# CONTEXTUAL INFLUENCES OF PRENATAL AND POSTNATAL ENVIRONMENTS ON EXECUTIVE FUNCTION RISK FOR ADOLESCENT SUBSTANCE USE

by

**Emily Rolan**

**A Dissertation**

*Submitted to the Faculty of Purdue University*

*In Partial Fulfillment of the Requirements for the degree of*

**Doctor of Philosophy**


Department of Human Development and Family Studies

West Lafayette, Indiana

May 2020

# THE PURDUE UNIVERSITY GRADUATE SCHOOL
# STATEMENT OF COMMITTEE APPROVAL

**Dr. Kristine Marceau, Chair**

Department of Human Development and Family Studies

**Dr. Shawn Whiteman**

Department of Human Development and Family Studies

**Dr. Valerie Knopik**

Department of Human Development and Family Studies

**Dr. Sara Schmitt**

Department of Human Development and Family Studies

**Approved by:**

Dr. Doran French

*"Whoever touches the life of a child, touches the most sensitive part of a whole which has roots in the most distant past and climbs toward the infinite future." – Maria Montessori*

# ACKNOWLEDGMENTS

I would like to thank **Dr. Kristine Marceau** for her incredible mentorship. From the first time I came to her office to excitedly convince her that my sibling research and behavior genetics belonged together, to the many, many more times that I ran through her door excited about a new idea, Dr. Marceau has remained patient and excited about all avenues of research. She has supported me to extend her work into a whole different realm. Dr. Marceau showed me what I am capable of and continues to inspire me to be a better researcher. I would also like to thank **Dr. Shawn Whiteman** for his brilliance in sibling literature and methodology. While his mentorship has been long distance, he has never failed to support me in my research. I appreciate **Dr. Sara Schmitt** for taking me under her wing, encouraging me to keep pushing forward, and introducing me to the wonderful world of executive functioning. I can honestly say that she is partially responsible for my success in graduate school. I first met **Dr. Valerie Knopik** at a conference, I shook her hand and asked her to remember my name because I wanted to work with her when she moved into our department. She said she would and kept her word. Her door has always been open to me, whether it was for research questions or moral support. I always know that I can turn to her. Dr. Knopik's knowledge of behavior genetics and adolescence were a crucial part of my training and have truly bolstered my program of research.

I stand certain that each of the mentors I have been fortunate enough to have through graduate school will continue to be a strong network of support for the remainder of my career. I sincerely thank all of you.

I would also like to thank the graduate students of the Purdue HDFS department, all of whom work tirelessly and still find time to build each other up.

Finally, I would like to thank Dylan Doner and my family for their unwavering support and compassion.

# TABLE OF CONTENTS

# LIST OF TABLES

# LIST OF FIGURES

# ABSTRACT

Due to the great transitions and turmoil uniquely attributed to the period of adolescence, youth experience a greater risk for substance use and the multitude of concerns that coincide with the early onset of substance use. Many biological and environmental factors have been investigated as predictors of adolescent substance use. Executive function and disruptive behaviors are two important individual characteristics linked to adolescent substance use. Both smoking during pregnancy and sibling relationships are separate contexts that can mitigate or exacerbate the associations of executive function and adolescent substance use. The present study focuses on development of substance use through executive function deficits and disruptive behavior, while considering smoking during pregnancy and sibling relationships as unique moderators of these pathways. This work addresses a novel, interrelated set of questions with a series of three studies. The central hypothesis driving this program of research is that smoking during pregnancy and sibling relationships are under-studied contexts that can mitigate or exacerbate the associations of executive function, disruptive behavior, and adolescent substance use. This dissertation examines whether: (1) executive function mediates the smoking during pregnancy-disruptive behavior association and smoking during pregnancy exacerbates the executive function-disruptive behavior association, (2) smoking during pregnancy exacerbates the association between executive function and disruptive behavior during adolescence using a sibling comparison design, and (3) sibling relationship quality moderates developmental trajectories of executive function on the transition from disruptive problems to adolescent substance use using a high-risk, longitudinal sample. Findings challenge the link between exposure to smoking during pregnancy and both executive function and disruptive behavior. Further, these findings reinforce the need to utilize genetically-informed designs when examining potential effects of smoking during pregnancy. Additionally, this dissertation found support for the link between executive function and disruptive behavior, but not executive function and substance use.

# INTRODUCTION OF KEY CONCEPTS AND DISSERTATION AIMS

Adolescence is often termed a unique developmental and sensitive period. This stage of development consists of transitions and turmoil due to the onset of puberty and shifts in brain structure that coincide with cascading social and cognitive changes (e.g., Crone & Dahl, 2012; Ernst, 2014; Hollenstein & Lougheed, 2013; Mendle & Ferrero, 2012; Rowe, Maugham, Worthman, Costello, & Angold, 2004; Schultz, Molenda-Figueira, & Sisk, 2009; Ullsperger & Nikolas, 2017). Importantly, adolescent transitions are linked to increases in risky behavior, a quintessential part of adolescence. During adolescence, through the combined influence of biological predisposition, as well as both environmental and biological changes, some adolescents show increases in risky behaviors (e.g., Blakemore & Choudhury, 2006; Gray & Squeglia, 2018; Marceau, Kirisci, & Tarter, in press; Mendle & Ferrero, 2012, Ullsperger & Nikolas, 2017). Further, adolescence is a period in which the initiation of adverse behavioral outcomes may set youth on a trajectory for life-persistent patterns of maladjustment (Baggio et al., 2015; Blanco et al., 2016; Gray & Squeglia, 2018). Because of the profound transformation in development (e.g., significant brain development), neuroscientists studying adolescence compare the period to the zero to three developmental stage due to it being a sensitive period in which behavior is malleable (e.g., Zelazo, Blaire, & Willoughby, 2016). Research aimed at understanding and generating knowledge about adolescent behavior and development is critical for prevention and intervention efforts, as implementation may be most impactful during this sensitive period and could possibly offset life-persistent maladjustment. Many biological and environmental factors have been investigated as predictors of adolescent substance use. The present study focuses on development of substance use through executive function deficits and disruptive behavior, while considering smoking during pregnancy and sibling relationships as unique contexts that may mitigate or exacerbate earlier developmental influences on adolescent substance use. This chapter will offer a brief background on the development of key study constructs (disruptive behavior, substance use, executive function, smoking during pregnancy, and sibling relationships), outline the overall conceptual model, discuss the interdisciplinary nature of this dissertation, and present the study aims.

## Behavioral Disinhibition

Behavioral disinhibition is defined as a generalized vulnerability to externalizing behavior (behaviors including substance use, conduct disorder, attention-deficit/hyperactivity disorder, and novelty seeking; Young et al., 2009). For the purpose of this dissertation, I have separated substance use from disruptive behavior. Disruptive behavior includes conduct disorder, oppositional disorder, attention-deficit/hyperactivity disorder (Tolan & Leventhal, 2013). Both substance use and disruptive behavior are considered to be situated under an umbrella of behavioral disinhibition (Young et al., 2009). From early adolescence (8th grade) to late adolescence (12th grade) researchers see a rapid increase in the rates of adolescent substance use across illicit substances (Johnston et al., 2019), with rates being the lowest in early adolescence. Literature suggests, early disruptive behavior is one of the strongest predictors of substance use in late adolescence (e.g., Dodge, Malone, Lansford, Miller, Pettit, & Bates, 2009), which coincides with the data regarding the developmental rates of adolescent substance use. Developmental studies highlight that disruptive behavior precedes later adolescent delinquent behavior (including substance use; e.g., Eiden, Lessard, Colder, Livingston, Casey & Leonard, 2016; Meyers et al., 2014). Thus, earlier disruptive behaviors often predict later adolescent substance use, as a part of a behavioral disinhibition developmental trajectory.

Another complementary view of the development of adolescent substance use is the latent behavior disinhibition factor, with overlapping constructs (i.e., substance use, conduct disorder, attention-deficit/hyperactivity disorder, and novelty seeking) changing in importance across adolescence (Young et al., 2009). When examining these constructs from a developmental perspective, Young and colleagues (2009) found that in early adolescence (12 years of age) attention-deficit/hyperactivity disorder and conduct disorders largely drive the latent construct of behavioral disinhibition. This is likely due to the salience of these behaviors earlier in adolescence. For example, age 12 is likely too early for the initiation of substance use for the majority of youth that will go on to initiate during adolescence. However, later in adolescence (age 17) when substance use behavior becomes more prominent, substance use is largely involved in the latent construct (above other behaviors). Specifically, research suggests that while these constructs (i.e., substance use, conduct disorder, attention-deficit/hyperactivity disorder, and novelty seeking) are interrelated within the latent construct of behavioral disinhibition, developmentally, constructs are differentially important in early adolescence

versus later adolescence.

My view driving the research questions and hypotheses in the current dissertation is that disruptive behaviors and substance use are unique but overlapping constructs because they are correlated, and both conceptually fall under the umbrella of behavioral disinhibition. Specifically, in line with the literature, disruptive behavior and substance use are a part of the larger behavioral disinhibition concept, however, from a developmental perspective, disruptive behavior precedes substance use and is highly predictive earlier in adolescence for later substance use behaviors (e.g., Meyers et al., 2014). Thus, while the disruptive behavior and substance use are highly correlated cross-sectionally, disruptive behaviors are more prevalent prior to substance use initiation from a developmental perspective. The focal outcome of interest in this dissertation is adolescent substance use, however, as described here, in order to understand the development of adolescent substance use, I must address disruptive behavior.

## Disruptive Behavior

***Definition.*** Disruptive behaviors are often defined as behaviors that include, but are not limited to, physical and covert aggression, oppositional behavior, emotion dysregulation, and rule-breaking (Tolan & Leventhal, 2013). Often, disruptive behaviors consist of co-occurring disorders during childhood, such as oppositional defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder (Boyle & Offord, 1991; Fergusson, Horwood, & Lynskey, 1994; Ford, Goodman, & Meltzer, 2003; Kandel et al., 1997). Importantly, early research suggests that disruptive behavior is a common and persistent form of childhood maladjustment (Campbell, 1995). Disruptive behaviors in childhood predict a host of outcomes, including but not limited to, midlife mortality (Jokiela, Ferrie, & Kivimakie, 2009), adolescent parent-child relationship (Burt, McGue, Krueger, & Iacono, 2005), and the likelihood of receiving a high school diploma and college enrollment (McLeod, & Kaiser, 2004). Further, disruptive behaviors in childhood predict disruptive behavior in adolescence (e.g., Bornstein, Hahn, & Haynes, 2010). Critically, disruptive behavior during adolescence predicts substance use (both early regular use and advanced use; King, Iacono, & McGue, 2004), long-term violence, as well as economical and health problems (Odgers et al., 2008).

***Genetic Influences.*** Studies have established the heritability of disruptive behaviors (Burt, 2009). Adoption and twin studies have examined the behaviors encompassed in disruptive

behaviors (as defined in this dissertation) and found that components of adolescent disruptive behaviors are differentially influenced by genetics and shared environment. Specifically, aggressive behaviors are more heritable whereas shared environmental influences are more impactful for rule-breaking behavior (Deater-Deackard and Plomin, 1999; Eley et al., 1999; Eley et al., 2003; Hudziak et al., 2003; Tackett, Krueger, Iacono, & McGue, 2005; van der Valk, 1998). Further, behavior genetics research has found that genetic influences interact with a variety of youths' environments that increase risk for the development of disruptive behaviors (e.g., Holz et al., 2018). In sum, genetic influence largely explains the transmission and development of disruptive behavior, however, 15%-20% of variation in disruptive behavior (excluding ADHD) is attributed to shared environment, suggesting direct environmental effects (Miles & Carey, 1997; Moffit, 2005; Rhee & Waldman, 2002).

***Familial Influences.*** The home environment has extensively been investigated in the development of youths' disruptive behavior. Interestingly, shared environmental effects are stronger for disruptive behavior (i.e., antisocial personality and conduct disorder) than substance use (Kendler, Prescott, Myers, & Neale, 2003). A particularly salient component of the home environment for the development of disruptive behavior is parenting behavior. Baumrind's parenting styles have been examined extensively, and research has linked authoritarian parenting with increased disruptive behavior (e.g., Braza, et al., 2013), as well as inconsistent parenting (Dwairy, 2008). Further, siblings serve as unique socializers of youth, and are linked to adolescent disruptive behaviors (Fagan & Najman, 2005; Kothari, Sorenson, Bank, & Snyder, 2014). Through observation/modeling, reinforcement, and extensive opportunities for practice, siblings influence the development of youths' delinquent behavior (Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017). For example, perceived sibling social support has been linked to fewer behavioral problems during adolescence via modeling processes (Branje, van Lieshout, van Aken, & Haselager, 2004).

***Development of disruptive behavior.*** When reviewing the development of disruptive behaviors from middle childhood to adolescence, one of the strongest longitudinal predictors is prior disruptive behavior (e.g., Bornstein, Hahn, & Haynes, 2010; Reef, Diamantopoulou, van Meurs, Verhulst, & van der Ende, 2010). When examining the home environment for the development of disruptive behavior, parent behaviors have shown to be a particularly important context. For example, the development of autonomy is a critical part of adolescent development

(Arnett, 2002), and parental behaviors surrounding adolescent autonomy development have been found to be influential in the development of adolescent disruptive behaviors (e.g., psychological control and parental monitoring). For example, in a longitudinal study across adolescence, Lansford and colleagues (2014) found that adolescents' perceptions of psychological control predicted disruptive behaviors in later adolescence in girls, such that more perceived psychological control was linked to greater rates of disruptive behavior. Relatedly, lack of parental monitoring in late childhood and early adolescence has been linked to increases in youths' disruptive behaviors (Pettit, Laird, Dodge, Bates, & Criss, 2001). Although less studied, another influential component of the home environment in the development of adolescent disruptive behavior are siblings. For example, longitudinal studies of older sibling disruptive behaviors in adolescence were predictive of younger sibling disruptive behaviors during adolescence (Defoe et al., 2013).

## Substance Use

***Definition.*** Adolescent substance use is a ubiquitous public health problem, as evidenced by recent statistics suggesting over 55% of seniors in high school have consumed alcohol and a wide-ranging decline in youth's perception of risk of harm and condemnation of substance use (Monitoring the Future Survey: High school and Youth Trends, 2016). In the United States 90% of those with a substance use disorder, initiated substance use prior to age 18 (The National Center on Addiction and Substance Abuse at Columbia University, 2011), suggesting that early onset is linked with long-term problem use. During adolescence, alcohol continues to be the most common substance used (64%), followed by marijuana (45%), and cigarette use (31%) with percentages remaining relatively unchanging over the past several years (30-day use; Johnston, O'Malley, Miech, Bachman, & Schulenberg, 2017). While a certain amount of early experimentation with substances is normative during adolescence, an alarming rate of adolescents meet the criteria for alcohol (15%) and drug (16%) abuse by 18 years-old (Swendsen et al., 2012). Critically, earlier onset of substance use is associated with greater risk for developing a substance use disorder (Blanco et al., 2016; Gray & Squeglia, 2018) and disengagement in education, employment, and training (Baggio et al., 2015).

***Genetic influences***. Notably, both genetics and environmental context play a crucial role in the development of substance use behavior (e.g., alcohol use; Enoch, 2012; Guerrini, Quadri,

& Thomson, 2014). Adoption studies conducted in the United States (Hicks et al., 2012; McGue et al., 2007) found significant support for the parent-child transmission of alcohol dependence. Twin studies examining adolescent alcohol (Knopik, Heath, Bucholz, Madden, & Waldron, 2009; Rose, Dick, Viken, Pulkkinen, & Kaprio, 2004) suggest a smaller genetic effect with shared environment contributing substantially. Notably, these studies are unlikely to index the transmission of specifically alcohol dependence, but rather a nonspecific genetic risk for various disruptive behavior (Hicks et al., 2012). Further, genetic influence on adolescent substance use has been found to depend on contexts associated with the home. For example, when parental monitoring is low, the genetic influence on smoking behavior increases during adolescence, whereas when parental monitoring is high, the genetic influence nearly vanishes (Dick et al., 2007). Importantly, the genetic nature of adolescent substance use lessens across development, such that environmental factors become more important predictors of substance use later in adolescence (compared to increased heritability in early adolescence; Young et al., 2009).

***Familial influences.*** The home environment has extensively been investigated in the development of adolescent substance use, particularly the role of parents. Parenting styles have been related to adolescent substance use, in particular authoritarian parenting styles (Paiva, Bastos, & Ronzani, 2012). Further, early substance use initiation for teen girls have been linked to maternal drinking and mother-daughter relationship quality (Schinke, Fang, & Cole, 2008). Findings in a sample of European adolescents suggest that living with both parents, perception of being able to confide in youths' mother, and supervision (more for males than females) are linked to drug use (McArdle et al., 2002). In addition to parenting styles and behaviors, sibling influence has been found to be a prominent and unique influencer for adolescent substance use. Siblings are uniquely influential for the development of substance use during adolescence, above and beyond the social influences of parents and peers (Defoe et al., 2013; Jenkins & Dunn, 2009) Observation/modeling, reinforcement, and extensive opportunities for practice are mechanisms hypothesized to explain similarities in sibling substance use (Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017). Further, an adolescent's risk for substance use increases when they have a sibling who uses substances (Whiteman et al., 2013).

***Development of adolescent substance use.*** Due to the great transitions and turmoil uniquely attributed to the period of adolescence, youth experience a greater risk for substance use and the multitude of concerns that coincide with the early onset of substance use (e.g.,

disruptive behaviors; Gray & Squeglia, 2018). A number of earlier predictors have been linked to the imitation of substance use during adolescence, including individual traits (e.g., sex and inhibition; Chen & Jacobson, 2012; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014), parents (e.g., monitoring, relationship quality and early parenting behaviors; Clark, Donnella, Robins, & Conger, 2015; Eiden et al., 2016; Pinquart, 2017; Rusby, Light, Crowley, & Westling, 2018), and risky peers (e.g., Clark et al., 2015). As noted above, disruptive behavior is one of the best predictors of adolescents' earlier transitions to substance use (Dodge et al., 2009) and is often considered a risk factor for later substance use initiation. According to cascade models, adolescents' access to substances increases as they age, likely due to both disruptive behavior and risky peers (Trucco, Hicks, Villafuerte, Nigg, Burmeister, & Zucker, 2016). Further, adolescent substance use is linked to poor academic achievement (e.g., GPA and high school completion; Kelly et al., 2015; Meier, Hill, Small & Luthar, 2015) and poor social skills (e.g., peer rejection; Moilanen, Shaw, & Maxwell, 2010), often suggesting a reciprocal progression across development leading to more problematic substance use (Trucco et al., 2016).

## Executive Function

***Definition.*** Executive function is a set of interrelated cognitive skills used to conduct goal-directed actions through control and coordination of information (Zelazo, Blair, & Willoughby, 2016). While there are ongoing debates on the unity versus diversity of executive functions, the primary consensus is that three components of executive function, working memory, response inhibition, and set shifting, are related yet distinct cognitive components that make up executive function (Garon, Bryson, & Smith, 2008; Miyake, Friedman, Emerson, Witki, Howerter, & Wager, 2000). Working memory is conceptualized as information being updated and manipulated while completing a complex task, as opposed to simpler tasks where information is simply held in mind (Gathercole, 1998). Response inhibition is defined as the ability to withhold or refrain from responding with a preferred or dominant response, in order to respond appropriately (Garon et al., 2008). Set shifting is defined as the ability to shift from one mental state to another conflicting mental state (Garon et al., 2008).

***Genetic influences.*** A large body of literature has investigated genetic influences on executive function as well as the individual components that executive function is comprised of during childhood and adolescence. During early childhood ($M$ = 5 years of age) working

memory is moderately heritable (55%), and in late childhood (*M* = 12 years of age) working memory is highly heritable (73%; Heutink et al., 2006). Additionally, for 3rd to 8th graders, latent constructs of executive function components (i.e., inhibition, switching, working memory, and updating) showed moderate heritability for the switching latent construct (59%) but no other components had significant heritability estimates. Further, in the same sample, a common executive function factor (comprised of the latent constructs inhibition, switching, working memory, and updating) was highly heritable (100%; Engelhardt, Briley, Mann, Harden, & Tucker-Drob, 2015). In a sample of adolescent and adult twins (16-29 years old), both spatial and verbal working memory (one component of executive function) were moderately heritable (43% - 49%; Ando, Ono, & Wright, 2001). Additionally, when evaluating set shifting using the Wisconsin Card Sorting Test (one component of executive function) using a sample of female twins aged 17-28 years, researchers found moderate heritability (37%-46%; Anokhin, Heath, & Ralano, 2003). Consistently, in a sample of adolescents (16-17 years of age), when examining individual executive function tasks (i.e., Antisaccade, Stop-Signal, Stroop, Keep Track, Letter Memory, Spatial 2-Back, Number-Letter, Color Shape, and Category Switch tasks), researchers found moderate heritability across tasks (Friedman, Miyake, Young, Defris, Corley, & Hewitt, 2008).

When investigating latent constructs of working memory (including Keep Track, Letter Memory, and Spatial 2-Back tasks), set shifting (including Number-Letter, Color Shape, and Category Switch tasks), and inhibition (including Antisaccade, Stop-Signal, and Stroop tasks), the latent constructs were highly heritable (81% - 100%; Friedman et al., 2008). Finally, in that same study, when examining a common executive function variable (including working memory, set shifting, and inhibition latent constructs), the common executive function factor was also highly heritable (99%; Friedman et al., 2008). Notably, results from childhood (Engelhardt et al., 2015) compared to adolescence (Friedman et al., 2008), in terms of genetic influence, suggest that genetic influences that differentiate components of executive function may not develop until adolescence (Engelhardt et al., 2015). In sum, across development (early childhood, adolescence, and into emerging adulthood), there is evidence of genetic influence on executive function.

***Familial influences.*** Literature on executive function suggests that the home is a particularly important context for the development of executive function (e.g., parenting and sibling presence). Parenting and parent behavior have been studied as an important social

facilitator of youths' executive function. Parenting quality is linked to greater executive functioning (Bernier, Carlson, & Whipple, 2010). For example, the parenting literature has found that the practice of mind-mindedness (i.e., interacting with youth like they have minds of their own), facilitates youth's executive functioning (Bernier et al., 2010). Further, in line with attachment theory, more sensitive and responsive parents promote children's internalization of executive function skills (Bernier, Carlson, Deschenes, & Matte-Gagne, 2012). Youth are afforded greater opportunities to develop executive functioning skills through positive interactions with parents (e.g., reading; Bradley, McKelvey, & Whiteside-Mansell, 2011). Additionally, parental scaffolding predicts greater executive function skills (Hammond, Muller, Carpendale, Bibok, & Lierbermann-Finestone, 2012).

Whereas parenting and parent behavior have been explored in depth as a meaningful context for the development of executive function, less is known about the role of siblings. An emergent body of research has begun to consider whether sibling presence is linked to the youths' executive function. Siblings act as bidirectional models via presence and interactions, which may facilitate executive function development (Harris, 2005; McAlister & Peterson, 2013). Two studies found that sibling presence is linked to greater executive functioning, utilizing observational measured of executive function (McAlister & Peterson, 2006; McAlister & Peterson, 2013). In contrast, utilizing parent-report of executive function, another study found that sibling presence was related to poorer executive function (Rolan, Schmitt, Purpura, & Nichols, 2018). In sum, the home environment comprised of both parents and siblings, provide a salient context for the development of executive function.

***Development of executive function*.** Perspectives of executive function development are studied as processes of neural systems (Diamond, 2013), genetic factors (Friedman et al., 2008), socialization (Lewis & Carpendale, 2009), and a combination of both biological and contextual factors (Zelazo, 2013). The Cognitive Complexity and Control (CCC) theory posits that as children age, they have increased capabilities in terms of the number and complexity of rules they can maintain while solving problems (Frye, Zelazo & Burak, 1998). Executive function is continually developing based on youth's reactions to their environment and the support or constraints afforded to them by their environment (Sameroff, 2010). The development of youth's executive function skills is impacted by personal characteristics (e.g., age or developmental constraints) and can be exacerbated or mitigated by contextual factors (McClelland et al., 2015).

By the end of the first year of life, brain systems association with the executive attention network begins to emerge (e.g., prefrontal cortex; Berger, Tzur, & Posner, 2006; Kochanska & Knaack, 2003; Rothbart, Derryberry, & Posner, 1994) and executive function develops most rapidly during the early years (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997) showing modest stability in individual differences by the age of 4 (Kochanska & Knaack, 2003).

Components of executive function (i.e., inhibition) develop rapidly throughout the preschool years, but there is evidence that working memory and set shifting develop more gradually (Best & Miller, 2010). Importantly, during adolescence, executive function continues to develop with the maturational growth occurring during this period (e.g., brain development; Crone & Dahl, 2012; Ernst, 2014; Zecevic & Rakic, 2011). The myelination of the prefrontal cortex is responsible for reeling in the newfound impulsivity, components that assist executive functioning (e.g., Crone & Dahl, 2012; Ernst, 2014). Further, the prefrontal cortex is related to emotional responses (Levens et al., 2014) and plays a highly complex role in neural function and is believed to be responsible for short term memory, framing plans, strategizing, and initiation of action (Blakemore & Choudhury, 2006; Carlson & Birkett, 2017). However, the prefrontal cortex remains relatively immature until later in adolescence (e.g., Crone & Dahl, 2012; Ernst, 2014), thus highlighting the continued growth of executive function skills throughout adolescence and into late adolescence. In sum, both early childhood and adolescence are crucial periods in the development of executive function and are considered sensitive periods (Zelazo, Blaire, & Willoughby, 2016), during which functions related to executive function are particularly susceptible to environmental influences.

## Smoking During Pregnancy

***Definition.*** Another potentially sensitive period for the development of executive function is the prenatal period, particularly if the child is exposed to smoking during pregnancy. Smoking during pregnancy is a phenomenon that still affects, on average, 7.2% of women in the United States, with several states (i.e., Montana, Missouri, Kentucky, West Virginia, and Vermont) reporting rates of 20% and above (Drake, Driscoll, Mathews, 2016). Further, smoking during pregnancy is associated with a number of outcomes that also increase disruptive behavior (e.g., D'Onofrio et al., 2008; Salatino-Oliveira et al., 2016; Wakschlag et al., 2010) and poorer

executive function (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono, Carlson, Taylor, Elkins & McGue, 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). Smoking during pregnancy is associated with increased disruptive behavior and worse executive function, in part, through a teratogenic role of smoking during pregnancy on brain development (e.g., atypical frontal lobe development and myelination of the prefrontal cortex; Ekblad, Korkeila, & Lehtonen, 2014; Peterson et al., 2003). However, a limitation of work examining the effects of smoking during pregnancy is that the potential for familial confounding (i.e., genetic and environmental influences) is largely ignored.

***Genetic influence.*** Smoking during pregnancy is also a familial influence on later developmental outcomes. For example, mothers who experience executive function deficits and/or who are nicotine dependent may have more difficulty quitting smoking when they become pregnant and thus confer correlated genes and environmental exposures to their offspring. This could result in non-causal associations between smoking during pregnancy, executive function, and adolescent substance use that are the result of common familial (genetic and environmental) influences. Or, the children of mothers who smoke may present with executive function deficits and substance use, and the executive function - substance use association could be exacerbated by the environmental context of smoking during pregnancy. As such, poor and inconsistent control for potential confounders preclude concluding causal effects of smoking during pregnancy on executive function and disruptive behavior and their association (Knopik, 2009). As such, a critical component of the conceptual model is the utilization of genetically-informed samples to test hypotheses. Sibling comparison studies can be utilized to control for familial confounds as a function of their design. A growing literature of genetically sensitive studies on the effects of smoking during pregnancy have demonstrated a potentially causal effect on ADHD symptoms (i.e., increased hyper-activity and impulsivity; Knopik et al., 2016; Marceau et al., 2017). However, the effects of smoking during pregnancy were completely attenuated by familial confounds for a total ADHD score, disruptive behavior (excluding multi-rater composite scores; Ekblad et al., in press), and children's inhibitory control (Micalizzi et al., 2018). More work is needed to determine whether smoking during pregnancy may play an organizing role for aspects of executive function as it relates to disruptive behavior, or whether familial factors completely confound smoking during pregnancy-executive function associations.

***The influence of smoking during pregnancy on disruptive behavior development.*** In addition to direct effects, prenatal influences, including smoking during pregnancy, are hypothesized to have an organizing effect on later biological (e.g., brain) and behavioral development (Gluckman, Hanson, Cooper, & Thornburg, 2008). Exposure to smoking during pregnancy may be influential well past the prenatal period (e.g., attention-deficit/hyperactivity disorder; Knopik et al., 2016; Thapar et al., 2003; Weissman et al., 1999), and may be a context for later behavior by influencing the trajectory of brain development that occurs later (e.g., during adolescence; Crone & Dahl, 2012; Ernst, 2014; Zecevic & Rakic, 2011). Adolescence is associated with shifts in dopamine release that are linked to risky behaviors (Spear, 2000). Notably, in animal studies prenatal nicotine exposure predicts alterations in catecholamine systems that come online later in development (e.g., neurotransmitters such as dopamine; Azam et al., 2007; Ribary & Lichtensteiger, 1989; Onal et al., 2004). Exposure to smoking during pregnancy predicts later neurobehavioral deficits, possibly related to smoking during pregnancy-related catecholaminergic dysfunction in the adolescent brain (e.g., attention-deficit/hyperactivity disorder; Dwyer, McQuown, & Leslie, 2009; Knopik et al., 2016; Thapar et al., 2003; Weissman et al., 1999).

Notably, genetically-informed studies suggest that the link between exposure to smoking during pregnancy and later behavior may not be direct (Ekblad et al., in press; D'Onofrio, Van Hulle, Goodnight, Rathouz, & Lahey, 2011; Knopik, 2009; Kuja-Halkola, D'Onofrio, Larsson, & Lichtenstein, 2014; Rydell, Granath, Cnattingius, Magnusson, & Galanti, 2014). Given the teratogenic role of exposure to smoking during pregnancy on brain development, such as the prefrontal cortex (e.g., atypical frontal lobe associated with executive function; Crone & Dahl, 2012; Ekblad, Korkeila, & Lehtonen, 2014; Ernst, 2014 ; Peterson et al., 2003) and alterations in the catecholamine system (Azam et al., 2007; Ribary & Lichtensteiger, 1989; Onal et al., 2004), executive function may be a process through which smoking during pregnancy influences later disruptive behavior. However, to the best of my knowledge, this idea has yet to be investigated.

In addition to executive function mediating the smoking during pregnancy-disruptive behavior association, smoking during pregnancy may interact with executive function to provide an environment of catecholaminergic dysfunction exacerbating the effect of executive function on disruptive behavior. There is precedent for earlier influences serving as a developmental

context moderating later associations. Genetic influences (i.e., familial risk to externalzing behavior) have been shown to moderate later smoking during pregnancy effects on disruptive behavior (Buschgens et al., 2009), illustrating how earlier developmental influences can moderate later associations. However, smoking during pregnancy also has been identified as a context moderating the effects of familial influences on disruptive behavior (Marceau et al., 2019; Neiderhiser et al., 2016), depicting the potential for smoking during pregnancy to serve as an environment for the development of disruptive behavior. While temporally, smoking during pregnancy occurs prior to the concurrent association between executive function and disruptive behavior, distinct effects of the exposure may not become salient for disruptive behavior until preadolescence/adolescence when shifts in brain structure (e.g., the prefrontal cortex; Crone & Dahl, 2012; Ernst, 2014; Hollenstein & Lougheed, 2013; Mendle & Ferrero, 2012; Rowe, Maugham, Worthman, Costello, & Angold, 2004; Schultz, Molenda-Figueira, & Sisk, 2009; Ullsperger & Nikolas, 2017) implicated in both executive function and risky behavior come online (Blakemore & Choudhury, 2006; Carlson & Birkett, 2017; Crone & Dahl, 2012; Ernst, 2014; Levens et al., 2014; Zecevic & Rakic, 2011). In sum, given the organizational influences of smoking during pregnancy on brain development, smoking during pregnancy is also considered as a context (e.g., moderator) of the executive function-disruptive behavior association.

## Sibling Relationships

***Definition.*** I have defined and reviewed literature on disruptive behavior, substance use, executive function, and smoking during pregnancy in the context of the family, as I view my program of research through the lens of family research. However, a particularly salient and understudied component of the family is the sibling relationship. Siblings are a particularly important relationship as, of households with children in the United States, 81% have more than one child (Census Bureau, 2017). Beyond the prevalence of siblings in the home, the sibling relationship is one of the most significant and enduring relationships throughout one's life and siblings continually shape each other's environment within the family (e.g., Dunn, 1983). Further, sibling relationships are unique from other relationships youth have (both within and outside the family unit), as they consist of both reciprocity and complementarity (Dunn, 1983).

Given the salience of siblings' presence throughout youths' development, understanding siblings as a context for adolescent adjustment (e.g., disruptive behaviors and substance use) is critical.

***Genetic influences.*** In the field of behavior genetics, researchers have begun to examine the genetic influences that contribute to the sibling relationship quality. Utilizing a twin study, Neiderhiser and colleagues (2013) found that sibling negativity is heritable, that adolescents' genes contributed to associations of marital conflict, sibling negativity, and adolescent substance use, but also that increased sibling negativity acted as a unique shared environmental influence on the initiation of adolescent substance. Further, in an adoption study, researchers found that sibling levels of competition, as well as both positive and negative behavior, had underlying genetic influences (Rende, Slomkowski, Stocker, Fulker, & Plomin, 1992). However, genetic influence on sibling relationships has not been examined extensively in the literature to fully understand the genetic nuances that contribute to the development of the sibling relationship (e.g., sibling interactions or conflict).

***Environmental influences.*** There are many individual and family influences that have been linked to variations in sibling relationships. Individual characteristics, such as gender (both individual gender and the sibling gender constellation), age-spacing, temperament, and birth-order are thought to operate via environmental social mechanisms to impact sibling relationships (Campione-Barr, Greer, Schwab, & Kruse, 2013; McHale, Updegraff, & Whiteman, 2012; Stoneman & Brody, 1993; Stoneman, Brody, Churchill, & Winn, 1999). For example, domains of sibling conflict differ by sibling gender composition, such that sister-sister pairs more frequently have conflict surrounding invasion of the personal domain and equality/fairness, whereas all other dyads most frequent conflict surrounds equality and fairness (Campione-Barr et al., 2013). Reports of conflict also differ by birth order, such that older siblings tend to report conflicts being more frequent and surrounding the invasion of the personal domain compared to their younger counterparts (Campione-Barr & Smetana, 2010). Family influences, such as marital discord and parenting behavior have also been linked to sibling relationships. One particular parenting behavior that has been linked to the sibling relationship is parental differential treatment, or when one sibling perceives themselves to be more dis/favored or treated differently in comparison to their sibling. Parental differential treatment also predicts more negative sibling relationship quality (Brody, Stoneman, & Burke, 1987; Brody, Stoneman, & McCoy, 1992; McHale & Pawletko, 1992). For example, the sibling that reported being

disciplined more often, also reported a more negative sibling relationship (McHale, Crouter, McGuire, & Updegraff, 1995). Further, marital discord and parent hostility have been linked to greater sibling relationship hostility (e.g., Stocker & Youngblade, 1999).

***Development from childhood to adolescence.*** Literature on sibling relationships from middle childhood to adolescence suggest that as sibling dyads grow older, their relationship grows more egalitarian, less asymmetrical, and less intense (Buhrmester & Furman, 1990). Across adolescence, research suggests that relative power declines, with the majority of power being conceded by older siblings, but only for siblings that have less positive relationship quality (Lindell & Campione-Barr, 2017). The development of the sibling relationship may depend on characteristics of the sibling dyad, such as sibling gender constellation. For example, opposite-sex dyads have increased intimacy from late childhood to late adolescence, whereas same-sex dyads see declines in intimacy across the same age range (Kim, McHale, Osgood, & Crouter, 2006). Additionally, sibling conflict declines for both older and younger siblings when the older sibling reaches early adolescence (e.g., the older sibling may be an early adolescent, while the younger sibling is in late childhood, but conflict declines similarly; Kim et al., 2006). Early home environment may further contribute to trends in sibling relationship development, longitudinal studies of family relationships suggest that parent-child relationship quality and parental differential treatment predict sibling relationship quality. For example, high mother-child conflict is associated with later conflict and aggression in the sibling relationship (Volling & Belsky, 1992).

***Siblings as a context for behavioral development.*** In addition to the direct effects of siblings on executive function and behavioral development, sibling relationship quality and characteristics of one's sibling are also likely a key family-level contextual influence on the development of executive function, disruptive behavior, and substance use (e.g., Buist, Dekovic, & Prinzie, 2013; Recchia & Howe, 2009). Further, one perspective on siblings as a training ground, suggests that negative sibling relationships facilitate more negative, conflictual, and coercive interactions across relationships throughout development (Natsuaki et al., 2009; Patterson, 1984; Patterson et al., 1989). Persistent coercive interactions and behaviors are linked to a lack of self-control (Feinberg, Solmeyer, & McHale, 2011). Hence, negative sibling relationship quality may interact with developmental influences that predict greater risk for youth disruptive behavior and substance use. Finally, Windle (2000) found that having a sibling that

used substances may be linked to consuming alcohol when faced with stressful life events and an inclination for negative coping strategies via sibling role modeling or imitation. Thus, sibling substance use may provide access to substances that would strengthen a youth at risk to initiate substance use (e.g., executive function deficits or increased disruptive behavior). In sum, the sibling literature suggests that sibling characteristics (e.g., sibling substance use) and the quality of the sibling relationship may be a risk factor for maladjustment and interact with or exacerbate other developmental influences (e.g., early executive function deficits and disruptive behavior) to predict adolescent substance use.

## Overarching Gaps in the Literature

Executive function develops most rapidly in early childhood (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997) and is associated with later disruptive behavior (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Notably, through a teratogenic role on brain development (Ekblad et al., 2014; Peterson et al., 2003), exposure to smoking during pregnancy predicts decreased childhood executive function (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono, Carlson, Taylor, Elkins & McGue, 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). Despite evidence that 1) smoking during pregnancy predicts executive function, 2) executive function predicts disruptive behavior, and 3) evidence that executive function may represent a biological mechanism (e.g., index of brain development in key regions such as the prefrontal cortex), no research has examined the role of early childhood executive function as a process through which smoking during pregnancy may predict disruptive behavior. Therefore, one of the aims of the current dissertation is to examine whether early childhood executive function is a mediator through which smoking during pregnancy is associated with later disruptive behavior.

Sibling comparison designs have demonstrated a causal effect of smoking during pregnancy on increased attention-deficit/hyperactivity disorder symptoms (i.e., hyper-activity and impulsivity, based on a composite parent-teacher reports and the Strengths and Weaknesses of ADHD-Symptoms and Normal-Behavior scale; Knopik et al., 2016; Marceau et al., 2017) and reduced birth weight (Knopik, Marceau, Palmer, Smith, & Heath, 2015). However, smoking

during pregnancy effects on total attention-deficit/hyperactivity disorder and attention-deficit/hyperactivity disorder symptomology (excluding hyper-activity and impulsivity, based on a composite parent-teacher reports and normative ranges of symptomology; Knopik et al., 2016; Marceau et al., 2017), disruptive behavior (excluding multi-rater composite scores including both parent and teacher reports; Ekblad et al., in press), as well as children's inhibitory control (Micalizzi et al., 2018) showed complete familial confounding. In a study of smoking during pregnancy and substance use initiation, there was no direct effect of exposure to smoking during pregnancy on initiation of alcohol, tobacco, or marijuana use (Bidwell et al., 2017). However, the sibling comparison design has not yet been used to examine global executive function or the role of smoking during pregnancy in this executive function-substance use association. Thus, the second part of my dissertation will investigate whether smoking during pregnancy moderates the association between adolescent executive function and disruptive behavior.

In a cross-sectional study, Giancola and colleagues (2001) found evidence of a link from executive function to substance use through anti-social behavior. However, longitudinal studies from late adolescence/early adulthood to adulthood failed to find a link between executive function and substance use (e.g., Gale, Deary, Boyle, Barefoot, Mortensen, & Batty, 2008; Wilens et al., 2011). Otherwise, to my knowledge, there is no study that has examined this developmental pathway, longitudinally, from childhood to adolescence. The aim of study three is to investigate whether disruptive behavior mediates the executive function-substance use association in adolescence. In addition, an established literature suggests that sibling relationships are particularly important to consider for adolescent substance use, in part, because siblings influence each other's environment (Dunn, 1983). Indeed, warmer sibling relationships are associated with lower rates of substance use (East & Khoo, 2005), and adolescents are more likely to use substances when their sibling engages in substance use (Whiteman et al., 2013). The potential moderating role of sibling relationships for the developmental pathways from executive function to disruptive behavior and transitions to substance use have not yet been examined. To my knowledge there is no literature on the role of sibling relationships for executive function development during adolescence, or associations of executive function and substance use. Thus, sibling relationships are a significant, but under-studied, influence that may affect the pathways between executive function, disruptive behavior, and substance use, as well as a point of prevention and intervention for family-based programs targeting adolescent problem behavior.

Part of the aim of study three is to examine whether sibling relationship quality and siblings' substance use moderate associations of executive function with disruptive behavior and the disruptive behavior-substance use association.

