13, 5.93)
Hispanic	1.04	(0.69, 1.57)	0.41	(0.00, 75.46)
Asian	0.73	(0.21, 2.55)	0.00[a]	
Other race	0.55*	(0.34, 0.90)	0.03	(0.00, 745.76)
High parent education	0.77*	(0.61, 0.98)	0.64	(0.19, 2.17)
Low parent education	--		--	
1976-1991 marijuana use cohort	--		--	
1992-1997 marijuana use cohort	1.13	(0.89, 1.43)	1.06	(0.41, 2.77)
1998-2006 marijuana use cohort	1.07	(0.86, 1.33)	0.80	(0.26, 2.45)
Late adolescent factors (W1)				
C+ or lower	0.68**	(0.54, 0.87)	0.46	(0.13, 1.67)
College plans	1.79***	(1.44, 2.22)	5.53*	(1.22, 25.01)
Cut ≥1 class/week	0.52***	(0.42, 0.65)	0.28*	(0.09, 0.87)
3+ evenings with friends	0.49***	(0.39, 0.62)	0.39	(0.13, 1.16)
Binge drinking	0.70***	(0.66, 0.74)	0.88	(0.65, 1.18)
Self-esteem	1.09	(0.94, 1.28)	2.14**	(1.21, 3.77)
Sensation seeking	0.89*	(0.80, 0.98)	0.32	(0.18, 0.56)
Interpersonal agg.	0.77**	(0.63, 0.94)	0.71	(0.28, 1.79)
Young adult factors				
Binge drinking (W5)	1.00	(0.91, 1.10)	1.31	(0.98, 1.76)
Self-esteem (W5)	1.03	(0.83, 1.28)	0.67	(0.37, 1.23)
Sensation seeking (W5)	0.99	(0.86, 1.14)	1.21	(0.67, 2.18)
Interpersonal aggression (W5)	1.32	(0.79, 2.20)	0.13	(0.00, 6.56)
Enrolled in college (W2-W5)	2.16***	(1.43, 3.26)	0.30	(0.06, 1.43)
Graduated college (W2-5)	1.72**	(1.18, 2.49)	1.15	(0.39, 3.38)
Married (W2-5)	0.64*	(0.44, 0.93)	0.52	(0.16, 1.69)
Parent (W2-5)	0.90	(0.64, 1.29)	2.39	(0.56, 10.18)

Note. OR = odds ratio; 95% confidence interval in parentheses; [a]uninterpretable due to small sample size; – reference group; agg. = aggression; W1 = wave 1; W2 = wave 2; W5 = wave 5.

**p* < 0.05 ***p* < 0.01 ****p* < 0.001

Table 12

Growth Mixture Model Fit for Binge Drinking and Marijuana Use, Chapter Three

	BIC	Entropy	Class proportions	L-M-R test	L-M-R *p*-value
Binge drinking model					
2 classes	15389.15	0.99	3.78 96.22	274.96	<0.01
3 classes	**15242.77**	**0.97**	**11.21 3.52 85.28**	**155.28**	**<0.01**
4 classes	15175.08	0.95	2.82 78.58 9.91 8.69	80.79	0.68
Marijuana use model					
2 classes	5841.40	0.95	73.96 26.04	300.58	<0.001
3 classes	**5691.71**	**0.95**	**10.88 18.15 70.98**	**158.41**	**<0.001**
4 classes	5653.50	0.94	17.96 69.34 6.63 6.10	52.89	0.36

Note. Model fit is shown for the linear binge drinking model and linear marijuana use model; BIC = Bayesian Information Criteria; class proportions for the latent class patterns based on estimated posterior probabilities; L-M-R Test = Lo-Mendell-Rubin adjusted likelihood ratio value; L-M-R *p*-value = *p* value associated with Lo-Mendell Rubin adjusted likelihood ratio value.

Table 13

Correlations Between Predictor Variables Examined in Logistic Regression Models Predicting Resilient Versus Risk Groups

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Male	1																
2. High parent education	0.07	1															
3. Number of parents with SUD	0.02	0.01	1														
4. Resiliency (12-14)	0.06	-0.04	0.09	1													
5. Reactive control (12-14)	-0.11	0.06	-0.07	-0.21**	1												
6. Sensation seeking (12-14)	-0.10	0.11	0.02	0.15*	-0.22**	1											
7. Internalizing behaviors (12-14)	-0.12	-0.07	0.03	-0.13	-0.07	-0.02	1										
8. Externalizing behaviors (12-14)	0.04	-0.00	-0.01	-0.01	-0.34***	0.01	0.50***	1									
9. Resiliency (17-18)	-0.14	-0.03	-0.05	0.16	0.11	0.23**	-0.23**	-0.24**	1								
10. Reactive control (17-18)	-0.01	-0.06	-0.16*	-0.05	0.36***	-0.12	-0.14	-0.35***	0.25**	1							
11. Sensation seeking (17-18)	-0.06	-0.03	-0.15	-0.04	-0.05	0.22*	0.00	0.10	0.14	-0.13	1						
12. Internalizing behaviors (17-18)	-0.14*	-0.04	0.09	-0.10	0.12	-0.07	0.36***	0.13	-0.22**	-0.06	-0.21*	1					
13. Externalizing behaviors (17-18)	0.08	0.02	0.07	0.05	-0.08	-0.09	0.20**	0.42***	-0.15	-0.44***	0.03	0.51***	1				
14. Enrolled in college (18-26)	-0.01	0.11	-0.16*	-0.03	0.05	0.17*	-0.07	-0.09	0.27**	0.32***	0.07	-0.11	-0.19**	1			
15. Graduated college (18-26)	-0.05	0.16*	-0.13	0.14	-0.07	0.18*	-0.03	-0.01	0.26**	0.20*	-0.04	-0.02	0.08	0.35***	1		
16. Married (18-26)	-0.11	-0.05	-0.10	0.10	-0.05	-0.01	0.09	0.05	0.09	0.04	-0.09	0.01	-0.04	-0.12	0.06	1	
17. Parent (18-26)	-0.18**	-0.15*	0.02	0.07	-0.08	-0.12	0.10	0.01	-0.10	-0.17*	0.07	-0.06	-0.00	-0.31***	-0.21**	0.41***	1

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 14

Participants' Characteristics – Resilient Versus Risk Groups

	Resilient	Risk	X^2 *or t*-value
	N = 84	*N* = 151	
Sociodemographic characteristics			
Male[a]	59.52%	84.11%	17.55***
High parent education[b]	86.90%	84.77%	0.20
Two parents with SUD[c]	50.00%	55.63%	0.69
Substance use			
Binge drinking (17-18)	2.13 (8.42)	42.16 (70.46)	-5.12***
Binge drinking (19-20)	4.81 (9.150	82.74 (90.00)	-6.22***
Binge drinking (21-22)	7.58 (11.28)	105.16 (85.58)	-9.00***
Binge drinking (23-24)	5.40 (10.44)	84.63 (85.72)	-7.47***
Binge drinking (25-26)	3.94 (8.55)	88.77 (88.66)	-7.38***
Marijuana use (17-18)	0.33 (0.89)	3.08 (2.91)	-8.34***
Marijuana use (19-20)	0.24 (0.52)	3.76 (3.11)	-8.16***
Marijuana use (21-22)	0.28 (0.74)	3.65 (3.20)	-8.25***
Marijuana use (23-24)	0.16 (0.68)	3.69 (3.23)	-8.77***
Marijuana use (25-26)	0.11 (0.48)	3.47 (2.30)	-7.85***
Early adolescent factors (12-14)			
Resiliency	5.69 (0.93)	5.76 (0.87)	-0.50
Reactive control	5.45 (1.17)	4.89 (1.01)	3.51**
Sensation seeking	5.85 (1.93)	5.91 (1.81)	-0.24
Internalizing behaviors	8.34 (6.51)	9.59 (7.52)	-1.12
Externalizing behaviors	8.46 (5.55)	12.23 (7.74)	-3.68***
Late adolescent factors (17-18)			
Resiliency	5.99 (1.03)	5.53 (1.18)	2.45*
Reactive control	5.36 (0.93)	4.49 (1.07)	5.12***
Sensation seeking	5.62 (2.15)	6.00 (1.89)	-1.16
Internalizing behaviors	7.60 (7.03)	8.74 (6.84)	-1.16
Externalizing behaviors	7.83 (5.20)	12.86 (6.66)	-5.79***
Young adult social roles (18-26)			
Enrolled in college	73.81%	66.44%	2.55
Graduated college	25.00%	20.13%	1.02
Married	20.23%	10.07%	5.23*
Parent	21.43%	17.45%	0.77

Note. Total *N* = 235. Mean differences between categorical variables are shown by X^2 tests; early adolescent factors are from ages 12-14; late adolescent factors are from ages 17-18; young adult social roles are from ages 18-26; [a]reference group female; [b]reference group low parent education; [c]reference group one parent with SUD.