***Behavior genetic designs.*** In order to obtain minimally biased findings regarding the predictors of substance use, we can only effectively understand the unique contribution of environmental influences by accounting for the confound of the heritability of substance use. Studies have established genetic influence on disruptive behaviors (e.g., Burt, 2009), executive function (e.g., Engelhardt, Briley, Mann, Harden, & Tucker-Drob, 2015), and substance use (e.g., Hicks et al., 2012; McGue et al., 2007; Young et al., 2009). Thus, when considering the context for the development of youth behavior (i.e., substance use, disruptive behavior, and executive function), genetic influence is an important component to consider. For full siblings, genetic influence could result in both siblings having more substance use related problems and upwardly bias the importance of siblings' modeling in studies where this shared genetic liability is not accounted for. The little work on sibling influence conducted with genetically informed designs tends to show that siblings are likely to influence each other via environmental mechanisms even beyond their shared genetic influences (Samek et al., 2015; Slomkowski, Rende, Conger, Simons, & Conger, 2001; Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005). In work examining the association between smoking during pregnancy and youth behavior, relatively few studies have considered the potential for familial confounding (i.e., genetic and environmental influences). Developmental scientists are, at best, losing valuable information and at worst significantly biasing and misinterpreting results when not accounting for genetics in studies of the development of substance use. Thus, including designs that can begin to control for or test genetic influence is imperative to avoid losing valuable information or significantly biasing/misinterpreting results when examining the developmental cascade in middle childhood and adolescence from executive functioning through disruptive behavior to substance use, in the context of exposure to smoking during pregnancy or sibling relationships.

## Conceptual Model

In order to address these gaps in the literature, I propose an interdisciplinary approach to examine prenatal and sibling influences on the development of substance use through executive function deficits using a multiple design strategy including genetically-informed and longitudinal

samples. The conceptual model guiding my work (Figure 1) focuses on the transitions from executive function to disruptive behavior and substance use across childhood and adolescence, considering executive functioning as a mediator of associations of smoking during pregnancy with disruptive behavior (Aim 1a), as well as moderating role of smoking during pregnancy (Aim 1b & Aim 2a), the mediating role of disruptive behavior in the executive function-substance use association (Aim3a) and of sibling relationships for the development of disruptive behavior and substance use (Aim3b).

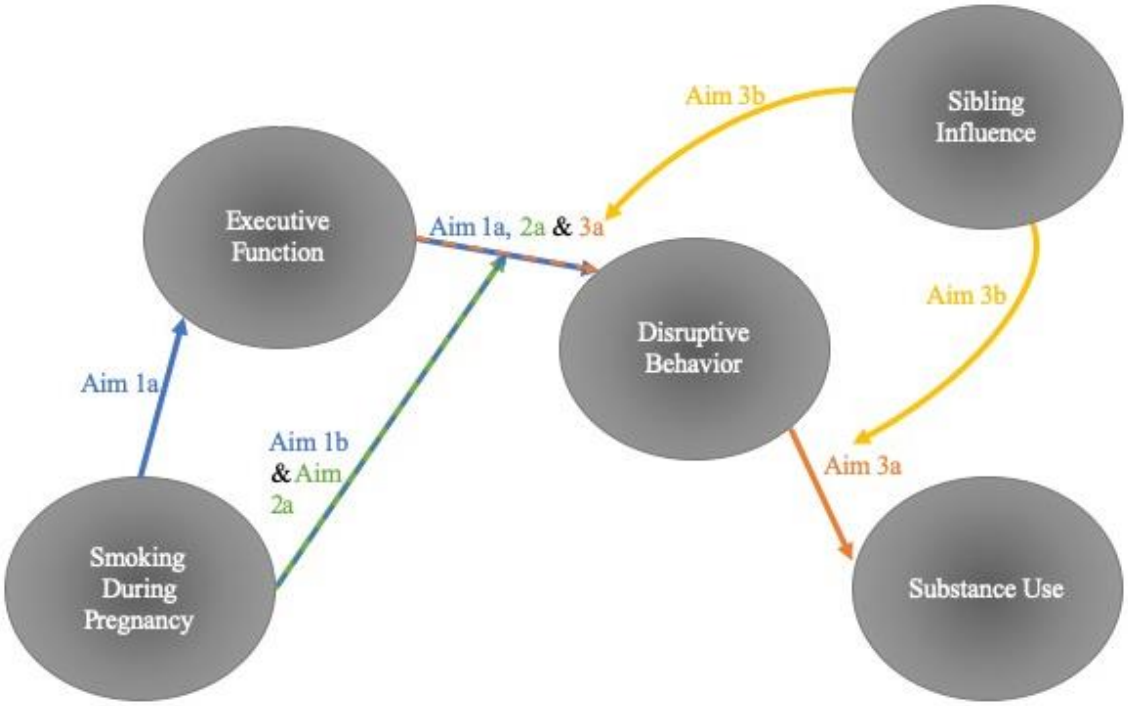



Figure 1. The Conceptual model guiding my work.

## Rationale for Conceptual Model Pathways

### Aim 1

***Executive function as a process through which smoking during pregnancy impacts disruptive behavior*.** Studies have begun to explore the role of smoking during pregnancy on youth disruptive behavior and found that smoking during pregnancy is linked to increased disruptive behavior (only utilizing a multi-rater composite score of disruptive behavior from both parent and teacher; Ekblad et al., in press). The research examining the process through which smoking during pregnancy is thought to impact youth disruptive behavior has primarily focused

on biological factors (e.g., teratogenic role on brain development; Ekblad, Korkeila, & Lehtonen, 2014). However, there is a long developmental gap from smoke exposure during pregnancy to childhood and adolescent behavior. Theoretically, it may be more plausible that developmental phenotypes that are more proximal temporally and biologically may serve as a mechanism supporting the association.

Childhood executive function is particularly salient as executive function develops most rapidly in early childhood (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997) and offers a foundation for the ongoing development of executive function skills (Caspi, Henry, McGee, Moffitt, & Silva, 1995; Eisenberg et al., 1997; Mischel, Shoda, & Rodriguez, 1989; Raffaelli, Crockett, & Shen, 2005). Further, early executive function has been linked to later disruptive behavior (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Smoking during pregnancy is associated with poorer executive function in early childhood (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono, Carlson, Taylor, Elkins & McGue, 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). Smoking during pregnancy is associated with worse executive function, in part, through a teratogenic role of smoking during pregnancy on brain development (e.g., atypical frontal lobe development and myelination of the prefrontal cortex; Ekblad et al., 2014; Peterson et al., 2003). Importantly, those parts of the brain found to be impacted by smoking during pregnancy have been linked with the development of executive function (Anderson, 2002). In a study of 296 five-year-olds, children exposed to smoking during pregnancy had poorer working memory and inhibition, two of the three components of executive function (Clark, Espy, & Wakschlag, 2016). In other studies, maternal report of smoking during pregnancy was associated with poorer set-shifting, global executive function (Daseking, Peterman, Tischler, & Waldmann, 2015), and the ability to plan or organize during adolescence (Piper & Corbett, 2011). Despite this evidence, no research has examined the role of early childhood executive function as a process through which smoking during pregnancy may predict disruptive behavior. Thus, the current study examines whether early childhood executive function is a mediator through which smoking during pregnancy is associated with later disruptive behavior.

***Smoking during pregnancy as a context for the executive function-disruptive behavior association.*** Findings from sibling-comparison designs and other genetically-informed studies suggest that familial confounding accounts for associations of smoking during pregnancy with executive function and with adolescent disruptive behavior (Ekblad et al., in press; D'Onofrio, Van Hulle, Goodnight, Rathouz, & Lahey, 2011; Knopik, 2009; Kuja-Halkola, D'Onofrio, Larsson, & Lichtenstein, 2014; Rydell, Granath, Cnattingius, Magnusson, & Galanti, 2014), rendering the direct effect of smoking during pregnancy unlikely to be causal. Given the organizing effect of smoking during pregnancy on later biological (e.g., brain) and behavioral development (Gluckman et al., 2008), and it's interaction with familial risk for externalizing-type behavior (Buschgens et al., 2009; Marceau et al., 2019; Neiderhiser et al., 2016), smoking during pregnancy may be an important context for the executive function-disruptive behavior association. Executive function develops rapidly during early childhood (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997) and predicts the trajectory of more complex executive function skills (e.g., Tillman et al., 2015) as well as later externalizing-type behavior (e.g., Eisenberg et al., 2005; Eisenberg et al., 2009; Nigg et al., 2006). In addition to smoking during pregnancy being related to those early executive function deficits that put youth at increased risk for later disruptive behavior, through its organizing role on other brain systems, smoking during pregnancy could potentially provide an environment of catecholaminergic dysfunction during late childhood/early adolescence which compounds risk (e.g., moderates) for disruptive behavior. In sum, although several behavioral genetic studies of smoking during pregnancy suggest exposure associations are confounded by familial effects, there is evidence that it is relevant through and/or in interaction with other developmental influences (e.g., early executive function deficits) on later disruptive behavior. Therefore, in addition to testing early childhood executive function as a mechanism by which smoking during pregnancy affects late childhood disruptive behavior, I will also consider whether smoking during pregnancy is a moderator serving to exacerbate the association between executive function and disruptive behavior.

**Aim 2**

***Smoking during pregnancy as a context for the executive function-disruptive behavior association in early adolescence.*** Expanding developmentally from the aim 1, examining the

link between executive function, smoking during pregnancy, and disruptive behavior from middle childhood into adolescence is critical, given the extensive brain development that occurs during this period. During adolescence, youth experience many shifts in their brain structure that offer an additional biological mechanism that creates a sensitive period. Importantly, brain changes at the beginning of adolescence (e.g., the development of the prefrontal cortex and cerebellum) have been associated with increases in impulsivity, and risk taking , key facets of disruptive behavior (Casey, Getz, & Galvan, 2008; Chambers, Taylor, & Potenza, 2003; Nelson et al., 2002; Steinberg, 2008; Spear, 2009). The development of the brain (e.g., myelination of the prefrontal cortex) that assists in early adolescent executive function, responsible for reeling in the newfound impulsivity, does not become impactful until late adolescence. Executive function consists of behaviors (e.g., response inhibition) that have been related to adolescent delinquent behavior (Nigg et al., 2006), while the cerebellum controls emotional reactivity is relatively developed, the prefrontal cortex (implicated in executive function skills) remains relatively immature until later in adolescence (e.g., Crone & Dahl, 2012; Ernst, 2014). Because in childhood there is synaptic proliferation or amounts of synapses that greatly exceed that of adult levels, the brain must prune unused synapses for accuracy, efficiency, and speed (Zecevic & Rakic, 2011). This research corresponds with findings that suggest from age 10 to 30, impulsivity steadily declines (Steinberg et al., 2008). Further, the prefrontal cortex is also linked to emotional responses (e.g., emotional response to regret comparisons in gambling tasks; Levens et al., 2014) and is implicated in other critical executive function skills (short term memory, framing plans, strategizing, and initiation of action; Blakemore & Choudhury, 2006; Carlson & Birkett, 2017). Thus, smoking during pregnancy is salient for examining executive function during adolescence when these areas are becoming central in supporting appropriate behaviors (Wiebe et al., 2015). In sum, during this time in the brain's development, adolescents are most at risk for influences that are associated with delinquent behavior (e.g., disruptive behavior and substance use).

The literature on smoking during pregnancy has considered exposure as a context (e.g., moderator) for later behavior problems. In line with the reasons outlined in study one (i.e., smoking during pregnancys may have an organizing role for catecholaminergic dysfunction in adolescence), study two extends to a complementary genetically-informed design meant to examine exposure to smoking during pregnancy. Thus, the second aim of this dissertation

examines smoking during pregnancy as a context that may exacerbate the executive function-disruptive behavior association. Thus, smoking during pregnancy is salient for examining executive function during adolescence when these areas are becoming central in supporting appropriate behaviors (Wiebe et al., 2015). In sum, the second aim of this dissertation seeks to examine smoking during pregnancy as a context for the executive function-disruptive behavior association, such that during smoking during pregnancy becomes a salient context for the development of executive function when adolescent brains are experiencing a sensitive period linked to disruptive behavior.

**Aim 3**

***Disruptive behavior as a process through which executive function predicts substance use.*** Executive functions are foundational cognitive processes that are used in service of many outcomes (e.g., academic success, behavioral regulation). For example, children with lower executive function are more likely to have poorer physical health, substance dependence, poorer personal finances, and criminal charges later in life (Moffit et al., 2011). Critically, executive function deficits have been associated with increased adolescent disruptive behavior and substance use (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Further, McGue and colleagues (2001) found that the presence of childhood disorders, characterized by disinhibition, are related to earlier initiation of alcohol use. Notably, executive function deficits are related to preadolescents' impulsivity (Cassidy, 2015; Romer et al., 2009) which may translate to poor decision-making and adolescent substance use. Thus, the current dissertation will focus on executive function as a key predictor of both adolescent disruptive behavior and substance use. Further, disruptive behavior is one of the strongest predictors of later substance use and considered a risk factor for earlier substance use initiation (Dodge et al., 2009). Cascade models of substance use initiation suggest that adolescents' access to substances increases as they age, likely due in part to disruptive behavior (Marceau, Brick, Knopik, & Reijneveld, in press; Trucco et al., 2016). These findings suggest that disinhibition or executive function deficits may foster problem behavior (e.g., disruptive behavior) which may lead to greater risk for adolescent substance use. Therefore, the current study focuses on examining

disruptive behavior as a process through which executive function is related to adolescent substance use.

***The sibling relationship as a context for disruptive behavior as a process through which executive function predicts substance use.*** A number of studies illustrate that children's sibling relationship qualities are uniquely linked to numerous outcomes from childhood into adolescence. For example, negative sibling relationship qualities for young children (e.g., agonism) are associated with internalizing (e.g., depression, loneliness and low self-worth; Stocker, 1994) and disruptive behaviors (e.g., aggressive behavior, behavior problems and associations between jealousy and poor emotional understanding; Mandell & Gamble, 2006; Volling, McElwain, & Miller, 2002). In contrast, warm and affectionate sibling relationships are negatively associated with disruptive behaviors and positively associated with socio-cognitive development (Modry-Mandell, Gamble & Taylor, 2007). Additionally, the variety and intensity of emotions within sibling interactions are largely impactful as well, and the quality of those interactions is thought to shape the course of children's development (Dunn, Slomkowksi, & Beardsall, 1994). For example, sibling conflict is positively related to a number of suboptimal outcomes for children, including risky and antisocial behavior (Criss & Shaw, 2005; Solmeyor, McHale, & Crouter, 2014) as well as depressive symptoms (Kim, McHale, Crouter, & Osgood, 2007).

Critically, during adolescence siblings are unique socializers, influencing adolescent behaviors such as disruptive behaviors and substance use (Fagan & Najman, 2005; Kothari, Sorenson, Bank, & Snyder, 2014). Research into sibling relationships suggests that sibling relationship quality is associated with disruptive behavior and substance use, and findings are often interpreted such that negative sibling relationships and/or siblings acting as facilitators or models of risky behaviors subsequently predicts behavior problems in the co-sibling (Modry-Mandell, Gamble & Taylor, 2006; Rende, Slomkowski, Lloyd-Richardson, & Niaura, 2005; Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005; Solmeyer, McHale & Crouter, 2014). For example, Jenkins and Dunn (2009) found that siblings are one of the most influential social factors during adolescence, and are influential for the development of disruptive behaviors and substance use during adolescence, above and beyond the parent-child relationship, peer disruptive behavior, and adolescent-peer negative interactions (Defoe et al., 2013). Specifically, research suggests that in adolescence there is a bidirectional, positive association between

siblings' disruptive behavior and alcohol use (Whiteman et al., 2017). Together, associations of sibling influence has been explained by hypothesized mechanisms that include observation/modeling, reinforcement, and extensive opportunities for practice (e.g., older siblings providing cigarettes or alcohol and being 'partners in crime'; Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017).

Modeling has been shown to increase when siblings have a high social connection. For example, there is increased similarity in sibling tobacco and alcohol use when siblings have a more positive relationship, after controlling for both parent and peer smoking (Rende et al., 2005; Slomkowski et al., 2005). However, siblings with a warmer relationship are less likely to experience adolescent substance use (East & Khoo, 2005). Further, while an adolescent's risk for substance use increases when they have a sibling who uses substances (Whiteman et al., 2013). Importantly, siblings may be a training ground for negative and coercive interactions linked to a lack of self-control (Natsuaki et al. 2009; Patterson 1984; Patterson et al. 1989), suggesting that negative sibling relationship quality may exacerbate executive function deficits and increased disruptive behavior predicting later substance use. Importantly, sibling substance use may provide access to substances that would strengthen a youth at risk likelihood to initiate substance use. For example, in a study of early adolescents, almost half of youth that smoked reported receiving cigarettes from their sibling (Forster et al., 2003). Additionally, in a study of adolescents, sibling substance use was linked to youth utilizing substance use as a way of coping with stressful life events (Windle, 2002).

In sum, the sibling literature suggests that sibling substance use and the quality of the sibling relationship may be risk factors for maladjustment and interact with or exacerbate other developmental influences (e.g., early executive function deficits and disruptive behavior) to predict adolescent substance use. Taken together, these studies highlight the importance of investigating siblings as a context for the development of both disruptive behaviors and substance use. However, sibling relationships remain the least studied close relationship (McHale, Updegraff & Whiteman, 2012). Thus, the current dissertation examines the role of the sibling relationship quality and whether a sibling uses substances as a context for the executive function-disruptive behavior and executive function-substance use associations (Aim 3).

## Interdisciplinary Approach

The current dissertation utilizes an interdisciplinary approach, incorporating family research, behavior genetics, and a developmental perspective (Figure 2). By utilizing a developmental perspective along with family research, this dissertation is able to examine the varying influence of families across time, shaping youth's environment. Additionally, utilizing a developmental perspective along with behavior genetics and incorporating behavior genetics in family research, this dissertation is able to capitalize on familial risk and genetically-informed designs to better control for familial confounding in developmental pathways. As a whole, this interdisciplinary approach allows for understanding how prenatal environment, executive function, and sibling relationships work together across development situated in genetic relatedness, to influence disruptive behavior and the development of adolescent substance use. Critically, this dissertation includes two genetically-informed studies and a longitudinal study capitalizing on familial risk to better investigate the possibility of familial confounding in associations in the developmental pathway from executive function deficits to adolescent substance use. Further, utilizing family research on both smoking during pregnancy and siblings' impact on youth's environment across time is significant in understanding how families effect development, possibly influencing adolescent substance use.

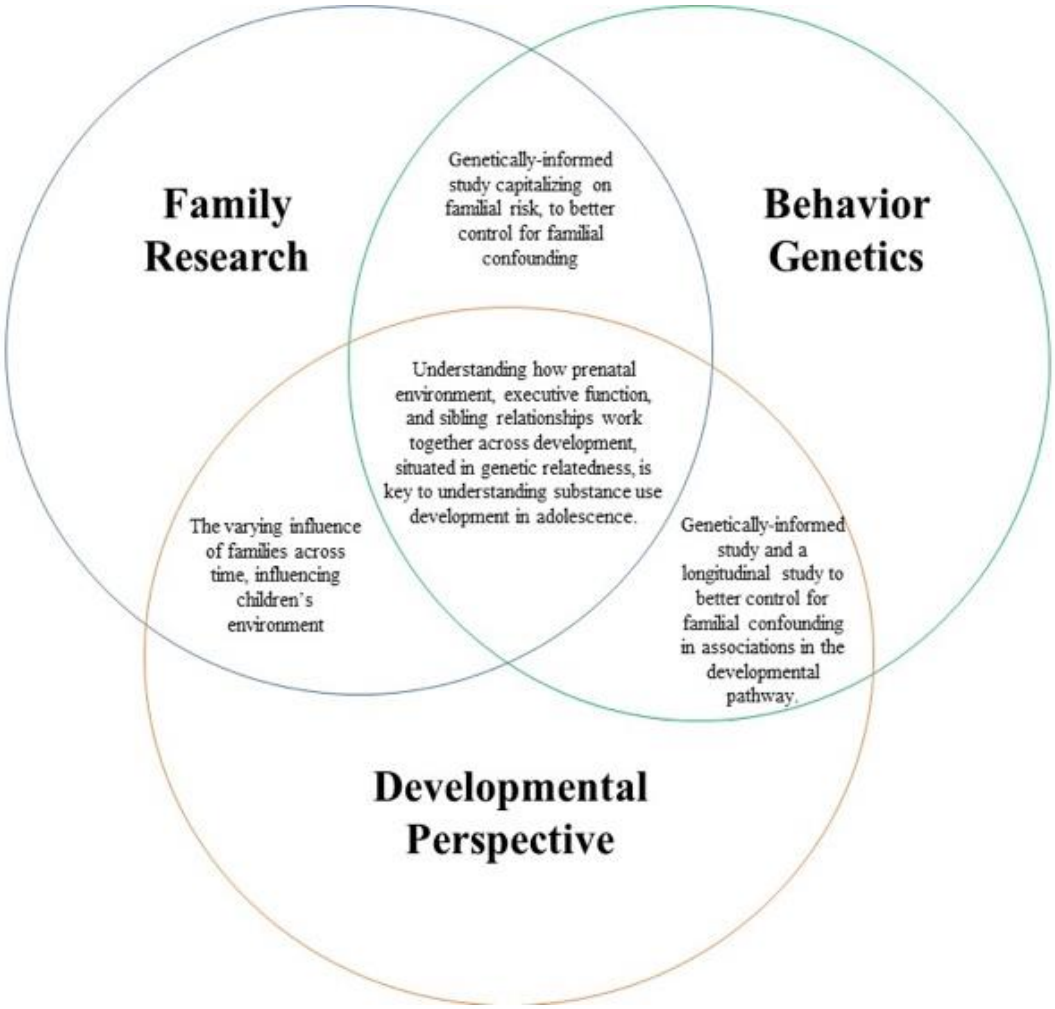



Figure 2. The figure depicts the interdisciplinary approaches utilized in the current dissertation, how they are distinct and interrelated to best answer dissertation research questions.

**Family Research**

Research suggests that, within the population, substance use is not equally nor randomly distributed (Tarter, Vanyukov, Giancola, Dawes, Blacksin, Mezzich, & Clark 1999). Importantly, family research designs can help to understand the components that go into high or low liability in risk for substance use by implementing designs that target at risk populations. By utilizing a design that incorporates information from all family members (e.g., mothers, fathers, and children), for groups with high risk (e.g., for substance use liability, fathers with substance use disorders; Tarter, et al., 2001) and low risk (e.g., for substance use liability, fathers with no disorders; Tarter, et al., 2001), researchers can examine and compare children from both high and low risk families across development to assess antecedents of risk for substance use. Thus,

utilizing a longitudinal family risk design allows researchers is a strong method to examine the developmental pathways or specific, independent influences associated with a phenotype or behavior.

**Developmental Perspective**

This dissertation is guided by dynamic theories of development, including environmental and individual characteristics. For example, the relational-developmental-systems (RDS; Lerner, Johnson, & Buckingham, 2015) theory suggests that individual characteristics (e.g., genetics and cognitive abilities) and environments (e.g., prenatal and sibling relationships) do not occur separately, but are interwoven in a bidirectional and dynamic process manipulating development. Secondly, the work comprising this dissertation focuses on the importance of sensitive developmental periods of great change, particularly the prenatal period and adolescence. Thirdly, this research is grounded in how transactional and bidirectional influences shape development across sensitive periods. For example, dialectical theory (Kuczynski & Mol, 2015) suggests that development is dependent on interactions among individuals' personal characteristics and their environment. Thus, individuals are continually developing based on reactions to, and provisions or restraints offered by their environment. Further, utilizing longitudinal data enables this dissertation to examine associations across sensitive periods and development. Notably, adolescence is a significant period of transition, where individuals experience a various physical, social, cognitive, and emotional changes. Understanding how prenatal environment, cognitive abilities, and sibling relationships influence each other and work together, situated in designs that can control for genetic relatedness, is both fascinating and integral to understanding the development of risk for substance use during adolescence.

**Behavior Genetics**

Genetically-informed studies allow for researchers to control for familial confounding by design when examining both environmental and genetic influences on behavior. As noted above, smoking during pregnancy, sibling relationships, executive function, disruptive behaviors, and substance use are heritable traits (Friedman et al., 2008; Hicks, Iacono & McGue, 2012; Mark, Pike, Latham & Oliver, 2016: Moffit, 2005), introducing the potential for genetic confounding.

Genetic confounding is when the variance in a phenotype that is perceived to be predicted by environmental factors is at least partially explained by underlying genetic risk or predisposition that isn't properly accounted for in a model. Utilizing genetically-informed research is necessary to either test or account for genetic confounding. Therefore, the proposed dissertation harnesses several genetically sensitive designs in order to more clearly understand the development of adolescence substance use.

Prior literature highlights the importance of considering both biological and social components of the development of substance use, and importantly, the prominence of considering familial (e.g., genetic and home environment) confounds (Iacono et al., 1999). However, few studies relating smoking during pregnancy to executive function have utilized genetically-sensitive designs (Micalizzi et al., 2018), and studies relating executive function to adolescent substance use have not considered smoking during pregnancy as a critical early environmental context. Similarly, parents with a substance use disorder are likely to pass down genetic risk for substance use as well as poorer functioning to offspring, and siblings also experiencing that same familial risk may serve as models for substance use compounding risk for earlier substance use engagement. To control for potential genetic/familial confounds and improve interpretation of the associations between smoking during pregnancy, sibling relationships, executive function, disruptive behaviors and substance use as either potentially environmental or due to familial confounding, the current study incorporates two types of genetically-informed designs (i.e., adoption study and sibling comparison design) to examine the development of adolescent substance use.

Quantitative genetics does not examine specific genes, but instead estimates the extent to which discernable distinctions among individuals are due to genetic and/or environmental differences. A strength of quantitative genetic designs (e.g., twin/sibling and adoption studies) is the ability to utilize family samples, with varying degrees of genetic relatedness, to parse the variance of a phenotype into three variance components: genetic, shared, and non-shared environmental influences. Genetic components refer to similarities among family members that are attributable to shared DNA material. For example, two siblings in the same family may have similar personality traits that were passed on genetically to them both from their parents. Shared environmental influences include any non-genetic factors that serve to make siblings more similar, whereas non-shared environmental influences include any non-genetic factors that serve

to make siblings dissimilar. For example, parental differential treatment commonly acts as a non-shared environmental influence, where two siblings in the same home experience divergent parenting that leads to one sibling (who perceives themselves as being less favored) initiating delinquent behaviors and the other (who perceives themselves as being favored) does not. On the other hand, parental education often acts as a shared environmental influence, frequently controlled for in the study of sibling relationships as a control for the overall home environment, siblings share an environment that may have implications for the both of them.

***Adoption study design (Aim 1)***. One class of genetically informed designs that can be leveraged for understanding sibling influence are adoption designs. There are many variations in adoption studies. The two most frequently used types include (i) adopted-at-birth samples, which include a target child is adopted immediately or very closely following birth and both biological and adoptive parents, and (ii) samples of adopted children and their siblings: both biological siblings (reared apart) and non-genetically related siblings (reared together). Both adoption study designs can be used to explore how parenting is related to child behavior- whether it's genetically confounded or environmental in nature. Given that genes are passed down from parent to child, and that genes can also drive children's environment, separating the birth parent's genetic contribution to a child's development from the adoptive parent's environmental contribution, by design, disentangles and controls for genetic confounds. The strength of the adopted-at-birth sample is that it allows researchers to explore whether associations of parents' characteristics and behaviors with child outcomes are attributable to genetic or environmental influences.

Specifically, one type of adoption study design utilizes children who were adopted at or close to birth (adopted-at-birth design), gathering data from both the biological and adoptive parents (e.g., The Early Growth and Development Study**;** Leve, Neiderhiser, Shaw, Ganiban, Natsuaki, & Reiss, 2013). In this case, child-biological parent associations are attributed to genetic or prenatal influence, whereas child-adoptive parent associations are attributed to environmental influences. The assumption of the adopted-at-birth study design is that, theoretically, children have not been exposed to their birth parents' environment (except for prenatally), and thus any similarities must be due to the genetics that they share (if the prenatal environment has been controlled for). On the other hand, the child and their adoptive parents share no genetics; the adoptive parent has only contributed to the child's environment. Thus, we

assume that any similarities between the child and the adoptive parent must be environmental influences. The adopted-at-birth design does a good job of parsing apart genetic and environmental influences of parent-child associations but is less relevant to studying the influence of siblings, unless siblings are also included (in the same way as described below).

Unique to adoption studies that include both biological and adoptive siblings, we have the opportunity to examine the impact of a non-related sibling as a support system, and to compare that relationship to that of the genetic sibling relationship (studies of this design have consistently been similar to the population utilized in sibling relationship research). Similar to twin studies, adoption studies allow researchers to compare genetically related and genetically unrelated dyads to examine the contribution of additive genetic influences, and shared environmental influences. However, adoption studies are unique from twin studies because the adopted youth develop in an environment separate from their biological or genetic relatives (e.g., biological parents and sibling/s), resulting in stronger separation of genetic and environmental influences. In genetically unrelated sibling dyads (including both step siblings but also adoptive siblings), any sibling correlation has to be attributed to shared environmental influences as siblings share no genes and associations cannot be confounded by genetic influences. Thus, the adoption study design allows researchers to isolate environmental pathways for sibling influence.

***Limitations of adoption studies*.** The adopted children and their siblings design is a robust method to isolate environmental pathways of sibling influence but the design does have several weaknesses. Functionally, there are challenges in finding linked families that include biological and adoptive parents and siblings in sufficient numbers to be adequately power for the complex questions most developmental sibling research are seeking to examine. Further, adoption itself is not common and thus requires more intensive recruitment and a potentially smaller sample size. Ethically, researchers must be sensitive when approaching biological families about the child they placed for adoption (especially if the adoption occurred further in the past). Additionally, there are concerns surrounding the representativeness of biological and adoptive parents, as well as adopted children. Furthermore, when considering the prenatal environment, there is not as clean of a separation between genes and environmental influences, as similarities between biological mother and adopted child may be attributable to either genetic effects or the prenatal environment. Importantly, a majority of domestic adoptions in the United States are at least partially open, meaning information is shared between biological and adoptive

parents. This threatens the assumption that youths' environment with their adoptive parents is entirely independent from genetic influence (i.e., biological parents). Finally, a major critique of the adoption design is that placement may not be random, also known as selective placement. This occurs when adopted children are placed with genetic relatives or parents that resemble their biological parents, both of which serve to inflate estimations of heritability as adopted children may look more similar to biological parents for reasons other than additive genetic influences.

***Sibling comparison design (Aim 2).*** Experimental designs with random assignment can assume causal influence if a controlled experimental environment (opposed to the control group) leads to an outcome of interest. However, it is not often ethical to subject individuals to certain environments. For example, subjecting a fetus to teratogenic substances during neo-natal development. Sibling comparison designs are a quasi-experimental design that controls for genetic and environmental confounds that utilizes natural experiences for research (see Lahey & D'Onofrio, 2010). The sibling comparison design strives to account for this confound (disentangling genetic and environmental influences) by utilizing siblings from the same family who have had disparate experiences with a given observable phenotype. The strongest form of this design utilizes monozygotic twins (who shared 100% of their genes), however, full siblings are still informative and in some cases (e.g., differential intrauterine exposures) necessary. The siblings' environments overlap because they share a home created by the parents, and they share 50% of their genes (if they are full siblings). Thus, siblings are "matched" on these familial factors, so when controlling for genetic environmental differences between families that could confound the association of interest (e.g., neighborhood or socioeconomic status), researchers can assume that variation in a phenotype is due to the disparate experience of the siblings. For example, a sibling comparison design where siblings are disparate for smoking during pregnancy (i.e., a mother smoked during one pregnancy but not the other). Any differences in the outcome of interest (e.g., ADHD; Knopik et al., 2016) is potentially causally influenced by prenatal smoking.

***Limitations of sibling comparison designs.*** Not unlike other research designs, the sibling comparison design has several limitations that must be noted. First, sibling comparison designs must be conducted with disparate experience, meaning that one member of the dyad must have a unique experience from the other member that researchers are interested in utilizing as a focal

predictor of an outcome. Secondly, the effect of one sibling's exposure to the disparate experience cannot impact the other sibling. For example, if one sibling experienced smoking during pregnancy and the other did not, we assume that the sibling experiencing prenatal smoking did not somehow change the experience of the sibling who was not subjected to smoking during pregnancy. Thirdly, researchers must confirm that findings are generalizable, for example from full siblings to only children. Further, understanding why siblings were differentially exposed to a given environmental risk factor is critical to avoid confounding environmental factors or self-selection, as the strength of causal inference can be weakened if this is not accounted for. Finally, when utilizing a design with full siblings, conducting sensitivity analyses by replicating findings with a sample of monozygotic twins can strengthen study findings (e.g., Mendle, Ferrero, Moore, & Harden, 2013).

A strength of this work is the use of samples at familial risk for both disruptive behavior and substance use, as well as complementary genetically-informed and longitudinal study designs. The Early Growth and Development Study (EDGS) is a longitudinal adoption study and research shows that adopted youth are more likely to experience substance use disorder in adulthood (Yoon, Westermeyer, Warwick, & Kuskowski, 2012). Further, in EGDS, there is increased genetic risk, as birth parents had higher rates of substance use disorders (59% of birth mothers, 72% of birth fathers) as compared to the National Comorbidity Study (30% for females, 42% for males). Youth also had higher than average exposure to smoking during pregnancy. The Missouri Mothers and Their Children project (MO-MATCH) is a sibling comparison design that captures familial risk because all mothers were smokers. Also, MO-MATCH had a high proportion of mothers and fathers with nicotine dependence (62% and 39%, respectively) and alcohol abuse (45% and 53%, respectively), and higher than average exposure to smoking during pregnancy (57.8%). Smoking during pregnancy is also a familial influence on later developmental outcomes, with correlated genes and environmental exposures transferred to children potentially leading to compounded risk for disruptive behavior and substance use. The Center for Education and Drug Abuse Research (CEDAR) by design recruited half the sample to be at familial risk of substance use because fathers with substance use disorders (44%) were identified and recruited. This recruitment strategy captures greater risk as children of parents with substance use disorders have greater liability for psychopathology (e.g., Clark, Moss,

Kirisci, Mezzich, Miles, & Ott, 1997; Hill & Muka, 1996; Schuckit & Smith, 1996; Sher, Walitzer, Wood, & Brent, 1991; Tarter et al., 1999).

## Dissertation Aims

Together my conceptual model and interdisciplinary framework leads to three aims that will be conceptualized and presented as three papers. I begin to examine the process through which smoking during pregnancy impacts later adolescent adjustment in **Aim 1** using a longitudinal (birth through middle childhood) genetically sensitive parent-child adoption design. Specifically, I will test whether early childhood executive function is a mediator through which smoking during pregnancy is associated with disruptive problems in late childhood, a key behavioral risk for adolescent substance use (1a). Further, I will test whether smoking during pregnancy may serve as an organizing influence that moderates the association between early childhood executive function and late childhood disruptive behavior, a key behavioral risk for later adolescent substance use (1b). Next, **Aim 2** utilizes a complementary genetically sensitive (sibling comparison) design during late childhood/early adolescence to replicate the first aim in examining smoking during pregnancy as an organizing influence that moderates the association between executive function and disruptive behavior, a key behavioral risk for adolescent substance use (2a). Finally, I will extend the developmental pathway of disruptive behavior to adolescent substance use in **Aim 3** utilizing a family risk design. Specifically, I will examine whether disruptive behavior mediates the executive function-substance use association in adolescence (3a). Further, I will test whether sibling relationship quality and siblings' substance use serve as later contextual influences that moderate associations of executive function with disruptive problems and disruptive problems with substance use (3b). Together, the proposed studies address how prenatal and postnatal contexts may affect the developmental pathway from executive function deficits to adolescent substance use.

### Hypotheses

***Aim 1. To examine the process through which smoking during pregnancy impacts later adjustment and whether smoking during pregnancy moderates the early childhood executive function-disruptive behavior in late childhood association.*** Using the Early Growth and

Development Study (EGDS): a genetically-informed study of children adopted at birth, for aim 1a I tested whether early childhood executive function is a mediator through which smoking during pregnancy is associated with disruptive behavior in late childhood. It is hypothesized that smoking during pregnancy will be associated with decreased executive function and decreased executive function will be associated with increased disruptive behavior. For aim 1b, using the EGDS, I will examine whether smoking during pregnancy moderates the association of early childhood executive function with disruptive behavior in late childhood. It is hypothesized that the relation between executive function and disruptive behavior will be stronger for the sibling who experienced smoking during pregnancy than the sibling who did not. The longitudinal adoption study allows me to control for both genetic and family environmental confounds while testing developmental trajectory of executive function and disruptive behavior.

***Aim 2. To examine smoking during pregnancy as a moderator of the association between early adolescent executive function and disruptive behavior.*** I will use the Missouri Mothers and Their Children project (MO-MATCH; Knopik et al., 2015): a genetically-informed sibling-comparison sample of late childhood/early adolescent siblings and their parents where mothers smoked (or smoked more) during one pregnancy and not the other to examine whether smoking during pregnancy moderates the early adolescent executive function-disruptive behavior association (2a). It is hypothesized that the relation between early adolescent executive function and disruptive behavior will be stronger for the sibling who experienced smoking during pregnancy than the sibling who did not. The sibling comparison design allows me to elucidate whether associations might be environmental or explained by between-family differences (including genetics).

***Aim 3. To extend previous aims by examining the sibling relationship as a context for development.*** Using data from the Center for Education and Drug Abuse Research (CEDAR; Tarter & Vanyukov, 2001): a sample including youth at elevated familial risk (e.g., youth who had a father with a substance use disorder) for substance use and a control sample, I will examine whether there is an indirect effect of late childhood executive function on adolescent substance use through early adolescent disruptive behavior (3a). It is hypothesized that lower executive function will be linked to greater rates of disruptive behavior, which in turn will be associated with greater substance use. For aim 3b, I will test whether sibling relationship quality and sibling substance use moderates this developmental pathway. It is hypothesized that the paths will be

stronger for siblings who have a more negative sibling relationship and a sibling that has reported substance use. Finally, I will also test whether findings hold for youth at familial risk (e.g., youth who had a father with a substance use disorder) vs. control youth to explore whether familial risk (including genetics related to addiction) plays a role in these pathways. Utilizing a longitudinal design with at-risk youth allows me to examine the developmental pathways or specific, independent influences (if a developmental pathway is not confirmed) associated with adolescent substance use.

# STUDY 1. EXECUTIVE FUNCTION AS A PROCESS FOR WHICH SMOKING DURING PREGNANCY INFLUENCES DISRUPTIVE BEHAVIOR

Emily Rolan, M.S.[1], Kristine Marceau, Ph.D. [1], Valerie Knopik, Ph.D. [1], Sara Schmitt, Ph.D. [1], Shawn Whiteman, Ph.D. [2], Leslie D. Leve, Ph.D. [3], Daniel S. Shaw, Ph.D. [4], Jody M. Ganiban, Ph.D. [5], David Reiss, M.D. [6], Misaki Natsuaki, Ph.D. [7], Linda Mayes, Ph.D. [8], Jenae M. Neiderhiser, Ph.D. [9]

[1]Department of Human Development and Family Studies, Purdue University (Rolan@purdue.edu; KristineMarceau@purdue.edu; vknopik@purdue.edu; saraschmitt@purdue.edu); [2]Department of Human Development and Family Studies, Utah State University (shawn.whiteman@usu.edu); [3]Prevention Science Institute, University of Oregon (leve@uoregon.edu); [4]Department of Psychology, University of Pittsburgh (casey@pitt.edu); [5]Department of Psychology, George Washington University (ganiban@gwu.edu); [6]Child Study Center, Yale University (dxreiss@earthlink.net); [7]Department of Psychology, University of California, Riverside (misaki.natsuaki@ucr.edu); [8]Department of Psychology, Yale University (linda.mayes@yale.edu); [9]Department of Psychology, Penn State University (jenaemn@psu.edu)

Anticipated submission to *Developmental Psychology*

## Abstract

Exposure to smoking during pregnancy is linked to both disruptive behavior and executive function. Additionally, evidence suggests that smoking during pregnancy may be a context under which executive function becomes more prominent in the development of disruptive behavior. The current study examined whether smoking during pregnancy placed youth on a path to, or exacerbated, a negative developmental trajectory of early childhood executive function deficits to late childhood disruptive behavior. Utilizing a longitudinal adoption study design (*N*=361), a series of regressions were analyzed in MPlus. Our hypotheses of an indirect effect of smoking during pregnancy on disruptive behavior through executive function and that smoking during pregnancy would moderate the executive function-disruptive behavior association were not supported. Findings suggest there is no mediation from smoking during pregnancy to disruptive behavior through executive function. Further, there is no interaction between smoking during pregnancy and executive function predicting disruptive behavior.

## Executive Function as a Process for Which Smoking During Pregnancy Influences Disruptive Behavior

Executive function and disruptive behavior are related to youth adjustment and development (Blair & Razza, 2007; Burt et al., 2005; Jokela et al., 2009; McClelland et al., 2007; McLeod, & Kaiser, 2004; Zelazo et al., 2016). Executive function deficits are a key predictor of disruptive behavior (Aytaclar et al., 1999; Fairchild et al., 2009; Piehler et al., 2012; Rose-Jacobs et al., 2011; Squeglia et al., 2014), and deficits are especially salient during early childhood when executive function is developing most rapidly (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997). Executive function has been associated with disruptive behavior (Hummer et al., 2011; Clark, Prior, & Kinsella, 2000); however, these effects are not always found (Fairchild et al., 2009; Moffitt & Henry, 1989; Pennington & Ozonoff, 1996). Thus, the current study sought to examine a developmental link between childhood executive function and early adolescent disruptive behavior

Smoking during pregnancy is a phenomenon that still affects, on average, 7.2% of women in the United States, with several states (i.e., Montana, Missouri, Kentucky, West Virginia, and Vermont) reporting rates of 20% and above (Drake et al., 2016). Importantly, exposure to smoking during pregnancy predicts disruptive behavior (e.g., Ekblad et al., in press; Wakschlag, Pickett, Kasza, & Loeber, 2006) and executive function (Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono et al., 1999; Micalizzi & Knopik, 2017; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). Therefore, given the link between executive function and disruptive behavior, it is conceivable that executive function deficits, at least in part, mediate the effect of smoking during pregnancy on disruptive behavior. There is evidence of genetic influences (i.e., familial risk to externalzing behavior) moderating later effects of smoking during pregnancy on disruptive behavior (Buschgens et al., 2009), depicting the ways in which earlier developmental influences can be a context for later associations. Smoking during pregnancy has been found to serve as a context moderating the association between familial influences and disruptive behavior (Marceau et al., 2019; Neiderhiser et al., 2016), exemplifying that smoking during pregnancy may be a context for disruptive behavior development. Therefore, the current study examines whether early childhood executive function is a mediator through which smoking during pregnancy is associated with disruptive behavior in late childhood and if smoking during

pregnancy moderates the association of early childhood executive function with disruptive behavior in late childhood.

### Executive Function as a Process for the Smoking During Pregnancy-Disruptive Behavior Association

Studies have begun to explore the role of smoking during pregnancy on youth disruptive behavior and have found that smoking during pregnancy is linked to increased disruptive behavior (only utilizing a multi-rater composite score of disruptive behavior from both parent and teacher; Ekblad et al., in press). Disruptive behavior is a common and persistent form of childhood maladjustment (Campbell, 1995) that includes but is not limited to oppositional defiant disorder, conduct disorder, and attention-deficit/hyperactivity disorder (Boyle & Offord, 1991; Fergusson et al., 1994; Ford et al., 2003; Kandel et al., 1997). The research examining the process through which smoking during pregnancy is thought to impact both youth disruptive behavior has primarily focused on biological factors (e.g., teratogenic role on brain development; Ekblad, Korkeila, & Lehtonen, 2014). However, there is a long developmental gap from smoke exposure during pregnancy to childhood and adolescent behavior. Theoretically, it may be more plausible that developmental phenotypes that are relatively more proximal temporally and more closely tied to biological development may serve as a mechanism supporting the association.

Similar to behavior problems, smoking during pregnancy is associated with poorer executive function in early childhood (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono, Carlson, Taylor, Elkins & McGue, 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). Executive function is a set of interrelated cognitive skills used to conduct goal-directed actions through control and coordination of information (Zelazo et al., 2016) and includes three components: working memory, set-shifting, and inhibition (Garon, Bryson, & Smith, 2008; Miyake, Friedman, Emerson, Witki, Howerter, & Wager, 2000). Childhood executive function is particularly salient as executive function develops most rapidly in early childhood (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997) and offers a foundation for the ongoing development of executive function skills (Caspi, Henry, McGee, Moffitt, & Silva, 1995; Eisenberg et al., 1997; Mischel, Shoda, & Rodriguez, 1989). Notably, smoking during pregnancy may have a teratogenic role on brain development partially responsible for the

development of executive function in early childhood, (e.g., prefrontal cortex; Anderson, 2002; Berger, Tzur, & Posner, 2006; Diamond, 2013; Ekblad et al., 2014; Kochanska & Knaack, 2003; Peterson et al., 2003; Rothbart, Derryberry, & Posner, 1994), exposure to smoking during pregnancy predicts decreased childhood executive function (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono, Carlson, Taylor, Elkins & McGue, 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011).

The parts of the brain found to be impacted by smoking during pregnancy have also been linked with the development of executive function (Anderson, 2002). Further, alterations in brain structure and function related to exposure to smoking during pregnancy are also linked to disruptive behavior (e.g., Bublitz & Stroud, 2012; Chatterton et al., 2017; Ekblad et al., 2014; Ekblad et al., 2010; Knopik, 2009; Latimer et al., 2012). Despite evidence that: 1) smoking during pregnancy predicts executive function; 2) executive function predicts disruptive behavior; and 3) evidence that executive function may represent a mechanism for the smoking during pregnancy-disruptive behavior association, no research has examined the role of early childhood executive function as a process through which smoking during pregnancy may predict disruptive behavior. Thus, the current study examines whether early childhood executive function is a mediator through which smoking during pregnancy is associated with later disruptive behavior.

Given the genetic influence on both executive function (Ando et al., 2001; Anokhin et al., 2003; Friedman et al., 2008; Engelhardt et al., 2015; Heutink et al., 2006) and disruptive behavior (Burt, 2009), utilizing genetically-informed designs is critical to obtain minimally biased findings (Burt, 2009; Engelhardt et al., 2015). An adopted-at-birth design allows researchers to elucidate whether associations of parents' characteristics and behaviors with child outcomes are attributable to genetic or environmental influences by gathering data from both the biological and adoptive parents. A longitudinal adopted-at-birth study enables researchers to control for both genetic and family environmental confounds while testing the developmental trajectory of executive function and disruptive behavior. The prenatal environment is a context provided by the birth mother, thus, similarities between youth and birth mothers in this study may not be solely due to smoking during pregnancy, but genetic risk as well. By controlling for the biological parents' executive function and disruptive behavior, the study can partially account for genetic influence to isolate the effects of smoking during pregnancy. Additionally, including measures of adoptive parents executive functioning and disruptive behaviors controls

for familial confounding induced by adoptive parent risk factors (e.g., executive function deficits or increased disruptive behavior) on the rearing environment. Thus, by leveraging a longitudinal adopted-at-birth design in this way, the current study extends previous work by isolating smoking during pregnancy as a predictor that may influence youths' individual executive function and disruptive behavior across development.

### Smoking During Pregnancy as a Context for the Executive Function-Disruptive Behavior Association

Prenatal influences, including smoking during pregnancy, have been shown to have an organizing effect on later biological (e.g., brain) and behavioral development (Gluckman et al., 2008). Literature has begun to investigate smoking during pregnancy as a context for development, notably, often without genetically sensitive designs able to control for familial confounding (Becker et al., 2008; Hohmann et al., 2016; Salatino-Oliveira et al., 2016). The adolescent stage of development is related to alterations in dopamine release which are associated with risky behaviors (Spear, 2000). Animal studies suggest that prenatal nicotine exposure predicts changes in catecholamine systems (e.g., dopamine; Azam et al., 2007; Ribary & Lichtensteiger, 1989; Onal et al., 2004). Prenatal smoking during pregnancy is associated with later neurobehavioral deficits, potentially linked to smoking during pregnancy-related catecholaminergic dysfunction in the adolescent brain (e.g., Dwyer et al., 2009; Knopik et al., 2016; Thapar et al., 2003; Weissman et al., 1999). Executive function develops rapidly in early childhood (Bell & Deater-Deckard, 2007; Blair & Razza, 2007; Espy, Kaufmann, Glisky, & McDiarmid, 2001; Zelazo, Carter, Reznick, & Frye, 1997), predicts more complex executive function skills (e.g., Tillman et al., 2015) as well as externalizing-type behavior in late childhood and preadolescence (e.g., Eisenberg et al., 2005; Eisenberg et al., 2009; Nigg et al., 2006). Therefore, executive function deficits in late childhood, along with smoking during pregnancy-related catecholaminergic dysfunction, may predict greater disruptive behavior. Although the smoking during pregnancy precedes the development and transitions in executive functioning temporally, various effects may not become salient for disruptive behavior until much later during adolescence. In sum, although several behavioral genetic studies of smoking during pregnancy suggest exposure associations are confounded by familial effects, there is evidence

that it is relevant through and/or in interaction with other developmental influences (e.g., early executive function deficits) on later disruptive behavior.

## Current Study

Previous work has tested the associations between smoking during pregnancy and executive function, between smoking during pregnancy and disruptive behavior as well as between adolescent executive function and the development of adolescent disruptive behavior. However, no previous study has tested whether executive function mediates the association between smoking during pregnancy and disruptive behavior, or whether the developmental relation of executive function on disruptive behavior in childhood is exacerbated by exposure to smoking during pregnancy. When examining the link between exposure to smoking during pregnancy and disruptive behavior, there is a substantial developmental gap. Given the teratogenic role of exposure to smoking during pregnancy on brain regions linked to executive function (e.g., prefrontal cortex; Anderson, 2002; Ekblad et al., 2014; Peterson et al., 2003) and the established association between executive function and later externalzing-type behaviors (e.g., Eisenberg et al., 2005; Eisenberg et al., 2009; Nigg et al., 2006), it may be more plausible that executive function, a more proximal characteristic, may serve as a mechanism supporting the smoking during pregnancy-disruptive behavior association. Further, there is evidence that suggests smoking during pregnancy has an organizing effect on later biological (e.g., brain) and behavioral development (Gluckman et al., 2008), and interacts with familial risk to predict externalizing-type behavior (Buschgens et al., 2009; Marceau et al., 2019; Neiderhiser et al., 2016), suggesting that smoking during pregnancy may be a context for that exacerbates the executive function-disruptive behavior association. Thus, the current study examined the role of smoking during pregnancy as putting youth on or exacerbating a negative developmental trajectory of childhood executive function deficits and subsequent early adolescent disruptive behavior using a longitudinal adoption study design. The first aim of the current study is to examine whether there is an indirect effect of exposure to smoking during pregnancy on late childhood disruptive behavior through earlier executive function (Figure 3). It was hypothesized that exposure to smoking during pregnancy would be related to executive function deficits (age 6), and those deficits would be linked to greater disruptive behavior (age 11). The second aim of the study was to examine the role of smoking during pregnancy as a context for the early

childhood executive function-disruptive behavior association (Figure 4). It was hypothesized that the link between executive function (age 7) and disruptive behavior (age 11) would be stronger for youth exposed to smoking during pregnancy.

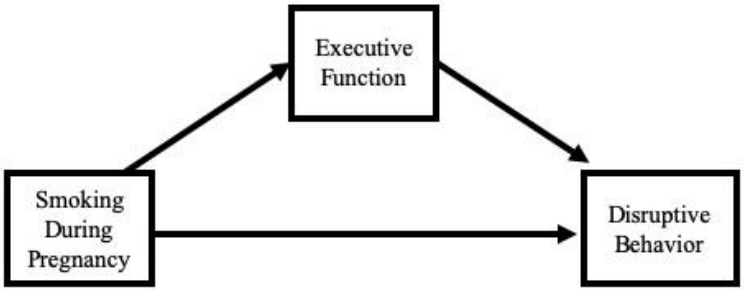



Figure 3. The figure depicts the first aim of study one, the association of smoking during pregnancy and disruptive behavior through executive function.

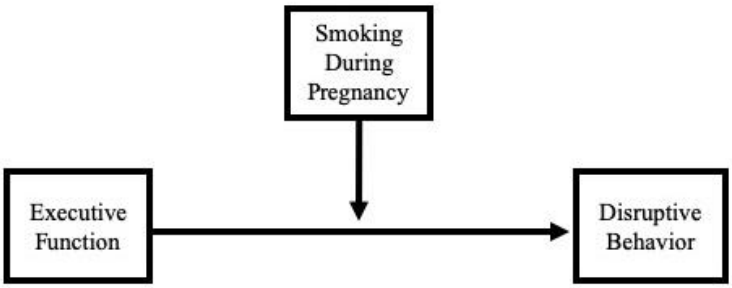



Figure 4. This figure depicts the second aim of study one, the moderating role of smoking during pregnancy on the executive function-disruptive behavior association.

## Methods

### Participants and Procedures

The Early Growth and Development Study (EGDS) is a sample of 561 adopted children, as well as their adoptive and birth parents. The sample is about half male (57.2%) and Caucasian (55.6%). Children were adopted between January 2003 and May 2009, on average 6.2 days after birth. Data from these participants were collected in two cohorts (Cohort I recruited from 2003-2006; Cohort II recruited from 2008-2010). Recruitment was facilitated by 45 adoption agencies in 15 states reflecting the full range of adoption agencies in the US (e.g., public vs. private, religious vs. secular, favoring more open vs. more closed adoptions). Families were eligible if the adoption was domestic, placement occurred within 3 months postpartum, the child was

placed with a non-relative, the child had no major medical conditions, and birth parents and adoptive parents could understand English at the 8th grade level.

Data were collected in-home and via web-based questionnaires and phone interviews beginning 3-6 months post-partum and extending across infancy through middle childhood (and further assessments are ongoing), assessing a wide range of birth parent and adoptive parent characteristics, prenatal and postnatal environments, and child behavioral and cognitive outcomes. In the current study solely Cohort 1 ($N$ = 361) is used, as this Cohort has the measures required at the specific ages hypothesized (i.e., data available through 11 years of age). About half the youth in Cohort 1 is male (57.3%) and Caucasian (55.6%), and the median adopted parent income ranged from $70,000-$100,000. The majority of the adopted parent sample is Caucasian (91.4%) and married (90.9%).

## Measures

***Smoking during pregnancy*.** Frequency of maternal smoking during pregnancy was measured via biological mothers self-report using a pregnancy history calendar (adapted version of the life history calendar; Caspi et al., 1996) assessed at 4 months post-partum. In cases where pregnancy use frequency data were missing, if biological mothers reported no lifetime use, or no pregnancy use, frequency of use during pregnancy was assigned a 0 (none). For smoking during pregnancy, mothers were asked about the average number of cigarettes smoked per day in each trimester. Many smoking during pregnancy effects follow a dose-response pattern (Marceau et al., 2016; Kramer et al., 2001). Exposure to smoking during pregnancy in the second and third trimesters of pregnancy are distinct from exposure during the first trimester, and may be more harmful (Hebel et al., 1988; Dwyer et al., 2009). Thus, a severity score was created that aligns with previous literature (e.g., Bidwell et al., 2017; Knopik et al., 2016, 2015; Marceau et al., 2017; Micalizzi et al., 2018) and captures the quantity and length of pregnancy smoking occurred which may be salient for outcomes (e.g., Dwyer, McQuown, & Leslie, 2009; Hebel, Fox, & Sexton, 1988). The severity score includes a discrete indicator specific to each trimester (0=No, 1=Yes) and the quantity of cigarettes smoked in each trimester. Thus, smoking during pregnancy exposure is operationalized as 1=no smoking during pregnancy, 2= smoking during pregnancy in the first trimester only, 1–10 cigarettes per day, 3= smoking during pregnancy in the first trimester only, 11–19 cigarettes per day, 4= smoking during pregnancy in the first trimester only,

20+ cigarettes per day, 5= smoking during pregnancy beyond the first trimester, 1–10 cigarettes per day (max of all trimesters), 6= smoking during pregnancy beyond the first trimester, 11–19 cigarettes per day (max of all trimesters), 7= smoking during pregnancy beyond the first trimester, 20+ cigarettes per day (max of all trimesters). Descriptive statistics for the severity score of smoking during pregnancy can be found in Table 1. The severity score of smoking during pregnancy was used as one of the primary predictors of interest in analyses. However, an alternate operationalization of smoking during pregnancy was used to confirm the pattern of findings found with the severity score in sensitivity analyses. Specifically, the average number of cigarettes smoked per day across the three trimesters was utilized as another measure of smoking during pregnancy, a score used in a previously published paper (Marceau et al., 2019). Alternative measures of smoking during pregnancy used in sensitivity analyses included a discrete indicator, the maximum quantity of cigarettes smoked in any one trimester, the sum quantity of cigarettes smoked across pregnancy, and the number of trimesters mothers smoked during (See Appendix Table A1 for descriptive statistics).

***Executive Function*.** The Go-No-Go task is a computerized task that assesses early inhibitory control, measured at 6 years of age (see Nosek & Banaji, 2001). There are 84 trials and the task take approximately 5 minutes to complete. For each trial, a letter was displayed in the center of the computer monitor. The children are instructed to press a button for every letter except for the letter, X. Following an incorrect response, auditory performance feedback (i.e., a brief buzz) is presented. The task produces several scores, the inhibit go trials (percent correctly responded to inhibit trial go stimuli) and the inhibit NoGo trials (percent correctly responded to for inhibit trial no go stimuli). The no-go consisted of intermixed Xs and non-Xs (participants are asked to press the button for only non-Xs). Whereas the inhibit go trials consisted of all non-Xs with varying time elapsing between each stimulus, acting as a control. The inhibit go score measures response inhibition and was utilized for data analysis. Descriptive statistics for youth executive function can be found in Table 1.

***Disruptive Behavior*.** Adoptive mothers and fathers reported on the Child Behavior Checklist (Achenbach, 1991) for children's disruptive behaviors at age 11 years old. Adoptive parents reported on youth's problem behaviors (e.g., "destroys things belonging to his or her family or to other children," "gets in many fights," and "physically attacks people") that occurred in the 2 months prior to the time of the questionnaire. Adoptive parents' reports on behaviors on

a 3-point scale that ranged from *not true* to *very true*, such that higher scores indicate increased reports of behavior. These items were used to create subscales according to the Achenbach and Rescorla (2000) manual, including T-score versions for oppositional defiant disorder symptoms (e.g., "defiant" or "disobedient"), conduct disorder symptoms (e.g., "Doesn't seem to feel guilty after misbehaving"), and attention-deficit/hyperactivity disorder symptoms (e.g., "can't concentrate"). Correlations for the oppositional defiance disorder symptoms, conduct disorder symptoms, and attention deficit ranged from 0.55-.80. Thus, in line with the literature on disruptive behavior, a composite score was created from the averaged T-scores for oppositional defiance disorder symptoms, conduct disorder symptoms, and attention deficit disorder symptoms (Cronbach's $\alpha = 0.87$). This composite score of disruptive behavior was used as the main outcome of interest in analyses. However, to gain a more nuanced understanding of associations, the components of the disruptive behavior score (subscales including oppositional defiance disorder symptoms, conduct disorder symptoms, and attention-deficit/hyperactivity disorder symptoms) were examined individually as outcome variables. Descriptive statistics for youth disruptive behavior and its components can be found in Table 1.

***Covariates*.** We controlled for adoption openness and knowledge at baseline to minimize the potential confound of adoption process on effects of smoking during pregnancy with child outcomes. Adoption openness refers to a continuum of contact and communication reported by birth and adoptive parents. Adoption knowledge refers to the knowledge known about one another (i.e., birth parent knowledge of adoptive parent and vice versa) regarding physical and mental health, cultural/ethnic background, reasoning behind adoption, and extended family health.

We also controlled for birth and adoptive parents' scores of executive function and disruptive behavior to control for familial confounding. Biological and adoptive parent executive function were measured when the adopted child was between four and five years old, using the Go-No-Go task (birth parents) and the Stroop task (adoptive parents). The adult and child Go-No-Go task differed in the type of stimuli shown on the computer screen (i.e., parents saw letters and the child saw shapes like a cross, diamond, square, star, or triangle). The computerized Stroop task consists of color words (e.g., "red" or "green") that are printed in color, such that the font color is or is not congruent with the color word (e.g., color word red, font it red) and the participant must press a key that indicates the font color of the color word. Birth mothers' and

fathers' externalizing problems (as an index of genetic risk for disruptive behavior) were measured using a composite score previously published (Marceau et al., 2019). The composite score was created with a principal component analysis that included measures of conduct and antisocial disorder and their symptoms as well as substance use (the composite score utilized the best score from either the assessment when the adopted child was 1.5 or when they were 5 years old; see Marceau et al., 2019 for details). Adoptive mothers' and fathers' disruptive behavior (as an index of environmental risk for youth disruptive behavior) were measured with an adapted version of the Antisocial Action questionnaire when youth were 1.5 years-old (e.g., psychopathy and antisocial behavior like gossiping and lying; Levenson, Kiehl, & Fitzpatrick, 1995).

Additional covariates included disruptive behavior at age 7, in analyses to control for previous behavior in order to assess the development of disruptive behavior. Additionally, paternal secondhand smoke is included as a covariate. In studies of active (i.e., maternal smoking) and passive (i.e., exposure to second hand smoke) both were found to be impactful for fetal development, but active smoking was more strongly associated with outcomes (e.g., Jaddoe et al., 2008; Vardavas et al., 2016), suggesting passive exposure may be an independent factor related to development. In order to isolate the effect of maternal smoking during pregnancy, paternal secondhand smoke was utilized as a covariate. Finally, one indicator of socioeconomic status at age 11 was included in analyses, as a proximal context for disruptive behavior, measured via adoptive parents report of "making ends meet" (e.g., difficulty paying bills) on a scale of 1 (*great difficulty*) to 5 (*no difficulty*) with higher scores indicating more difficulty (Conger, Conger, Elder, Lorenz, Simons, & Whitbeck, 1992; Conger et al., 1994). Descriptive statistics for covariates can also be found in Table 1.

## Analytic Strategy

***Hypothesis testing aim 1.*** To test the hypothesis that there is an indirect effect of exposure to smoking during pregnancy on disruptive behavior through executive function deficits, such that smoking during pregnancy is related to lower executive function and lower executive function is related to increased rates of disruptive behavior, a structural equation model (SEM; Figure 6) was fit in Mplus. We utilized bootstrapping, which is preferred to test indirect effects because it tests with higher power and is more accurate. Further, bootstrapping also addresses issues with non-normal data in models (Hayes, 2013). An effect of smoking during

pregnancy after controlling for birth parents scores indexing genetic risk for disruptive behavior and executive function indicates the potential for the smoking during pregnancy effect to be environmental in nature. That is, it can be concluded that adolescents that experienced the prenatal environment of smoking during pregnancy have executive function deficits and subsequently disruptive problems as a result of the exposure, not genetic risk (controlled via birth parent executive function deficits and disruptive problems). Further, by controlling for adoptive parent executive function and disruptive behavior, it can be concluded that associations are a result of exposure to smoking during pregnancy and not postnatal environmental risks (controlled via adoptive parent executive function deficits and disruptive problems, and by design, as different parents provided the prenatal and postnatal environments).

***Hypothesis testing aim 2.*** To test the hypothesis that the association between executive function and adolescent disruptive behavior is stronger for those adolescents who experienced exposure to smoking during pregnancy, a series of regression analyses were conducted in in R(lavaan). First, we tested a model (2a) with covariates predicting disruptive behavior, in order to establish a baseline model to facilitate the examination of the R-square change ($R2\,\Delta$) as an estimate of effect size in each model following. Second, a model (2b) with the main effects was fit for executive function, exposure to smoking during pregnancy. In the second model (2c), the two-way interaction between executive function and exposure to smoking during pregnancy was entered into the model. In the instance of a significant interaction effect, interactions were probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936), this technique is optimal when the moderator is continuous due to its method of solving for the values of smoking during pregnancy for which the effect of executive function on risk for disruptive behavior stops being significant (Carden, Holtzman, & Strube, 2017). This program will output the significance of simple slopes as well as the regions of significance for the interaction term (e.g., at what levels of executive function are smoking during pregnancy significantly influential on adolescent disruptive behavior). Notably, the lm function was used to test simple slopes and utilize the Johnson-Neyman approach to plotting the interaction, which is only possible with listwise deletion.

***Missing data.*** For missing data, to determine if data are missing at random (MAR), three dummy variables were created for whether each of key study concepts (smoking during pregnancy, executive function, and disruptive behavior) are missing (i.e., 0 = missing and 1 =

observed) and run t-tests and chi-square tests were utilized to examine whether the missingness on variables is meaningfully linked to specific characteristics (e.g., child age, socio-economic status, or openness/contact in the adoption, and study variables). Data was found to be Missing-Not-At-Random (MNAR; see appendix A for results of tests and patterns of missingness), thus, Full Information Maximum Likelihood (FIML) was used, as it has been shown to be an appropriate method for handling data MNAR (Acock, 2005).

## Results

Correlations were not as expected. Specifically, smoking during pregnancy was not correlated with executive function or disruptive behavior. Further, childhood executive function was not correlated with early adolescent disruptive behavior. For full correlations, see Table 2.

Table 1. The table depicts descriptive statistics of key study variables

| Variable | N | Mean(SD) | Minimum-Maximum | Skew | Kurtosis |
|---|---|---|---|---|---|
| Executive Function | 287 | 65.09(19.86) | 4.76-100.00 | -0.71 | -0.02 |
| Smoking During Pregnancy Severity Score | 145 | 6.50(1.23) | 1.00-7.00 | -2.37 | 5.04 |
| Disruptive Behavior | 236 | 55.74(5.36) | 50.00-76.50 | 1.37 | 1.59 |
| Oppositional Defiant Disorder Symptoms | 236 | 55.67(5.75) | 50.00-75.00 | 1.36 | 1.23 |
| Conduct Disorder Symptoms | 236 | 55.22(5.90) | 50.00-76.50 | 1.34 | 1.22 |
| ADHD Symptoms | 236 | 56.33(6.36) | 50.00-80.00 | 1.11 | 0.62 |
| **Covariates** | | | | | |
| Disruptive Behavior | 214 | 55.15(4.50) | 50.00-72.17 | 1.24 | 1.35 |
| Oppositional Defiant Disorder Symptoms | 214 | 55.08(4.96) | 50.00-73.00 | 1.40 | 1.80 |
| Conduct Disorder Symptoms | 214 | 55.11(5.03) | 50.00-71.50 | 1.01 | 0.23 |
| ADHD Symptoms | 214 | 55.25(5.56) | 50.00-75.50 | 1.34 | 1.36 |
| AP Maternal Executive Function | 317 | 0.90(0.30) | 0.00-1.00 | -2.70 | 5.28 |
| AP Paternal Executive Function | 317 | 0.87(0.34) | 0.00-1.00 | -2.08 | 2.33 |
| AP Maternal Anti-Social Behavior | 338 | 16.91(2.46) | 13.00-28.00 | 1.03 | 1.54 |
| AP Paternal Anti-Social Behavior | 322 | 17.03(2.57) | 13.00-28.00 | 0.89 | 1.15 |
| BP Externalizing Risk Score | 351 | 0.25(1.83) | -3.62-5.49 | 0.38 | -0.47 |
| BP Maternal Executive Function | 325 | 86.14(11.50) | 14.29-100.00 | -1.73 | 5.64 |
| BP Paternal Executive Function | 108 | 86.60(10.76) | 52.38-100.00 | -0.81 | 0.08 |
| Secondhand Smoke Exposure | 347 | 0.15(8.68) | -5.92-54.08 | 1.70 | 4.10 |
| Openness of Adoption | 349 | 0.04(0.93) | -2.06-1.84 | -0.21 | -0.54 |
| Knowledge of Adoption | 349 | 0.00(0.66) | -2.00-1.54 | -0.31 | -0.19 |
| Socioeconomic status (age 11) | 236 | 3.72(1.26) | 2.00-8.00 | 1.02 | 0.74 |

Table 2. The table depicts correlation statistics of key study variables.

| **Variable** | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. | 11. | 12. | 13. | 14. | 15. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1.Smoking During Pregnancy Severity Score | -- | | | | | | | | | | | | | | |
| 2.Executive Function | -0.01 | -- | | | | | | | | | | | | | |
| 3.AP Maternal Anti-Social Behavior | 0.14 | -0.09 | -- | | | | | | | | | | | | |
| 4.AP Paternal Anti-Social Behavior | 0.04 | 0.08 | 0.20** | -- | | | | | | | | | | | |
| 5.AP Maternal Executive Function | -0.10 | -0.00 | -0.00 | -0.001 | -- | | | | | | | | | | |
| 6.AP Paternal Executive Function | 0.04 | 0.01 | -0.09 | 0.01 | 0.48** | -- | | | | | | | | | |
| 7.BP Externalizing Risk Score | 0.03 | -0.07 | 0.00 | 0.05 | 0.04 | -0.04 | -- | | | | | | | | |
| 8.BP Paternal Executive Function | -0.22 | -0.02 | -0.14 | 0.09 | 0.03 | -0.03 | 0.10 | -- | | | | | | | |
| 9.BP Maternal Executive Function | 0.11 | 0.00 | 0.04 | -0.05 | -0.08 | -0.02 | -0.10 | -0.14 | -- | | | | | | |
| 10.Openness of Adoption | -0.10 | 0.05 | 0.04 | 0.01 | -0.01 | 0.05 | 0.05 | -0.07 | -0.04 | -- | | | | | |
| 11.Knowledge of Adoption | -0.15 | 0.02 | 0.05 | 0.02 | 0.01 | -0.01 | 0.05 | -0.07 | 0.02 | 0.45** | -- | | | | |
| 12.Secondhand Smoke Exposure | 0.06 | 0.01 | -0.01 | -0.01 | 0.06 | 0.01 | 0.35** | -0.04 | -0.07 | 0.04 | -0.01 | -- | | | |
| 13. Socioeconomic Status Age 11 | -0.06 | -0.06 | 0.11 | 0.07 | -0.10 | -0.12+ | -0.01 | 0.21+ | -0.07 | -0.07 | 0.03 | 0.11+ | -- | | |
| 14. Disruptive Behavior Age 11 | -0.04 | 0.04 | -0.03 | 0.14* | 0.05 | 0.04 | -0.01 | 0.02 | -0.13 | 0.02 | 0.00 | 0.14* | 0.04 | -- | |
| 15. Disruptive Behavior Age 7 | -0.12 | -0.03 | 0.02 | 0.10 | 0.01 | 0.09 | -0.03 | -0.14 | -0.11 | 0.00 | -0.02 | 0.19** | 0.07 | 0.74** | -- |

Note. AP = adoptive parent; BP = birth parent. *p < .05, **p<.01, ***p<.001.

**Model 1**

The model testing the indirect effect of smoking during pregnancy on disruptive behavior through executive function provided an adequate fit to the data (Chi-Square = 0.000(0), p < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.001). Biological and adoptive parents' executive function and disruptive behavior did not predict youth executive function or disruptive behavior (see Table 3 for full results). Earlier disruptive behavior predicted later disruptive behavior ($b$ = 0.90, $SE$ = 0.09, $p$ < .001), such that youth with greater disruptive behavior at age seven were related to greater rates of disruptive behavior at age eleven. Smoking during pregnancy was not related to executive function ($b$ = -1.05, $SE$ = 2.67, $p$ = 0.69) or disruptive behavior ($b$ = 0.40, $SE$ = 0.75, $p$ = 0.59). Childhood executive function was not related to early adolescent disruptive behavior ($b$ = 0.02, $SE$ = 0.02, $p$ = 0.35). Further, contrary to hypotheses, there was no indirect effect from smoking during pregnancy to early adolescent disruptive behavior through childhood executive function ($b$ = -0.02, $SE$ = 0.13, $p$ = 0.87).

Table 3. The table shows the full results of the a priori model 1 (N = 361).

Table 1.

| | Executive Function | | | Disruptive Behavior | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| Intercept | 111.72 * | 52.64 | 0.034 | -2.68 | 16.72 | 0.873 |
| Smoking During Pregnancy | -1.05 | 2.67 | 0.694 | 0.40 | 0.75 | 0.596 |
| AP Maternal Executive Function | 0.29 | 5.74 | 0.960 | 1.67 | 1.78 | 0.347 |
| AP Paternal Executive Function | -1.85 | 5.06 | 0.714 | -0.37 | 1.36 | 0.788 |
| AP Maternal Anti-social Behavior | -0.88 | 0.63 | 0.164 | -0.18 | 0.15 | 0.228 |
| AP Paternal Anti-social Behavior | 1.16 + | 0.62 | 0.060 | 0.16 | 0.15 | 0.278 |
| BP Maternal Executive Function | 0.03 | 0.13 | 0.840 | -0.02 | 0.03 | 0.615 |
| BP Paternal Executive Function | -0.20 | 0.32 | 0.535 | 0.05 | 0.10 | 0.615 |
| BP Externalizing Behavior Risk Score | -0.86 | 0.77 | 0.268 | -0.12 | 0.19 | 0.540 |
| Sex | -12.44 *** | 2.49 | <0.001 | 0.96 | 0.74 | 0.198 |
| Socioeconomic Status (age 11) | -0.64 | 1.57 | 0.684 | 0.08 | 0.32 | 0.806 |
| BP Knowledge | -0.28 | 2.41 | 0.906 | 0.04 | 0.57 | 0.945 |
| Openness of Adoption | 1.33 | 1.66 | 0.423 | 0.12 | 0.41 | 0.765 |
| Disruptive Behavior (age 7) | -0.35 | 0.37 | 0.352 | 0.90 *** | 0.09 | <0.001 |
| Secondhand Smoke Exposure | 0.11 | 0.17 | 0.543 | 0.00 | 0.06 | 0.994 |
| EF | -- | -- | -- | 0.02 | 0.02 | 0.348 |
| Indirect effect | | **Estimate** | **SE** | **P-Value** | | |
| | | -0.02 | 0.13 | 0.87 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error. *$p$ < .05, ** $p$ <.01, ***$p$ < .001. Chi-Square = 0.000(0), $p$ < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.002

**Model 2**

For the model testing the moderating effect of smoking during pregnancy on the childhood executive function-early adolescent disruptive behavior association, a series of regression analyses were conducted. First, we tested a model (2a) with covariates predicting early adolescent disruptive behavior ($R^2 = 0.604$). Greater disruptive behavior at age 7 ($b = 0.92$, $SE = 0.07$, $p < .001$) predicted more disruptive behavior at age 11. Further, increased adoptive mother anti-social behavior was linked to decreased early adolescent disruptive behavior ($b = -0.11$, $SE = 0.10$, $p = 0.03$), although this association did not hold in following models. Second, a model (2b) with the main effects was fit ($R^2 \Delta = 0.01$) and neither childhood executive function ($b = 0.01$, $SE = 0.03$, $p = 0.80$) nor exposure to smoking during pregnancy ($b = -0.03$, $SE = 0.51$, $p = 0.96$) were linked to early adolescent disruptive behavior. In the final model (2c) that included the interaction effect ($R^2 \Delta = 0.03$), contrary to hypotheses, there was not an interaction between childhood executive function and smoking during pregnancy predicting early adolescent disruptive behavior ($b = 0.05$, $SE = 0.04$, $p = 0.26$). See Table 4 for full results of all models.

Table 4. This table depicts the full results of model building steps for model 2 (N = 361).

| | Model 2A | | | Model 2B | | | Model 2C | | |
|---|---|---|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 8.65 + | 4.76 | 0.069 | 15.04 + | 8.44 | 0.075 | 16.51 + | 8.91 | 0.064 |
| Openness | -0.02 | 0.02 | 0.244 | -0.02 | 0.03 | 0.455 | -0.02 | 0.03 | 0.529 |
| Knowledge | -0.00 | 0.00 | 0.282 | -0.00 | 0.01 | 0.656 | -0.00 | 0.01 | 0.589 |
| Disruptive Behavior (age 7) | 0.92 *** | 0.07 | <0.001 | 0.81 *** | 0.12 | <0.001 | 0.78 *** | 0.13 | <0.001 |
| BP Externalizing Behavior Risk Score | -0.02 | 0.14 | 0.889 | -0.07 | 0.30 | 0.819 | -0.13 | 0.30 | 0.667 |
| AP Maternal Anti-Social Behavior | -0.22 * | 0.10 | 0.032 | -0.08 | 0.24 | 0.727 | -0.13 | 0.25 | 0.614 |
| AP Paternal Anti-Social Behavior | 0.20 | 0.15 | 0.180 | 0.05 | 0.29 | 0.859 | 0.07 | 0.28 | 0.794 |
| Sex | -1.16 * | 0.54 | 0.032 | -0.63 | 0.98 | 0.518 | -0.44 | 0.96 | 0.647 |
| Socioeconomic Status (age 11) | 0.09 | 0.25 | 0.733 | -0.32 | 0.49 | 0.513 | -0.28 | 0.46 | 0.535 |
| Secondhand Smoke Exposure | -0.04 | 0.05 | 0.395 | 0.02 | 0.09 | 0.855 | -0.00 | 0.09 | 0.988 |
| Executive Function | -- | -- | -- | 0.01 | 0.03 | 0.795 | -0.00 | 0.04 | 0.970 |
| Smoking During Pregnancy | -- | -- | -- | -0.03 | 0.51 | 0.957 | -0.61 | 0.80 | 0.445 |
| EF*SDP | -- | -- | -- | -- | -- | -- | 0.05 | 0.04 | 0.257 |
| R-Square | 0.604 | | | 0.590 | | | 0.615 | | |

Note. AP = adoptive parent; BP = birth parent; EF = executive function; SDP = smoking during pregnancy; SE = standard error. +$p < .10$, *$p < .05$, **$p < .01$, *** $p < 0.001$.

**Sensitivity Analyses: Model 1**

Given an observation in the literature that boys might be more susceptible to smoking during pregnancy effects on disruptive behavior (Marceau et al., 2019), sex-specific sensitivity analyses were conducted to examine whether the pattern of findings differed by sex.

***Sex difference for model 1***. Using the grouping command in MPlus, model 1 was run in a multiple group analysis to examine sex differences. Sex differences included: paternal anti-social behavior and the birth parent risk score. Paternal anti-social behavior predicted female executive function at age six whereas it did not for males and the birth parent risk score predicted female disruptive behavior at age 11 whereas it did not for males (see Table 5 for full results). There were no differences in the pattern of results based on sex in associations between smoking during pregnancy, executive function, and disruptive behavior.

***Sex difference for model 2.*** Using the group command in R (Lavaan), model 2 was run in a multiple group analysis to examine sex differences. The only sex difference was that for girls' disruptive behavior at age seven predicted disruptive behavior at age eleven ($b = 0.77$, $SE = 0.19$, $p < 0.011$), whereas it did not for boys ($b = 0.49$, $SE = 0.42$, $p = 0.24$). There were no differences in the pattern of results based on sex in associations between smoking during pregnancy and executive function with disruptive behavior (age 11), or for the interaction between executive function and smoking during pregnancy (see Table 6 for full results).

Table 5. Summary of results for model 1 sex differences.

| | Females | | Males | |
|---|---|---|---|---|
| | Executive Function b(SE) | Disruptive Behavior b(SE) | Executive Function b(SE) | Disruptive Behavior b(SE) |
| Intercept | 94.86(103.45) | -17.59(19.97) | 135.56(91.11) | 5.09(21.78) |
| Smoking During Pregnancy | -0.50(3.98) | 0.78(0.87) | 2.90(7.53) | -2.51(1.35)+ |
| AP Maternal Executive Function | -4.50(10.70) | 4.40(2.62) | 7.86(16.02) | -7.44(4.46)+ |
| AP Paternal Executive Function | 1.64(21.45) | -3.47(2.51) | -12.03(12.91) | 3.40(3.43) |
| AP Maternal Anti-social Behavior | -1.16(1.04) | -0.20(0.23) | -1.57(1.36) | 0.29(0.32) |
| AP Paternal Anti-social Behavior | 1.86(-.89)* | 0.44(0.24)+ | 0.34(1.12) | -0.08(0.30) |
| BP Maternal Executive Function | 0.15(0.37) | 0.05(0.04) | -0.43(0.37) | 0.09(0.07) |
| BP Paternal Executive Function | -0.21(0.71) | 0.14(0.18) | -0.50(0.66) | 0.15(0.13) |
| BP Externalizing Behavior Risk Score | 0.34(2.10) | -0.75(0.35)* | -1.61(1.17) | 0.17(0.21) |
| Socioeconomic Status (age 11) | 1.67(2.67) | -0.29(0.61) | -0.10(4.55) | -0.31(0.75) |
| BP Knowledge | -0.18(4.37) | -0.28(1.13) | -4.71(7.56) | 0.98(1.26) |
| Openness of Adoption | 1.95(4.67) | -0.14(0.64) | 2.16(3.24) | 0.42(0.83) |
| Disruptive Behavior (age 7) | -0.56(0.64) | 0.89(0.11)*** | 0.21(0.77) | 0.83(0.25)** |
| Secondhand Smoke Exposure | -0.18(0.31) | 0.02(0.10) | -0.00(0.42) | 0.09(0.10) |
| EF | -- | -0.01(0.03) | -- | 0.03(0.03) |
| Indirect effect | | 0.00(0.21) | | 0.10(0.30) |

Note. AP = adoptive parent; BP = birth parent; EF = executive function. $+p < .10$, $*p < .05$, $** p < .01$, $*** p < .001$.

Table 6. Summary of results for model 2 sex differences.

| | **Girls** | | | **Boys** | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 11.55 | 15.56 | 0.458 | 34.04 | 22.82 | 0.136 |
| Openness | -0.04 | 0.05 | 0.363 | 0.02 | 0.06 | 0.770 |
| Knowledge | 0.01 | 0.01 | 0.563 | -0.00 | 0.01 | 0.920 |
| Disruptive Behavior (age 7) | 0.77 *** | 0.18 | <0.001 | 0.49 | 0.44 | 0.266 |
| BP Externalizing Behavior Risk Score | -0.64 | 0.54 | 0.234 | -0.03 | 0.77 | 0.970 |
| AP Maternal Anti-Social Behavior | -0.49 | 0.60 | 0.414 | -0.23 | 0.49 | 0.642 |
| AP Paternal Anti-Social Behavior | 0.66 | 0.63 | 0.292 | -0.13 | 0.45 | 0.778 |
| Socioeconomic Status (age 11) | 0.93 | 1.22 | 0.447 | -0.43 | 1.51 | 0.777 |
| Secondhand Smoke Exposure | -0.32 | 0.25 | 0.211 | 0.17 | 0.16 | 0.284 |
| Executive Function | 0.03 | 0.10 | 0.764 | -0.01 | 0.11 | 0.918 |
| Smoking During Pregnancy | 1.14 | 2.60 | 0.662 | -1.20 | 1.85 | 0.516 |
| EF*SDP | 0.00 | 0.13 | 0.997 | 0.05 | 0.20 | 0.805 |
| R-Square | 0.780 | | | 0.561 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function; SE = standard error; SDP = smoking during pregnancy. $+p < .10$, $*p < .05$, $** p < .01$, $*** p < .001$.

A series of structural equation models were fit in Mplus (Muthén, & Muthén, 1998) post-hoc, to examine alternative measures of smoking during pregnancy for model 1 to examine if findings from the main analyses are consistent across diverse measures of defining and capturing exposure. For descriptive statistics on the different measures of exposure to smoking during pregnancy, see Table 17.