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 15

Hierarchical Multivariable Logistic Regression Models Predicting Resilient Versus Risk Groups

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Sociodemographic characteristics						
Male[a]	0.38*	(0.16, 0.93)	0.32*	(0.12, 0.87)	0.28*	(0.93, 0.87)
High parent education[b]	1.17	(0.34, 4.00)	1.55	(0.40, 6.04)	2.30	(0.52, 10.11)
Two parents with SUD[c]	1.16	(0.52, 2.60)	1.38	(0.57, 3.37)	1.66	(0.64, 4.28)
Early adolescent factors (12-14)						
Resiliency	0.99	(0.63, 1.58)	0.99	(0.60, 1.63)	1.00	(0.57, 1.73)
Reactive control	1.45	(0.96, 2.21)	1.35	(0.84, 2.16)	1.34	(0.83, 2.18)
Sensation seeking	0.92	(0.72, 1.17)	0.89	(0.68, 1.17)	0.91	(0.69, 1.21)
Internalizing behaviors	0.99	(0.92, 1.06)	0.98	(0.91, 1.07)	0.96	(0.88, 1.06)
Externalizing behaviors	0.96	(0.89, 1.03)	1.03	(0.94, 1.13)	1.04	(0.95, 1.14)
Late adolescent factors (17-18)						
Resiliency			1.14	(0.71, 1.84)	1.16	(0.71, 1.92)
Reactive control			1.85*	(1.09, 3.13)	2.04*	(1.15, 3.62)
Sensation seeking			0.98	(-0.77, 1.25)	1.00	(0.78, 1.29)
Internalizing behaviors			1.03	(0.95, 1.13)	1.04	(0.95, 1.14)
Externalizing behaviors			0.88*	(0.78, 0.99)	0.87*	(0.77, 0.99)
Young adult social roles (18-26)						
Enrolled in college					1.00	(0.26, 3.84)
Graduated college					0.50	(0.14, 1.80)
Married					4.57*	(1.01, 20.73)
Parent					0.71	(0.13, 3.71)
Nagelkerke R^2	0.17		0.34		0.38	
Model χ^2	15.22		33.09**		38.28**	

Note. OR = odds ratio; 95% confidence intervals in parentheses; [a]reference group female; [b]reference group low parent education; [c]reference group one parent with SUD.

**p* < 0.05, ***p* < 0.01, ****p* < 0.001

Table 16

Participants' Characteristics by Binge Drinking Trajectory Classes – Resilient Versus Risk Groups

	Resilient	Risk	X^2 or *t*-value
	N=21	*N*=36	
Sociodemographic characteristics			
Male[a]	66.67%	75.00%	0.50
Two parents with SUD	42.90%	52.80%	-0.47
Mean age at Go/No-Go scan	20.68 (1.74)	19.88 (1.78)	1.64
Mean age at MIDT scan	20.83 (1.45)	20.51 (1.20)	0.86
Substance use			
Binge drinking (17-18)	5.00 (15.31)	49.74 (77.57)	-2.60*
Binge drinking (19-20)	5.06 (9.72)	96.21 (101.16)	-3.69**
Binge drinking (21-22)	3.97 (9.57)	112.02 (100.20)	-4.91***
Binge drinking (23-24)	3.13 (6.36)	68.77 (66.09)	-4.52***
Binge drinking (25-26)	2.85 (77.10)	77.10 (71.34)	-3.86***
Marijuana use (17-18)	0.52 (1.25)	2.69 (3.00)	-3.16**
Marijuana use (19-20)	0.24 (0.53)	2.91 (2.97)	-3.67**
Marijuana use (21-22)	0.12 (0.31)	2.94 (3.01)	-4.26***
Marijuana use (23-24)	0.05 (0.15)	2.53 (2.90)	-3.90***
Marijuana use (25-26)	0.00 (0.00)	2.48 (3.19)	-2.90**
Early adolescent factors (12-14)			
Reactive control	5.61 (1.28)	4.77 (1.04)	2.60*
Externalizing behaviors	8.14 (5.18	13.11 (8.24)	-2.49*
Late adolescent factors (17-18)			
Reactive control	5.19 (1.06)	4.65 (0.91)	1.75
Externalizing behaviors	7.38 (3.96)	12.45 (5.56)	-3.66**

Note. N = 57. SUD = substance use disorder; MIDT = monetary incentive delay task; Mean differences between categorical variables are shown by X^2 tests; early adolescent factors are from ages 12-14; late adolescent factors are from ages 17-18; [a]reference group female; [b]reference group one parent with SUD.

**p* < 0.05, ***p* < 0.01, ****p* < 0.001

Table 17

Mean Task Performance Data for the Go/No-Go Task and Monetary Incentive Delay Task for Resilient Versus Risk Groups

	Resilient	Risk	*t*-value
Go/No-Go Task			
Hit accuracy (%)	98.64 (4.01)	98.33 (2.55)	0.37
Hit reaction time (ms)	421.27 (34.59)	420.38 (42.22)	0.07
Correct inhibition rate (%)	79.05 (15.14)	76.67 (10.88)	0.69
MIDT			
Hit accuracy (%)			
Reward target trials[a]	63.75 (15.25)	61.53 (17.24)	0.47
Loss target trials[a]	62.91 (16.45)	59.90 (15.49)	0.66
Neutral target trials	51.00 (17.21)	45.81 (17.85)	1.03
Reaction time (ms)			
Reward target trials[a]	192.46 (33.97)	178.67 (39.60)	1.28
Loss target trials[a]	193.36 (33.12)	181.68 (37.45)	1.14
Neutral target trials	191.10 (39.83)	183.73 (35.91)	0.69

Note. MIDT = Monetary Incentive Delay Task; Standard deviations are shown in parentheses; [a]Combined reward trials were calculated by the mean of small and large amount for both reward and loss trials.