***Yes/no*.** This measure of exposure to smoking during pregnancy was a dichotomous variable of exposure, such that 0 is no exposure and 1 is exposure to smoking during pregnancy. There were no differences from the models including the severity score, as exposure to smoking during pregnancy did not predict executive function ($b$ = -2.24, $SE$ = 26.63, $p$ = 0.93), disruptive behavior ($b$ = 6.25, $SE$ = 11.69, $p$ = 0.59), and there was no indirect effect ($b$ = -0.05, $SE$ = 1.01, $p$ = 0.96; See Table 7).

Table 7. Results for the discrete indicator of exposure to smoking during pregnancy.

| | **Executive Function** | | | **Disruptive Behavior** | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| Intercept | 107.57 * | 53.94 | 0.046 | -5.98 | 17.47 | 0.732 |
| Smoking During Pregnancy (Yes/No) | -2.24 | 26.63 | 0.933 | 6.25 | 11.69 | 0.593 |
| AP Maternal Executive Function | 0.86 | 5.69 | 0.880 | 1.82 | 2.14 | 0.395 |
| AP Paternal Executive Function | -2.26 | 5.39 | 0.675 | -0.65 | 1.96 | 0.742 |
| AP Maternal Anti-social Behavior | -0.96 | 0.65 | 0.141 | -0.17 | 0.16 | 0.281 |
| AP Paternal Anti-social Behavior | 1.12 + | 0.60 | 0.060 | 0.15 | 0.17 | 0.378 |
| BP Maternal Executive Function | 0.01 | 0.13 | 0.951 | -0.01 | 0.03 | 0.774 |
| BP Paternal Executive Function | -0.18 | 0.31 | 0.549 | 0.05 | 0.09 | 0.597 |
| BP Externalizing Behavior Risk Score | -0.92 | 0.76 | 0.230 | -0.12 | 0.19 | 0.529 |
| Sex | -12.42 *** | 2.53 | <0.001 | 0.78 | 0.74 | 0.291 |
| Socioeconomic Status (age 11) | -0.52 | 1.50 | 0.728 | 0.08 | 0.37 | 0.832 |
| BP Knowledge | 0.08 | 2.19 | 0.696 | -0.02 | 0.48 | 0.966 |
| Openness of Adoption | 1.38 | 1.66 | 0.406 | 0.19 | 0.42 | 0.654 |
| Disruptive Behavior (age 7) | -0.32 | 0.39 | 0.413 | 0.89 *** | 0.09 | <0.001 |
| Secondhand Smoke Exposure | 0.09 | 0.17 | 0.579 | -0.00 | 0.06 | 0.965 |
| EF | -- | -- | -- | 0.02 | 0.02 | 0.339 |
| Indirect effect | | **Estimate** | **SE** | **P-Value** | | |
| | | -0.05 | 1.01 | 0.964 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function. +$p$ < .10, *$p$ < .05, ** $p$ < .01, *** $p$ < .001. Chi-Square = 0.000(0), p < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.001

***Maximum quantity.*** This measure of exposure to smoking during pregnancy was the maximum quantity smoked (i.e., number of cigarettes) in any one trimester. There were no differences from the models including the severity score, as exposure to smoking during pregnancy did not predict executive function ($b$ = -0.26, $SE$ = 0.27, $p$ = 0.32), disruptive behavior ($b$ = 0.04, $SE$ = 0.07, $p$ = 0.55), and there was no indirect effect ($b$ = -0.01, $SE$ = 0.01, $p$ = 0.59; See Table 8).

Table 8. Results for the maximum quantity smoked in any one trimester.

| | **Executive Function** | | | **Disruptive Behavior** | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| Intercept | 96.10 | 50.07 | 0.055 | 1.50 | 13.24 | 0.910 |
| Smoking During Pregnancy (Max Quantity) | -0.26 | 0.27 | 0.324 | 0.04 | 0.07 | 0.545 |
| AP Maternal Executive Function | -0.87 | 6.09 | 0.887 | 1.69 | 1.68 | 0.314 |
| AP Paternal Executive Function | -2.40 | 4.87 | 0.622 | -0.14 | 1.23 | 0.909 |
| AP Maternal Anti-social Behavior | -0.68 | 0.72 | 0.344 | -0.19 | 0.17 | 0.252 |
| AP Paternal Anti-social Behavior | 1.18 * | 0.58 | 0.041 | 0.16 | 0.16 | 0.312 |
| BP Maternal Executive Function | 0.07 | 0.15 | 0.654 | -0.02 | 0.03 | 0.581 |
| BP Paternal Executive Function | -0.15 | 0.31 | 0.636 | 0.04 | 0.09 | 0.709 |
| BP Externalizing Behavior Risk Score | -0.80 | 0.72 | 0.266 | -0.11 | 0.17 | 0.531 |
| Sex | -12.00 *** | 2.58 | <0.001 | 0.95 | 0.72 | 0.186 |
| Socioeconomic Status (age 11) | -0.54 | 1.49 | 0.718 | 0.05 | 0.31 | 0.869 |
| BP Knowledge | 0.46 | 2.18 | 0.833 | -0.17 | 0.47 | 0.722 |
| Openness of Adoption | 0.91 | 1.76 | 0.604 | 0.19 | 0.40 | 0.627 |
| Disruptive Behavior (age 7) | -0.25 | 0.38 | 0.505 | 0.88 *** | 0.09 | <0.001 |
| Secondhand Smoke Exposure | 0.19 | 0.20 | 0.356 | -0.01 | 0.06 | 0.855 |
| EF | -- | -- | -- | 0.02 | 0.02 | 0.286 |
| Indirect effect | | **Estimate** | **SE** | **P-Value** | | |
| | | -0.01 | 0.01 | 0.594 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function. +$p$ < .10, *$p$ < .05, ** $p$ < .01, *** $p$ < .001. Chi-Square = 0.000(0), p < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.001

***Sum quantity.*** This measure of exposure to smoking during pregnancy was the sum total of the quantity (i.e., number of cigarettes) smoked across all three trimesters. There were no differences from the models including the severity score, as exposure to smoking during pregnancy did not predict executive function ($b$ = -0.20, $SE$ = 0.15, $p$ = 0.20), disruptive behavior ($b$ = 0.03, $SE$ = 0.04, $p$ = 0.50), and there was no indirect effect ($b$ = -0.01, $SE$ = 0.01, $p$ = 0.55; See Table 9).

Table 9. Results for the sum quantity smoked across pregnancy.

| | Executive Function | | | Disruptive Behavior | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| Intercept | 100.45 | 48.54 | 0.039 | 0.41 | 13.24 | 0.975 |
| Smoking During Pregnancy (Sum Quantity) | -0.20 | 0.15 | 0.195 | 0.03 | 0.04 | 0.504 |
| AP Maternal Executive Function | -0.81 | 6.41 | 0.900 | 1.65 | 1.72 | 0.338 |
| AP Paternal Executive Function | -2.78 | 5.13 | 0.588 | -0.14 | 1.28 | 0.912 |
| AP Maternal Anti-social Behavior | -0.70 | 0.70 | 0.318 | -0.18 | 0.16 | 0.246 |
| AP Paternal Anti-social Behavior | 1.22 | 0.58 | 0.034 | 0.16 | 0.15 | 0.303 |
| BP Maternal Executive Function | 0.09 | 0.15 | 0.560 | -0.02 | 0.03 | 0.555 |
| BP Paternal Executive Function | -0.17 | 0.31 | 0.587 | 0.04 | 0.09 | 0.668 |
| BP Externalizing Behavior Risk Score | -0.71 | 0.75 | 0.346 | -0.11 | 0.17 | 0.511 |
| Sex | -12.13 | 2.47 | <0.001 | 0.98 | 0.71 | 0.167 |
| Socioeconomic Status (age 11) | -0.58 | 1.55 | 0.709 | 0.06 | 0.31 | 0.861 |
| BP Knowledge | -0.04 | 2.19 | 0.986 | -0.09 | 0.47 | 0.850 |
| Openness of Adoption | 0.95 | 1.80 | 0.595 | 0.17 | 0.40 | 0.679 |
| Disruptive Behavior (age 7) | -0.31 | 0.37 | 0.391 | 0.89 | 0.09 | <0.001 |
| Secondhand Smoke Exposure | 0.22 | 0.20 | 0.278 | -0.01 | 0.06 | 0.829 |
| EF | -- | -- | -- | 0.02 | 0.02 | 0.300 |
| Indirect effect | | **Estimate** | **SE** | **P-Value** | | |
| | | -0.01 | 0.01 | 0.553 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function. $+p < .10$, $*p < .05$, $** p < .01$, $*** p < .001$. Chi-Square = 0.000(0), p < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.000

***Number of trimesters*.** This measure of exposure to smoking during pregnancy was the number of trimesters that mothers smoked during, ranging from 0 (no smoking during pregnancy) to 3 (smoked during all three trimesters). There were no differences from the models including the severity score, as exposure to smoking during pregnancy did not predict executive function ($b$ = -7.53, $SE$ = 8.04, $p$ = 0.35), disruptive behavior ($b$ = 0.67, $SE$ = 2.54, $p$ = 0.79), and there was no indirect effect ($b$ = -0.16, $SE$ = 0.45, $p$ = 0.73; See Table 10).

Table 10. Results for the number of trimesters smoked during pregnancy.

| | Executive Function | | | Disruptive Behavior | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| Intercept | 122.48 *** | 34.92 | <0.001 | 12.15 *** | 2.23 | <0.001 |
| Smoking During Pregnancy | -7.53 | 8.04 | 0.349 | 0.67 | 2.54 | 0.790 |
| AP Maternal Executive Function | 3.76 | 7.70 | 0.626 | 1.23 | 2.00 | 0.540 |
| AP Paternal Executive Function | -2.58 | 5.16 | 0.618 | -0.22 | 1.34 | 0.870 |
| AP Maternal Anti-social Behavior | -0.94 | 0.64 | 0.139 | -0.15 | 0.15 | 0.308 |
| AP Paternal Anti-social Behavior | 1.18 + | 0.65 | 0.069 | 0.17 | 0.16 | 0.296 |
| BP Maternal Executive Function | 0.03 | 0.13 | 0.796 | -0.01 | 0.03 | 0.670 |
| BP Paternal Executive Function | -0.30 | 0.36 | 0.406 | 0.06 | 0.12 | 0.631 |
| BP Externalizing Behavior Risk Score | -0.58 | 0.89 | 0.515 | -0.12 | 0.20 | 0.534 |
| Sex | -12.42 *** | 2.65 | <0.001 | 1.00 | 0.78 | 0.198 |
| Socioeconomic Status (age 11) | -0.43 | 1.79 | 0.812 | 0.04 | 0.37 | 0.915 |
| BP Knowledge | -1.21 | 2.78 | 0.663 | -0.00 | 0.73 | 0.996 |
| Openness of Adoption | 1.18 | 1.80 | 0.512 | 0.14 | 0.44 | 0.748 |
| Disruptive Behavior (age 7) | -0.34 | 0.38 | 0.382 | 0.89 *** | 0.09 | <0.001 |
| Secondhand Smoke Exposure | 0.11 | 0.17 | 0.520 | 0.00 | 0.06 | 0.961 |
| EF | -- | -- | -- | 0.02 | 0.03 | 0.426 |
| Indirect effect | | **Estimate** | **SE** | **P-Value** | | |
| | | -0.16 | 0.45 | 0.728 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function. +$p < .10$, *$p < .05$, ** $p < .01$, *** $p < .001$. Chi-Square = 0.000(0), p < .001; RMSEA = 0.000; CFI/TLI = 1.000/1.000; SRMR = 0.001

In summary, for models including alternative measures of smoking during pregnancy, there were no direct or mediation effects, thus findings are robust across measures of exposure.

**Sensitivity Analyses: Model 2**

A series of structural equation models were fit in R (lavaan) post-hoc, to examine alternative measures of smoking during pregnancy for model 2. For descriptive statistics on other measures of smoking during pregnancy see Appendix Table A1.

***Yes/no*.** This measure of exposure to smoking during pregnancy was a dichotomous variable of exposure, such that 0 is no exposure and 1 is exposure to smoking during pregnancy. There was no association between the discrete indicator of smoking during pregnancy ($b$ = -0.61, $SE$ = 0.82, $p$ = 0.46) and executive function ($b$ = -0.31, $SE$ = 0.31, $p$ = 0.30) with disruptive behavior, there was also no significant interaction ($b$ = 0.05, $SE$ = 0.04, $p$ = 0.28; See Table 11).

Table 11. Results for the discrete indicator of exposure to smoking during pregnancy.

| | Model 2B | | | Model 2C | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 15.22 + | 8.96 | 0.089 | 20.50 * | 10.42 | 0.049 |
| Openness | -0.02 | 0.03 | 0.454 | -0.02 | 0.03 | 0.524 |
| Knowledge | -0.00 | 0.01 | 0.648 | -0.00 | 0.01 | 0.612 |
| Disruptive Behavior (age 7) | 0.81 *** | 0.12 | <0.001 | 0.78 *** | 0.13 | <0.001 |
| BP Externalizing Behavior Risk Score | -0.07 | 0.31 | 0.824 | -0.13 | 0.32 | 0.680 |
| AP Maternal Anti-Social Behavior | -0.08 | 0.24 | 0.724 | -0.13 | 0.24 | 0.605 |
| AP Paternal Anti-Social Behavior | 0.05 | 0.28 | 0.856 | 0.07 | 0.28 | 0.790 |
| Sex | -0.63 | 0.98 | 0.518 | -0.33 | 1.02 | 0.667 |
| Socioeconomic Status (age 11) | -0.32 | 0.48 | 0.502 | -0.28 | 0.49 | 0.566 |
| Secondhand Smoke Exposure | 0.02 | 0.10 | 0.858 | -0.00 | 0.10 | 0.988 |
| Executive Function | 0.01 | 0.03 | 0.802 | -0.31 | 0.30 | 0.301 |
| Smoking During Pregnancy (Yes/No) | -0.03 | 0.53 | 0.959 | -0.61 | 0.82 | 0.455 |
| EF*SDP | -- | -- | -- | 0.05 | 0.04 | 0.276 |
| R-Square | 0.590 | | | 0.615 | | |

Note. AP = adoptive parent; BP = birth parent; SE = standard error; EF = executive function; SE = standard error; SDP = smoking during pregnancy; Yes/No = the discrete indicator of exposure, such that 0= no smoking and 1= smoking. $+p < .10$, $*p < .05$, $** p < .01$, $*** p < .001$.

***Maximum quantity.*** This measure of exposure to smoking during pregnancy was the maximum quantity smoked (i.e., number of cigarettes) in any one trimester. There was no association between the maximum quantity smoking during pregnancy variable ($b$ = -0.00, $SE$ = 0.00, $p$ = 0.50) and disruptive behavior, but there was for executive function ($b$ = 0.11, $SE$ = 0.06, $p$ = 0.04) and a significant interaction ($b$ = -0.00, $SE$ = 0.00, $p$ = 0.02; See Table 12). The interaction was probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936). Specifically, as the maximum quantity smoked in any one trimester increases, the effect of higher executive function being linked to lower disruptive behavior gets stronger. Further, among youth with no smoking during pregnancy exposure higher executive function predicts more disruptive behavior (See Figure 5 and Table 13).

Table 12. Results for the maximum quantity smoked in any one trimester.

| | Model 2B | | | | Model 2C | | | |
|---|---|---|---|---|---|---|---|---|
| | **Estimate** | | **SE** | **P-Value** | **Estimate** | | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 15.60 | + | 8.66 | 0.072 | 16.88 | + | 8.61 | 0.050 |
| Openness | -0.02 | | 0.04 | 0.574 | -0.02 | | 0.03 | 0.544 |
| Knowledge | -0.00 | | 0.01 | 0.621 | -0.00 | | 0.01 | 0.445 |
| Disruptive Behavior (age 7) | 0.80 | *** | 0.12 | <0.001 | 0.77 | *** | 0.13 | <0.001 |
| BP Externalizing Behavior Risk Score | -0.09 | | 0.32 | 0.770 | -0.18 | | 0.30 | 0.561 |
| AP Maternal Anti-Social Behavior | -0.12 | | 0.21 | 0.568 | -0.06 | | 0.20 | 0.756 |
| AP Paternal Anti-Social Behavior | 0.06 | | 0.27 | 0.832 | 0.01 | | 0.25 | 0.955 |
| Sex | -0.62 | | 0.93 | 0.506 | -0.96 | | 0.83 | 0.249 |
| Socioeconomic Status (age 11) | -0.30 | | 0.43 | 0.485 | -0.26 | | 0.44 | 0.555 |
| Secondhand Smoke Exposure | 0.01 | | 0.08 | 0.903 | 0.03 | | 0.09 | 0.733 |
| Executive Function | 0.01 | | 0.03 | 0.726 | 0.11 | * | 0.06 | 0.040 |
| Smoking During Pregnancy (Max) | 0.00 | | 0.00 | 0.763 | 0.00 | | 0.00 | 0.503 |
| EF*SDP | -- | | -- | -- | -0.00 | * | 0.00 | 0.018 |
| R-Square | 0.590 | | | | 0.629 | | | |

Note. AP = adoptive parent; BP = birth parent; EF = executive function; SDP = smoking during pregnancy; Max = Maximum cigarettes smoked in any one trimester. *$p$ < .05, ** $p$ < .01, *** $p$ < .001.

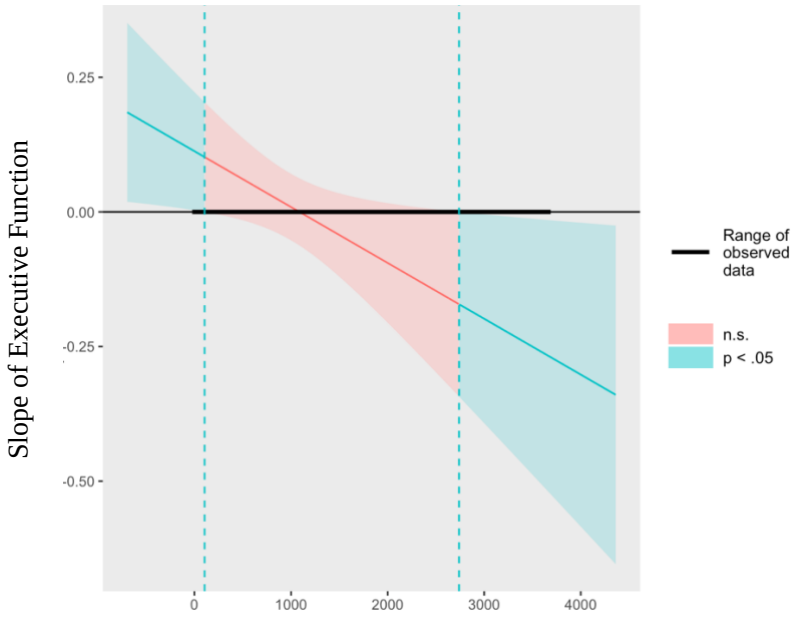



Figure 5. The interaction between executive function and the max quantity of cigarettes smoked in any on trimester.

Note. The y-axis is the slope of executive function on disruptive behavior, the x-axis is the value of the maximum quantity of cigarettes smoked in any one trimester (centered at the sample average, 906.34). The blue shaded area indicates at what value of exposure there is a significant effect of executive function on disruptive behavior.

Table 13. Simple slopes test for the interaction between max quantity of cigarettes smoked in any one trimester and executive function

| | Estimate | Standard Error | P-Value |
|---|---|---|---|
| **-1 Standard Deviation** | 0.10 | 0.05 | 0.05 |
| **Mean** | 0.02 | 0.03 | 0.46 |
| **+1 standard deviation** | -0.05 | 0.04 | 0.23 |

***Sum quantity.*** This measure of exposure to smoking during pregnancy was the sum total of the quantity (i.e., number of cigarettes) smoked across all three trimesters. There was a significant interaction ($b$ = -0.00, $SE$ = 0.00, $p$ = 0.05; See Table 14). The interaction was probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936). The Johnson-Neyman plot as well as a simple slope analysis suggest that this interaction is not significant contrary to the structural equation model (See Figure 6 and Table 15). This suggests that the interaction was not robust enough to a different way of handling missing data (i.e., list-wise deletion in the lm function of R).

Table 14. Results for the sum quantity smoked across pregnancy.

| | Model 2B | | | Model 2C | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 14.86 | 9.07 | 0.101 | 14.39 + | 7.62 | 0.059 |
| Openness | -0.02 | 0.03 | 0.468 | -0.02 | 0.03 | 0.413 |
| Knowledge | -0.00 | 0.01 | 0.639 | -0.00 | 0.01 | 0.398 |
| Disruptive Behavior (age 7) | 0.81 *** | 0.12 | <0.001 | 0.81 *** | 0.12 | <0.001 |
| BP Externalizing Behavior Risk Score | -0.06 | 0.31 | 0.857 | -0.11 | 0.31 | 0.730 |
| AP Maternal Anti-Social Behavior | -0.07 | 0.21 | 0.730 | -0.03 | 0.20 | 0.890 |
| AP Paternal Anti-Social Behavior | 0.05 | 0.25 | 0.831 | 0.03 | 0.24 | 0.893 |
| Sex | -0.64 | 0.95 | 0.505 | -0.94 | 0.86 | 0.273 |
| Socioeconomic Status (age 11) | -0.32 | 0.47 | 0.495 | -0.33 | 0.44 | 0.444 |
| Secondhand Smoke Exposure | 0.02 | 0.08 | 0.802 | 0.02 | 0.08 | 0.771 |
| Executive Function | 0.01 | 0.03 | 0.830 | 0.10 | 0.06 | 0.102 |
| Smoking During Pregnancy (Sum) | -0.00 | 0.00 | 0.846 | 0.00 | 0.00 | 0.729 |
| EF*SDP | -- | -- | -- | -0.00 * | 0.00 | 0.045 |
| R-Square | 0.590 | | | 0.624 | | |

Note. AP = adoptive parent; BP = birth parent; EF = executive function; SDP = smoking during pregnancy; Sum = the sum of cigarettes smoked across pregnancy. *$p$ < .05, ** $p$ < .01, *** $p$ < .001.

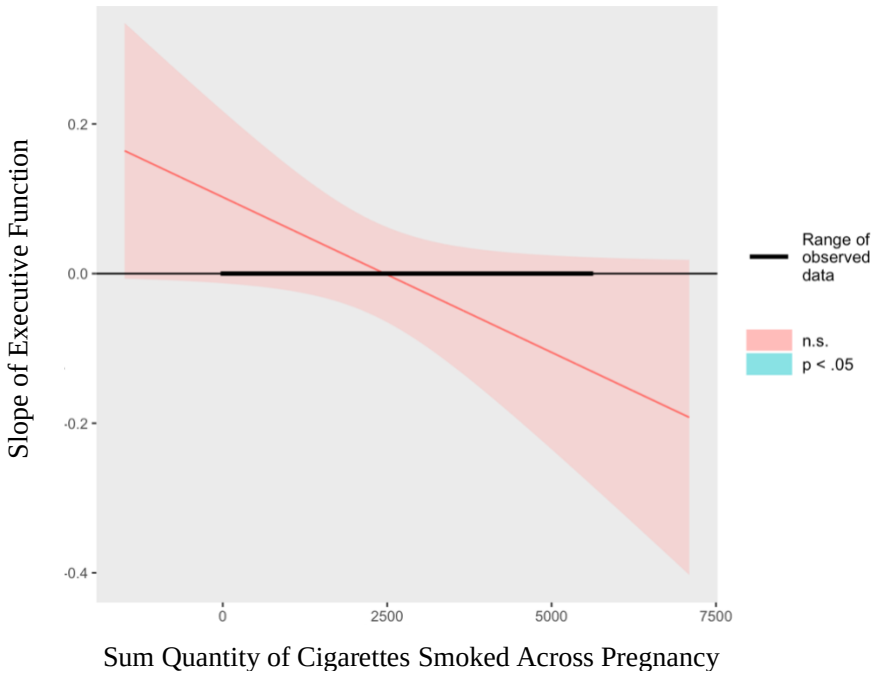



Figure 6. The interaction between executive function and the sum quantity of cigarettes smoked across pregnancy.

Note. The y-axis is the slope of executive function on disruptive behavior, the x-axis is the value of the sum quantity of cigarettes smoked (centered and the sample average, 2070.20).

Table 15. Simple slopes test for the interaction between sum quantity of cigarettes smoked across pregnancy and executive function

| | **Estimate** | **Standard Error** | **P-Value** |
|---|---|---|---|
| **-1 Standard Deviation** | 0.09 | 0.05 | 0.10 |
| **Mean** | 0.02 | 0.03 | 0.46 |
| **+1 standard deviation** | -0.04 | 0.04 | 0.33 |

***Number of trimesters*.** This measure of exposure to smoking during pregnancy was the number of trimesters that mothers smoked during, ranging from 0 (no smoking during pregnancy) to 3 (smoked during all three trimesters). There was no association between the maximum quantity smoking during pregnancy variable ($b$ = -0.98, $SE$ = 1.33, $p$ = 0.46) and executive function ($b$ = -2.38, $SE$ = 1.53, $p$ = 0.12) with disruptive behavior, there was also no significant interaction ($b$ = -0.015, $SE$ = 0.10, $p$ = 0.15; See Table 16).

Table 16. Results for the number of trimesters mothers smoked during pregnancy.

| | Model 2B | | | Model 2C | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SE** | **P-Value** | **Estimate** | **SE** | **P-Value** |
| **Disruptive Behavior (intercept)** | 16.32 + | 8.63 | 0.065 | 20.66 * | 9.68 | 0.033 |
| Openness | -0.02 | 0.01 | 0.499 | -0.02 | 0.03 | 0.526 |
| Knowledge | -0.00 | 0.01 | 0.677 | -0.00 | 0.01 | 0.543 |
| Disruptive Behavior (age 7) | 0.80 *** | 0.12 | <0.001 | 0.78 *** | 0.13 | <0.001 |
| BP Externalizing Behavior Risk Score | -0.14 | 0.29 | 0.629 | -0.17 | 0.31 | 0.580 |
| AP Maternal Anti-Social Behavior | -0.07 | 0.23 | 0.761 | -0.11 | 0.23 | 0.635 |
| AP Paternal Anti-Social Behavior | 0.07 | 0.29 | 0.824 | 0.09 | 0.28 | 0.751 |
| Sex | -0.63 | 1.02 | 0.535 | -0.40 | 1.02 | 0.693 |
| Socioeconomic Status (age 11) | -0.32 | 0.44 | 0.478 | -0.28 | 0.44 | 0.521 |
| Secondhand Smoke Exposure | 0.02 | 0.10 | 0.799 | -0.00 | 0.10 | 0.986 |
| Executive Function | 0.00 | 0.03 | 0.911 | -0.28 | 0.20 | 0.153 |
| Smoking During Pregnancy (Number) | -0.98 | 1.33 | 0.461 | -2.38 | 1.46 | 0.103 |
| EF*SDP | -- | -- | -- | 0.15 | 0.10 | 0.147 |
| R-Square | 0.588 | | | 0.609 | | |

Note. AP = adoptive parent; BP = birth parent; EF = executive function; SDP = smoking during pregnancy; Number = Number of Trimesters. *$p$ < .05, ** $p$ < .01, *** $p$ < .001.

In summary, there was evidence that the alternative measure of smoking during pregnancy, maximum quantity smoked in any one trimester, contradicted the severity score and interacted with executive function to predict disruptive behavior. Further, results for the sum quantity of cigarettes smoked across pregnancy was significant when using FIML to handle missing data, but not when using listwise deletion (although the effect was in the same direction). However, these interactions did not survive correction for multiple testing (Bonferroni adjusted $p$-value = 0.002). Considering the sparse pattern of findings across alternative measers, we believe the effect is not robust and likely a Type I error.

## Discussion

A body of literature is steadily growing surrounding the effect of exposure to smoking during pregnancy. Exposure to smoking during pregnancy has been linked to behaviors such as disruptive behavior (e.g., Ekblad et al., in press; Wakschlag, Pickett, Kasza, & Loeber, 2006) and executive function (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono et al., 1999; Micalizzi & Knopik, 2017; Rose-Jacobs et al., 2011; Piper & Corbett, 2011), but much research is limited by familial confounding, especially given that in most instances of studies that have been able to control for familial (including genetic) confounds the most prominent pattern is that the effects of smoking during pregnancy are greatly reduced if they survive at all (Boutwell & Beaver, 2010; D'Onofrio et al., 2010; Ekblad et al., in press; Langleu, Heron, Smith, & Thapar, 2012; Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014). Our hypotheses that there would be an indirect effect of smoking during pregnancy on disruptive behavior through executive function and that smoking during pregnancy would exacerbate the link between executive function and disruptive behavior were not supported. Contrary to previous literature, there was no executive function-disruptive behavior, nor smoking during pregnancy-executive function associations found in the current study.

### Smoking During Pregnancy and Disruptive Behavior

The current study included parent report of disruptive behavior, consistent with much of the sibling comparison literature that shows that familial confounding explains the association of smoking during pregnancy and disruptive behavior (Boutwell & Beaver, 2010; D'Onofrio et al., 2010; Langleu, Heron, Smith, & Thapar, 2012; Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014). However, parent report alone may not encompass as broad of symptoms across environments that a multi-rater approach would have. For example, in a recent sibling comparison design controlling for familial confounds, Ekblad and colleagues (in press) found that the smoking during pregnancy-disruptive behavior association was only significant when utilizing a multi-rater composite score of disruptive behavior that included both parent and teacher reports. Teacher reports offer a unique perspective, as the school environment is a context where youth have more opportunity to engage in disruptive behavior, as well as provides teachers with a perception of youth behavior relative to their peers (Deater-Deckard & Plomin,

1999). Further, teacher reports may capture more severe behavior traits since they are more predictive of both the use of mental health services (Stanger & Lewis, 1993) and later behavioral disorders (Sutin, Flynn, & Terraciano, 2017). Since parents and teachers provide unique information on varying contexts (e.g., home versus school), the multi-rater approach is likely to cover a wider range of symptoms that are observable from both reporters and thus may best capture disruptive behavior (Stanger & Lewis, 1993). Utilizing a multi-rater measure of disruptive behavior would offer greater power to detect effects of smoking during pregnancy, as this approach encompasses the highest amount of, and more accurate, symptomology. Future work examining disruptive behavior should consider utilizing a multi-rater approach to best capture problem behavior.

The majority of sensitivity analyses regarding alternative measures of smoking during pregnancy support the main findings. Specifically, there was no mediation of executive function on the smoking during pregnancy-disruptive behavior association and executive function does not interact with smoking exposure to predict disruptive behavior. There was one model that suggested an interaction between both executive function and working memory with maximum quantity smoked in any one trimester. However, the effect did not survive correction for multiple testing (Bonferroni adjusted *p*-value = 0.002). Coupled with the sparse pattern of findings when assessing smoking during pregnancy, we believe it is not robust and is likely a Type I error.

**Executive Function**

Although executive function has been linked to disruptive behavior in several studies (Hummer et al., 2011; Clark, Prior, & Kinsella, 2000), these effects are not always found (Fairchild et al., 2009; Moffitt & Henry, 1989; Pennington & Ozonoff, 1996) including in the current study. Further, studies that found a significant link also utilized samples with youth that had clinical ranges of disruptive behavior (Hummer et al., 2011; Clark, Prior, & Kinsella, 2000). Thus, the executive function-disruptive behavior link may also depend on researchers' sampling for studies of disruptive behavior. For example, in a meta-analysis, researchers found an association between executive function and disruptive behavior in pre-school children and found that community samples had a weaker association compared to referred or selected samples with increased rates of disruptive behavior (Schoemaker, Mulder, Dekovic, & Matthys, 2013). Thus, it may be that normative variation in executive function may not be important for normative

variations of disruptive behavior. Instead, future work may consider more severe deficits in executive function and symptoms of disruptive behavior.

Alternatively, the current study was limited to a measure that is specific to a single component of executive function, inhibition. From a hierarchical perspective of executive function, inhibition is thought to be the foundation from which youths' working memory and set-shifting develop from. Thus, poor inhibition in early childhood could potentially hinder the development of working memory or set-shifting deficits later on (Tillman et al., 2015). Thus, our null findings of the relation from early childhood executive function to preadolescent disruptive behavior may be explained by the lack of information regarding both working memory and set-shifting. Future work may consider examining whether inhibition predicts working memory and set-shifting in middle childhood, and how those complex executive functions predict disruptive behavior in preadolescence. A developmental approach may elucidate whether early childhood inhibition predicts preadolescent disruptive behavior through working memory and/or set-shifting in middle childhood.

Previous studies examining executive function have begun to tease apart hot versus cold aspects of these cognitive skills (Zelazo & Muller, 2002). What differentiates the two (i.e., hot versus cold) aspects is the contexts in which inhibition is measured. Hot executive function involves executive functions used emotional or stressful situations, where more is at stake (Zelazo & Carlson, 2012). In studies of executive function and smoking during pregnancy, cool inhibition was not related to exposure to smoking during pregnancy (Micalizzi et al., 2018; Zelazo & Muller, 2002), whereas hot inhibition was (Huijbregts, de Sonneville, & Swaab-Barneveld, 2008; Zelazo & Muller, 2002). Consistent with these findings, the current study utilized a cold measure of inhibition and did not find a link with smoking during pregnancy. Thus, future work examining smoking during pregnancy and executive function should consider utilizing both cool and hot measures of inhibition to understand whether one is more related than the other.

Altogether, results suggest that the link between executive function and both disruptive behavior and smoking during pregnancy may be more nuanced. Studies of executive function and its components have historically used a variety of measures without consensus (Miyake et al., 2000), which may potentially lead to inconclusive findings across studies. Lack of replicability across studies may suggest that associations are task specific. This becomes a larger

issue when considering task impurity, the phenomena that occurs when a measure of executive function or its components may involve other skills to complete. This phenomenon is intuitive and difficult to amend as executive function skills are recorded as building off of other skills (e.g., nonexecutive processes like language or visuospatial processing; Miyake et al., 2000), which has the potential to skew or bias results. Thus, when controlling for non-executive function skills (e.g., language), effects between executive function and disruptive behavior may become clearer such that we could detect effects. For example, the Go-No-Go task requires youth to quickly recognize letters, coordination of pressing a button, and responding to auditory feedback, thus deficits could be attributed to a number of impairments. Future studies of the link between executive function and both smoking during pregnancy and disruptive behavior should consider utilizing a latent variable approach with multiple measures for each component of executive function (Miyake et al., 2000). Utilizing a latent variable approach of executive function, the score would better measure the underlying process that produced correlations among the components of executive function. Potentially, the latent variable approach would produce a purer measure of executive function. Ideally, researchers may also choose tasks that measure specific components of executive function while also being relatively different from one another regarding the non-executive skills require to complete the tasks.

**Limitations**

The current study should be interpreted considering the following limitations. As noted above, the sample has limited executive function data. As a result, the analyses only encompass a single component of executive function (i.e., inhibitory control) as opposed to measures of all three components (i.e., inhibitory control, set shifting, and working memory) enabling the use of a latent factor. Additionally, we used only parent report of youth disruptive behavior, which limits the amount of information we are able to ascertain regarding problem behaviors. Also, the study may not be generalizable to the general population as the sample was comprised of only youth adopted at birth. Despite these limitations of the data, this current study has the advantage of being able to examine the longitudinal link between smoking during pregnancy, childhood executive function, and disruptive behavior.

## Conclusions

The current study found further evidence that the smoking during pregnancy does not predict disruptive behavior in genetically sensitive designs when controlling for familial confounds – at least when using parent reported disruptive behavior. Further, our findings support the emerging literature that hints that smoking during pregnancy may be more predictive of hot inhibition opposed to cold inhibition. Additionally, these findings challenge the longitudinal link between executive function and disruptive behavior, potentially executive function may only be linked to disruptive behavior concurrently and in adolescence or in clinical ranges of disruptive behavior. Future directions include probing the conceptual model guiding this work by utilizing measures of hot inhibition as it relates to smoking during pregnancy, in boys specifically, and sampling more severe cases of executive function deficits and disruptive behavior to examine associations.

# STUDY 2. CONTEXTUAL INFLUENCE OF SMOKING DURING PREGNANCY EXPOSURE ON EXECUTIVE FUNCTION AND DISRUPTIVE BEHAVIOR

Emily Rolan, M.S.[1], Kristine Marceau, Ph.D. [1], Sara Schmitt, Ph.D. [1], Shawn Whiteman, Ph.D. [2], Lauren Micalizzi, Ph.D.[3], Mikael Ekblad, Ph.D.[4], Rohan Palmer, Ph.D.[5], Allison Evans, Ph.D.[6], Alexandre Todorov, Ph.D.[7], Andrew Heath, Ph.D.[7], Valerie Knopik, Ph.D. [1]

[1]Department of Human Development and Family Studies, Purdue University (Rolan@purdue.edu; KristineMarceau@purdue.edu; vknopik@purdue.edu; saraschmitt@purdue.edu); [2]Department of Human Development and Family Studies, Utah State University (shawn.whiteman@usu.edu); [3]Brown University, Providence, Rhode Island (Lauren_Micalizzi@brown.edu); [4]Department of General Practice, University of Turku (moekbl@utu.fi); [5]Department of Psychology, Emory University; [6]Private Practice; [7] Department of Psychiatry, Washington University School of Medicine

Anticipated submission to *Nicotine & Tobacco Research*

## Abstract

Heritability, individual characteristics, and the family environment are all implicated in the development of youth disruptive behavior. During adolescence, the development of brain regions linked to executive functioning put adolescents at greater risk for delinquent behavior. Further, changes in dopamine release during adolescence is linked to risky behaviors and prenatal exposure to nicotine is related to alterations in the catecholamine systems (e.g., dopamine release). Thus, the current study sought to investigate whether the unique contribution of smoking during pregnancy exacerbated the global executive function-disruptive behavior association by accounting for the confound of genetic influence on youths' executive function and disruptive behavior. Utilizing a sibling-comparison framework, the goal of the current study was to explore whether a sibling exposed to smoking during pregnancy had a stronger association between executive function deficits and disruptive behavior compared to a sibling that was not exposed. The Missouri Mothers and Their Children sample consists of 173 families in which siblings are discordant for exposure to smoking during pregnancy (aged 8-15 years; full sibling pairs). A series of multi-level models were fit in MPlus to account for the nested structure of siblings within families. A severity score of smoking during pregnancy did not predict

disruptive behavior and sensitivity analyses showed a similar pattern of results. Executive function predicted disruptive behavior; however, there was no interaction between the executive function and the smoking during pregnancy severity score predicting disruptive behavior. In sensitivity analyses, there was evidence that alternate measures of smoking during pregnancy interacted with executive function to predict disruptive behavior.

## Contextual Influence of Smoking During Pregnancy Exposure on Executive Function and Disruptive Behavior

Disruptive behaviors are considered behaviors that entail physical and covert aggression, oppositional behavior, emotion dysregulation, and rule-breaking, as well as three potentially co-occurring components: oppositional defiant, conduct, and attention-deficit/hyperactivity disorders (Boyle & Offord, 1991; Fergusson et al., 1994; Ford et al., 2003; Kandel et al., 1997). Disruptive behavior is relatively common and is persistent across development (Campbell, 1995) with research suggesting that disruptive behavior in childhood is linked to later adjustment, including adolescent disruptive behavior (e.g., Bornstein et al., 2010), greater substance use (regular and advance use; Kind et al., 2004), poorer adolescent parent-child relationship quality (Burt et al., 2005), long-term violence, as well as economic and health problems (e.g., midlife mortality and probability of completing high school or enrolling in a university; Jokiela et al., 2009; McLeod & Kaiser, 2004; Odgers et al., 2008). The developmental trajectory of disruptive behavior is considered to be affected by many complex components (e.g., executive function), which are influenced by both genetics and environment. Executive function is a critical set of cognitive skills related to various developmental domains, including adolescent disruptive behavior (Fairchild et al., 2009). Additionally, exposure to smoking during pregnancy may be an important context for the development of problem behaviors. Smoking during pregnancy is thought to be related to catecholaminergic dysfunction (i.e., dysfunction of neurotransmitters including dopamine, epinephrine, and norepinephrine) in the adolescent brain and changes in dopamine release are linked to risky behaviors (Spear, 2000). Thus, youth with executive function deficits that also experience catecholaminergic dysfunction may be at increased risk for disruptive behavior. Whether smoking during pregnancy plays a role in associations between executive function-disruptive behavior during early adolescence has not been investigated but will be addressed here utilizing a genetically-informed design. Therefore, the goal of the current

study is to examine whether youth that were exposed to smoking during pregnancy have a stronger association between executive function deficits and disruptive behavior compared to those who did not.

### The Critical Role of Executive Function During Early Adolescence

Executive function consists of a set of skills that have been related to a host of outcomes across the lifespan, including adolescent delinquent behavior (Nigg et al., 2006). Executive function is considered a set of interconnected cognitive skills, utilized for controlling and coordinating information in order to manage goal-directed actions (Zelazo et al., 2016). A body of literature has examined the unity of executive function skills and largely agreed on executive function being made up of three related, yet distinct cognitive components: working memory, response inhibition, and set shifting (Garon et al., 2008; Miyake et al., 2000). The frontal lobes are largely implicated in executive function skills based on both lesion and functional imaging studies (e.g., Casey et al., 1997; Goldman-Rakic, 1987; Rakic, Bourgeois, & Goldman-Rakic, 1994; Rubia et al., 2001; Rubia, Smith, Brammer, & Taylor, 2003). One particularly important portion of the frontal lobe for executive function is the prefrontal cortex (e.g., D'Esposito & Postle, 2015). The prefrontal cortex is also linked to emotional responses (e.g., emotional response to regret comparisons in gambling tasks; Levens et al., 2014) and is implicated in other critical executive function skills (short term memory, framing plans, strategizing, and initiation of action; Blakemore & Choudhury, 2006; Carlson & Birkett, 2017). Notably, the prefrontal cortex remains relatively immature until later in adolescence (e.g., Crone & Dahl, 2012; Ernst, 2014). During childhood there is synaptic proliferation or amounts of synapses that greatly exceed that of adult levels. Thus, the brain must prune unused synapses for accuracy, efficiency, and speed across adolescence (Zecevic & Rakic, 2011). This research corresponds with findings that suggest from age 10 to 30, impulsivity steadily declines (Steinberg et al., 2008). Thus, the development of the brain (e.g., myelination of the prefrontal cortex) that assists in executive function progresses across adolescence and becomes fully developed by late adolescence. During this time of brain development, adolescents are likely at greater risk for risky behavior (e.g., disruptive behavior and substance use) given the ongoing changes in executive function development.

## The Role of Exposure to Smoking During Pregnancy

Smoking during pregnancy is linked with various indicators of youth adjustment, including greater rates of disruptive behavior (e.g., D'Onofrio et al., 2008; Salatino-Oliveira et al., 2016; Wakschlag et al., 2010) and poorer executive function (e.g., Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono et al., 1999; Micalizzi & Knopik, 2018; Rose-Jacobs et al., 2011; Piper & Corbett, 2011). However, the potential for familial confounding (i.e., genetic and environmental influences) has been largely ignored in the literature and is a critical limitation of work examining the effects of exposure to smoking during pregnancy. Specifically, mothers that smoke during pregnancy also have a constellation of other traits that could be transmitted to their children via genetics or shared environment (e.g., executive function deficits or disruptive behavior). A genetically-informed sibling comparison study of siblings disparate for exposure to smoking during pregnancy found that the association of smoking during pregnancy and childhood inhibitory control (one aspect of executive function) was fully attenuated by familial confounds (Micalizzi et al., 2018).

Further, the effects of smoking during pregnancy on disruptive behavior were generally attenuated by familial confounds (except when disruptive behavior was measured using multi-rater composite scores; Boutwell & Beaver, 2010; D'Onofrio et al., 2010; Ekblad et al., in press; Langleu, Heron, Smith, & Thapar, 2012; Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014). However, during early adolescence, biological processes (e.g., dopamine release) that are both affected by exposure to smoking during pregnancy and related to executive function become influential in the development of problem behaviors. It may be that exposure to smoking during pregnancy does not play a direct role in the development of disruptive behavior but plays a contextual role in the executive function-disruptive behavior association. To our knowledge, others have not considered the link between executive function and early adolescent disruptive behavior in the context of exposure to smoking during pregnancy.

## Smoking During Pregnancy Exacerbating the Executive Function-Disruptive Behavior Association

Familial risk (e.g., parent report of anxiety, depression, substance dependence, antisocial behavior, and psychosis) is more strongly associated with preadolescent delinquency in those exposed to smoking during pregnancy compared to those not exposed (Buschgens et al., 2009).

During adolescence there are changes in dopamine release, linked to risky behaviors (Spear, 2000). In animal studies of exposure to nicotine, rats experience profound alterations in the catecholamine systems (e.g., norepinephrine and dopamine; Azam et al., 2007; Ribary & Lichtensteiger, 1989; Onal et al., 2004). Exposure to smoking during pregnancy has been shown to have a long-standing role in neurobehavioral deficits (e.g., Knopik et al., 2016; Thapar et al., 2003; Weissman et al., 1999), speculated to be related to the catecholaminergic dysfunction in the adolescent brain. Thus, youth in late childhood with executive function deficits, who also experience catecholaminergic dysfunction, may be at increased risk for disruptive behavior. In other words, while the exposure to smoking during pregnancy occurred prior to the development and transitions in executive functioning at the onset of adolescence, specific effects of the exposure may not become apparent or impactful for disruptive behavior until adolescence. To date, whether smoking during pregnancy could also play a role in organizing associations of early adolescent executive function and disruptive behavior, exacerbating the likelihood of transitioning to disruptive behavior in youth experiencing executive function deficits, has not been investigated. Therefore, the current study seeks to examine smoking during pregnancy as a context for the executive function-disruptive behavior association.

Disruptive behavior has familial origins – including both genetic influence as well as being influenced by the family environment. Studies have recognized that genetic influence largely explains the development of disruptive behavior, however, environmental effects explain 15%-20% of variation in disruptive behavior (excluding attention-deficit/hyperactivity disorder; Burt, 2009; Miles & Carey, 1997; Moffit, 2005; Rhee & Waldman. 2002). Further, specific environmental exposures, such as smoking during pregnancy, have also been linked to later development of disruptive behavior. However, smoking during pregnancy may also be linked to genetic risk for disruptive behavior (e.g., D'Onofrio et al., 2010; Ernst et al., 2001; Ramsay & Reynolds, 2000). For example, D'Onofrio and colleagues (2010) examined the link between exposure to smoking during pregnancy and violent and non-violent convictions in a Swedish population registry study. They found that when controlling for paternal and maternal criminality, siblings discordant for smoking during pregnancy had the same likelihood of being convicted and associations were not due to smoking during pregnancy, but rather familial background factors (D'Onofrio et al., 2010). Utilizing a sibling comparison design with multilevel models allows researchers to compare siblings who experience similar home

environments, controlling for familial confounding by design (e.g., characteristics of parenting or home environment, as well as genetics that siblings share). Thus, the current study is able to focus on differences among siblings with disparate exposure to smoking during pregnancy and confidently attribute variation in the executive function-disruptive behavior association to the specific context of smoking during pregnancy. In sum, to fully understand the magnitude and role of specific environmental influences (e.g., smoking during pregnancy), environmental effects need to be examined utilizing genetically-informed study designs that can methodologically disentangle environmental from genetic influences on behavior.

## Current Study

The current study utilizes a genetically-informed sibling-comparison sample of siblings and their parents where mothers smoked (or smoked more) during one pregnancy and did not smoke (or smoked less) during the other pregnancy to examine whether smoking during pregnancy moderates the early adolescent executive function-disruptive behavior association (Figure 8). This study uses a disruptive behavior score previously created in a study utilizing the current sample (Ekblad et al., in press). In that study, there was a potentially causal within-family association of smoking during pregnancy on a multi-rater composite score of disruptive behavior. The present study extends the Ekblad and colleagues (in press) study by including smoking during pregnancy as a moderator of a unique executive function-disruptive behavior association. It is hypothesized that the relationship between early adolescent executive function and disruptive behavior will be stronger for the sibling who experienced smoking during pregnancy than the sibling who did not, on the basis of smoking during pregnancy's role on brain development (Ekblad et al., 2014; Peterson et al., 2003). The sibling comparison design allows further elucidation about whether associations might be environmental or explained by within-family differences (including genetics). Specifically, the sibling comparison design is a quasi-experimental design that utilizes natural experiences to disentangle genetic and environmental influences by recruiting siblings from the same family with disparate experiences and comparing outcomes within-family (i.e. between siblings). Thus, "matching" for familial factors and other confounding factors (e.g., neighborhood and socioeconomic status), any sibling differences in outcomes of interest may be potentially causally influenced by the disparate experience (in this case, smoking during pregnancy).

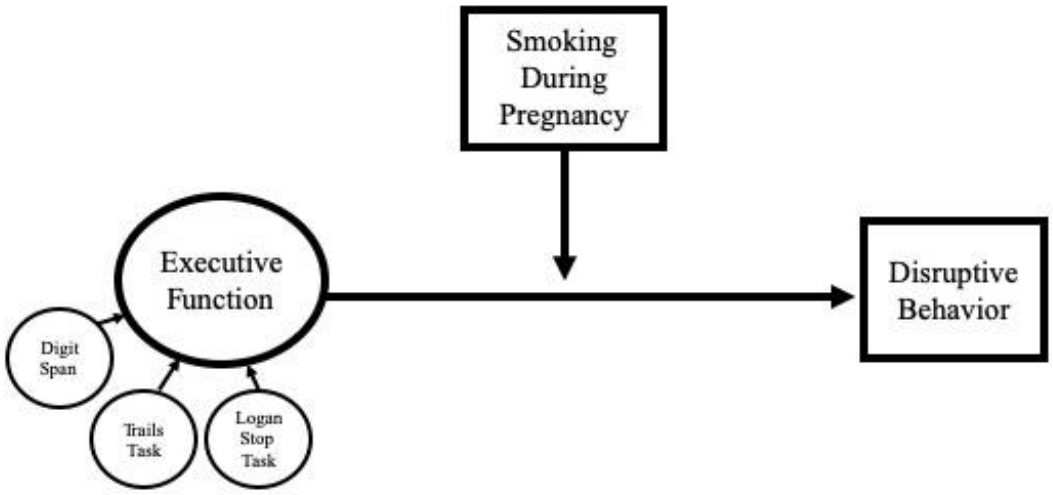



Figure 7. The figure depicts the conceptual model for study 2, the moderating effect of smoking during pregnancy on the executive function-disruptive behavior association.

## Method

### Participants and Procedures

***The Missouri Mothers and Their Children Project (MO-MATCH).*** The MO-MATCH (Knopik et al., 2015) sample consists of 173 families in which mothers smoked during one pregnancy but not the other ($N$=346 children). Birth records were used to identify and enroll families with two children (aged 8-15 years, average older sibling age is 12.99, younger is 10.19; full sibling pairs) discordant for maternal smoking during pregnancy and their parents (173 mothers, 94 fathers). Following a maternal interview about her pregnancies and her children's behavior, families were brought into the lab for in-depth neuropsychological assessment of children and parents (including cognitive ability, memory, receptive language, reading, executive function, as well as pregnancy and early life exposures and complications).

## Measures

***Smoking during pregnancy*.** Smoking during pregnancy severity was assessed with the Missouri Assessment of Genetics Interview for Children–Parent on Child (Todd, Joyner, Heath, Neuman, & Reich, 2003), separately for each pregnancy. Any smoking during pregnancy was assessed as a discrete indicator specific to each trimester (0=No, 1=Yes), overall quantity of smoking during pregnancy (0= no smoking during pregnancy, 1=21 or less, 2=21–99, 3=100 + cigarettes), and the quantity of cigarettes smoked in each trimester (continuous variable from 0-98 cigarettes) were assessed. Many smoking during pregnancy effects follow a dose-response pattern (Marceau et al., 2016; Kramer et al., 2001). Exposure to smoking during pregnancy in the second and third trimesters of pregnancy are distinct from exposure during the first trimester, and may be more harmful (Hebel et al., 1988; Dwyer et al., 2009) and to be consisten with previous work (Bidwell et al., 2017; Ekblad et al., in press; Knopik et al., 2016, 2015; Marceau et al., 2017; Micalizzi et al., 2018). Thus, using the above indicators of smoking during pregnancy, a severity score is created specific to each child's exposure to smoking during pregnancy, where 1 = no smoking during pregnancy, 2 = smoking during pregnancy in the first trimester only, 1–10 cigarettes per day, 3 = smoking during pregnancy in the first trimester only, 11–19 cigarettes per day, 4 = smoking during pregnancy in the first trimester only, 20+ cigarettes per day, 5 = smoking during pregnancy beyond the first trimester, 1–10 cigarettes per day (max of all trimesters), 6 = smoking during pregnancy beyond the first trimester, 11–19 cigarettes per day (max of all trimesters), 7 = smoking during pregnancy beyond the first trimester, 20+ cigarettes per day (max of all trimesters). The score is meant to capture the severity of exposure later in pregnancy, as literature suggests it may be more harmful compared to earlier in pregnancy (e.g., Dwyer et al., 2009; Hebel et al., 1988). For descriptive statistics on smoking during pregnancy severity score, see Table 19. Alternative measures of smoking during pregnancy used in sensitivity analyses included a discrete indicator, the maximum quantity of cigarettes smoked in any one trimester, the sum quantity of cigarettes smoked across pregnancy, and the number of trimesters mothers smoked during (See Appendix Table B1 for descriptive statistics).

***Executive function*.** During the neuropsychiatric assessment, all three components of executive function (i.e., set shifting, response inhibition, and working memory) were assessed in both siblings and parents. The Delis Kaplan Executive Function System (DKEFS; Delis, Kaplan, Kramer, 2001) was administered to both children to assess set shifting. The DKEFS Trail

Making Test consists of five conditions (Trails 1–Trails 5). The contrast score from the Number Letter Switching Score (Trails 4) minus the Combined Number and Letter Sequencing Score will be used to assess set shifting. To assess response inhibition, the Logan Stop task, commonly used to measure response inhibition in a rapid decision context, was administered. The computer screen displayed either an X or an O on a black and white screen and participants were required to respond to each letter by pressing buttons labeled 'X' and 'O' rapidly and withhold responding when a tone was heard. The Digit Span Backward task (Wechsler, 2003) of the Wechsler Intelligence Scale for Children was administered to assess auditory working memory and the Spatial Span Backward task (Wechsler, 2003) was used to assess visual working memory. The Wechsler Adult Intelligence Scale (Wechsler, 1997) assessed each component of working memory in parents, which will be used as covariates to control for familial confounding. For descriptive statistics on executive function, see Table 19.

***Disruptive behavior.*** A composite score including measures of oppositional defiant disorder symptoms and conduct disorder symptoms (Ekblad et al., in press) was measured using parent and teacher reports on the Child Behavior Checklist (CBCL/parent report and TRF/teacher report; Achenbach 1991, 1991b). The CBCL/TRF measure behavior for the previous 6 months, on a scale of 1 (*not true*) to 3 (*very true/often true*). Parent and teacher reports were combined utilizing the "or" rule for each item (Knopik et al., 2016). Items exclusive to the CBCL or the TRF were included in the composite scores for oppositional defiant disorder symptoms and conduct disorder symptoms (see Ekblad et al., in press for details). Scores for oppositional defiant disorder symptoms and conduct disorder symptoms were created from a sum of items. These scores were then combined to create a measure of disruptive behavior. The combined score for disruptive behavior is the main outcome of interest, however, scores for oppositional defiant disorder symptoms and conduct disorder symptoms were examined as outcomes in separate sensitivity analyses. For descriptive statistics on disruptive behavior, see Table 19.

***Covariates.*** Characteristics of youths' parents can act as familial confounds for the associations of smoking during pregnancy with executive function and disruptive behavior. Thus, maternal age, maternal executive function, maternal attention-deficit/hyperactivity disorder, and maternal conduct were included as covariates. Further, maternal marital status,

qualification for food stamps (yes/no) and education at the birth of each child were included as covariates, consistent with prior studies (e.g., Knopik et al., 2016). Fathers' smoking across the entire pregnancy was included as a measure of youths' passive exposure to smoking during pregnancy (0 = none, 1 = < 21, 2 = 22–99, 3 = 100+). Finally, characteristics of the youth were included as covariates, specifically, sibling birth order, and child sex. Notably, birth order and age are highly correlated in this sample (r = −0.87), introducing a multicollinearity problem. Thus, birth order was used as a covariate rather than age because the study is comprised of discordant siblings where mothers smoked more in the first pregnancy rather than the second pregnancy (Knopik et al., 2015). For descriptive statistics on study covariates, see Table 19.

**Analytic Strategy**

***Additional variable creation*.** First, a global factor score of executive function was created, derived from an exploratory factor analysis, which was used for main hypothesis testing. Next, following published methods (Knopik et al., 2015, 2016; Bidwell et al., 2017; Marceau et al., 2017; Ekblad et al, in press), in order to separate between-family and within-family effects of predictors, family-average and child-specific variables were created for smoking during pregnancy, executive function, and the interaction of smoking during pregnancy and executive function (i.e., the interaction consisted of the smoking during pregnancy by executive function child-specific variables). For example, the *family-average smoking during pregnancy severity* score is the average of smoking during pregnancy severity across both siblings within a family; the *child-specific smoking during pregnancy severity score is calculated by subtracting each siblings' smoking during pregnancy severity score from the family average (i.e. within-family centered), and thus reflects child-specific smoking during pregnancy relative to the family average,* tapping within-family differences in exposure. *Family average* variables were included as covariates, whereas child-specific variables provided a within-family test of hypotheses.

***Hypothesis testing*.** In order to test for a potentially causal role of smoking during pregnancy on the association of executive function and disruptive behavior, and to clarify the role of environment in the development of adolescent disruptive behavior, a multilevel model in Mplus (Muthén, & Muthén, 1998) was used, where level 1 is specified as:

$$Disruptive\ Behavior_{ij} = \beta_{0j} + \beta_{1j}(EF_{ij}) + \beta_{2j}(SDP_{ij}) + \beta_{3j}(EF_{ij} * SDP_{ij}) + \ldots + e_{ij}$$

where, $Disruptive\ Behavior_{ij}$ is the disruptive behavior outcome for child *i* in family *j*. The $\beta_{0i}$ coefficient is the estimated intercept level of disruptive behavior. The $\beta_{1i}$ coefficient tests the linear effect of child-specific executive function on disruptive behavior. The $\beta_{2i}$ coefficient tests the linear effect of child-specific smoking during pregnancy and disruptive behavior. The $\beta_{3i}$ coefficient tests the interaction of child-specific smoking during pregnancy and child-specific executive function on disruptive behavior. Finally, the $e_{ij}$ is a series of individual-specific residuals.

Level 2 is specified as:

$$\beta_{0j} = \gamma_{00} + \gamma_{01}(\text{Family Average SDP}_j) + \gamma_{02}(\text{Family Average EF}_j) + \mu_{0j}$$

$$\beta_{1j} = \gamma_{10}$$

$$\beta_{2j} = \gamma_{20}$$

$$\beta_{3j} = \gamma_{30}$$

The $\gamma_{00}$ estimates the average level of disruptive behavior across the various families. The $\gamma_{01}$ estimates the between-family effect of smoking during pregnancy on disruptive behavior. The $\gamma_{02}$ estimates the family-level effect of executive function on disruptive behavior. The $\mu_{0j}$ is a random effect that estimates the unique effect of family *j* on disruptive behavior. The $\gamma_{10}$ estimates the fixed effect or sample-average within-family effect of executive function on disruptive behavior. The $\gamma_{20}$ estimates the fixed effect or sample-average within-family effect of smoking during pregnancy on disruptive behavior. The $\gamma_{30}$ estimates the fixed effect or sample-average within-family effect for the executive function*smoking during pregnancy interaction, addressing the hypothesis that the relation between executive function and disruptive behavior will be stronger for the sibling who experienced smoking during pregnancy. These equations only describe the hypothesized main effects and interactions. Covariates were included on the appropriate equation based on whether they varied within family, and included parents' family-average executive function and disruptive behavior, family-average smoking during pregnancy (entered on the level two equation for $\beta_{0j}$), and demographic covariates (e.g., child specific age and father smoking during pregnancy, entered on the level one equation).

An unconditional model was run initially to assess within-and between-family variance in disruptive behavior. Intraclass correlations were calculated, to examine the proportion of

variance in disruptive behavior explained by the family grouping variable, by dividing the variance of level two variables by the sum of the variance of both level one and level two:

$$ICC = r = \frac{t_{00}}{t_{00} + s^2}$$

The second model included covariates only. Next, a third model included covariates and key study constructs (i.e., child-specific executive function and child-specific smoking during pregnancy), and finally a fourth model added the interaction term. The percent of reduction in error (PRE) was calculated for each model to measure within-family variance explained by the addition of variables as a measure of effect size. The PRE was calculated by subtracting the level 1 residual of the outcome variable of the target model from the preceding model and dividing the value by the level 1 residual of the outcome variable from the preceding model.

Sensitivity analyses included examining individual components of disruptive behavior (i.e., conduct disorder symptoms and oppositional defiant disorder symptoms), sex differences, individual components of executive function (i.e., working memory, set-shifting, and inhibition), and alternative measures of smoking during pregnancy. Hypothesis testing remained the same as it was for the main analyses for individual components of both disruptive behavior and executive function. Sex differences were examined in a multi-level model using Mplus with a three-way interaction between executive function, child-specific sex (e.g., the within-family effect), and smoking during pregnancy for both disruptive behavior and conduct disorder. For alternative measures of smoking during pregnancy, the final model was run with either a discrete indicator, maximum quantity of cigarettes smoked in any one trimester, the sum quantity of cigarettes smoked across pregnancy, or the number of trimesters smoked in, as opposed to the main anlysis that use the severity score of smoking during pregnancy. Interactions were probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936), this technique is optimal as it solves for the values of smoking during pregnancy for which the executive function-disruptive behavior association is no longer significant (Carden, Holtzman, & Strube, 2017). Notably, the lmer function was used to test simple slopes and utilize the Johnson-Neyman approach, which is only possible with listwise deletion.

***Missing data.*** For missing data, to determine if data were missing at random (MAR), three dummy variables were created for whether each of the key study concepts (smoking during pregnancy, executive function, and disruptive behavior) were missing (i.e., 0 = missing and 1 =

observed). Following, a series of chi-square tests were used to confirm the missingness on variables wasn't meaningfully linked to specific characteristics (e.g., child sex, age food stamps, and maternal executive function). Full Information Maximum Likelihood (FIML) was used for data missing not at random (MNAR), as it is less biased and more robust compared to listwise deletion (Acock, 2005). See Appendix B. for results of tests and patterns of missingness.

## Results

More severe smoking during pregnancy was correlated with lower executive function. However, disruptive behavior was not correlated with any key study variables (see Table 18).

Table 17. Correlation of key study two variables

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Maternal Education | -- | | | | | | | | | | | |
| 2. Maternal Age | .23** | -- | | | | | | | | | | |
| 3. Food Stamp Usage | .03 | .03 | -- | | | | | | | | | |
| 4. Paternal Secondhand Smoke | -.114* | -.36** | .09 | -- | | | | | | | | |
| 5. Sex | .05 | .03 | .03 | -.07 | -- | | | | | | | |
| 6. Birth Order | .21** | .87** | .11 | -.42** | .05 | -- | | | | | | |
| 7. Maternal Executive Function | .00 | .00 | .00 | .00 | .00 | .00 | -- | | | | | |
| 8. Maternal ADHD | .00 | .00 | .00 | .00 | .00 | .00 | -.09 | -- | | | | |
| 9. Maternal Conduct Disorder | .00 | .00 | .00 | .00 | .00 | .00 | .12 | -.02 | -- | | | |
| 10. Executive Function | -.01 | .17** | -.11 | -.06 | .11* | .07 | .00 | .00 | .00 | -- | | |
| 11. Smoking During Pregnancy | -16** | -.47** | .05 | .44** | -.01 | -.51** | .00 | .00 | .00 | -.15** | -- | |
| 12. Disruptive Behavior | .09 | .02 | .01 | .09 | -.10 | .00 | -.06 | .03 | -.06 | -.11 | .06 | -- |

Note. Sex is coded as 0 = female, 1 = male; ADHD = attention-deficit/hyperactivity disorder *$p < .05$, ** $p < .01$, *** $p < .001$

Table 18. Descriptive statistics for study 2.

| Study variables | Child 1 (older) | | | | | | Child 2 (younger) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | N | Mean | (SD) | Range | Skew | Kurtosis | N | Mean | (SD) | Range | Skew | Kurtosis |
| SDP Severity | 173 | 3.95 | 2.05 | 6.00 | -0.70 | -0.49 | 171 | 2.04 | 1.77 | 6.00 | 0.70 | -0.49 |
| Child Executive Function | 164 | -0.05 | 0.60 | 3.60 | -0.06 | 0.80 | 164 | 0.03 | 0.96 | 5.16 | -0.31 | 0.08 |
| Maternal Executive Function | 164 | 0.01 | 1.00 | 6.48 | -0.18 | 0.78 | 166 | -0.01 | 1.00 | 6.48 | -0.16 | 0.73 |
| Maternal ADHD | 169 | 0.11 | 0.51 | 3.00 | 4.88 | 23.72 | 169 | 0.11 | 0.51 | 3.00 | 4.88 | 23.72 |
| Maternal Past ODD | 169 | 0.02 | 0.13 | 1.00 | 7.24 | 50.71 | 169 | 0.02 | 0.13 | 1.00 | 7.24 | 50.71 |
| Maternal Present ODD | 169 | 0.01 | 0.11 | 1.00 | 8.95 | 78.54 | 169 | 0.01 | 0.11 | 1.00 | 8.95 | 78.54 |
| Maternal Conduct Disorder | 169 | 0.01 | 0.08 | 1.00 | 12.77 | 162.04 | 169 | 0.01 | 0.08 | 1.00 | 12.77 | 162.04 |
| **Disruptive behavior disorder** | | | | | | | | | | | | |
| CBCL | 162 | 1.76 | 1.28 | 5.20 | 0.14 | -0.73 | 160 | 1.74 | 1.26 | 6.16 | 0.37 | -0.16 |
| TRF | 109 | 1.04 | 1.27 | 4.24 | 0.86 | -0.48 | 111 | 1.38 | 1.29 | 4.58 | 0.57 | -0.68 |
| CBCL/TRF multi-rater total | 165 | 2.13 | 1.25 | 5.66 | -0.08 | -0.47 | 164 | 2.13 | 1.31 | 6.40 | 0.23 | -0.19 |
| **Oppositional defiant disorder** | | | | | | | | | | | | |
| CBCL | 162 | 1.21 | 0.92 | 2.83 | -0.24 | -1.46 | 160 | 1.19 | 0.90 | 3.16 | -0.01 | -1.06 |
| TRF | 109 | 0.65 | 0.85 | 2.83 | 0.78 | -0.94 | 111 | 0.86 | 0.94 | 3.00 | 0.46 | -1.29 |
| CBCL/TRF multi-rater total | 165 | 1.48 | 0.83 | 3.16 | -0.65 | -0.64 | 164 | 1.48 | 0.89 | 3.32 | -0.31 | -0.71 |
| **Conduct disorder** | | | | | | | | | | | | |
| CBCL | 162 | 1.09 | 1.12 | 4.47 | 0.62 | -0.52 | 160 | 1.10 | 1.09 | 5.29 | 0.69 | 0.08 |
| TRF | 109 | 0.73 | 1.00 | 3.74 | 1.13 | 0.26 | 111 | 0.93 | 1.06 | 3.61 | 0.81 | -0.51 |
| CBCL/TRF multi-rater total | 165 | 1.37 | 1.16 | 4.69 | 0.33 | -0.74 | 164 | 1.36 | 1.19 | 5.57 | 0.47 | -0.33 |
| **Covariates** | | | | | | | | | | | | |
| Maternal age at birth | 162 | 26.48 | 5.55 | | -0.82 | 0.40 | 163 | 29.22 | 5.75 | | 0.71 | 0.32 |
| Maternal education (in years) at birth | 162 | 13.28 | 2.12 | | -4.35 | 38.19 | 163 | 13.5 | 1.94 | | 4.43 | 39.54 |
| Second-hand smoke exposure by fathers | 171 | 1.84 | 1.44 | | 0.54 | 0.04 | 161 | 1.15 | 1.43 | | -0.48 | -0.08 |
| | **N** | **%** | | | | | **N** | **%** | | | | |
| Food stamp usage at birth | 149 | 9% | | | | | 150 | 13% | | | | |
| Marital status (percent married) at birth | 155 | 85% | | | | | 159 | 83% | | | | |

Note. SDP = smoking during pregnancy; ADHD = attention-deficit/hyperactivity disorder; ODD = oppositional defiant disorder; CBCL = child behavior checklist; TRF = teacher report form (of the child behavior checklist).

***Executive function factor scores*.** Utilizing Lavaan in R, three factor scores of executive function were created for the child and mother (individually) with a promax rotation using the regression method to estimate factor scores. For youth, components of executive function were correlated from .26 to .29 ($p < .001$), these are relatively low correlations. Thus, we created the factor score to measure global executive function but conducted sensitivity analyses examining components of executive function separately. The EFA for youth executive function indicated one conceptually distinct factor that represented children's executive function (RMSR = 0.00). Item loadings were 0.56, 0.52, and 0.28 for set-shifting, inhibition and auditory working memory, respectively. Set-shifting was removed from the maternal factor analyses due to poor factor loadings (0.00). For mothers, components of executive function were correlated from .35 to .83 ($p < .001$). The EFA for mothers' executive function indicated one conceptually distinct factor that represented maternal executive function (RMSR = 0.00). Item loadings were 0.95, and 0.70 for working memory and inhibition, respectively.

**Disruptive Behavior Multi-Rater Composite Score**

The unconditional model showed that 75% of variance in the composite parent and teacher report of disruptive behavior is attributable to within-family differences (ICC = 0.25). From the unconditional model, the addition of level 1 and 2 covariates accounted for 11% of the within family variation in disruptive behavior (PRE = 0.11). In model 3, the addition of the predictors (i.e., executive function and smoking during pregnancy), the model accounted for 4% of the residual within family variance from model 2 (PRE = 0.04). Finally, in model 4, the addition of the interaction between executive function and smoking during pregnancy account for none of the residual within family variance from model 3 (PRE = 0.00). There was evidence that executive function predicted disruptive behavior ($b$ = -0.27, $SE$ = 0.11, $p$ = 0.02). Specifically, worse executive function predicted more disruptive behavior. Further, there was no evidence that smoking during pregnancy predicted disruptive behavior ($b$ = 0.05, $SE$ = 0.04, $p$ = 0.26), contrary to Ekblad et al. (in press) that found a smoking during pregnancy-disruptive behavior association. Finally, there was not an interaction between executive function and smoking during pregnancy ($b$ = -0.15, $SE$ = 0.10, $p$ = 0.14; See Table 20 for full results).

**Sensitivity Analyses**

***Oppositional defiant disorder multi-rater composite score***. The unconditional model showed that 72% of variance in the composite parent and teacher report of oppositional defiance disorder symptoms is attributable to within-family differences (between-family ICC = 0.18). From the unconditional model, the addition of level 1 and 2 covariates accounted for 7% of the within family variance (PRE = 0.07). In model 3, with the addition of the predictors (i.e., executive function and smoking during pregnancy), the model accounted for 1% of the residual within family variance from model 2 (PRE = 0.01). The full model (including the interaction term) accounted for none of the residual within family variance from model 3 (PRE = 0.00). There was no evidence that executive function predicted oppositional defiance disorder symptoms ($b$ = -0.11, $SE$ = 0.09, $p$ = 0.242). Further, there was no evidence that smoking during pregnancy predicted oppositional defiant disorder symptoms ($b$ = 0.02, $SE$ = 0.04, $p$ = 0.559). Finally, there was not an interaction between executive function and smoking during pregnancy ($b$ = -0.10, $SE$ = 0.07, $p$ = 0.155; See Table 20 for full results).

***Conduct disorder multi-rater composite score*.** The unconditional model showed that 82% of variance in the composite parent and teacher report of conduct disorder symptoms is attributable to within-family differences (between-family ICC = 0.28). From the unconditional model, the addition of the level 1 and 2 covariates accounted for 12% of the within-family variance (PRE =0.12). In model 3, with the addition of predictors (i.e., executive function and smoking during pregnancy) accounted for 17% of the residual within family variance from model 2 (PRE = 0.17). Finally, the full model (including the interaction term) accounted for none of the residual within family variance from model 3 (PRE = 0.00). There was evidence that executive function predicted conduct disorder symptoms ($b$ = -0.28, $SE$ = 0.11, $p$ = 0.01). Specifically, lower executive function predicted more conduct disorder symptoms. However, there was no evidence of a within-family effect of smoking during pregnancy, such that more severe exposure did not predict greater conduct disorder symptoms ($b$ = 0.05, $SE$ = 0.04, $p$ = 0.16). Finally, there was not an interaction between executive function and smoking during pregnancy ($b$ = -0.09, $SE$ = 0.10, $p$ = 0.40; See Table 20 for full results).

Table 19. Full results for study two: disruptive behavior, oppositional defiant disorder symptoms, and conduct disorder symptoms.

| **Variable Name** | **Disruptive Behavior** | | | **Oppositional Defiant Disorder** | | | **Conduct Disorder** | | |
|---|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | | | | | | | |
| EF | -0.27* | 0.11 | 0.015 | -0.11 | 0.08 | 0.164 | -0.28* | 0.11 | 0.014 |
| SDP | 0.05 | 0.04 | 0.257 | 0.02 | 0.03 | 0.575 | 0.05 | 0.04 | 0.157 |
| EF*SDP | -0.15 | 0.10 | 0.144 | -0.10 | 0.06 | 0.111 | -0.09 | 0.10 | 0.395 |
| Birth order | 0.07 | 0.25 | 0.794 | -0.00 | 0.18 | 0.995 | 0.14 | 0.21 | 0.526 |
| Mother education | 0.21* | 0.08 | 0.010 | 0.09+ | 0.05 | 0.064 | 0.21* | 0.08 | 0.010 |
| Mother age | 0.25+ | 0.14 | 0.079 | 0.17+ | 0.10 | 0.089 | 0.18 | 0.14 | 0.199 |
| Food Stamp Usage | -0.03 | 0.44 | 0.940 | 0.12 | 0.34 | 0.718 | -0.06 | 0.42 | 0.891 |
| Father SDP | 0.13 | 0.09 | 0.150 | 0.07 | 0.06 | 0.211 | 0.14+ | 0.08 | 0.098 |
| Child Sex | -0.37* | 0.17 | 0.031 | -0.16 | 0.13 | 0.219 | -0.36* | 0.15 | 0.014 |
| Level 2 (family-level variables) | | | | | | | | | |
| SDP | 0.14+ | 0.07 | 0.054 | 0.07 | 0.05 | 0.121 | 0.12+ | 0.07 | 0.079 |
| EF | -0.09 | 0.14 | 0.493 | -0.10 | 0.09 | 0.298 | -0.05 | 0.13 | 0.681 |
| Mother education | -0.08+ | 0.05 | 0.096 | -0.05 | 0.03 | 0.134 | -0.06 | 0.04 | 0.172 |
| Mother age | -0.00 | 0.02 | 0.835 | -0.01 | 0.01 | 0.463 | 0.01 | 0.02 | 0.735 |
| Food Stamp Usage | 0.03 | 0.28 | 0.927 | -0.10 | 0.17 | 0.548 | 0.18 | 0.28 | 0.513 |
| Father SDP | 0.00 | 0.07 | 1.000 | 0.00 | 0.04 | 0.982 | 0.02 | 0.06 | 0.760 |
| Child Sex | -0.73** | 0.22 | 0.001 | -0.33* | 0.15 | 0.028 | -0.68** | 0.20 | 0.001 |
| Maternal EF | -0.21 | 0.29 | 0.476 | -0.17 | 0.19 | 0.372 | -0.11 | 0.29 | 0.714 |
| Maternal ADHD | 0.05 | 0.24 | 0.837 | 0.13 | 0.17 | 0.440 | 0.01 | 0.23 | 0.949 |
| Maternal Conduct Disorder | 0.03 | 0.67 | 0.962 | 0.16 | 0.45 | 0.728 | 0.05 | 0.60 | 0.937 |
| Random effects: Individual-level | | | | | | | | | |
| Variance Intercept | 0.33*** | 0.12 | 0.004 | 0.11* | 0.05 | 0.048 | 0.36*** | 0.09 | <0.001 |
| Residual Variance | 1.06*** | 0.15 | <0.001 | 0.56*** | 0.06 | <0.001 | 0.82*** | 0.11 | <0.001 |

Note EF = executive function; SDP = smoking during pregnancy; ADHD = attention deficit-hyperactivity disorder. *$p$ < .05, ** $p$ < .01, *** $p$ <.001

***Sex differences***. In post hoc analyses, to examine whether there were sex differences in the effects, the full model was run with a three-way interaction between executive function, smoking during pregnancy, and within- and between family sex. Within-family sex examines sex differences across siblings whereas between family examines sex differences across families. There was no indication of sex differences for within family executive function and smoking during pregnancy on disruptive behavior for disruptive behavior ($b$ = -0.23, $SE$ = 0.19, $p$ = 0.23) or conduct disorder symptoms ($b$ = -0.20, $SE$ = 0.19, $p$ = 30; See Table 21).

Table 20. Summary of results for sex differences.

| **Variable Name** | **Disruptive Behavior** | | | **Conduct Disorder** | | |
|---|---|---|---|---|---|---|
| | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | | | | |
| Executive Function | -0.69 | 0.49 | 0.159 | -1.074** | 0.40 | 0.007 |
| SDP | 0.23+ | 0.13 | 0.064 | 0.15 | 0.11 | 0.192 |
| Executive Function*SDP | -0.68* | 0.29 | 0.018 | -0.58* | 0.29 | 0.043 |
| Executive Function*Within-Family Sex | 0.02 | 0.50 | 0.974 | -0.23 | 0.53 | 0.666 |
| SDP*Within-Family Sex | 0.13 | 0.11 | 0.233 | -0.01 | 0.11 | 0.931 |
| Executive Function*Between-Family Sex | 0.29 | 0.33 | 0.385 | 0.55 | 0.27 | 0.038 |
| SDP*Between-Family Sex | -0.12 | 0.08 | 0.114 | -0.06 | 0.07 | 0.378 |
| Executive Function*SDP*Within-Family Sex | -0.23 | 0.19 | 0.231 | -0.20 | 0.19 | 0.295 |
| Executive Function*SDP*Between-Family Sex | 0.35+ | 0.18 | 0.055 | 0.33+ | 0.18 | 0.065 |
| Birth order | 0.07 | 0.24 | 0.763 | 0.15 | 0.21 | 0.456 |
| Mother education | 0.23** | 0.09 | 0.006 | 0.23** | 0.09 | 0.008 |
| Mother age | 0.26+ | 0.14 | 0.066 | 0.18 | 0.14 | 0.189 |
| Food Stamp Usage | -0.04 | 0.40 | 0.920 | -0.07 | 0.38 | 0.858 |
| Father SDP | 0.12 | 0.09 | 0.211 | 0.14+ | 0.08 | 0.077 |
| Child Sex | -0.38* | 0.09 | 0.033 | -0.37* | 0.15 | 0.015 |
| Level 2 (family-level variables) | | | | | | |
| SDP | 0.16* | 0.07 | 0.033 | 0.13+ | 0.07 | 0.061 |
| Executive Function | -0.12 | 0.14 | 0.394 | -0.06 | 0.12 | 0.605 |
| Mother education | -0.08 | 0.05 | 0.121 | -0.06 | 0.04 | 0.202 |
| Mother age | -0.01 | 0.02 | 0.783 | 0.01 | 0.02 | 0.766 |
| Food Stamp Usage | -0.03 | 0.31 | 0.923 | 0.12 | 0.29 | 0.685 |
| Father SDP | -0.01 | 0.07 | 0.837 | 0.02 | 0.06 | 0.740 |
| Child Sex | -0.68** | 0.23 | 0.003 | -0.64** | 0.20 | 0.002 |
| Maternal EF | -0.30 | 0.29 | 0.307 | -0.14 | 0.30 | 0.644 |
| Maternal ADHD | -0.01 | 0.28 | 0.971 | -0.07 | 0.24 | 0.755 |
| Maternal Conduct Disorder | 0.13 | 0.70 | 0.851 | 0.06 | 0.61 | 0.919 |
| Random effects: Individual-level | | | | | | |
| Variance Intercept | 0.35** | 0.12 | 0.002 | 0.371*** | 0.09 | <0.001 |
| Residual Variance | 0.991*** | 0.15 | <0.001 | 0.762*** | 0.11 | <0.001 |

Note. SDP = smoking during pregnancy; EF = executive function; ADHD = attention-deficit/hyperactivity disorder, + $p$ < .10, * $p$ < .05, ** $p$ < .01, *** $p$ < .001.

Post-hoc analyses also included a series of multi-level models conducted in MPlus for each component of executive function: working memory, set-shifting, and inhibition.

***Working memory***. The unconditional model showed that 75% of variance in the composite parent and teacher report of disruptive behavior is attributable to within-family differences (ICC = 0.25). From the unconditional model, the addition of level 1 and 2 covariates accounted for 11% of the within family variation in disruptive behavior (PRE = 0.11). From model 2 (level 1 and 2 covariates), the addition of the predictors (i.e., working memory and smoking during pregnancy), the model accounted for 3% of the within family variance (PRE = 0.03). Finally, from model 3 (i.e., level 1 and 2 covariates with predictors), the addition of the interaction between working memory and smoking during pregnancy account for 0% of the within family variance (PRE = 0.00). There was evidence that working memory predicted disruptive behavior ($b$ = -0.06, $SE$ = 0.03, $p$ = 0.05), such that lower working memory predicted more disruptive behavior. Further, there was no evidence that smoking during pregnancy predicted disruptive behavior ($b$ = 0.13, $SE$ = 0.06, $p$ = 0.03). Finally, there was not an interaction between working memory and smoking during pregnancy ($b$ = -0.04, $SE$ = 0.02, $p$ = 0.07; See Table 22 for full results).

Table 21. Summary of results for the working memory component of executive function

| Variable Name | Disruptive Behavior | | |
|---|---|---|---|
| | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | |
| Working Memory | -0.06* | 0.03 | 0.046 |
| SDP | 0.05 | 0.04 | 0.221 |
| Working Memory*SDP | -0.04+ | 0.02 | 0.065 |
| Birth order | 0.09 | 0.25 | 0.726 |
| Mother education | 0.21* | 0.08 | 0.011 |
| Mother age | 0.22 | 0.14 | 0.108 |
| Food Stamp Usage | 0.08 | 0.43 | 0.856 |
| Father SDP | 0.12 | 0.09 | 0.186 |
| Child Sex | -0.40* | 0.17 | 0.018 |
| Level 2 (family-level variables) | | | |
| SDP | 0.14+ | 0.07 | 0.051 |
| Working Memory | -0.01 | 0.04 | 0.891 |
| Mother education | -0.09+ | 0.05 | 0.065 |
| Mother age | -0.01 | 0.02 | 0.741 |
| Food Stamp Usage | 0.02 | 0.30 | 0.942 |
| Father SDP | -0.01 | 0.06 | 0.919 |
| Child Sex | -0.72** | 0.22 | 0.001 |
| Maternal EF | -0.22 | 0.29 | 0.434 |
| Maternal ADHD | 0.02 | 0.27 | 0.927 |
| Maternal Conduct Disorder | 0.16 | 0.70 | 0.819 |
| Random effects: Individual-level | | | |
| Variance Intercept | 0.33** | 0.12 | 0.005 |
| Residual Variance | 1.08*** | 0.15 | <0.001 |

Note. SDP = smoking during pregnancy; EF = executive function; ADHD = attention-deficit/hyperactivity disorder, + $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

***Set-shifting***. The unconditional model showed that 75% of variance in the composite parent and teacher report of disruptive behavior is attributable to within-family differences (ICC = 0.25). From the unconditional model, the addition of level 1 and 2 covariates accounted for 11% of the within family variation in disruptive behavior (PRE = 0.11). From model 2 (level 1 and 2 covariates), the addition of the predictors (i.e., set-shifting and smoking during pregnancy), the model accounted for 4% of the within family variance (PRE = 0.04). Finally, from model 3 (i.e., level 1 and 2 covariates with predictors), the addition of the interaction between set-shifting and smoking during pregnancy account for 0% of the within family variance (PRE = 0.00). There was evidence that set-shifting predicted disruptive behavior ($b$ = -0.07, $SE$ = 0.03, $p$ = 0.04), such that less set-shifting predicted more disruptive behavior. Further, there was no evidence that smoking during pregnancy predicted disruptive behavior ($b$ = 0.05, $SE$ = 0.04, $p$ =

0.20). Finally, there was not an interaction between set-shifting and smoking during pregnancy (*b* = -0.02, *SE* = 0.03, *p* = 0.47; See Table 23 for full results).