Table 18

Whole-Brain Task Activation During Go/No-Go Task and Monetary Incentive Delay Task

Region of Interest	MNI Coordinates *x*, *y*, *z*	k	Peak *t*	Cluster level *p* (FWE corrected)
Go/No-Go Task				
Correct inhibition versus baseline				
Right dorsolateral prefrontal cortex	40, 44 26	159	7.23	$p < 0.005$
Right inferior orbitofrontal gyrus	48, 46, -10	56	6.43	$p < 0.05$
Left middle frontal gyrus	-32, 52, 18	37	5.81	$p < 0.05$
MIDT				
Reward anticipation versus neutral				
Left ventral striatum	-10, 4, 2	769	11.86	$p < 0.00005$
Right ventral striatum	8, 10, 0	645	11.51	$p < 0.00005$
Positive versus negative reward feedback				
Left ventral striatum	-14, 10, -12	67	6.00	$p < 0.05$
Right ventral striatum	14, 10, -14	50	6.64	$p < 0.05$

Note. MNI = Montreal Neurological Institute; k = extent threshold in voxels; MIDT = Monetary Incentive Delay Task; FEW = family-wise error; standard deviations are shown in parentheses; MNI coordinates

Table 19

Correlations Between Variables Examined in Hierarchical Logistic Regression Models

	1	2	3	4	5	6	7	8	9	10	11	12	13
1. Male	1												
2. Number of parents with SUD	0.30*	1											
3. Reactive control (12-14)	0.12	-0.02	1										
4. Externalizing behaviors (12-14)	-0.27*	-0.06	-0.41**	1									
5. Reactive control (17-18)	0.18	-0.22	0.52**	-0.31*	1								
6. Externalizing behaviors (17-18)	-0.22	-0.07	-0.17	0.46***	-0.24	1							
7. Right DLPFC - GNG	0.01	0.22	-0.01	-0.07	-0.08	-0.23	1						
8. Right iOFG – GNG	0.17	0.13	0.21	-0.18	0.11	-0.26*	0.57***	1					
9. Left MFG – GNG	0.00	0.03	0.06	-0.18	0.01	-0.02	0.48***	0.59***	1				
10. Left VS – MID (Reward)	0.16	0.13	-0.10	0.16	-0.33*	0.09	0.23	0.27	0.19	1			
11. Right VS – MID (Reward)	0.20	0.13	-0.17	0.19	-0.32	0.15	0.12	0.22	0.15	0.95***	1		
12. Left VS – MID (Feedback)	0.02	0.10	-0.04	0.19	-0.26	0.24	-0.02	0.15	-0.04	0.16	0.22	1	
13. Right VS – MID (Feedback)	0.12	0.15	-0.07	0.16	-0.17	0.22	-0.03	0.15	0.07	0.28*	0.36*	0.84***	1

Note. DLPFC = dorsolateral prefrontal cortex; iOFG = inferior orbital frontal gyrus; MFG = medial frontal gyrus; VS = ventral striatum

*$p < 0.05$, **$p < 0.01$, ***$p < 0.001$

Table 20

Hierarchical Multivariable Logistic Regression Models Predicting Substance Use Resilient Versus Risk Groups – Go/No-Go Task (Correct Inhibition)

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Sociodemographic Characteristics						
Male[a]	0.74	(0.13, 4.31)	0.45	(0.06, 3.44)	0.96	(0.09, 10.36)
Number of parents with SUD	0.86	(0.18, 4.20)	0.88	(0.14, 5.61)	0.09	(0.00, 2.01)
Early Adolescence (12-14)						
Reactive control	1.61	(0.83, 3.12)	1.72	(0.80, 3.72)	3.28*	(1.07, 10.08)
Externalizing behaviors	0.93	(0.82, 1.05)	0.97	(0.85, 1.12)	1.01	(0.87, 1.17)
Late Adolescence (17-18)						
Reactive control			1.28	(0.45, 3.63)	0.83	(0.24, 2.82)
Externalizing behaviors			0.78*	(0.62, 0.98)	0.70*	(0.51, 0.96)
Neural Activation Go/No-Go Task						
Right dorsolateral prefrontal cortex (Correct inhibition vs. Baseline)					1.88*	(1.03, 3.44)
Nagelkerke R^2	0.22		0.40		0.55	
Model χ^2	6.78		13.48*		20.11**	

Note. OR = odds ratio; CI = 95% confidence intervals; SUD = substance use disorder; [a]reference group female.

**p* < 0.05. ***p* < 0.01. ****p* < 0.001

Table 21

Hierarchical Multivariable Logistic Regression Models Predicting Substance Use Resilient Versus Risk Groups – Monetary Incentive Delay Task (Reward Anticipation)

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Sociodemographic Characteristics						
Male[a]	0.74	(0.13, 4.31)	0.45	(0.06, 3.44)	0.59	(0.07, 5.20)
Number of parents with SUD	0.86	(0.18, 4.20)	0.88	(0.14, 5.61)	0.85	(0.12, 6.18)
Early Adolescence (12-14)						
Reactive control	1.61	(0.83, 3.12)	1.72	(0.80, 3.72)	1.57	(0.73, 3.39)
Externalizing behaviors	0.93	(0.82, 1.05)	0.97	(0.85, 1.12)	0.98	(0.84, 1.15)
Late Adolescence (17-18)						
Reactive control			1.28	(0.45, 3.63)	1.33	(0.46, 3.85)
Externalizing behaviors			0.78*	(0.62, 0.98)	0.81	(0.64, 1.04)
Neural Activation MIDT						
Left ventral striatum (Reward vs. neutral anticipation)					2.91	(0.24, 34.98)
Right ventral striatum (Reward vs. neutral anticipation)					0.37	(0.03, 4.50)
Nagelkerke R^2	0.22		0.40		0.36	
Model χ^2	6.78		13.48*		10.57	

Note. OR = odds ratio; CI = 95% confidence intervals; SUD = substance use disorder; MIDT = Monetary Incentive Delay Task; [a]reference group female.

*p < 0.05. **p < 0.01. ***p < 0.001

Table 22

Hierarchical Multivariable Logistic Regression Models Predicting Substance Use Resilient Versus Risk Groups – Monetary Incentive Delay Task (Reward Feedback)

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Sociodemographic Characteristics						
Male[a]	0.74	(0.13, 4.31)	0.45	(0.06, 3.44)	0.58	(0.05, 6.22)
Number of parents with SUD	0.86	(0.18, 4.20)	0.88	(0.14, 5.61)	1.40	(0.18, 10.98)
Early Adolescence (12-14)						
Reactive control	1.61	(0.83, 3.12)	1.72	(0.80, 3.72)	1.49	(0.65, 3.40)
Externalizing behaviors	0.93	(0.82, 1.05)	0.97	(0.85, 1.12)	1.00	(0.84, 1.18)
Late Adolescence (17-18)						
Reactive control			1.28	(0.45, 3.63)	1.73	(0.53, 5.66)
Externalizing behaviors			0.78*	(0.62, 0.98)	0.80	(0.59, 1.08)
Neural Activation MIDT						
Left ventral striatum (Positive versus negative reward feedback)					1.72	(0.77, 3.86)
Right ventral striatum (Positive versus negative reward feedback)					0.55	(0.27, 1.11)
Nagelkerke R^2	0.22		0.40		0.40	
Model χ^2	6.78		13.48*		11.81	

Note. OR = odds ratio; CI = 95% confidence intervals; SUD = substance use disorder; MIDT = Monetary Incentive Delay Task; [a]reference group female.