Table 22. Summary of results for the set-shifting component of executive function.

| **Variable Name** | **Disruptive Behavior** | | |
|---|---|---|---|
| | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | |
| Set-shifting | -0.07* | 0.03 | 0.039 |
| SDP | 0.05 | 0.04 | 0.199 |
| Set-shifting*SDP | -0.02 | 0.03 | 0.469 |
| Birth order | 0.11 | 0.25 | 0.663 |
| Mother education | 0.21* | 0.08 | 0.011 |
| Mother age | 0.24+ | 0.14 | 0.090 |
| Food Stamp Usage | -0.10 | 0.44 | 0.826 |
| Father SDP | 0.13 | 0.09 | 0.145 |
| Child Sex | -0.39* | 0.17 | 0.025 |
| Level 2 (family-level variables) | | | |
| SDP | 0.15+ | 0.08 | 0.061 |
| Set-shifting | 0.00 | 0.04 | 0.981 |
| Mother education | -0.08+ | 0.05 | 0.086 |
| Mother age | 0.00 | 0.02 | 0.990 |
| Food Stamp Usage | 0.07 | 0.28 | 0.816 |
| Father SDP | 0.00 | 0.07 | 0.947 |
| Child Sex | -0.73** | 0.23 | 0.001 |
| Maternal EF | -0.20 | 0.29 | 0.504 |
| Maternal ADHD | 0.07 | 0.25 | 0.791 |
| Maternal Conduct Disorder | -0.14 | 0.71 | 0.849 |
| Random effects: Individual-level | | | |
| Variance Intercept | 0.35** | 0.12 | 0.003 |
| Residual Variance | 1.06*** | 0.15 | <0.001 |

Note. SDP = smoking during pregnancy; EF = executive function; ADHD = attention-deficit/hyperactivity disorder, + $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$.

***Inhibition***. The unconditional model showed that 75% of variance in the composite parent and teacher report of disruptive behavior is attributable to within-family differences (ICC = 0.25). From the unconditional model, the addition of level 1 and 2 covariates accounted for 11% of the within family variation in disruptive behavior (PRE = 0.11). From model 2 (level 1 and 2 covariates), the addition of the predictors (i.e., inhibition and smoking during pregnancy), the model accounted for 2% of the within family variance (PRE = 0.02). Finally, from model 3 (i.e., level 1 and 2 covariates with predictors), the addition of the interaction between inhibition and smoking during pregnancy account for 0% of the within family variance (PRE = 0.00). There was no evidence that inhibition predicted disruptive behavior (*b* = -0.03, *SE* = 0.03, *p* =

0.28). Further, there was no evidence that smoking during pregnancy predicted disruptive behavior ($b$ = 0.05, $SE$ = 0.04, $p$ = 0.21). Finally, there was not an interaction between inhibition and smoking during pregnancy ($b$ = 0.01, $SE$ = 0.03, $p$ = 0.75; See Table 24 for full results).

Table 23. Summary of results for the inhibition component of executive function

| **Variable Name** | **Disruptive Behavior** | | |
|---|---|---|---|
| | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | |
| Inhibition | -0.03 | 0.03 | 0.284 |
| SDP | 0.05 | 0.04 | 0.209 |
| Inhibition*SDP | 0.01 | 0.03 | 0.752 |
| Birth order | 0.13 | 0.25 | 0.613 |
| Mother education | 0.22* | 0.09 | 0.010 |
| Mother age | 0.23 | 0.14 | 0.104 |
| Food Stamp Usage | 0.00 | 0.44 | 0.998 |
| Father SDP | 0.13 | 0.09 | 0.142 |
| Child Sex | -0.39* | 0.17 | 0.023 |
| Level 2 (family-level variables) | | | |
| SDP | 0.15 | 0.07 | 0.042 |
| Inhibition | -0.06 | 0.04 | 0.101 |
| Mother education | -0.07 | 0.05 | 0.126 |
| Mother age | -0.00 | 0.02 | 0.937 |
| Food Stamp Usage | 0.06 | 0.29 | 0.831 |
| Father SDP | -0.01 | 0.06 | 0.917 |
| Child Sex | -0.71 | 0.23 | 0.002 |
| Maternal EF | -0.20 | 0.29 | 0.498 |
| Maternal ADHD | 0.08 | 0.24 | 0.723 |
| Maternal Conduct Disorder | -0.31 | 0.66 | 0.636 |
| Random effects: Individual-level | | | |
| Variance Intercept | 0.33** | 0.12 | 0.007 |
| Residual Variance | 1.09*** | 0.15 | <0.001 |

Note. SDP = smoking during pregnancy; EF = executive function; ADHD = attention-deficit/hyperactivity disorder, + $p$ < .10, * $p$ < .05, ** $p$ < .01, *** $p$ < .001.

In summary, the sensitivity analyses examining the components of executive function (i.e., working memory, set-shifting, and inhibition) support the main analyses. Specifically, there was a main effect of both working memory and set-shifting with disruptive behavior, but no interaction between executive function or components of executive function with smoking during pregnancy to predict disruptive behavior.

A series of multilevel model in Mplus (Muthén, & Muthén, 1998) were run for post-hoc analyses to examine alternative measures of smoking during pregnancy, to explore whether findings are consistent across diverse measures of defining and capturing exposure. In sensitivity analyses of specific executive function components, working memory predicted disruptive

behavior and there was a trend-level interaction between working memory and smoking during pregnancy, whereas there was no interaction for the other components of executive function. Thus, this series of post-hoc analyses were also run with working memory in addition to the executive function factor score.

***Yes/no*.** This measure of exposure to smoking during pregnancy was a dichotomous variable of exposure, such that 0 is no exposure and 1 is exposure to smoking during pregnancy. There was no evidence that smoking during pregnancy predicted disruptive behavior ($b$ = 0.01, $SE$ = 0.19, $p$ = 0.95), but executive function did ($b$ = -0.29, $SE$ = 0.11, $p$ = 0.01) and there was a significant interaction ($b$ = -0.79, $SE$ = 0.39, $p$ = 0.04; See Table 25 for full results). Further, in models with working memory, working memory predicted disruptive behavior ($b$ = -0.06, $SE$ = 0.03, $p$ = 0.03). The dichotomous smoking during pregnancy variable did not predict disruptive behavior ($b$ = 0.02, $SE$ = 0.19, $p$ = 0.03), however, there was a significant interaction between working memory and dichotomous smoking during pregnancy ($b$ = -0.23, $SE$ = 0.11, $p$ = 0.03; See Table 26 for full result; and Figure 9). The interactions of executive function by the discrete indicator of exposure and working memory by the discrete indicator of exposure were probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936). The negative relationship between executive function and disruptive behavior was stronger for the sibling exposed to smoking during pregnancy (for simple slopes see Table 27).

***Maximum quantity*.** This measure of exposure to smoking during pregnancy was the maximum quantity smoked (i.e., number of cigarettes) in any one trimester. There was no evidence that smoking during pregnancy ($b$ = 0.00, $SE$ = 0.01, $p$ = 0.71) or executive function ($b$ = -0.03, $SE$ = 0.17, $p$ = 0.86) predicted disruptive behavior, but there was a significant interaction ($b$ = -0.04, $SE$ = 0.02, $p$ = 0.05; See Table 25 for full results). Further, in models with working memory, working memory predicted disruptive behavior ($b$ = -0.06, $SE$ = 0.03, $p$ = 0.04). The maximum quantity smoked in any one trimester variable did not predict disruptive behavior ($b$ = 0.01, $SE$ = 0.01, $p$ = 0.44), however, there was a significant interaction between working memory and the maximum quantity smoked in any one trimester ($b$ = -0.01, $SE$ = 0.01, $p$ = 0.03; See Table 26 for full result). The interactions of executive function by maximum quantity smoked in any one trimester and the working memory by maximum quantity smoked in any one trimester were probed using Johnson-Neyman regions of significance in R (Johnson & Neyman, 1936). Results indicated that the negative relationship between executive function and disruptive

behavior was stronger for the sibling exposed to smoking during pregnancy. However, for working memory the interaction with the maximum quantity smoking in any one trimester was not robust enough to an alternative way of handling missing data in a different program (R with lmer which uses list-wise deletion; See Figure 9 and 10; for simple slopes see Table 28).

***Sum quantity.*** This measure of exposure to smoking during pregnancy was the sum total of the quantity (i.e., number of cigarettes) smoked across all three trimesters. There was no evidence that smoking during pregnancy ($b$ = 0.01, $SE$ = 0.00, $p$ = 0.05) predicted disruptive behavior, but executive function did ($b$ = -0.27, $SE$ = 0.11, $p$ = 0.02). Further, there was no evidence of an interaction between smoking during pregnancy and executive function ($b$ = -0.02, $SE$ = 0.01, $p$ = 0.11; See Table 25 for full results). Further, in models with working memory, working memory did not predict disruptive behavior ($b$ = -0.06, $SE$ = 0.03, $p$ = 0.06), but the sum quantity of cigarettes smoked across all three trimesters did ($b$ = 0.01, $SE$ = 0.00, $p$ = 0.04). Specifically, the sibling with the greater quantity of cigarettes smoked across trimesters had more disruptive behavior. Further, there was no interaction between working memory and the sum quantity smoked across trimesters ($b$ = -0.00, $SE$ = 0.00, $p$ = 0.20; See Table 26 for full result).

***Number of trimesters*.** This measure of exposure to smoking during pregnancy was the number of trimesters that mothers smoked during, ranging from 0 (no smoking during pregnancy) to 3 (smoked during all three trimesters). There was no evidence that smoking during pregnancy ($b$ = 0.08, $SE$ = 0.07, $p$ = 0.23) predicted disruptive behavior, but executive function did ($b$ = -0.28, $SE$ = 0.11, $p$ = 0.01). Further, there was no evidence of an interaction between smoking during pregnancy and executive function ($b$ = -0.24, $SE$ = 0.15, $p$ = 0.11; See Table 25 for full results). Further, in models with working memory, working memory predicted disruptive behavior ($b$ = -0.06, $SE$ = 0.03, $p$ = 0.04), such that lower working memory predicted more disruptive behavior. However, the number of trimesters mothers smoked during did not ($b$ =0.09, $SE$ = 0.07, $p$ = 0.20), and there was no interaction with working memory ($b$ = -0.07, $SE$ = 0.04, $p$ = 0.11; See Table 26 for full results) to predict disruptive behavior.

Table 24. Results for other measures of smoking during pregnancy and executive function.

| Variable Name | Yes/No | | | Maximum Quantity | | | Sum Quantity | | | Number of Trimesters | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | | | | | | | | | | |
| Executive Function | -0.29 | 0.11 | 0.010 | -0.03 | 0.17 | 0.859 | -0.27 | 0.11 | 0.019 | -0.28 | 0.11 | 0.014 |
| SDP | 0.01 | 0.19 | 0.952 | 0.00 | 0.01 | 0.708 | 0.01 | 0.00 | 0.052 | 0.08 | 0.07 | 0.230 |
| Executive Function*SDP | -0.79 | 0.39 | 0.041 | -0.04 | 0.02 | 0.048 | -0.02 | 0.01 | 0.108 | -0.24 | 0.15 | 0.110 |
| Birth order | 0.01 | 0.25 | 0.957 | -0.02 | 0.26 | 0.946 | 0.06 | 0.25 | 0.796 | 0.08 | 0.25 | 0.753 |
| Mother education | 0.20 | 0.08 | 0.012 | 0.21 | 0.08 | 0.011 | 0.20 | 0.08 | 0.015 | 0.21 | 0.08 | 0.011 |
| Mother age | 0.22 | 0.14 | 0.101 | 0.23 | 0.13 | 0.092 | 0.23 | 0.13 | 0.080 | 0.25 | 0.14 | 0.067 |
| Food Stamp Usage | -0.00 | 0.44 | 0.993 | 0.06 | 0.45 | 0.898 | -0.02 | 0.44 | 0.956 | -0.03 | 0.43 | 0.947 |
| Father SDP | 0.16 | 0.09 | 0.072 | 0.13 | 0.09 | 0.136 | 0.13 | 0.09 | 0.140 | 0.13 | 0.09 | 0.167 |
| Child Sex | -0.35 | 0.18 | 0.043 | -0.37 | 0.17 | 0.030 | -0.35 | 0.17 | 0.041 | -0.36 | 0.17 | 0.036 |
| Level 2 (family-level variables) | | | | | | | | | | | | |
| SDP | 0.22 | 0.32 | 0.487 | 0.02 | 0.01 | 0.112 | 0.01 | 0.01 | 0.208 | 0.14 | 0.12 | 0.247 |
| Executive Function | -0.08 | 0.14 | 0.548 | -0.11 | 0.14 | 0.423 | -0.10 | 0.14 | 0.453 | -0.08 | 0.14 | 0.555 |
| Mother education | -0.08 | 0.05 | 0.085 | -0.08 | 0.05 | 0.115 | -0.08 | 0.05 | 0.136 | -0.08 | 0.05 | 0.080 |
| Mother age | -0.00 | 0.02 | 0.929 | 0.00 | 0.02 | 0.940 | 0.00 | 0.02 | 0.992 | -0.00 | 0.02 | 0.960 |
| Food Stamp Usage | 0.02 | 0.27 | 0.950 | 0.06 | 0.29 | 0.824 | 0.07 | 0.29 | 0.805 | 0.05 | 0.28 | 0.860 |
| Father SDP | 0.02 | 0.07 | 0.745 | 0.01 | 0.06 | 0.934 | 0.01 | 0.06 | 0.867 | 0.02 | 0.07 | 0.794 |
| Child Sex | -0.72 | 0.23 | 0.001 | -0.75 | 0.23 | 0.001 | -0.80 | 0.23 | 0.001 | -0.75 | 0.22 | 0.001 |
| Maternal EF | -0.21 | 0.28 | 0.446 | -0.17 | 0.28 | 0.545 | -0.18 | 0.29 | 0.527 | -0.21 | 0.29 | 0.454 |
| Maternal ADHD | 0.09 | 0.26 | 0.731 | -0.03 | 0.20 | 0.904 | -0.01 | 0.21 | 0.962 | 0.06 | 0.26 | 0.805 |
| Maternal Conduct Disorder | -0.42 | 0.60 | 0.488 | -0.53 | 0.60 | 0.380 | -0.40 | 0.60 | 0.503 | -0.25 | 0.65 | 0.698 |
| Random effects: Individual-level | | | | | | | | | | | | |
| Variance Intercept | 0.34 | 0.12 | 0.003 | 1.071 | 0.15 | <0.001 | 0.34 | 0.12 | 0.004 | 0.35 | 0.12 | 0.003 |
| Residual Variance | 1.08 | 0.15 | <0.001 | 0.33 | 0.12 | 0.004 | 1.06 | 0.15 | <0.001 | 1.06 | 0.15 | <0.001 |

Note. This table contains the full results for the sensitivity analyses on alternative measures of smoking during pregnancy (SDP). Columns correspond with the model run for working memory, such that the row SDP is actually a dichotomous predict (yes/no) in the first set of columns, maximum quantity smoked in any one trimester (Maximum Quantity) in the second set of columns, the sum of cigarettes smoked across trimesters (sum quantity) in the third set of columns, and the number of trimesters mothers smoked (number of trimesters) in the last set of columns. EF = executive function; ADHD = attention-deficit/hyperactivity disorder.

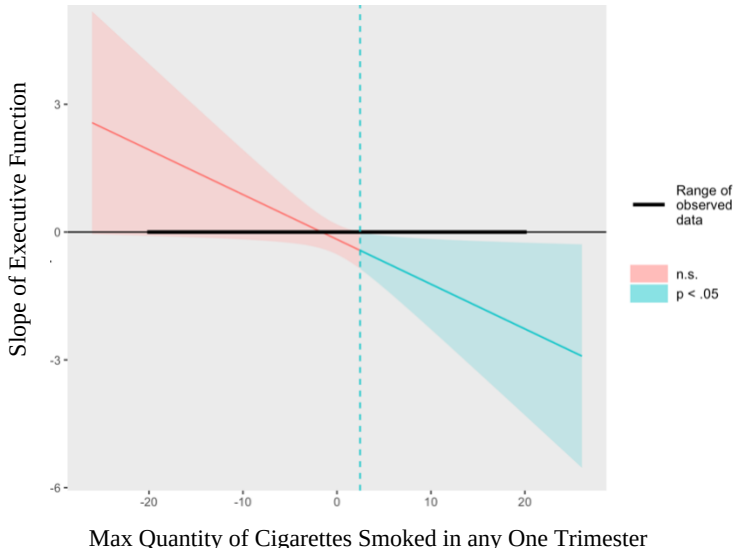
Table 25. Results for other measures of smoking during pregnancy and working memory.

| Variable Name | Yes/No | | | Maximum Quantity | | | Sum Quantity | | | Number of Trimesters | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value | Estimate | Standard Error | P-Value |
| Level 1 (child-specific variables) | | | | | | | | | | | | |
| Working Memory | -0.06 | 0.03 | 0.034 | -0.06 | 0.03 | 0.044 | -0.06 | 0.03 | 0.056 | -0.06 | 0.03 | 0.040 |
| SDP | 0.02 | 0.19 | 0.928 | 0.01 | 0.01 | 0.437 | 0.01 | 0.00 | 0.040 | 0.09 | 0.07 | 0.196 |
| Working Memory *SDP | -0.23 | 0.11 | 0.032 | -0.01 | 0.01 | 0.030 | -0.00 | 0.00 | 0.197 | -0.07 | 0.04 | 0.105 |
| Birth order | 0.03 | 0.25 | 0.891 | 0.07 | 0.25 | 0.793 | 0.09 | 0.25 | 0.735 | 0.10 | 0.25 | 0.692 |
| Mother education | 0.20 | 0.08 | 0.012 | 0.20 | 0.08 | 0.012 | 0.20 | 0.08 | 0.016 | 0.21 | 0.08 | 0.011 |
| Mother age | 0.20 | 0.13 | 0.131 | 0.21 | 0.13 | 0.116 | 0.21 | 0.13 | 0.113 | 0.23 | 0.13 | 0.089 |
| Food Stamp Usage | 0.12 | 0.44 | 0.790 | 0.10 | 0.43 | 0.822 | 0.08 | 0.43 | 0.848 | 0.09 | 0.43 | 0.842 |
| Father SDP | 0.15 | 0.09 | 0.089 | 0.15 | 0.09 | 0.097 | 0.12 | 0.09 | 0.170 | 0.12 | 0.09 | 0.206 |
| Child Sex | -0.39 | 0.17 | 0.025 | -0.39 | 0.17 | 0.024 | -0.38 | 0.17 | 0.026 | -0.39 | 0.17 | 0.022 |
| Level 2 (family-level variables) | | | | | | | | | | | | |
| SDP | 0.24 | 0.32 | 0.448 | 0.01 | 0.01 | 0.306 | 0.01 | 0.01 | 0.161 | 0.15 | 0.12 | 0.224 |
| Working Memory | -0.00 | 0.04 | 0.931 | -0.01 | 0.04 | 0.820 | -0.01 | 0.04 | 0.752 | -0.01 | 0.04 | 0.881 |
| Mother education | -0.09 | 0.05 | 0.058 | -0.09 | 0.05 | 0.076 | -0.08 | 0.05 | 0.122 | -0.09 | 0.05 | 0.062 |
| Mother age | -0.00 | 0.02 | 0.894 | 0.00 | 0.02 | 0.982 | -0.00 | 0.02 | 0.970 | -0.00 | 0.02 | 0.886 |
| Food Stamp Usage | 0.01 | 0.30 | 0.982 | 0.07 | 0.30 | 0.822 | 0.07 | 0.30 | 0.806 | 0.02 | 0.30 | 0.942 |
| Father SDP | 0.02 | 0.07 | 0.798 | 0.00 | 0.06 | 0.953 | 0.01 | 0.06 | 0.892 | 0.01 | 0.07 | 0.871 |
| Child Sex | -0.70 | 0.22 | 0.001 | -0.74 | 0.22 | 0.001 | -0.78 | 0.23 | 0.001 | -0.73 | 0.22 | 0.001 |
| Maternal EF | -0.23 | 0.28 | 0.410 | -0.18 | 0.28 | 0.513 | -0.20 | 0.29 | 0.495 | -0.24 | 0.29 | 0.411 |
| Maternal ADHD | 0.08 | 0.28 | 0.410 | -0.06 | 0.24 | 0.819 | -0.01 | 0.22 | 0.976 | 0.05 | 0.28 | 0.852 |
| Maternal Conduct Disorder | -0.22 | 0.65 | 0.730 | -0.36 | 0.62 | 0.559 | -0.38 | 0.62 | 0.543 | -0.11 | 0.69 | 0.870 |
| Random effects: Individual-level | | | | | | | | | | | | |
| Variance Intercept | 0.34 | 0.12 | 0.004 | 0.33 | 0.12 | 0.006 | 0.35 | 0.12 | 0.004 | 0.35 | 0.12 | 0.003 |
| Residual Variance | 1.09 | 0.15 | <0.001 | 1.08 | 0.15 | <0.001 | 1.07 | 0.15 | <0.001 | 1.07 | 0.15 | <0.001 |

Note. This table contains the full results for the sensitivity analyses on alternative measures of smoking during pregnancy (SDP). Columns correspond with the model run for working memory, such that the row SDP is actually a dichotomous predict (yes/no) in the first set of columns, maximum quantity smoked in any one trimester (Maximum Quantity) in the second set of columns, the sum of cigarettes smoked across trimesters (sum quantity) in the third set of columns, and the number of trimesters mothers smoked (number of trimesters) in the last set of columns. EF = executive function; ADHD = attention-deficit/hyperactivity disorder.

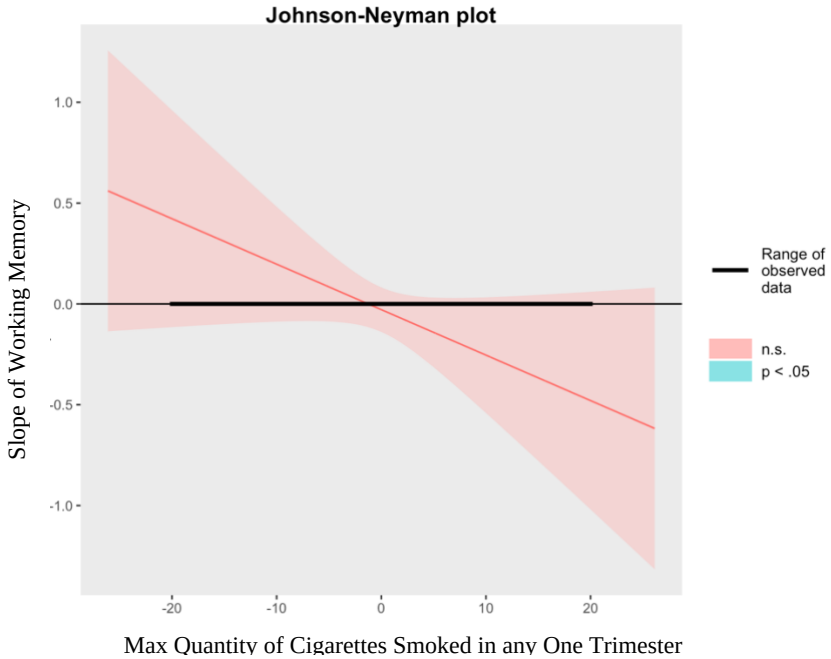
Table 26. Simple slopes test for the interaction between the discrete indicator of smoking during pregnancy and both executive function and working memory

| | Estimate | Standard Error | P-Value |
|---|---|---|---|
| **Executive Function** | | | |
| **SDP Yes** | -1.23 | 0.70 | 0.08 |
| **SDP No** | -0.22 | 0.17 | 0.21 |
| **Working Memory** | | | |
| **SDP Yes** | -0.06 | 0.05 | 0.25 |
| **SDP No** | -0.42 | 0.20 | 0.04 |




Note. The y-axis is the slope of executive function on disruptive behavior, the x-axis is the value of the max quantity smoked in any one trimester (centered at the sample average, 6.38). The blue shaded area indicates at what value of exposure there is a significant effect of executive function on disruptive behavior.

Figure 9. Interaction of executive function and the maximum quantity of cigarettes smoked in any one trimester.




Note. The y-axis is the slope of working memory on disruptive behavior, the x-axis is the value of the max quantity smoked in any one trimester (centered at the sample average, 6.38). The blue shaded area indicates at what value of exposure there is a significant effect of working memory on disruptive behavior.

Figure 8. Interaction of working memory and the maximum quantity of cigarettes smoked in any one trimester.

Table 27. Simple slopes test for the interactions between max quantity smoked in any one trimester and both executive function and working memory

| | Estimate | Standard Error | P-Value |
|---|---|---|---|
| **Executive Function** | | | |
| **-1 Standard Deviation** | 0.47 | 0.35 | 0.19 |
| **Mean** | -0.17 | 0.18 | 0.35 |
| **+1 standard deviation** | -0.80 | 0.35 | 0.02 |
| **Working Memory** | | | |
| **-1 Standard Deviation** | 0.11 | 0.10 | 0.27 |
| **Mean** | -0.03 | 0.06 | 0.59 |
| **+1 standard deviation** | -0.17 | 0.10 | 0.10 |

In summary, there was evidence that two alternative measures of exposure to smoking during pregnancy, the discrete indicator and the maximum quantity smoked in any one trimester, contradicted the severity score and interacted with both executive function and working memory to predict disruptive behavior. However, the interactions between executive function or working memory and measures of exposure did not survive correction for multiple testing (Bonferroni adjusted p-value = 0.003). Considering these interactions did not occur for the majority of

alternative measures of smoking during pregnancy, we believe the effect is not robust and likely a Type I error.

## Discussion

During adolescence, the development of brain regions linked to executive functioning put adolescents at greater risk for delinquent behavior (e.g., disruptive behavior and substance use; Blakemore & Choudhury, 2006; Carlson & Birkett, 2017; Crone & Dahl, 2012; D'Esposito & Postle, 2015; Ernst, 2014; Levens et al., 2014; Nigg et al., 2006). Further, changes in dopamine release during adolescence is linked to risky behaviors (Spear, 2000) and exposure to prenatal nicotine is related to alterations in the catecholamine systems (e.g., norepinephrine and dopamine; Azam et al., 2007; Ribary & Lichtensteiger, 1989; Onal et al., 2004). Thus, youth with lower executive function skills, in the context of smoking during pregnancy-related catecholaminergic dysfunction, may be more likely to experience greater rates of disruptive behavior. Thus, the current study sought to investigate the unique contribution of smoking during pregnancy as a context for the global executive function-disruptive behavior association by accounting for the confound of genetic influence on youths' executive function and disruptive behavior. In the main analyses, the severity score of smoking during pregnancy did not predict disruptive behavior, and this was confirmed in sensitivity analyses using alternative measures of smoking during pregnancy. Additionally, in the main analyses executive function did predict disruptive behavior, such that lower executive function was linked to more disruptive behavior. Further, in sensitivity analyses there was a similar effect on conduct disorder symptoms but not oppositional defiant disorder symptoms. However, there was no interaction between the executive function factor score and the smoking during pregnancy severity score predicting disruptive behavior, inconsistent with the study hypotheses. In sensitivity analyses, the negative effect of executive function on disruptive behavior was stronger for the sibling exposed to smoking during pregnancy. In summary, smoking during pregnancy does not have a robust within-family effect. Executive function does have an effext on disruptive behavior, likely driven by working memory and socioeconomic status, and possibly with conduct disorder. The pattern of interactions suggest smoking during pregnancy does not moderate the executive function-disruptive behavior association (See Table 29).

Table 28. Summary of main and sensitivity analyses.

| Predictor Variable | Disruptive Behavior | Oppositional Defiant Disorder | Conduct Disorder |
|---|---|---|---|
| **Smoking During Pregnancy** | | | |
| SDP Severity Score | 0.05(0.04) | 0.02(0.03) | 0.05(0.04) |
| Dichotomous SDP | 0.01(0.19) | -- | -- |
| Maximum Quantity | 0.00(0.01) | -- | -- |
| Sum Quantity | **0.01(0.00)** | -- | -- |
| Number of Trimesters | 0.08(0.07) | -- | -- |
| **Executive Function** | | | |
| Factor Score | **-0.27(0.11)*** | -0.11(0.08) | **-0.28(0.11)*** |
| Working Memory | **-0.06(0.03)*** | -- | -- |
| Set-Shifting | **-0.07(0.03)*** | -- | -- |
| Inhibition | -0.03(0.03) | -- | -- |
| Interaction Effects | | | |
| SDP Severity Score*EF Factor Score | -0.15(0.10) | -0.10(0.06) | -0.09(0.10) |
| SDP Severity Score*Working Memory | -0.04(0.02)+ | -- | -- |
| SDP Severity Score*Set-Shifting | -0.02(0.03) | -- | -- |
| SDP Severity Score*Inhibition | 0.01(0.03) | -- | -- |
| Dichotomous SDP*EF Factor Score | **-0.79(0.39)*** | -- | -- |
| Maximum Quantity*EF Factor Score | **-0.04(0.02)*** | -- | -- |
| Sum Quantity*EF Factor Score | -0.02(0.01) | -- | -- |
| Number of Trimesters*EF Factor Score | -0.24(0.15) | -- | -- |
| Dichotomous SDP* Working Memory | **-0.23(0.11)*** | -- | -- |
| Maximum Quantity* Working Memory | **-0.01(0.01)*** | -- | -- |
| Sum Quantity* Working Memory | -0.00(0.00) | -- | -- |
| Number of Trimesters* Working Memory | -0.07(0.04) | -- | -- |

Note. This table reflects the estimate(standard deviation) for both main and sensitivity analyses across this paper. Bolded items had a p-value of less than 0.05. SDP = smoking during pregnancy; dichotomous SDP = 0 is no exposure and 1 is exposure to smoking during pregnancy; Maximum quantity = the maximum quantity of cigarettes smoked in any one trimester; Sum quantity = the total number of cigarettes smoked across all three trimesters; Number of Trimesters = the number of trimesters that mothers smoked during, ranging from 0 (no smoking during pregnancy) to 3 (smoked during all three trimesters); EF = executive function. *p<.05, **p<.01, ***p<.001, +p<.10.

## The Critical Role of Executive Function During Early Adolescence

Executive function is a critical component of negotiating challenges across development, especially during late childhood and adolescence when youth are faced with increases in the complexities of their social, emotional, and cognitive environments (e.g., Blakemore & Choudhury, 2006; Gray & Squeglia, 2018; Mendle & Ferrero, 2012, Ullsperger & Nikolas, 2017). Consistent with hypotheses, the current study found that lower executive function predicted disruptive behavior. We utilized multi-level modeling to test the within-family association between executive function and disruptive behavior. Executive function was within-family centered; thus, our findings reflect that the sibling with lower executive function also exhibited more disruptive behavior than his/her co-sibling. Interestingly, in sensitivity analyses of the components of disruptive behavior, lower executive function predicted more conduct disorder symptoms but not oppositional defiant disorder symptoms. Both oppositional defiant disorder symptoms and conduct disorder symptoms occur similarly in community samples (i.e., 2-14% and 2-16%, respectively; Boylan, Vaillancourt, Boyle, & Szatmari, 2007; Loeber, Burke,

Lahey, Winters, & Zera, 2000) and are highly correlated (Loeber, Burkle, & Pardini, 2009; Rowe et al., 2002). However, there are distinct characteristics that differentiate the two disorders. Specifically, oppositional defiant disorder is often considered to be an emotional regulation or temperament deficit (Loeber et al., 2009) as its characteristics consist of developmentally inappropriate behavior toward authority figures, frequent and persistent patterns of irritable and angry mood, as well as vindictiveness (American Psychiatric Association, 2013). Conduct disorder is characterized by fighting, stealing, bullying, vandalism, and lying (American Psychiatric Association, 2013) and is considered to be more severe compared to oppositional defiant disorder (Rey et al., 1998). Thus, executive function deficits may be more salient for the severe form of disruptive behavior. For example, since oppositional defiant disorder precedes conduct disorder (e.g., Loeber, Green, Lahey, Christ, & Frick, 1992; Nock, Kazdin, Hiripi, & Kessler, 2007; Rowe, Costello, Angold, Copeland, & Maughan, 2010), youth with oppositional defiant disorder may have less opportunity to practice executive function skills (Eisenberg et al., 2010), potentially leading to poorer executive function which then snowballs into conduct disorder. Therefore, future work may consider using a developmental perspective to examine the progression of disruptive behavior (i.e., oppositional defiant disorder predicting conduct disorder) through executive function.

Executive function is theoretically made up of three components: working memory, set-shifting, and inhibition. These components have a common underlying process; however, they are distinguishable and utilized differentially depending on the context in young children as well as during late childhood (e.g., Lehto et al., 2003; Miyake et al., 2000). In the current study, sensitivity analyses of specific executive function components conducted post-hoc demonstrated that working memory and set-shifting predicted disruptive behavior but inhibition did not. Specifically, the sibling with greater working memory or set-shifting had lower rates of disruptive behavior. Interestingly, in studies of inhibition and externalizing behaviors measured with the child behavior checklist, there is a longitudinal association but not a concurrent one (Riggs, Blair, & Greenberg, 2003). Riggs and colleagues (2003) posit a "developmental lag" hypothesis, meaning youths' inhibitory abilities may develop prior to the behavior linked to it. This developmental lag could explain why inhibition is not related to disruptive behavior in this sample, with inhibition and disruptive behavior measured cross-sectionally.

Alternatively, one theory of executive function is the hierarchical perspective, where inhibition is considered to be the base of executive functions, which gives way to youths' ability to develop more complex executive function skills (i.e., working memory and set-shifting). For example, deficits in simple executive functioning in early childhood (e.g., poor inhibition) would be a foundation for the development of deficits in more complex executive functioning (e.g., working memory or set-shifting deficits) in late childhood or early adolescence. In line with this, there is research that suggests that inhibition is linked to attention-deficit/hyperactivity disorder until age 10, at which point working memory becomes predictive of attention-deficit/hyperactivity disorder from age 10 to 13 (Brocki & Bohlin, 2006). Given that attention-deficit/hyperactivity disorder often coexists with both conduct disorder and oppositional defiant disorder (Biederman, 2005), working memory, as compared to inhibition, may be more salient for disruptive behavior in late childhood. Additional research is necessary to understand how components of executive function build upon one another to predict disruptive behavior. This approach is in accordance with the hierarchical perspective that inhibition develops first in early childhood and predicts later working memory in late childhood (Tillman et al., 2015), which may then be linked to disruptive behavior. It may be that a longitudinal approach is necessary to test whether inhibition predicts later disruptive behavior through working memory and/or set-shifting.

**The Role of Exposure to Smoking During Pregnancy**

In the current study, when examining the effect of exposure to smoking during pregnancy in a sibling comparison design, the effect of the severity score on disruptive behavior was explained by familial confounds. The current study failed to recover an association between the smoking during pregnancy severity score and the combined disruptive behavior association, contradicting previous work that found an association (Ekblad et al., in press). Models run in previous work (i.e., Ekblad et al., in press) utilized listwise deletion on predictors. Alternatively, the current paper utilized full information maximum likelihood (FIML) to account for missing data. Studies comparing FIML to other methods of handling missing data have found that it produces less biased estimates and is more efficient compared to other methods (e.g., Acock, 2005; Enders & Bandalos, 2001). In post-hoc analyses without executive function in the model, when using listwise deletion on the predictors there is an effect of smoking during pregnancy on

disruptive behavior; however, when using FIML the association does not persist. Further, when using listwise deletion and adding the executive function predictor, there is an effect of executive function, but not smoking during pregnancy. Thus, while executive function explains some of the overlapping variance in disruptive behavior, it appears that the way missing data is handled in analyses is important.

In addition to the smoking during pregnancy severity score, sensitivity analyses also examined alternative measures of exposure to smoking during pregnancy in post-hoc models. The pattern of findings does not show robust evidence and therefore in order to avoid type I error, the findings should be replicated before they are interpreted. However, the findings also point to the possibility that working memory is a key component to consider in future replication attempts. Further, the pattern of findings suggest a need to better understand what the key timing and threshold effects of smoking during pregnancy may be, in order to improve our measurement of exposure, and to understand whether the pattern of findings across indicators here have a potentially better or worse ability to detect an effect or are just due to type I errors.

**Limitations**

This sibling-comparison design strives to account for familial confounding (disentangling genetic and environmental influences) by utilizing siblings from the same family who have differential exposure to smoking during pregnancy. The clear strength of the sibling-comparison design to control for familial confounding provides an excellent test of smoking during pregnancy effects on the executive function-disruptive behavior association. Second, in the factor score for youth executive function score, the measure of working memory did not load well. Third, in a subset of the data more than one teacher reported on a single participant, potentially biasing findings as those youths' scores may be higher compared to those who did not have multiple teacher reports. Finally, for sensitivity analyses (e.g., age difference and alternative measures of smoking during pregnancy), *p*-values did pass the threshold of significance ($p<0.05$), however associations were small and would not survive multiple testing adjustments. Further, in the sensitivity analyses for sex differences, due to the nature of the design, we cannot stratify by sex necessitating an interaction that the study is underpowered to examined. Thus, we cannot strongly conclude that there are no sex differences.

## Conclusions

In sum, these findings do not support work that suggests exposure to smoking during pregnancy may be causally linked to youth disruptive behavior. However, they confirm the link between executive function (particularly working memory and set-shifting) with disruptive behavior in late childhood. The novel contribution of the study was the within-family investigation of the executive function-disruptive behavior association, controlling for important familial confounds. This study suggests that within family, the sibling with decreased executive function exhibits more disruptive behavior. Interestingly, inhibition was not linked to disruptive behavior which suggests an interesting opportunity for future researchers to examine the hierarchical development of executive function as it relates to disruptive behaviors in late childhood and early adolescence.

# STUDY 3. TRANSITIONS FROM DISRUPTIVE BEHAVIOR TO SUBSTANCE USE AND THE ROLE OF EXECUTIVE FUNCTION AND SIBLING RELATIONSHIPS

Emily Rolan, M.S.[1], Shawn Whiteman, Ph.D. [2] , Sara Schmitt, Ph.D. [1], Valerie Knopik, Ph.D. [1], Kristine Marceau, Ph.D. [1]

[1]Department of Human Development and Family Studies, Purdue University (Rolan@purdue.edu; KristineMarceau@purdue.edu; vknopik@purdue.edu; saraschmitt@purdue.edu); [2]Department of Human Development and Family Studies, Utah State University (shawn.whiteman@usu.edu)

Anticipated Submission to the *Journal of Youth and Adolescence*

**Abstract**

Executive function predicts disruptive behavior, and disruptive behavior predicts rates of adolescent substance use. Also, characteristics of the sibling relationship are an important context to consider when examining the development of substance use. The current study used a study of at-risk youth (*N* = 775;71% male) to examine whether the late childhood executive function-adolescent substance use association would be mediated by disruptive behavior and if this path would be moderated by characteristics of the sibling relationship. There was no evidence of an executive function-substance use association, mediation, or interactions with characteristics of the sibling relationships. The results challenge the developmental cascade model of substance use, and highlights the need to further investigate the directionality of associations between executive function, disruptive behavior, and substance use.

## Transitions from Disruptive Behavior to Substance Use and the Role of Executive Function and Sibling Relationships

Adolescence is often termed a unique and sensitive developmental period. This stage of development consists of transitions and turmoil due to the onset of puberty and shifts in brain structure that coincide with cascading social and cognitive changes (e.g., Crone & Dahl, 2012; Ernst, 2014; Hollenstein & Lougheed, 2013; Mendle & Ferrero, 2012; Rowe, Maugham, Worthman, Costello, & Angold, 2004; Schultz, Molenda-Figueira, & Sisk, 2009; Ullsperger & Nikolas, 2017). During adolescence, through the combined influence of biological

predisposition, as well as both environmental and biological changes, some adolescents show increases in risky behaviors (e.g., Blakemore & Choudhury, 2006; Gray & Squeglia, 2018; Marceau, Kirisci, & Tarter, in press; Mendle & Ferrero, 2012, Ullsperger & Nikolas, 2017). Further, adolescence is a period in which the initiation of adverse behavioral outcomes may set youth on a trajectory for life-persistent patterns of maladjustment (Baggio et al., 2015; Blanco et al., 2016; Gray & Squeglia, 2018).