*$p < 0.05$. **$p < 0.01$. ***$p < 0.001$

Figures

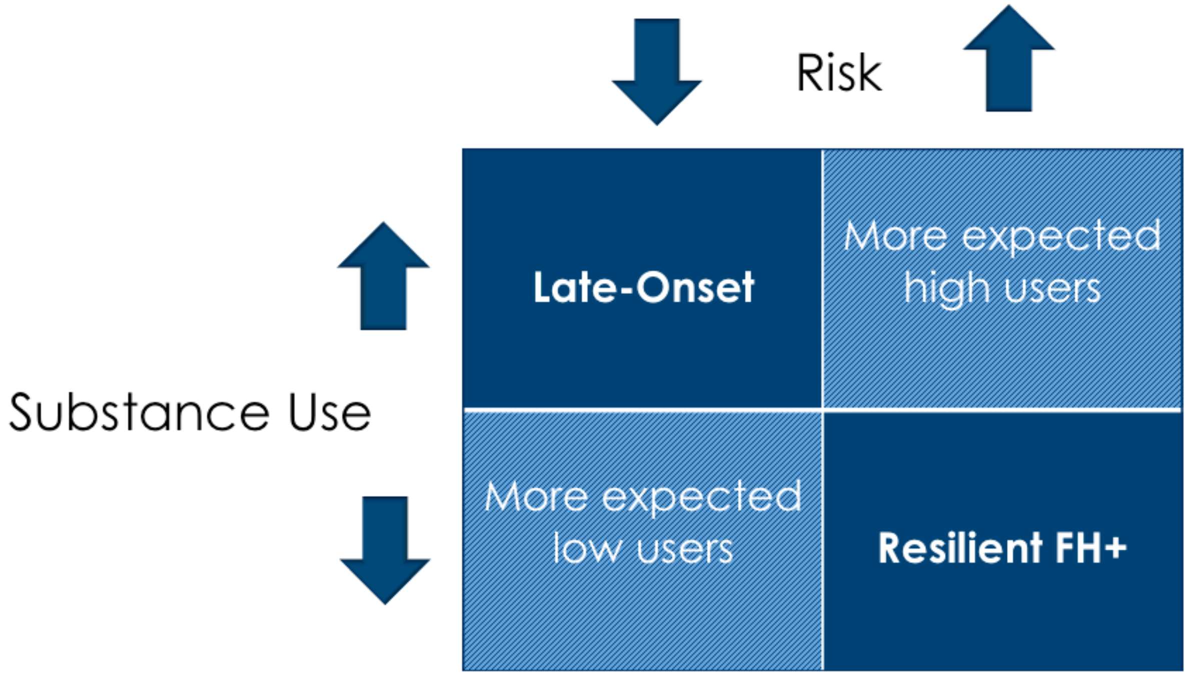

Figure 1. Off-diagonal substance use groups. Conceptual model for categorizations of off-diagonal substance use groups.

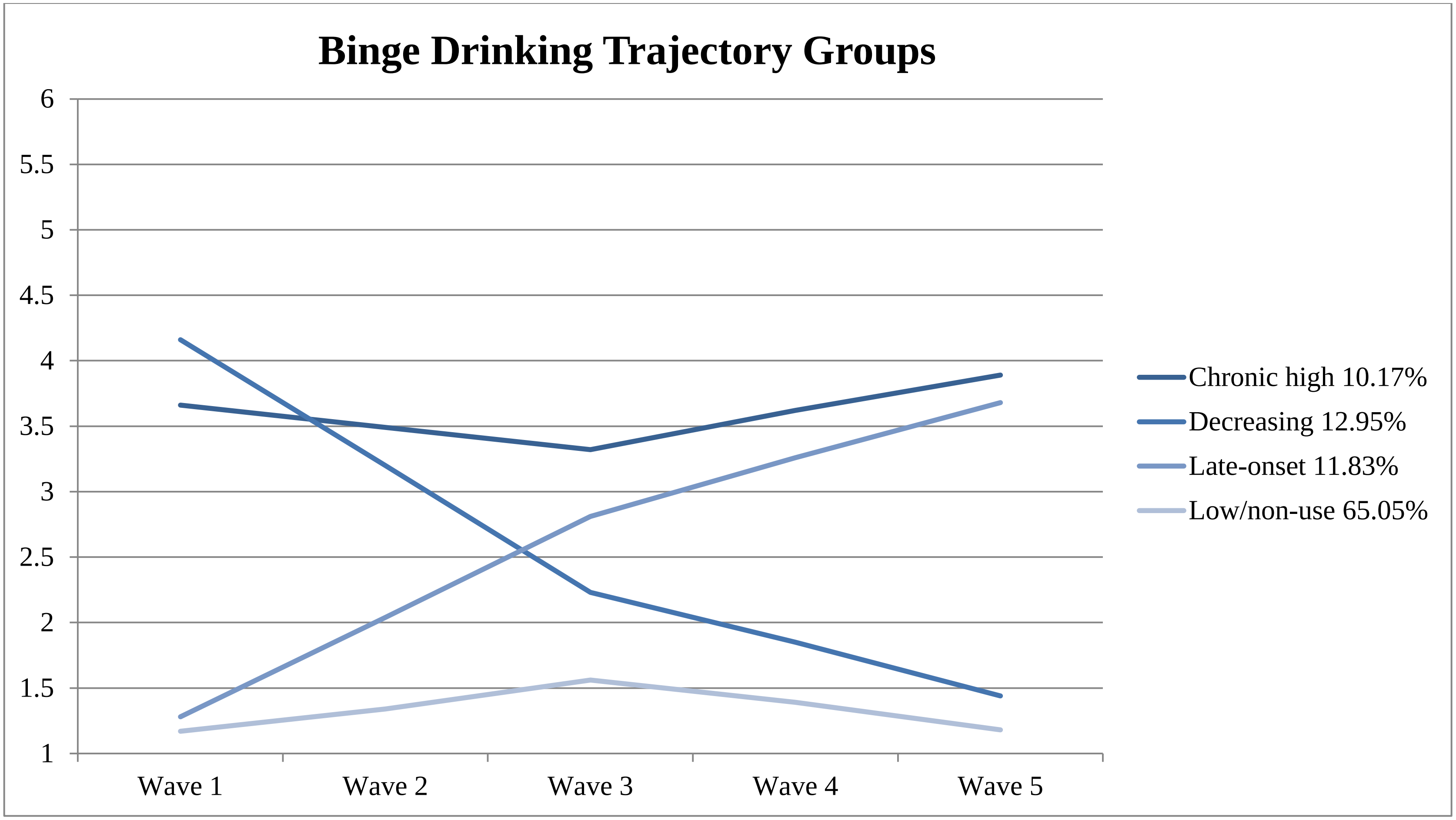

Figure 2. Binge drinking trajectory groups, Chapter Two. Estimated model means for the best fitting model (piecewise model) for binge drinking occasions during the past 2 weeks; Response options for binge drinking are 1 = None, 2 = Once, 3 = Twice, 4 = 3 to 5 times, 5 = 6 to 9 times, and 6 = 10 or more times.

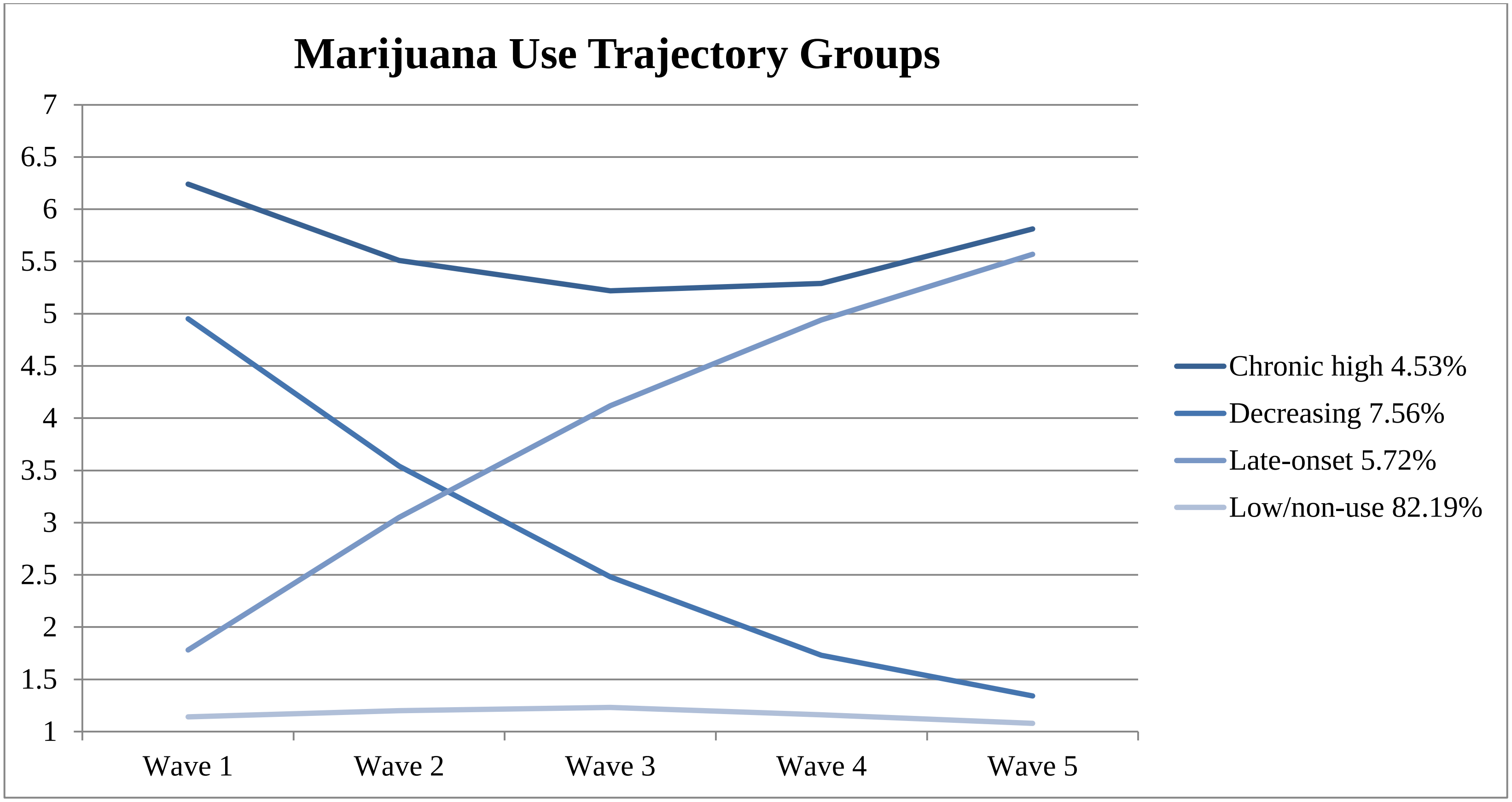

Figure 3. Marijuana use trajectory groups, Chapter Two. Estimated model means for the best fitting model (quadratic model) for marijuana use occasions during the past 30 days; Response options for marijuana use are 1 = 0 occasions, 2 = 1-2 occasions, 3 = 3-5 occasions 4 = 6-9 occasions, 5 = 10-19 occasions, 6 = 20-39 occasions, 7 = 40 or more occasions.

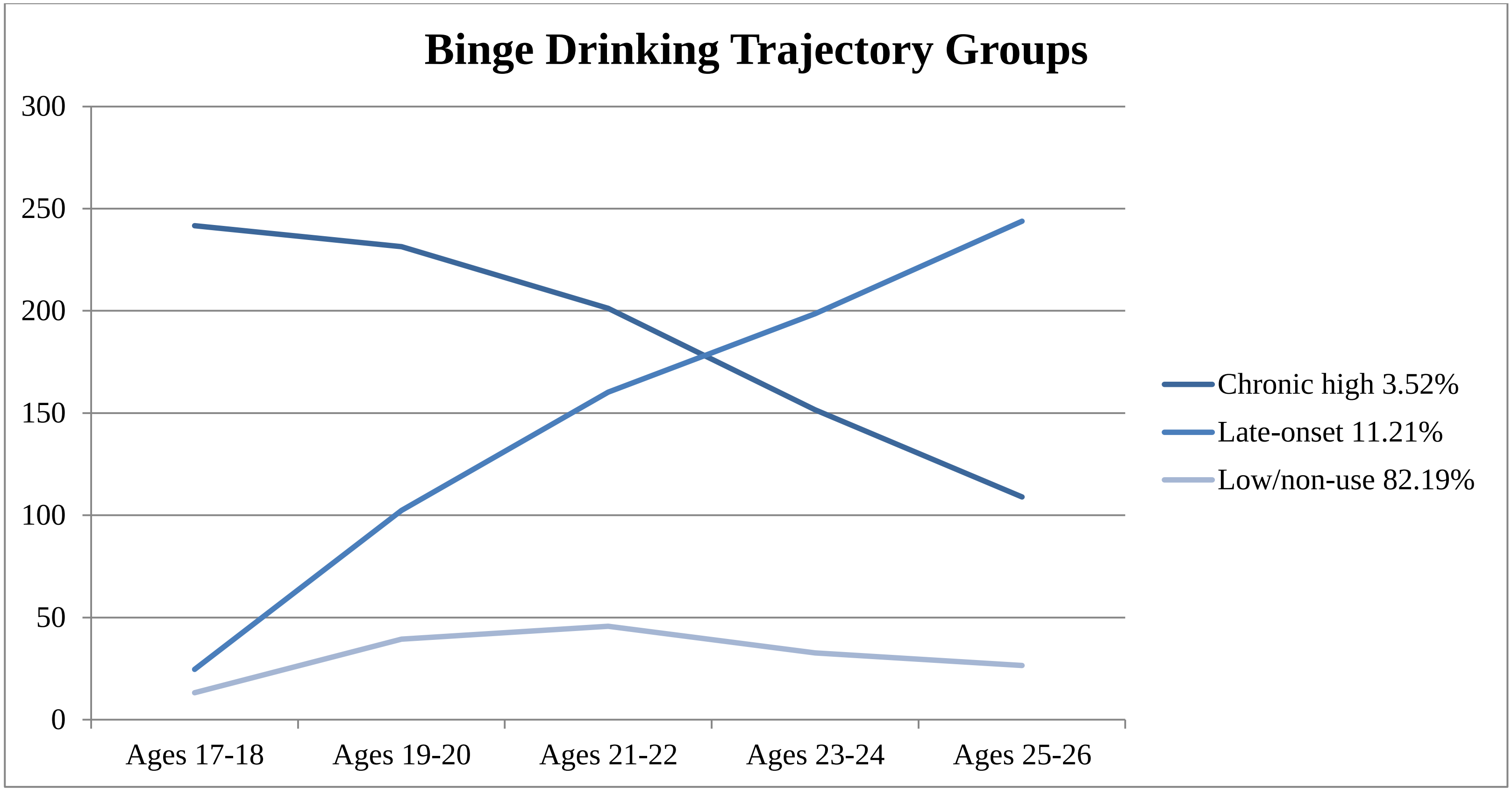

Figure 4. Binge drinking trajectory groups, Chapter Three. Estimated model means for the best fitting model (linear model) for binge drinking occasions during the past year. Vertical axis indicates number of days.