One critical problem behavior during adolescence is substance use. Adolescent substance use is a ubiquitous public health problem, as evidenced by recent statistics suggesting over 55% of seniors in high school have consumed alcohol and a wide-ranging decline in youth's perception of risk of harm and condemnation of substance use (Monitoring the Future Survey: High school and Youth Trends, 2016). While a certain amount of early experimentation with substances is normative during adolescence, an alarming rate of adolescents meet the criteria for alcohol (15%) and drug (16%) abuse by 18 years-old (Swendsen et al., 2012). Critically, earlier onset of substance use is associated with greater risk for developing a substance use disorder (Blanco et al., 2016; Gray & Squeglia, 2018) and disengagement in education, employment, and training (Baggio et al., 2015).

Many biological, individual, and environmental factors have been investigated as predictors of the developmental of adolescent substance use. Two important individual factors in the developmental trajectory of substance use are executive function and disruptive behavior. Executive function is a particularly important predictor of both disruptive behavior and substance use in the literature (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Moffit et al., 2011; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Further, earlier disruptive behavior has been related to the development of substance use (Dodge et al., 2009). Finally, sibling relationships are a particularly unique context for the development of problem behaviors (e.g., both disruptive behavior and substance use; Fagan & Najman, 2005; Kothari, Sorenson, Bank, & Snyder, 2014). Thus, the present study focuses on development of substance use through executive function deficits and disruptive behavior, while considering the sibling relationships as unique contexts that may mitigate or exacerbate earlier developmental influences on adolescent substance use.

## Disruptive Behavior and Substance Use

Both substance use and disruptive behavior are considered to be situated under an umbrella of behavioral disinhibition (Young et al., 2009). Behavioral disinhibition is defined as a generalized vulnerability to externalizing behavior (behavior including substance use, conduct disorder, attention-deficit/hyperactivity disorder, and novelty seeking; Young et al., 2009). Disruptive behavior includes specifically conduct disorder, oppositional disorder, and attention deficit/hyperactivity disorder (Tolan & Leventhal, 2013). One view of the development of adolescent substance use is that substance use and disruptive behavior are overlapping constructs across development that are both expressions of a latent behavior disinhibition factor. The expression of behavioral disinhibition changes across adolescence, with disruptive behavior waning and substance use waxing over time (Young et al., 2009). When examining these constructs from a developmental perspective, Young and colleagues (2009) found that in early adolescence (12 years of age) attention-deficit/hyperactivity disorder and conduct disorders loaded most strongly onto a latent behavioral disinhibition factor, demonstrating the salience of these behaviors earlier in adolescence. However, later in adolescence (age 17) substance use is loaded most strongly on the latent behavioral disinhibition factor, when substance use behavior becomes more prominent.

Thus, disruptive behavior and substance use are conceptually a part of the larger behavioral disinhibition concept, however, from a developmental perspective, disruptive behavior precedes substance use and is highly predictive earlier in adolescence for later substance use behaviors (e.g., Meyers et al., 2014). This makes disruptive behaviors a key indicator of risk for substance use initiation from a developmental perspective. Indeed, disruptive behavior is one of the strongest predictors of later substance use and considered a risk factor for earlier substance use initiation (Dodge et al., 2009). Cascade models of substance use initiation suggest that adolescents' access to substances increase as they age, likely due in part to disruptive behavior (Trucco et al., 2016). Therefore, in order to understand the development of adolescent substance use, we examine the transition from early adolescent disruptive behavior to later substance use.

***Disruptive behavior as a process through which executive function predicts substance use.*** Executive functions are foundational cognitive processes that are used in service of many outcomes (e.g., academic success, behavioral regulation) and consist of three primary

components: working memory, set-shifting, and inhibition (Garon, Bryson, & Smith, 2008; Miyake, Friedman, Emerson, Witki, Howerter, & Wager, 2000). For example, children with lower executive function are more likely to have poorer physical health, substance dependence, poorer personal finances, and criminal charges later in life (Moffit et al., 2011). Executive function deficits have been associated with increased adolescent disruptive behavior and substance use (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Notably, executive function deficits are related to preadolescents' impulsivity (Cassidy, 2015; Romer et al., 2009) which may translate to poor decision-making and substance use.

Despite evidence that executive function predicts both disruptive behavior and substance use (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Moffit et al., 2011; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014), as well as evidence that disruptive behavior precedes substance use (Dodge et al., 2009), only one study has examined whether disruptive behavior may be a mediator in associations of executive function deficits and substance use. In a sample of adolescent females, decreased executive function was associated with increased substance use, and antisocial behavior fully mediated the association between executive function and substance use at a single time point (age 16; Giancola et al., 2001). These findings suggest that executive function deficits may foster problem behavior (e.g., disruptive behavior) which may lead to greater risk for adolescent substance use, but is limited because it is cross-sectional evidence and only considers girls. Therefore, the current study focuses on examining disruptive behavior as a process through which executive function is related to adolescent substance use longitudinally, including a sample consisting of both males and females.

***Siblings as a context for the development of disruptive behavior and substance use during adolescence.*** During adolescence, siblings are unique socializers of youth, influencing adolescent behaviors including disruptive behaviors and substance use (Fagan & Najman, 2005; Kothari, Sorenson, Bank, & Snyder, 2014). Research into sibling relationships suggests that sibling relationship quality is associated with disruptive behavior and substance use, and findings are often interpreted such that negative sibling relationships and/or siblings acting as facilitators or models of risky behaviors subsequently predicts behavior problems in the co-sibling (Modry-Mandell, Gamble & Taylor, 2006; Rende, Slomkowski, Lloyd-Richardson, & Niaura, 2005;

Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005; Solmeyer, McHale & Crouter, 2014). For example, Jenkins and Dunn (2009) found that siblings are one of the most influential social factors during adolescence, and are influential for the development of disruptive behaviors and substance use during adolescence, above and beyond the parent-child relationship, peer disruptive behavior, and adolescent-peer negative interactions (Defoe et al., 2013). Specifically, research suggests that in adolescence there is a bidirectional, positive association between siblings' disruptive behavior and alcohol use (Whiteman et al., 2017). Together, associations of sibling influence has been explained by hypothesized mechanisms that include observation/modeling, reinforcement, and extensive opportunities for practice (e.g., older siblings providing cigarettes or alcohol and being 'partners in crime'; Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017). Modeling has been shown to increase when siblings have a high social connection. For example, there is increased similarity in sibling tobacco and alcohol use when siblings have a more positive relationship, after controlling for both parent and peer smoking (Rende et al., 2005; Slomkowski et al., 2005). However, siblings with a warmer relationship are less likely to experience adolescent substance use (East & Khoo, 2005). Further, while an adolescent's risk for substance use increases when they have a sibling who uses substances (Whiteman et al., 2013).

In addition to the direct effects of siblings on executive function and behavioral development, sibling relationship quality and characteristics of one's sibling are also likely a key family-level contextual influence on the development of executive function, disruptive behavior, and substance use. For example, siblings with a relationship characterized by greater conflict are differentially impacted by social comparisons, compared to siblings with less conflictual relationships. Further, one perspective on siblings as a training ground suggests that negative sibling relationships facilitate more negative, conflictual, and coercive interactions across relationships throughout development (Natsuaki et al., 200; Patterson, 1984; Patterson et al., 1989). Persistent coercive interactions and behaviors are linked to a lack of self-control (Feinberg, Solmeyer, & McHale, 2011). Hence, negative sibling relationship quality may interact with developmental influences that predict greater risk for youth disruptive behavior and substance use. Finally, Windle (2000) found that having a sibling that used substances may be linked to consuming alcohol when faced with stressful life events and an inclination for negative coping strategies via sibling role modeling or imitation. Thus, sibling substance use may provide

access to substances that would strengthen a youth at risk to initiate substance use (e.g., executive function deficits or increased disruptive behavior).

Taken together, these studies highlight the importance of investigating siblings as a context for the development of both disruptive behaviors and substance use. However, sibling relationships remain the least studied close relationship (McHale, Updegraff & Whiteman, 2012). Thus, the current study examines the role of the sibling relationship quality and whether a sibling uses substances as a context for the executive function-disruptive behavior and executive function-substance use associations.

**Current Study**

The aims of the current study were to examine 1) disruptive behavior as a process through which executive function predicts adolescent substance use longitudinally, and 2) the role of the sibling relationship quality and sibling substance use as a context for the executive function-disruptive behavior and disruptive behavior-substance use associations. As noted above, only one previous study used a cross-sectional design to test the indirect effect of executive function on substance use through a measure of antisocial behavior in sixteen-year-old adolescent females, from the same data used here (Giancola et al., 2001). The current study extended this research by examining both males and females, a measure of disruptive behavior that is broader than antisocial behavior, and longitudinal measurement. It was hypothesized that lower executive function at age 10-12 would be linked to greater rates of disruptive behavior at age 12-14, which in turn will be associated with greater substance use at age 16. Further, there has not been a model that incorporates the sibling relationship as a context that could moderate disruptive behaviors as a mechanism through which executive function is linked to adolescent substance use, despite plausible rationale based on findings that sibling relationships serve as a context for other pathways to substance use risk. It was hypothesized that the paths would be stronger for siblings who have a more negative sibling relationship and a sibling that has reported substance use. The current study utilized a longitudinal design with at-risk youth, which allowed me to examine the developmental pathways or specific, independent influences (if a developmental pathway was not confirmed) associated with adolescent substance use (Figure 11).

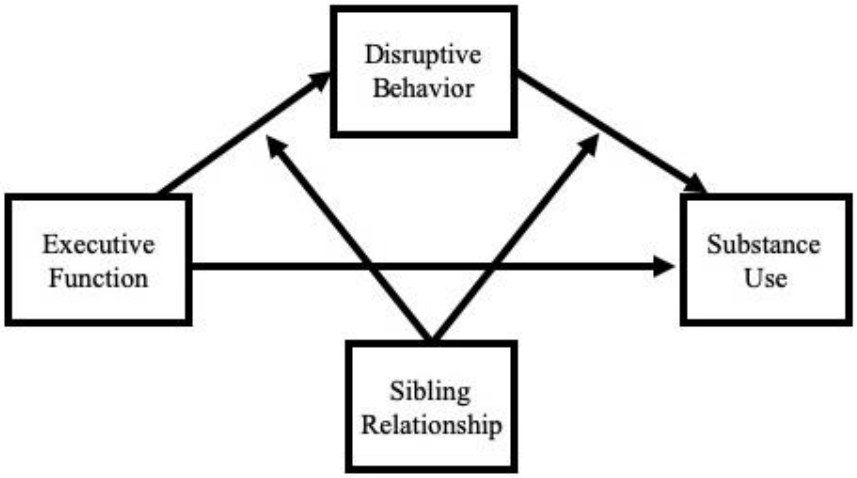



Figure 9. Conceptual model for study three, the link of executive function and substance use through disruptive behavior situated in the context of the sibling relationship.

## Method

### Participants and Procedures

The Center for Education and Drug Abuse Research (CEDAR; Tarter & Vanyukov, 2001) is a sample of 775 families (71% male). The sample consists of biological children of men either diagnosed with a substance use disorder (*n*=344), with a psychiatric disorder that was not substance use (*n*=81), or with no disorders (*n*=350). In the current study, risk groups are operationalized as dichotomous: having risk (i.e., paternal substance use disorder or psychiatric disorder) or no risk (i.e., no paternal disorders). Men were recruited via several mechanisms; random digit telephone dialing, advertisement, and public service announcements (from 1989 to 2009). Of the men recruited, 20% were currently in treatment for substance use disorder. Exclusion criteria for youth included teratogenic affects from maternal reports of exposure to alcohol or drug use during pregnancy, chronic medical or psychiatric illness, having been hospitalized for neurological injury, or having an IQ lower than 80 (Wechsler Intelligence Scale for Children, 3rd ed). Children and their parents were followed longitudinally, starting at age 10-12 (visit 1), 12-14 (visit 2), 16 (visit 3), 19, and annually thereafter until age 30. Data from the first, second and third wave were used in this study. (See Tarter & Vanyukov, 2001 for further details of the overarching study).

## Measures

***Substance use.*** Substance use involvement was measured utilizing a previously constructed score created with item response theory and validated in CEDAR (Marceau, Kirisci, & Tarter, 2019; Kirisci, Vanyukov, Dunn, & Tarter, 2002). Substance use was assessed in adolescents via self-report of type of substance and frequency of use at age 16 (CEDAR, 1989). Ten drug categories were created from 42 psychoactive substances (i.e., alcohol, cannabis, cocaine/crack, opiates, amphetamines, methylphenidate, sedative, tobacco, hallucinogens, PCP and inhalants), similarly to the National Institute of Mental Health Epidemiological Catchment Area Study (Anthony & Helzer, 1991). A dichotomous indicator of use (1 = yes, 0 = no) was used to examine whether youth tried a drug in each of the ten categories, the categories were then used as indicators of a two-parameter logistic item response model indexing a unidimensional model of substance use that was used to estimate latent trait scores. Descriptive statistics for youth substance use can be found in Table 30.

For sibling substance use, siblings of the participant reported on substance type used using the same self-report measure as the target adolescent (CEDAR, 1989). Siblings reported on drug use at visit 1, sibling age ranged from 11 to 30 years of age. We then created a dichotomous variable (0 = no, 1= yes) for any substances reported (no = 241, yes = 119). In some instances, there were multiple siblings reporting on their own substance use in the same family. However, this was not consistent across families as study protocols did not require all siblings to be included only those willing to participate. Thus, when calculating the dichotomous score for sibling substance use, a 1 was given if *any* sibling reported using substances, whereas a 0 was giving if no sibling substance use was reported. In instances that the target adolescent was an only child, data was treated as missing, as we could not be sure whether they had no sibling or no *participating* sibling.

***Disruptive behavior.*** Disruptive behavior was assessed for children age 12-14 using both mother and father reports on the Child Behavior Checklist (Achenbach, 1991). Reporters rated youth on a scale from *0 = not true* to *2 = very true or often true*. Items included in the externalizing score cover hyperactive (e.g., can't concentrate or restless), delinquent (e.g., truant or destroys own things) and aggressive (e.g., argue or teases) behavior. Mothers' and fathers' items were summed to create total scores across behaviors. Mother and father reports were

moderately correlated ($r$ = 0.65) and were averaged to create a single score of youth disruptive behavior. Descriptive statistics for youth disruptive behavior can be found in Table 30.

***Executive function*.** Executive function was measured at age 10-12 using the Go/No-Go (Langenecker et al., 2007). The Go/No-Go task consists of three levels completed according to ascending difficulty, where participants must press a button or withhold button-pressing depending on the stipulations of each level (e.g., press the button every time you see X or Y). This task yields a global executive function score that reliably measures a combination of participants' set-shifting, working memory, and inhibition (e.g., context-based inhibition as well as more complex executive functions; Langenecker et al., 2007). The Go/No-Go task outputs four scores for each participant: 1) bet on a "good" number (correct), 2) bet on a "bad" number (incorrect), 3) failure to respond to a bad number (correct), and 4) failure to respond to a good number (incorrect). Of these scores, betting on a "bad" number (commission error, failure to inhibit response to a known "bad" number) and failing to respond to a good number (omission error) are primarily used in the literature as dependent variables (see Yechiam et al., 2006). The current study utilized commission error as the primary outcome, because it best captures executive function from across both simple and complex components of executive function. Descriptive statistics for youth executive function can be found in Table 30.

***Sibling relationship quality*.** Sibling relationship quality was measured at age 12-14 via adolescent report of dyadic relationships with their mother, father, and sibling (Furman & Buhrmester, 1985). Adolescents were told to report on the sibling that was most important to them on a scale from 1 (little or none) to 5 (the most) for questions that pertained to the dyad's companionship, conflict, satisfaction, antagonism, intimacy, nurturance, affection, admiration, relative power and reliable alliance. The subscale items for companionship, satisfaction, intimacy, nurturance, affection, and admiration were positively correlated ($r$ = 0.42 to 0.71) and were summed to create a composite sibling relationship positivity score (Chronbach's $\alpha$ = .89). The subscale items for conflict and antagonism were positively correlated ($r$ = 0.11 to 0.81) and were summed to create a composite sibling relationship negativity score (Chronbach's $\alpha$ = .65). Composite scores for both sibling relationship positivity and negativity were coded so that a higher composite score indicates a more positive or negative sibling relationship (as two separate scores). Adolescent reports of parent-child relationship assessed on the same measure but referring to the parent-child relationship was used as a covariate to account for the overall home

environment. Descriptive statistics for sibling relationship quality variables (i.e., positive and negative sibling relationships) can be found in Table 30.

***Covariates*.** Age, sex, socioeconomic status, and risk/control group membership were included as covariates. Further, disruptive behavior and substance use at age 10-12 was included as a covariate in analyses to ensure that analyses are testing development (e.g., residualized change in youths' disruptive and substance use behavior). Additionally, measures of the adolescent reported parent-child relationship were used as a covariate to assess the contribution of the sibling relationship beyond the overall home environment, given that sibling relationships are related to the quality of other relationships (e.g., parent-child) within the home (Blackson et al., 1999). Descriptive statistics for study covariate variables can be found in Table 30.

## Analytic Strategy

***Hypothesis testing***. In order to test the hypothesis that there would be in indirect effect such that earlier executive function is linked to lower disruptive behavior two years later, which is subsequently associated with later substance use, a series of structural equation models (SEM; Figure 6) were fit in Mplus. Separate models were conducted that included main effects of sibling positivity (Model 1, base), negativity (Model 2, base), and siblings' own substance use (Model 3, base). Then, additional models were fit in Mplus to test the hypothesized moderation effects for the pathways from executive function to disruptive behavior, as well as from disruptive behavior to substance use by sibling positivity (Model 1, moderated mediation), negativity (Model 2, moderated mediation), and sibling's own substance use (Model 3, moderated mediation). Finally, a SEM was fit in Mplus to examine risk group as a potential moderator of the mediation analysis to examine whether the mediation pathways differed based on level of risk. We utilized a Bayesian estimator, given that literature on moderated mediation analyses suggests that this method yields less biased estimates and higher power than maximum likelihood methods with and without bootstrapping by calculating the posterior probability density distribution of the parameters (credibility intervals; Wang & Preacher, 2013). For the current study, an association is established when zero is not included within the 95% credibility interval values; meaning that the unobserved true effect has a 95% chance of falling somewhere within the range of the credibility interval. Missing data was missing not at random (MNAR). Thus, Full Information Maximum Likelihood (FIML) was used, because while still biased, FIML

is less so and more robust than listwise deletion, as FIML utilizes all available information from the model (including covariates associated with missingness) to specify a maximum likelihood estimation (Acock, 2005). See Appendix C for results of tests for data missingness and description of the pattern of missingness.

## Results

Correlations suggest that baseline (10-12 years-old) substance use was positively correlated with parent-child relationship quality (better relationship quality), increased baseline disruptive behavior, increased disruptive behavior at age 12-14, as well as increased substance use at age 16. Further, baseline disruptive behavior was positively correlated with better parent-child relationship quality, increased baseline substance use, increased disruptive behavior at age 12-14, and greater substance use at age 16. Baseline disruptive behavior was negatively correlated with lower socioeconomic status, poorer parent-child relationship quality, and less sibling positivity. Executive function was negatively correlated with lower socioeconomic status, and positively correlated with greater disruptive behavior at age 12-14. Disruptive behavior at age 12-14 was negatively correlated with lower socioeconomic status and less positive sibling relationship quality. Disruptive behavior at age 12-14 was positively correlated with greater parent-child relationship quality, more negative sibling relationship quality, and greater substance use at age 16. Finally, substance use at age 16 was negatively correlated with less positive sibling relationship quality. Substance use at age 16 was positively correlated with being older and better parent-child relationship quality. See Table 31 for full correlation results, including demographic covariates.

Table 29. Descriptive statistics of study three key variables.

| | N | Minimum-Maximum | Mean | Std. Deviation | Skewness | Kurtosis |
|---|---|---|---|---|---|---|
| Age | 653 | 11.29-15.66 | 13.47 | 0.96 | 0.02 | -1.02 |
| Maternal Socioeconomic Status | 459 | 9-66 | 40.39 | 13.04 | 0.09 | -0.79 |
| Parent-Child Relationship Quality | 275 | 42-128 | 81.78 | 16.49 | -0.37 | -0.23 |
| Baseline Disruptive Behavior | 739 | 0-50 | 8.86 | 9.10 | 1.68 | 3.28 |
| Baseline Substance Use | 770 | 0-13 | 0.14 | 0.92 | 8.63 | 89.68 |
| Executive Function (10-12 years-old) | 622 | 1-40 | 17.26 | 6.18 | 0.06 | 0.10 |
| Disruptive Behavior (12-14 years-old) | 532 | 0-51 | 2.78 | 1.35 | 0.38 | -0.17 |
| Positive Sibling Relationship Quality | 609 | 21-105 | 73.34 | 18.41 | -0.79 | 0.29 |
| Negative Sibling Relationship Quality | 609 | 9-45 | 22.62 | 7.23 | 0.09 | -0.55 |
| Substance Use (age 16) | 623 | -0.44-9.75 | 0.00 | 1.00 | 6.23 | 46.56 |

| | **Male** | **Female** |
|---|---|---|
| Sex | 509 | 202 |
| | **Yes** | **No** |
| Sibling Substance Use | 119 | 241 |
| | **Other** | **White** |
| Maternal Race | 119 | 340 |

Note. Baseline measurements were taken at age 10-12. Target youths' reports on sibling relationship quality were gathered at age 12-14.

Table 30. Correlations of key study three constructs.

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. Socioeconomic Status | -- | | | | | | | | | |
| 2. Age | .04 | -- | | | | | | | | |
| 3. Parent-Child Relationship Quality | -.15 | .06 | -- | | | | | | | |
| 4. Baseline Substance Use (Age 10-12) | .02 | .08 | .12* | -- | | | | | | |
| 5. Baseline Disruptive Behavior (Age 10-12) | -.12** | -.08 | .29** | .12** | -- | | | | | |
| 6. Positive Sibling Relationship (Age 12-14) | -.03 | -.02 | -.28** | .00 | -.13** | -- | | | | |
| 7. Negative Sibling Relationship (Age 12-14) | .10* | .06 | .15* | .04 | .01 | -.08* | -- | | | |
| 8. Executive Function (Age 10-12) | -.15** | -.04 | .03 | -.04 | .06 | .01 | .01 | -- | | |
| 9. Disruptive Behavior (Age 12-14) | -.18** | -.09 | .30** | .20** | .70** | -.12** | .10* | .10* | -- | |
| 10. Substance Use (Age 16) | -.07 | .10* | .14* | .27** | .12** | -.11** | .03 | -.08 | .15** | -- |

Note. *p < .05, **p<.01, ***p<.001. To see correlations by risk group, see Appendix C.

**Model 1 (Positive Sibling Relationship Quality as Moderator)**

In the base model, with mediation pathways but no interactions, there was no evidence of mediation from executive function at age 10-12 years-old to substance use at 16 years of age through disruptive behavior at 12-14 years-old. However, higher executive function at age 10-12 (*b* = 0.10, 95% credibility interval = 0.015 – 0.184, *SD* = 0.04), more substance use at age 10-12 (*b* = 0.72, 95% credibility interval = 0.221 – 1.234, *SD* = 0.26), and more disruptive behavior at 10-12 (*b* = 0.68, 95% credibility interval = 0.610 – 0.738, *SD* = 0.03) predicted increased disruptive behavior at age 12-14. Further, older age (*b* = 0.09, 95% credibility interval = 0.005 – 0.167, *SD* = 0.04) and more substance use at age 10-12 (*b* = 0.24, 95% credibility interval = 0.161 – 0.319, *SD* = 0.04) predicted increased substance use at age 16.

In the mediated moderation model, these effects persisted. Contrary to hypotheses, there was no interaction between executive function and positive sibling relationship quality (*b* = -0.00, 95% credibility interval = -0.005 – 0.003, *SD* = 0.00) nor disruptive behavior and positive sibling relationship quality (*b* = 0.00, 95% credibility interval = -0.001 – 0.000, *SD* = 0.00). Our hypothesis of moderated mediation was not supported. A loop plot of showed that zero remained within the credibility intervals across all levels of positive sibling relationship quality (see plot of moderated mediation model, Figure 12). For full results see Table 32 and Figure 13.

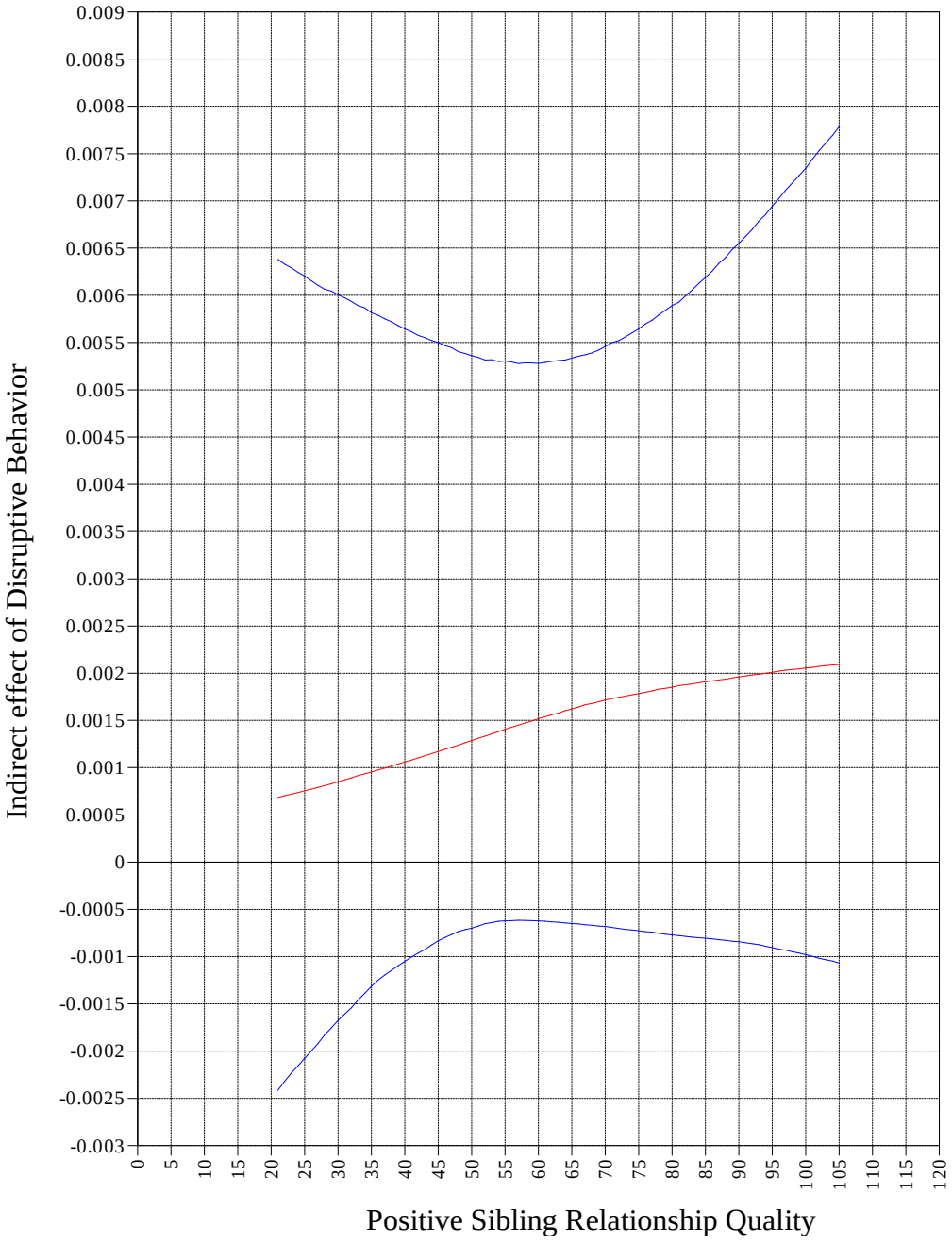



Figure 10. Loop plot of study three moderated mediation model one.

Note. The y-axis represents the indirect effect of executive function on substance use through disruptive behavior. The x-axis represents the effect of the moderator, positive sibling relationship quality. Blue lines indicate the credibility intervals and the red line indicates the estimate of the indirect effect

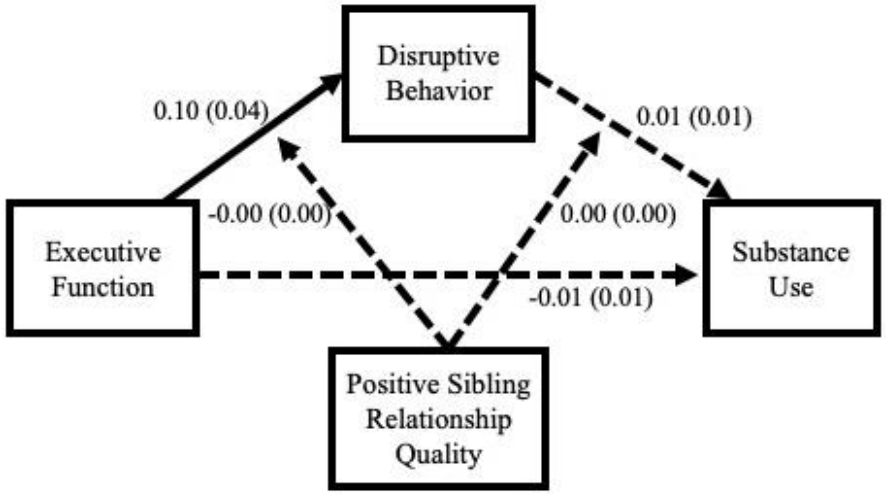



Figure 11. Study three mediation model.

Note. Dashed lines indicate zero falls within the credibility interval.

Table 31. Full results of study 3, model 1 (positive sibling relationship quality).

| | Base Mediation Model | | | Moderated Mediation Model | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SD** | **Credibility Interval** | **Estimate** | **SD** | **Credibility Interval** |
| **Disruptive Behavior (intercept)** | 2.91 | 1.42 | 0.134 – 5.692 | 2.16 | 0.83 | 0.536 – 3.7716 |
| Baseline Disruptive Behavior | 0.68 * | 0.03 | 0.610 – 0.738 | 0.68* | 0.03 | 0.619 – 0.746 |
| Baseline Substance Use | 0.72* | 0.26 | 0.221 – 1.234 | 0.71* | 0.26 | 0.200 – 1.217 |
| Executive Function | 0.10* | 0.04 | 0.015 – 0.184 | 0.10* | 0.04 | 0.014 – 0.186 |
| Positive Sib. Rel. Qual. | -0.01 | 0.02 | -0.041 – 0.020 | 0.01 | 0.04 | -0.061 – 0.084 |
| EF*Positive | -- | -- | -- | -0.00 | 0.00 | -0.005 – 0.003 |
| **Substance Use (intercept)** | -0.82 | 0.75 | -2.276 – 0.656 | -1.24 | 0.74 | -2.705 – 0.219 |
| Disruptive Behavior | 0.01 | 0.01 | -0.003 – 0.025 | 0.01 | 0.01 | -0.004 – 0.026 |
| Sex | 0.11 | 0.09 | -0.065 – 0.282 | 0.11 | 0.09 | -0.072 – 0.292 |
| Maternal SES | -0.00 | 0.00 | -0.011 – 0.003 | -0.01 | 0.00 | -0.012 – 0.002 |
| Age | 0.09* | 0.04 | 0.005 – 0.167 | 0.09* | 0.04 | 0.007 – 0.178 |
| Risk Group | 0.07 | 0.08 | -0.088 – 0.011 | 0.06 | 0.09 | -0.106 – 0.233 |
| Baseline Disruptive Behavior | -0.00 | 0.01 | -0.013 – 0.012 | -0.00 | 0.01 | -0.014 – 0.012 |
| Parent-Child Rel. Qual. | 0.00 | 0.01 | -0.008 – 0.011 | 0.00 | 0.01 | -0.008 – 0.012 |
| Baseline Substance Use | 0.24* | 0.04 | 0.161 – 0.319 | 0.24* | 0.04 | 0.164 – 0.324 |
| Executive Function | -0.01 | 0.01 | -0.026 – 0.000 | -0.01 | 0.01 | -0.027 – 0.000 |
| Positive Sib. Rel. Qual. | -0.01 | 0.00 | -0.013 – 0.012 | -0.00 | 0.00 | -0.008 – 0.003 |
| Disruptive Behavior*Pos Sib. Rel. Qual. | -- | -- | -- | 0.00 | 0.00 | -0.001 – 0.00 |

Note. Sib. Rel. Qual. = sibling relationship quality; EF = executive function; Rel. Qual. = relationship quality; SES = socioeconomic status. Baseline items were measured at age 10-12, disruptive behavior at age 12-14, and substance use at age 16. An association is indicated when zero is not included within the credibility interval values and marked with *.

**Model 2 (Negative Sibling Relationship Quality as Moderator)**

In the base model, with mediation pathways but no interactions, there was no evidence of mediation from executive function at age 10-12 years-old to substance use at 16 years of age through disruptive behavior at 12-14 years-old. The main effects were largely consistent with model 1:, higher executive function at age 10-12 (*b* = 0.09, 95% credibility interval = 0.009 – 0.178, *SD* = 0.04), more substance use at age 10-12 (*b* = 0.70, 95% credibility interval = 0.199 – 1.208, *SD* = 0.26), and more disruptive behavior at 10-12 (*b* = 0.68, 95% credibility interval = 0.612 – 0.738, *SD* = 0.03) predicted increased disruptive behavior at age 12-14. Older age (*b* = 0.09, 95% credibility interval = 0.004 – 0.167, *SD* = 0.04) and more substance use at age 10-12 (*b* = 0.24, 95% credibility interval = 0.157 – 0.315, *SD* = 0.04) predicted increased substance use at age 16. Further, more negative sibling relationship quality at age 12-14 (*b* = 0.08, 95% credibility interval = 0.008 – 0.158, *SD* = 0.04) predicted greater disruptive behavior at age 12-14 years-old.

In the full mediated moderation model, these effects persisted. Contrary to hypotheses, there were not interactions between executive function and negative sibling relationship quality (*b* = 0.00, 95% credibility interval = -0.012 – 0.012, *SD* = 0.01) nor disruptive behavior and negative sibling relationship quality (*b* = 0.00, 95% credibility interval = -0.002 – 0.001, *SD* = 0.00). Similar to model 1, our hypothesis of moderated mediation was not supported, as zero remained within the credibility intervals across all levels of negative sibling relationship quality (see plot of moderated mediation model, Figure 14). For full results see Table 33 and Figure 15.

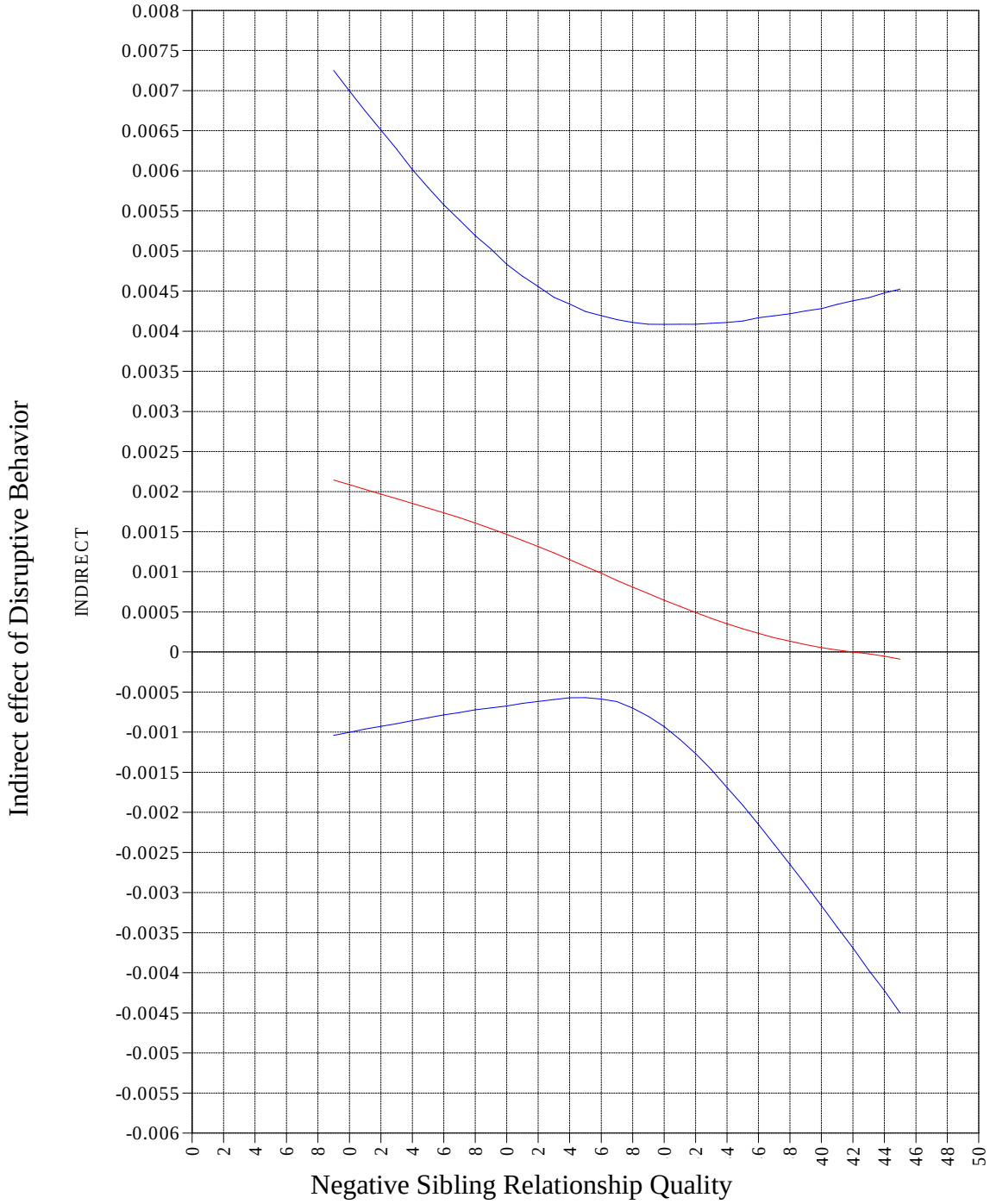



Figure 12. Loop plot of study three, model 2.

Note. The y-axis represents the indirect effect of executive function on substance use through disruptive behavior. The x-axis represents the effect of the moderator, negative sibling relationship quality. Blue lines indicate the confidence intervals and the red line indicates the estimate of the indirect effect.

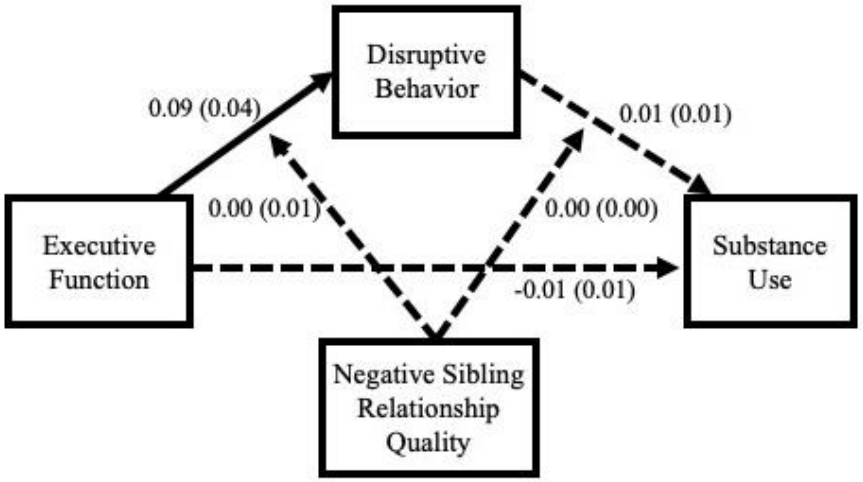



Figure 13. Full results of study 3, model 2 (negative sibling relationship quality).

Note. Dashed lines indicate zero falls within the credibility interval

Table 32. Full results of study three, model 2 (negative sibling relationship quality).

| | Base Mediation Model | | | Moderated Mediation Model | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SD** | **Credibility Interval** | **Estimate** | **SD** | **Credibility Interval** |
| **Disruptive Behavior (intercept)** | 0.41 | 1.14 | -1.793 – 2.647 | 3.91* | 0.37 | 3.176 – 4.645 |
| Baseline Disruptive Behavior | 0.68* | 0.03 | 0.612 – 0.738 | 0.68* | 0.03 | 0.620 – 0.746 |
| Baseline Substance Use | 0.70* | 0.26 | 0.199 – 1.208 | 0.68* | 0.26 | 0.176 – 1.189 |
| Executive Function | 0.09* | 0.04 | 0.009 – 0.178 | 0.09* | 0.04 | 0.006 – 0.178 |
| Negative Sib. Rel. Qual. | 0.08* | 0.04 | 0.008 – 0.158 | 0.09* | 0.04 | 0.013 – 0.165 |
| EF*Negative | -- | -- | -- | 0.00 | 0.01 | -0.012 – 0.012 |
| **Substance Use (intercept)** | -1.38 | 0.71 | -2.758 – 0.034 | -1.64* | 0.73 | -3.082 – -0.203 |
| Disruptive Behavior | 0.01 | 0.01 | -0.003 – 0.026 | 0.01 | 0.01 | -0.003 – 0.027 |
| Sex | 0.14 | 0.09 | -0.032 – 0.312 | 0.15 | 0.09 | -0.034 – 0.325 |
| Maternal SES | -0.00 | 0.00 | -0.011 – 0.003 | -0.00 | 0.00 | -0.012 – 0.003 |
| Age | 0.09* | 0.04 | 0.004 – 0.167 | 0.09* | 0.04 | 0.007 – 0.179 |
| Risk Group | 0.08 | 0.08 | -0.085 – 0.239 | 0.08 | 0.09 | -0.095 – 0.245 |
| Baseline Disruptive Behavior | 0.00 | 0.01 | -0.013 – 0.013 | 0.00 | 0.01 | -0.014 – 0.014 |
| Parent-Child Rel. Qual. | 0.00 | 0.01 | -0.006 – 0.013 | 0.00 | 0.01 | -0.007 – 0.013 |
| Baseline Substance Use | 0.24* | 0.04 | 0.157 – 0.315 | 0.23* | 0.04 | 0.154 – 0.315 |
| Executive Function | -0.01 | 0.01 | -0.026 – 0.000 | -0.01 | 0.01 | -0.027 – 0.000 |
| Negative Sib. Rel. Qual. | 0.00 | 0.01 | -0.013 – 0.013 | 0.01 | 0.01 | -0.009 – 0.018 |
| Disruptive Behavior*Neg Sib. Rel. Qual. | -- | -- | -- | 0.00 | 0.00 | -0.002 – 0.001 |

Note. Neg Sib. Rel. Qual. = negative sibling relationship quality; EF = executive function; Rel. Qual. = relationship quality; SES = socioeconomic status. Baseline items were measured at age 10-12, disruptive behavior at age 12-14, and substance use at age 16. An association is indicated when zero is not included within the credibility interval values, and marked with *

**Model 3 (Sibling Substance Use as Moderator)**

Results from the base model were entirely consistent with models 1 and 2: there was no evidence of mediation from executive function at age 10-12 years-old to substance use at 16 years of age through disruptive behavior at 12-14 years-old. However, higher executive function at age 10-12 ($b$ = 0.10, 95% credibility interval = 0.018 – 0.188, $SD$ = 0.04), more substance use at age 10-12 ($b$ = 0.72, 95% credibility interval = 0.206 – 1.224, $SD$ = 0.26), and more disruptive behavior at 10-12 ($b$ = 0.68, 95% credibility interval = 0.615 – 0.742, $SD$ = 0.03) predicted increased disruptive behavior at age 12-14. Further, older age ($b$ = 0.09, 95% credibility interval = 0.005 – 0.168, $SD$ = 0.04) and more substance use at age 10-12 ($b$ = 0.24, 95% credibility interval = 0.157 – 0.315, $SD$ = 0.04) predicted increased substance use at age 16.