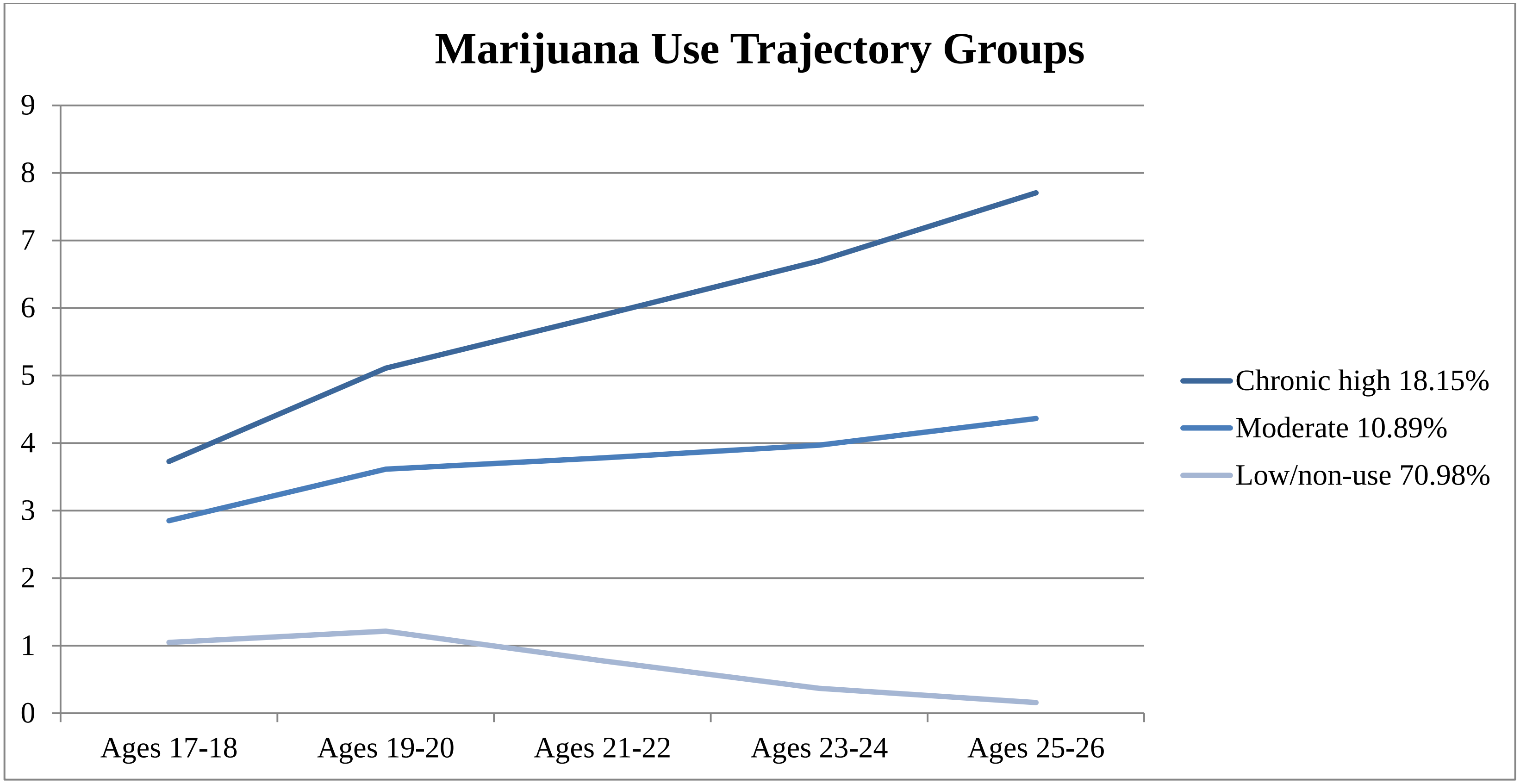

Figure 5. Marijuana use trajectory groups, Chapter Three. Estimated model means for the best fitting model (linear model) for marijuana use occasions during the past year; Response options for marijuana use are 0 = Never, 1 = 1 to 2 occasions, 2 = 3 to 5 occasions, 3 = 6 to 9 occasions, 4 = 10 to 19 occasions, 5 = 20 to 39 occasions, 6 = 40 to 99 occasions, 7 = 100 to 249 occasions, 8 = 250 to 499 occasions, or 9 = 500 or more occasions.

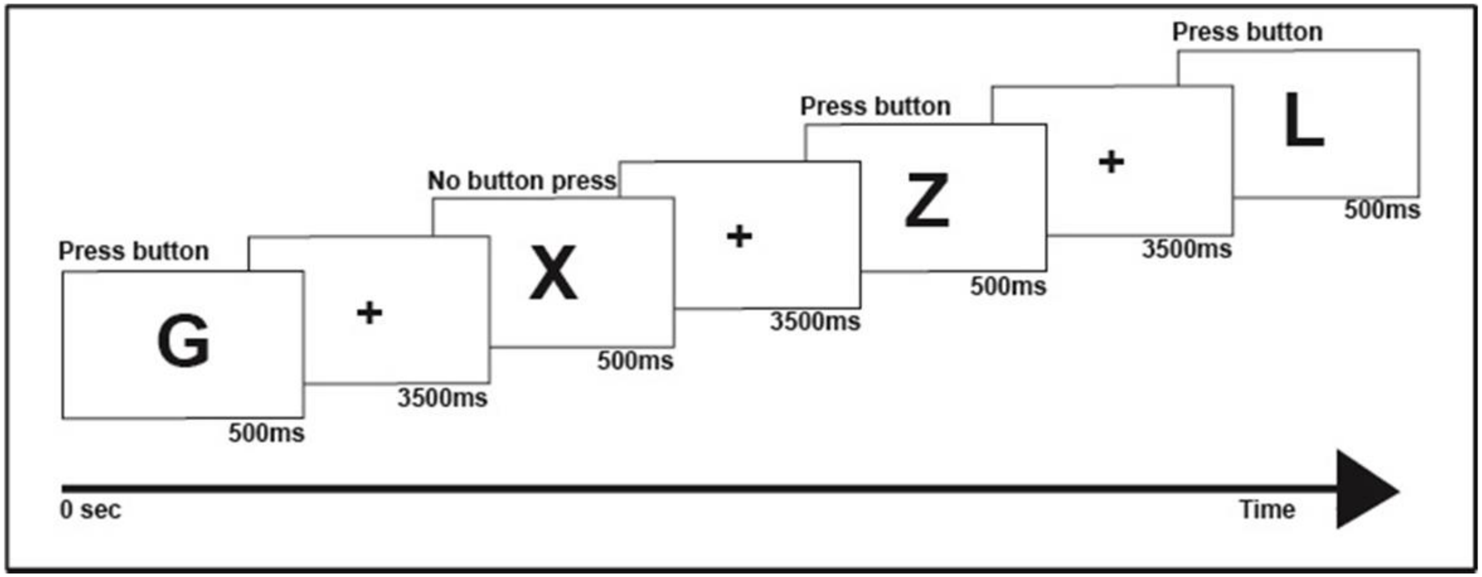

Figure 6. Schematic illustration of Go/No-Go task.

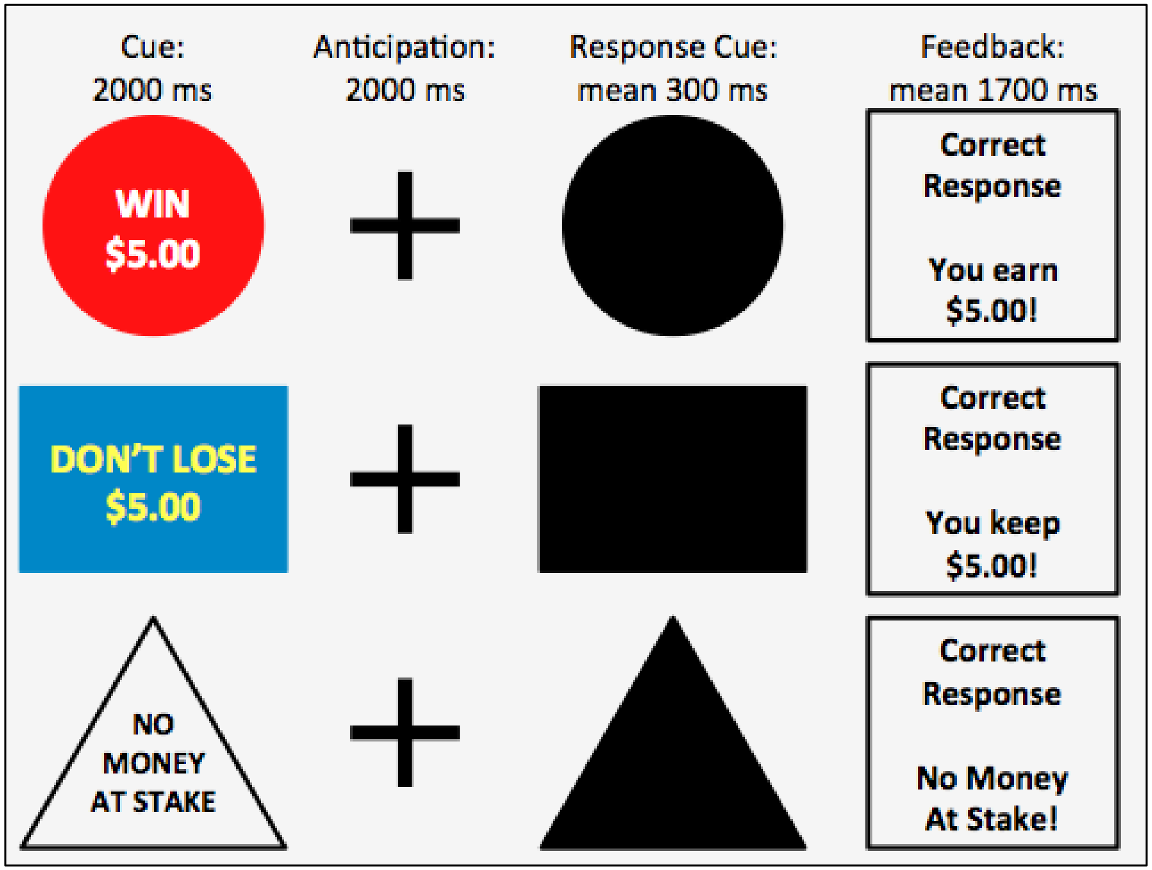

Figure 7. Schematic illustration of Monetary Incentive Delay Task (MIDT).

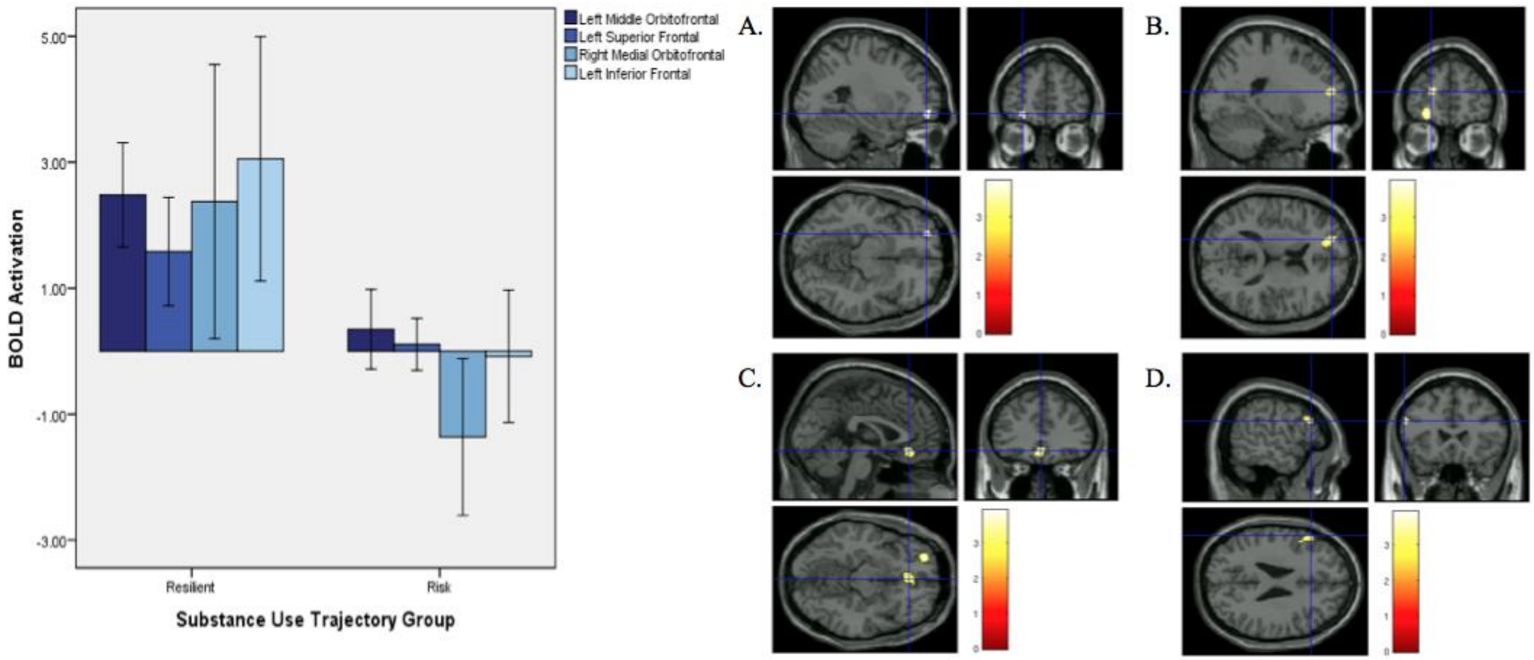

Figure 8. Brain activation differences between resilient and risk groups for correct inhibition. Differences were found in the (A.) left middle orbitofrontal gyrus (x = -26, y = 52, z = -10), (B.) left superior frontal gyrus (x = -20, y = 52, z = 14), (C.) right medial orbitofrontal cortex (x = 0, y = 34, z = -12), and (D.) left inferior frontal cortex (x = -56, y = 24, z = 26) all at $p < 0.005$ (uncorrected) and extent threshold of 77 voxels. Activations shown in the statistical parametric maps indicate greater activation in the resilient group compared to the risk group.

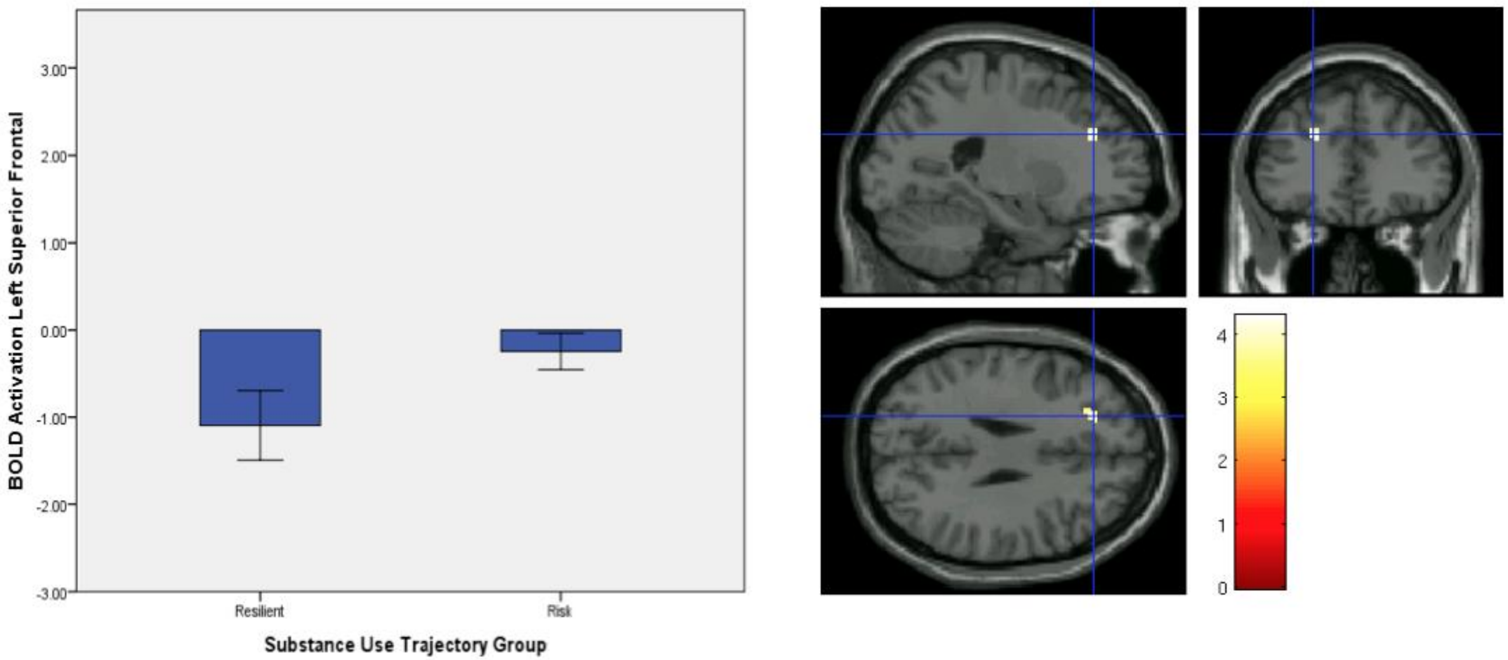

Figure 9. Brain activation differences between resilient and risk groups for reward anticipation. Differences were found in the left superior frontal gyrus (x = -22, y = 36, z = 28) at $p < 0.005$ (uncorrected) and extent threshold of 77 voxels. Activations shown in the statistical parametric maps indicate lower activation in the resilient group compared to the risk group.

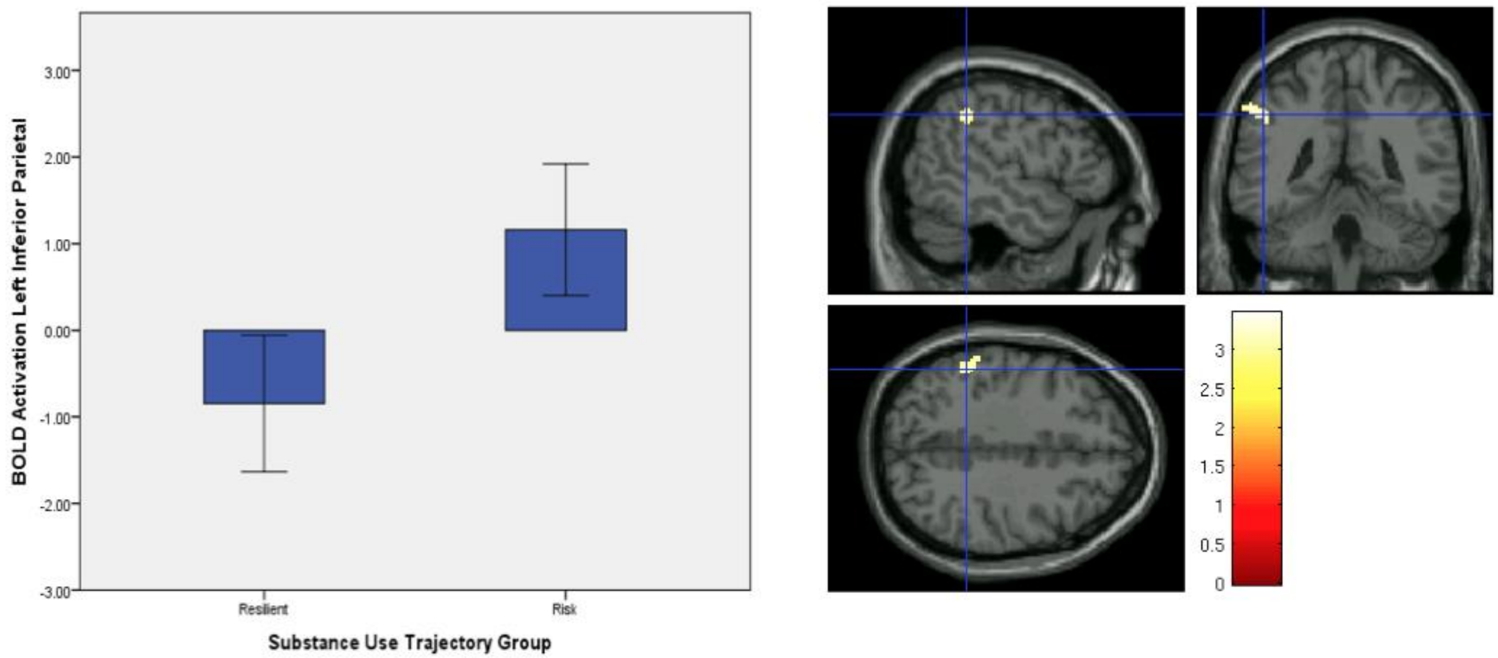

Figure 10. Brain activation differences between resilient and risk groups for reward feedback. Differences were found in the left inferior parietal (x = -56, y = -38, z = 44) at $p < 0.005$ (uncorrected) and extent threshold of 77 voxels. Activations shown in the statistical parametric maps indicate lower activation in the resilient group compared to the risk group.

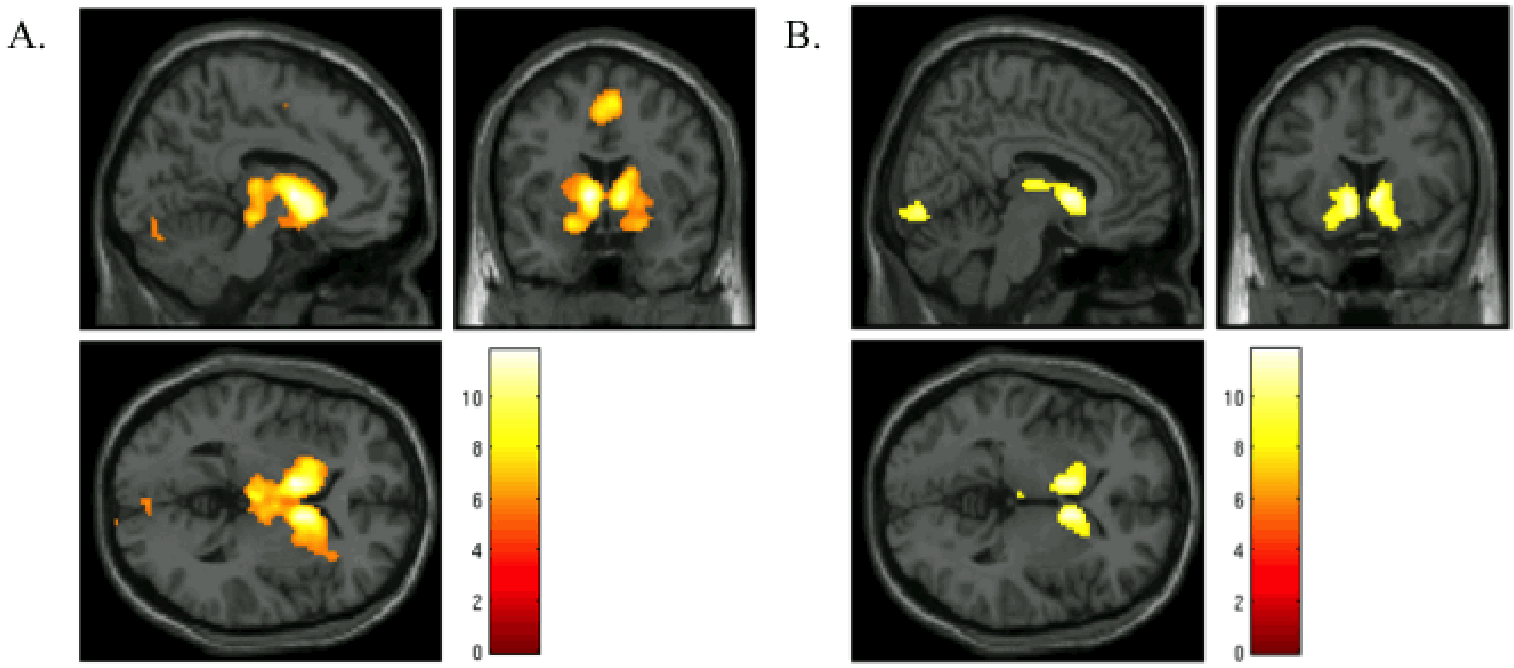

Figure 11. Left and right ventral striatum (VS) activation during reward anticipation. Whole-brain contrast maps for the reward anticipation versus neutral contrast for combined large and small incentive value at each scan are displayed at family-wise error (FWE) correction of $p < 0.05$ (Figure A) and FWE correction of $p < 0.00005$ (Figure B) minimum cluster size of 25. Left and right VS were not differentiated at $p < 0.05$ FWE with a cluster size of $k = 4{,}821$. At $p < 0.00005$ FWE left and right VS differentiated with left $k = 769$ and right $k = 645$.

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