In the full mediated moderation model, these effects were unchanged. Contrary to hypotheses, there were not interactions between executive function and siblings' own substance use ($b$ = 0.04, 95% credibility interval = -0.178 – 0.257, $SD$ = 0.11) nor disruptive behavior and siblings' own substance use ($b$ = -0.01, 95% credibility interval = -0.040 – 0.014, $SD$ = 0.01). Our hypothesis of moderated mediation was not supported, as zero remained within the credibility intervals across levels of sibling substance use (see plot of moderated mediation model, Figure 16). For full results see Table 34 and Figure 17.

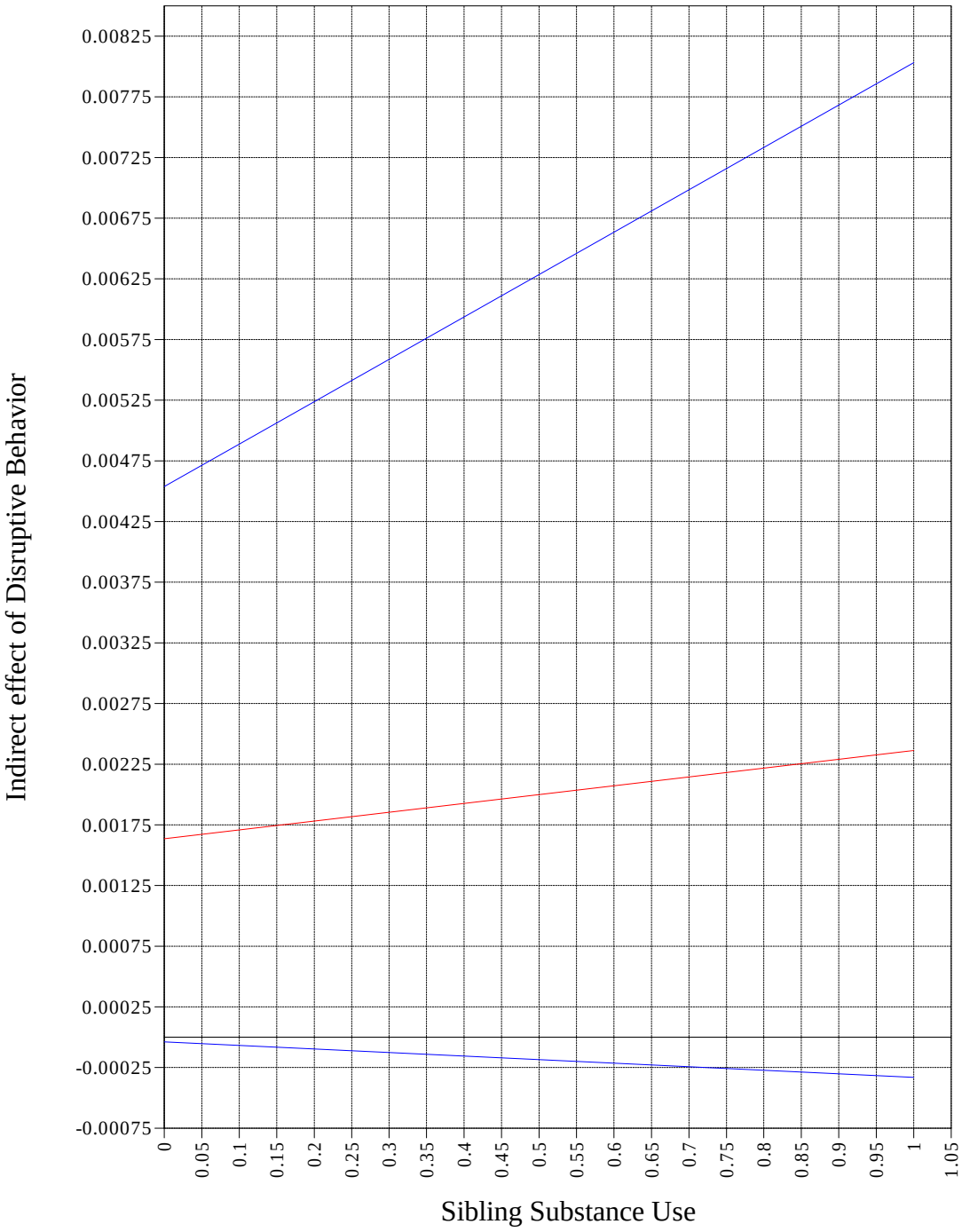



Figure 14. Loop plot of study three, model 3 moderated mediation model.

Note. The y-axis represents the indirect effect of executive function on substance use through disruptive behavior. The x-axis represents the effect of the moderator, sibling substance use. Blue lines indicate the confidence intervals and the red line indicates the estimate of the indirect effect.

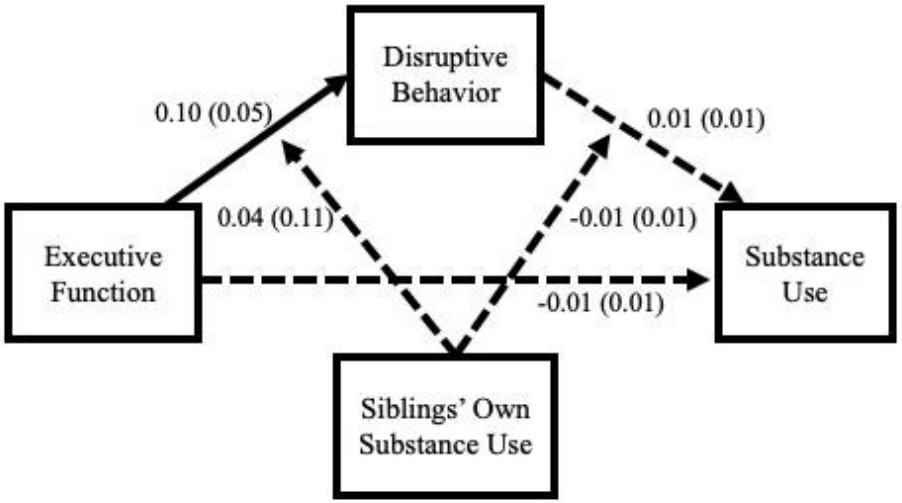



Figure 15. Full model for study three, model 3 moderated mediation.

Note. Dashed lines indicate zero falls within the credibility interval.

Table 33. Full results for study three, model three (sibling substance use).

| | Base Mediation Model | | | Moderated Mediation Model | | |
|---|---|---|---|---|---|---|
| | **Estimate** | **SD** | **Credibility Interval** | **Estimate** | **SD** | **Credibility Interval** |
| **Disruptive Behavior (intercept)** | 1.75* | 0.89 | 0.026 – 3.499 | 3.55* | 0.47 | 2.643 – 4.484 |
| Baseline Disruptive Behavior | 0.68* | 0.03 | 0.615 – 0.742 | 0.68* | 0.03 | 0.615 – 0.743 |
| Baseline Substance Use | 0.72* | 0.26 | 0.206 – 1.224 | 0.72* | 0.26 | 0.218 – 1.218 |
| Executive Function | 0.10* | 0.04 | 0.018 – 0.188 | 0.10* | 0.05 | 0.009 – 0.186 |
| Sibling Substance Use | 0.91 | 0.78 | -0.627 – 2.435 | 0.88 | 0.78 | -0.645 – 2.389 |
| EF*Sibling Substance Use | -- | -- | -- | 0.04 | 0.11 | -0.178 – 0.257 |
| **Substance Use (intercept)** | -1.35 | 0.71 | -2.730 – 0.053 | -1.58* | 0.70 | -2.946 – -0.204 |
| Disruptive Behavior | 0.01 | 0.01 | -0.003 – 0.026 | 0.01 | 0.01 | -0.001 – 0.029 |
| Sex | 0.14 | 0.09 | -0.032 – 0.310 | 0.14 | 0.09 | -0.031 – 0.311 |
| Maternal SES | -0.00 | 0.00 | -0.011 – 0.003 | -0.00 | 0.00 | -0.011 – 0.003 |
| Age | 0.09* | 0.04 | 0.005 – 0.168 | 0.09* | 0.04 | 0.005 – 0.169 |
| Risk Group | 0.08 | 0.08 | -0.086 – 0.238 | 0.08 | 0.08 | -0.086 – 0.234 |
| Baseline Disruptive Behavior | 0.00 | 0.01 | -0.013 – 0.013 | -0.00 | 0.01 | -0.026 – 0.001 |
| Parent-Child Rel. Qual. | 0.00 | 0.01 | -0.006 – 0.013 | 0.00 | 0.01 | -0.006 – 0.013 |
| Baseline Substance Use | 0.24* | 0.04 | 0.157 – 0.315 | 0.23* | 0.04 | 0.152 – 0.311 |
| Executive Function | -0.01 | 0.01 | -0.026 – 0.000 | -0.01 | 0.01 | -0.026 – 0.001 |
| Sibling Substance Use | -0.01 | 0.15 | -0.289 – 0.277 | 0.12 | 0.19 | -0.264 – 0.467 |
| Disruptive Behavior*Sibling Substance Use | -- | -- | -- | -0.01 | 0.01 | -0.040 – 0.014 |

Note. Baseline items were measured at age 10-12, disruptive behavior at age 12-14, and substance use at age 16. An association is indicated when zero is not included within the credibility interval values and marked with *.

**Sensitivity Analyses (Group Membership)**

Risk group membership was included in models 1-3 as a covariate. To examine whether the mediation pathway differed for those youth with fathers with substance use disorders or psychiatric disorders vs. control, we ran an additional model including group risk as a moderator (in place of sibling relationship quality/substance use; 1 = father with substance use disorder or psychiatric disorder, 0 = control group with no paternal diagnoses). Notably, group membership was not a significant predictor in Models 1-3 (see Tables 10-12). Further, greater risk did not interact with executive function ($b$ = 0.07, 95% credibility interval = -0.093 – 0.235, $SD$ = 0.08), or disruptive behavior ($b$ = -0.01, 95% credibility interval = -0.024 – 0.005, $SD$ = 0.01) in the mediation model. These findings suggest that for the current study, our findings for the mediation pathway from last childhood executive function to substance use at age 16 through disruptive behavior at age 12-14 did not differ by risk.

***Sex differences*.** To test whether the pathways from executive function to disruptive behavior and disruptive behavior to substance use differed for males and females, we examined a moderated mediation model, such that the paths from executive function to substance use through disruptive behavior would be moderated by sex. The pathways from executive function to substance use through disruptive behavior did not differ by sex (See Table 35).

Table 34. Results for sex differences.

| | Moderated Mediation Model | | |
|---|---|---|---|
| | **Estimate** | **SD** | **Credibility Interval** |
| **Disruptive Behavior (intercept)** | 3.03 | 0.57 | 1.916 – 4.166 |
| Baseline Disruptive Behavior | 0.68 | 0.03 | 0.612 – 0.740 |
| Baseline Substance Use | 0.69 | 0.26 | 0.179 – 1.195 |
| Executive Function | 0.10 | 0.08 | -0.048 – 0.258 |
| Sex | 1.23 | 0.63 | -0.015 – 2.458 |
| EF*Sex | -0.01 | 0.09 | -0.187 – 0.174 |
| **Substance Use (intercept)** | -1.65 | 0.73 | -3.065 – -0.197 |
| Disruptive Behavior | 0.02 | 0.01 | -0.002 – 0.035 |
| Sex | 0.18 | 0.10 | -0.026 – 0.375 |
| Maternal SES | -0.00 | 0.00 | -0.012 – 0.003 |
| Age | 0.09 | 0.04 | 0.005 – 0.176 |
| Risk Group | 0.07 | 0.09 | -0.095 – 0.240 |
| Baseline Disruptive Behavior | 0.00 | 0.01 | -0.027 – 0.000 |
| Parent-Child Rel. Qual. | 0.00 | 0.01 | -0.006 – 0.013 |
| Baseline Substance Use | 0.24 | 0.04 | 0.155 – 0.317 |
| Executive Function | -0.01 | 0.01 | -0.027 – 0.000 |
| Disruptive Behavior*Sex | -0.01 | 0.01 | -0.022 – 0.009 |

Note. EF = executive function.

## Discussion

There is limited research on disruptive behavior as a process through which executive function is linked to adolescent substance use. The current study extended this research by examining both males and females, a measure of disruptive behavior that is broader than antisocial behavior and utilized longitudinal data. Further, given the importance of siblings on development (Dunn, 1983; East & Khoo, 2005; Whiteman et al., 2013), the current study examined siblings as a context for associations between executive function, disruptive behavior, and adolescent substance use. Here, utilizing a longitudinal design with at-risk youth, we did not find an indirect effect of late childhood executive function on adolescent substance use through early adolescent disruptive behavior. However, executive function was linked to increased disruptive behavior two years later, but not to concurrent or later substance use. Further, more negative sibling relationship quality was linked to greater disruptive behaviors, however, no other sibling characteristic was associated with disruptive behavior or substance use in the final models. Finally, contrary to hypotheses, there was no evidence of interactions between sibling relationship qualities or behavior with executive function or disruptive behavior.

### Disruptive Behavior as a Process Through Which Executive Function Predicts Substance Use

The main purpose of the current study was to examine whether executive function deficits foster disruptive behavior which in turn lead to greater risk for adolescent substance use. However, in the current study, although executive function predicted disruptive behavior, disruptive behavior did not predict substance use after accounting for stability in both phenotypes, and there was no evidence of an executive function-substance use association. Importantly, the zero-order correlations suggested that more disruptive behavior at age 12-14 was linked to greater rates of substance use at age 16, but when covariates and the stability of each problem type (i.e., disruptive behavior and substance use at baseline, age 10-12) were entered in the model, the association was entirely attenuated. This suggests that previous associations between disruptive behavior and substance use may have been misattributed to stability in problem behaviors across time or directionality of associations, and that this link is likely not causal, at least during adolescence. Indeed, earlier substance use predicted later increased disruptive behavior during mid-adolescence in this sample. The zero-order correlations

in Appendix C (correlation tables that differ by risk group) suggest that the risk group drove the association between baseline substance use and disruptive behavior at age 12-14. Thus, the developmental cascade may differ for children at risk based on familial history and levels of early substance use. In other words, the current study challenges the conventional developmental cascade model of disruptive behavior to substance use and suggests that more work is needed to understand the directionality of associations between disruptive behavior and substance use across childhood and adolescence.

There was no evidence of mediation from executive function to substance use through disruptive behavior. There was no link between executive function and later substance use. There is work that has examined the longitudinal link between executive function and later externalizing behavior (e.g., conduct problems; Sulik, Blair, Mils-Koonce, Berry, & Greenberg, 2015) and, in the current study, we found that executive function predicted disruptive behavior. However, developmental studies of executive function and externalizing-type behaviors are primarily in early childhood and do not include substance use. To our knowledge, there is scant work that assesses a developmental association from earlier executive function to later substance use, specifically. In the few longitudinal studies examining adolescent executive function predicting early adult substance use, there was not an executive function-substance use association (e.g., Gale, Deary, Boyle, Barefoot, Mortensen, & Batty, 2008; Wilens et al., 2011), consistent with the current findings. Other findings suggest it may not be executive function that predicts later substance use, but instead substance use predicting worsening levels of executive functioning (Medina, Hanson, Schweinsburg, Cohen-Zion, Nagel, & Tapert, 2007; Schweinsburg, Brown, & Tapert, 2008), although in these studies only a single direction of effect was tested. Thus, future researchers should seek to disentangle whether executive function and substance use are a bidirectional association across development or clarify whether executive function predicts substance use or vice versa.

Interestingly, greater executive function was linked to *increased* disruptive behavior two years later. This positive executive function-disruptive behavior association contradicts previous literature that suggests executive function deficits contribute to greater rates of disruptive behavior (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). By design the current study recruited half the sample to be at familial risk of substance use. This

sample of youth are at greater risk for psychopathology, including executive function deficits and increased substance use disorder, as children of parents with substance use disorders (e.g., Clark, Moss, Kirisci, Mezzich, Miles, & Ott, 1997; Hill & Muka, 1996; Schuckit & Smith, 1996; Sher, Walitzer, Wood, & Brent, 1991; Tarter et al., 1999). One possibility could be that in this specific sample, youths' "increased" executive function is not necessarily the same as it would be in a population-based study. That is, if the sample as a whole has lower executive function skills than the population at large, 'higher' executive function in this sample could be an equivalent level as 'lower' executive function in better-off samples (which are commonly used for this type of work). If true, the findings may be specific to youth with greater risk for decreased executive function and increased disruptive behavior and not generalizable to the general population. Comparisons in average levels across samples is problematic because of differences in task type, age of the sample, or sample size, so we were not able to determine whether this is likely to be true. However, comparisons of the mean levels of executive function in the risk versus control group in this sample do not show the differences needed to support this explanation.

Alternatively, because we had sufficient risk for substance use and disruptive behavior in this sample, findings could be picking up an alternative path to externalizing problems such that in youth at familial (including genetic) risk for substance use problems, having higher executive function may enable the youth to better plan and execute their delinquent tendencies. For example, research suggests that in some individuals, highly rewarding circumstances may override top-down executive function (Hughes, 2011). Specifically, during peer engagement, executive function may interact with bottom-up motivation and emotion around risk/reward circumstances, leading to greater disruptive behaviors. In other words, literature suggests that it is important to not only understand youths' level of executive functioning but also how likely youth are to avoid risk and how they respond to rewards or peer influence. For example, youth with increased executive function, but does not avoid risk, is driven by rewards, and is easily influenced by peers, may experience increased disruptive behavior. Although an imperfect test, based on this explanation we would expect that there would be an interaction between executive function and risk group for disruptive behavior, such that this pathway was stronger or only existed in the risk group. However, we did not find evidence of risk group moderating the association of executive function and disruptive behavior in this sample. Future work is needed

to explore if this positive executive function-disruptive behavior association is unique to this sample and what may be driving this association.

### Siblings as a Context for the Development of Disruptive Behavior and Substance Use During Adolescence

Contrary to previous work (Modry-Mandell, Gamble & Taylor, 2006; Rende, Slomkowski, Lloyd-Richardson, & Niaura, 2005; Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005; Solmeyer, McHale & Crouter, 2014; Whiteman et al., 2017), there was only a significant main effect of negative sibling relationship quality with disruptive behavior, such that more negative sibling relationships were linked to greater disruptive behavior. Positive sibling relationship quality and sibling substance use did not predict disruptive behavior or substance use. There are many factors that contribute to the influence of siblings on youth substance use. For example, observation/modeling, reinforcement, and extensive opportunities for practice (e.g., older siblings providing cigarettes or alcohol and being 'partners in crime'; Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017) depend on qualities of the sibling relationship. Modeling has been shown to increase when siblings have a high social connection or when siblings are more similar (Rende et al., 2005; Slomkowski et al., 2005). Thus, it may be that only in certain circumstances do siblings influence youth substance use. While this study did not have the ability to do-so (i.e., statistical power and low numbers of participants in sub-groups), future work should consider examining sibling relationship quality along with sibling substance use. When siblings have a more positive sibling relationship, sibling modeling increases and there is increased similarity in sibling tobacco and alcohol use (Rende et al., 2005; Slomkowski et al., 2005). Thus, when examining siblings as a context in the development of substance use, future work should consider including a three-way interaction between sibling relationship quality and sibling substance use or utilizing a latent profile analysis to classify characteristics of sibling relationships (e.g., a subgroup with youth that have siblings who use substances and that also have a close, positive relationship). Also, measures of sibling similarities should be considered, such as sibling sex-constellation and age-spacing.

## Limitations

While the current study includes data from a longitudinal study designed to examine substance use, the findings should be considered in light of several limitations. First, there is a lack of sibling reports on substance use. CEDAR is not a genetically-informed design, however, it is an at-risk longitudinal sample that offers a more robust test for problem behaviors such as disruptive behaviors and substance use during adolescence. Parents with a substance use disorder likely provide genetic risk for substance use and poorer functioning to their children, and siblings experience the same familial risk and via modeling likely compound risk for the development of substance use. In CEDAR there is limited ability to examine group differences where one group has a higher chance of familial confounding for substance use outcomes (i.e., group where fathers was diagnosed with substance us disorder) compared to others (i.e., groups recruited where fathers had a psychiatric disorder not related to substance use, or fathers had no disorders). By including group membership and family-level measured covariates, analyses can only begin to test for familial confounding. Notably, only 288 siblings were willing to participate (53% of the sample's siblings), thus, the results may be biased due to a lack of information. Importantly, it was not systematic which sibling was chosen to participate in the study or how many siblings participated. Previous literature examines or controls for sibling influences that are connected to the importance or magnitude of sibling influence (e.g., sibling age-spacing or birth order; Whiteman, Jensen, Mustillo, & Maggs, 2016; Whiteman, Jensen, & Maggs, 2014), making it more likely to detect sibling effects. However, this was not in the case in the current study and we were unable to control for or examine further characteristics of the siblings (e.g., age, birth-order, sibling age-spacing, gender, gender composition, or whether they lived in the home together). Additionally, having low sibling participation attributed to the inability to conduct appropriate analyses such as a latent profile analyses noted above. This analysis was not feasible given low numbers in subgroups (e.g., youth that have siblings who use substances and that also have a close, positive relationship). In the current study, sibling negativity was relatively low ($M$ = 22.66, range = 9-45). Thus, there may not be enough variability to detect an effect. Finally, substance use is measured at age 16, and literature suggests that substance use becomes most prominent in late adolescence (i.e., age 17; Young et al., 2009).

## Conclusions

In conclusion, there was no evidence of a developmental pathway from executive function to disruptive behavior or disruptive behavior to substance use, after controlling for stability in both disruptive behavior and substance use. These findings challenge the concept of a developmental link between executive function and later substance use. Further, the current study suggests that the developmental cascade of disruptive behavior may differ by risk, familial history, and earlier substance use. Unaccounted for individual differences, such as likelihood of risk-aversion as well as response to rewards and peer influence may contribute to the positive link between executive function and disruptive behavior. It may also be that a high-risk sample introduces additional considerations that may explain the positive association. Additionally, for youth at high familial risk for delinquent behaviors having greater executive function may foster better planning and execution of their delinquent tendencies. The study's main hypotheses of moderated mediation were not supported. However, limitations including the sample size and relatively course measurement of sibling influences may have made it impossible to find the hypothesized effects. Future work may benefit from better harnessing the interlaced components of the sibling relationship. The replication of a positive disruptive behavior-substance use association highlights and further supports previous work that early disruptive behavior may be a flag for youth who may be more at risk for developing substance use and points of intervention.

# DISCUSSION

Many biological and environmental factors have been investigated as predictors of adolescent substance use. Two factors that have been implicated in the developmental trajectory of substance use are executive function and disruptive behavior. Further, both smoking during pregnancy and sibling relationships (i.e., positive and negative sibling relationship quality, as well as siblings' own substance use) are environments that may mitigate or exacerbate associations between executive function and disruptive behavior (sibling relationship and smoking during pregnancy) as well as disruptive behavior and substance use (sibling relationship). Thus, the conceptual model that guided my work focused on the transitions from executive function to disruptive behavior to substance use across childhood and adolescence. I also examined both processes and contexts for the transitions from executive function to disruptive behavior to substance use (i.e., smoking during pregnancy and the sibling relationship). I began by considering executive functioning as a mediator of associations of smoking during pregnancy with disruptive behavior (Aim 1a), as well as the moderating role of smoking during pregnancy (Aim 1b & Aim 2a). Then, I explored the later part of my conceptual trajectory to substance use by examining the mediating role of disruptive behavior in the executive function-substance use association (Aim3a) as well as the moderating role of sibling relationships for developmental associations from executing function through disruptive behavior to substance use (Aim3b). Using a longitudinal parent-child adoption design, I hypothesized that smoking during pregnancy would be associated with decreased executive function and decreased executive function would be associated with increased disruptive behavior. Extending from this, I utilized a longitudinal adoption study and a complementary sibling comparison design, I hypothesized that the relation between executive function and disruptive behavior would be stronger for the youth that experienced smoking during pregnancy than those who did not at the between family (Aim 1b) as well as within-family (Aim 2a) level. Finally, for the third aim of this dissertation, utilizing a longitudinal family risk design, I hypothesized that lower executive function would be linked to greater rates of disruptive behavior, which in turn would be associated with greater substance use. I also hypothesized that that the paths would be stronger for siblings who have a less positive sibling relationship, a more negative sibling relationship, or a sibling that reported substance use.

I proposed an interdisciplinary approach to examine prenatal and sibling influences on the development of substance use through executive function deficits using a multiple design strategy that included genetically-informed (i.e., adoption study and sibling comparison design) and longitudinal samples. The main findings are represented in terms of the conceptual model in Figure 18. First, there was no link between smoking during pregnancy and executive function or disruptive behavior at the between-family level during childhood (paths a and b respectively). Second, there were inconclusive findings across this dissertation regarding the link between executive function and disruptive behavior (path c). In the adoption study design there was no longitudinal association between executive function and parent reports of disruptive behavior, at the between-family level in childhood. In the sibling comparison design, there was a cross-sectional association between the global executive function factor score and a multi-rater composite score of disruptive behavior at the within-family level in early adolescence. In a longitudinal at-risk population, there was a positive association between early adolescent global executive function and parent report of disruptive behavior two years later at the between-family level. Third, there was no link between adolescent disruptive behavior and substance use two years later, after controlling for early adolescent disruptive behavior and substance use (path d). Finally, there was no direct link between sibling influences and substance use (paths e). There was no link between positive sibling relationship quality or siblings' own substance use and disruptive behavior (paths e). However, more negative sibling relationship quality was linked to greater disruptive behavior, concurrently (path e).

The current dissertation also examined both processes and contexts for the development of disruptive behavior and substance use. First, executive function was not a process through which smoking during pregnancy influenced disruptive behavior. Second, across the dissertation, there was no evidence that smoking during pregnancy moderated the executive function-disruptive behavior association in childhood or early adolescence at the between or within-family level longitudinally or cross-sectionally (path f), except in few sensitivity analyses utilizing other measures of exposure to smoking during pregnancy, although the overall pattern of findings across multiple tests does not indicate a robust effect. Third, there was no evidence of an association between executive function and substance use (path g), direct or mediated by disruptive behavior. Finally, characteristics of the sibling relationship (i.e., positive and negative sibling relationship quality, as well as siblings' own substance use) were not a context for the

pathway between executive function and disruptive behavior or disruptive behavior and substance use (path h). Despite the general lack of support for the conceptual model, the present dissertation yielded some new insights that may guide future work, described below.

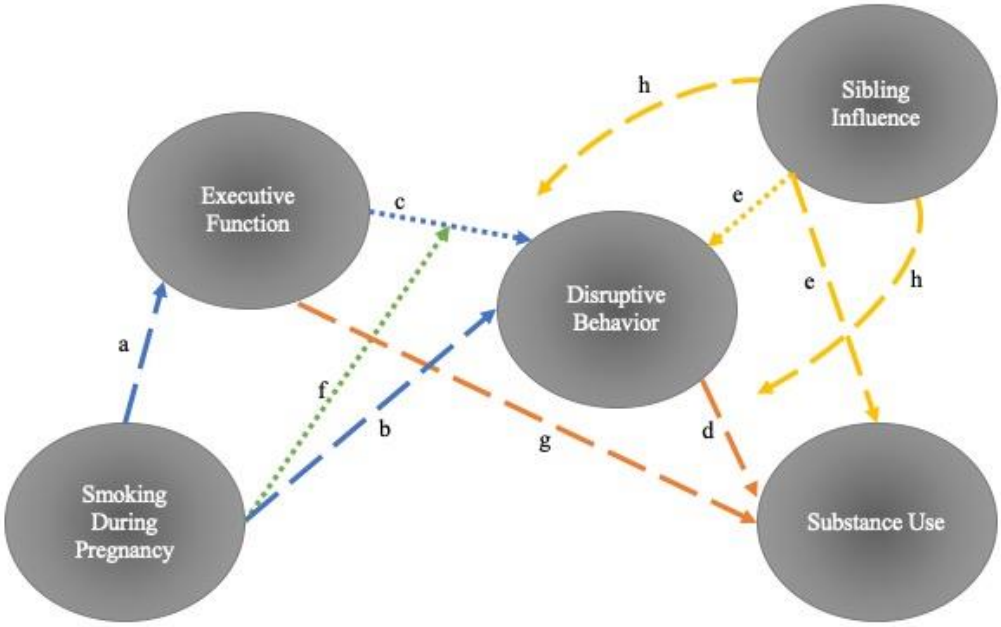



Figure 16. Final conceptual model showing hypothesized mediation and moderation results.

Note. Bold line indicates an association, dotted line indicates an association that was not consistent, and a dashed line indicates no association.

**Executive Function and Disruptive Behavior**

There were mixed findings regarding the link between executive function and disruptive behavior. On one hand, in one sample there was no link between executive function and disruptive behavior (study 1). However, in the sibling comparison and longitudinal at-risk sample I found an association. While all the samples were considered to have increased risk, such that I would be more likely to find associations, measurements of executive function varied across studies, in both age of measurement and tasks used. In the Early Growth and Development Study, a single component of executive function was measured, inhibitory control, at age 6. In the Missouri Mothers and Their Children Project all three components were

measured individually at an average age of 10 for the younger sibling and 13 for the older sibling and a latent score was created. Finally, in the Center for Education and Drug Abuse Research study a single task measured global executive function at age 10-12. Historically, researchers utilized various measures of executive function when examining similar associations (Miyake et al., 2000). The study with the null executive function-disruptive behavior association was limited to a single measure of inhibition, only one of the three components of executive function (i.e., inhibition). A hierarchical perspective of executive function suggests that inhibition is the base of executive function from which youths' working memory and set-shifting develop. Thus, the lack of findings regarding inhibition in early childhood and preadolescent disruptive behavior could potentially be due to the lack of information regarding both working memory and set-shifting. Specifically, according to the hierarchical perspective, early inhibition may not be linked directly to later disruptive behavior, but instead it is the base for more complex executive functions related to behavior (i.e., working memory and set-shifting). Notably, in the studies that did find the executive function-disruptive behavior association, a more global indicator of executive function was used. Further, in sensitivity analyses of the components in study two, working memory and set-shifting were related to disruptive behavior in late childhood/preadolescence whereas inhibition was not.

Interestingly, in one sample I found a positive association between executive function and disruptive behavior, such that greater executive function was linked to *increased* disruptive behavior two years later. The finding of a positive executive function-disruptive behavior association contradicts previous research that found executive function *deficits* predict greater disruptive behavior (Aytaclar, Tarter, Kirisci, & Lu, 1999; Fairchild et al., 2009; Piehler, Véronneau, & Dishion, 2012; Rose-Jacobs et al., 2011; Squeglia, Jacobus, Nguyen-Louie, & Tapert, 2014). Literature suggests that children of parents with substance use disorders are at greater risk for psychopathology, such as executive function deficits and increased substance use disorder (e.g., Clark, Moss, Kirisci, Mezzich, Miles, & Ott, 1997; Hill & Muka, 1996; Schuckit & Smith, 1996; Sher, Walitzer, Wood, & Brent, 1991; Tarter et al., 1999). Potentially, in an adolescent sample at higher risk for both executive function deficits and greater substance use, "increased" executive function is not comparable to a population-based study. Specifically, in the instance that youth in this specific sample have generally low executive function skills compared to the larger population, 'higher' executive function may not correspond with 'lower' executive

function in a sample less at-risk. In this case, the positive executive function-disruptive behavior association may not be generalizable to youth who are not at greater risk for decreased executive function and increased disruptive behavior, but specific to youth who are at greater risk. This unexpected association was also found in study one. Specifically, better executive function skills were associated with more disruptive behavior for youth that were not exposed to smoking during pregnancy, whereas for increases in the maximum quantity smoked in any one trimester the effect of higher executive function predicted lower disruptive behavior. Although the interaction between executive function and exposure was not part of a pattern of findings, potentially not robust and due to Type I error.

The samples used in this dissertation had sufficient risk for substance use and disruptive behavior. Thus, the particular finding of greater disruptive behavior predicting more disruptive behavior may be capturing an alternate path to externalizing problems. In particular, for youth with greater familial risk for substance use problems, increased executive functioning may support better planning and execution of their delinquent tendencies. For example, for some youth, more rewarding contexts potentially override top-down executive function (Hughes, 2011). In other words, when youth engage with peers, executive function may interact with bottom-up motivation and emotion surrounding risk/reward circumstances, resulting in greater disruptive behaviors. This suggests that when examining executive function as it relates to disruptive behavior it is important to understand youths' likelihood to avoid risk and their response to rewards and peer influences. More work is needed to investigate whether the positive executive function-disruptive behavior association is exclusive to this sample, as well as what could be driving this unexpected association.

***Smoking during pregnancy as a moderator of the executive function-disruptive behavior association.*** Genetically-informed studies suggest that associations of smoking during pregnancy with executive function and disruptive behavior are largely due to familial confounding (Ekblad et al., in press; D'Onofrio, Van Hulle, Goodnight, Rathouz, & Lahey, 2011; Knopik, 2009; Kuja-Halkola, D'Onofrio, Larsson, & Lichtenstein, 2014; Rydell, Granath, Cnattingius, Magnusson, & Galanti, 2014). This suggests the direct effect of smoking during pregnancy is likely not causal except under specific circumstances. However, smoking during pregnancy has shown an organizing effect on later brain and behavioral development (Gluckman et al., 2008), and interacts with familial risk for externalizing-type behavior (Buschgens et al.,

2009; Marceau et al., 2019; Neiderhiser et al., 2016). Thus, using complementary genetically-informed designs, I tested whether smoking during pregnancy was a developmental context for the executive function-disruptive behavior association. However, the smoking during pregnancy severity score did not interact with executive function, and sensitivity analyses with other smoking during pregnancy indicators did not reveal consistent or robust effects. In the current samples examining this link, the children are relatively young to experience the shifts in brain development linked to executive function, which is said not to finalize until late adolescence (e.g., prefrontal cortex; Berger et al., 2006; Kochanska & Knaack, 2003; Rothbart et al., 1994).

### The Smoking During Pregnancy-Disruptive Behavior Association Mediated by Executive Function

The current dissertation filled a gap in the literature by challenging the importance of smoking during pregnancy for both executive function and disruptive behavior. To this point, there have been mixed results regarding the impact of smoking during pregnancy. Studies of brain development consistently suggest that those who experience exposure to smoking during pregnancy have differential development in the frontal lobes (associated with executive function; Anderson, 2002) compared to their non-exposed peers (Ekblad et al., 2014; Peterson et al., 2003). However, when relating exposure to youth behavior, results are less clear. There is some evidence that smoking during pregnancy predicts both executive function and disruptive behavior (e.g., Ekblad et al., in press; Giancola & Tarter, 1999; Huizink & Mulder, 2006; Iacono et al., 1999; Micalizzi & Knopik, 2017; Rose-Jacobs et al., 2011; Piper & Corbett, 2011; Wakschlag, Pickett, Kasza, & Loeber, 2006). However, recent work that utilizes study designs able to control for both genetics and environment influences (e.g., adoption studies and sibling comparison designs) suggest otherwise (Boutwell & Beaver, 2010; D'Onofrio et al., 2010; Ekblad et al., in press; Langleu, Heron, Smith, & Thapar, 2012; Skoglund, Chen, D'Onofrio, Lichtenstein, & Larsson, 2014). In particular, the current dissertation used two complementary genetically-informed designs to examine smoking during pregnancy and found no link between smoking during pregnancy and executive function or disruptive behavior. Further, there was no evidence of executive functioning mediating the smoking during pregnancy-disruptive behavior association.

A growing body of research is exploring whether high levels of emotion may influence neurocognitive processes such as executive function, called "hot" and "cool" executive function (for a review see Zelazo et al., 2016). Specifically, "hot" executive function in measured with a component of heightened emotion or stress, whereas "cool" executive function is not (Zelazo and Muller, 2002). Prior work investigating the executive function-smoking during pregnancy association has begun to distinguish hot versus cold aspects of executive function (Huijbregts, de Sonneville, & Swaab-Barneveld, 2008; Zelazo & Muller, 2002). Specifically, cool inhibition has not been linked to smoking during pregnancy in the literature (Micalizzi et al., 2018; Zelazo & Muller, 2002), but hot inhibition is (Huijbregts, de Sonneville, & Swaab-Barneveld, 2008; Zelazo & Muller, 2002). The current dissertation utilized cool measures of executive function (i.e., measures with no substantial components of managing motivation or emotion) and did not find an association with smoking during pregnancy. Thus, future work studying the effects of smoking during pregnancy on executive function may consider utilizing both cool and hot measures of executive function to explore whether one type is more related to exposure compared to the other.

### The Mediating Role of Disruptive Behavior in the Executive Function-Substance Use Association

Executive function predicts both disruptive behavior and substance use (Aytaclar et al., 1999; Fairchild et al., 2009; Moffit et al., 2011; Piehler et al., 2012; Rose-Jacobs et al., 2011; Squeglia et al., 2014) and earlier disruptive behavior is linked to the development of substance use (Dodge et al., 2009). Thus, one component of the current dissertation was to test whether executive function deficits are linked to greater disruptive behavior which in turn would predict greater substance use. However, there was no evidence of mediation between the executive function-substance use association through disruptive behavior. More specifically, increased executive function skills predicted more disruptive behavior, disruptive behavior did not predict substance use severity, and there was no evidence of an executive function-substance use association. Importantly, zero-order correlations showed that disruptive behavior at age 12-14 was related to greater rates of later substance use. However, the association was attenuated by covariates and the stability of each problem type (i.e., disruptive behavior and substance use at baseline, age 10-12) in the structural equation models. Potentially, disruptive behavior-substance

use associations from the literature were misattributed to stability in problem behaviors across time or the directionality. Further, it suggests that, during adolescence, the disruptive behavior-substance use association is likely not causal. In the CEDAR sample, baseline substance use was linked to increased mid-adolescent disruptive behavior. When examining zero-order correlations that differed by risk group (see Appendix C) it appears that the level of risk drove the baseline substance use-later disruptive behavior association. It is possible that the developmental cascade could be different for youth at risk (e.g., familial history and levels of early substance use). Thus, this dissertation challenges the conventional developmental cascade model and highlights that additional research is necessary to realize the directionality of associations between disruptive behavior and substance use.

The association between executive function and substance use has been inconsistent in the literature, depending on whether the association was examined cross-sectionally or longitudinally. The longitudinal link between executive function and later externalizing-type behavior (e.g., conduct problems; Sulik, Blair, Mils-Koonce, Berry, & Greenberg, 2015) is well established. The current dissertation found evidence of a concurrent and longitudinal association between executive function in late childhood/preadolescence and disruptive behavior in late childhood/preadolescence. The concurrent association aligned with the literature suggesting greater executive function skills were related to less disruptive behavior. Although, the longitudinal link was found in the opposite direction to what the literature would suggest, such that greater executive function led to more disruptive behavior. However, this unexpected association was found in a unique, high-risk sample of adolescence. Importantly, literature on the longitudinal link between executive function and externalizing-type behaviors are primarily in early childhood and do not include substance use. Longitudinal studies from adolescent executive function to adult substance use do not find an association (e.g., Gale, Deary, Boyle, Barefoot, Mortensen, & Batty, 2008; Wilens et al., 2011), whereas cross-sectional studies of the executive function-substance use association have found an association (e.g., Giancola et al., 2001). To my knowledge, there has not be a previous study that has examined a longitudinal link from childhood executive function to adolescent substance use. Executive function is considered to be a malleable cognitive trait and may be bolstered across development (e.g., Zelazo et al., 2016). There is a large developmental gap between early childhood executive function and adolescent substance use. It may be that more proximal contexts are influencing this association.

Potentially there are enviornments not accounted for in this dissertation, such that for youth experiencing contexts that bolster executive function would not experience increased risk for substance use. For example, an extant literature exists examining both parenting (e.g., Hughes & Devine, 2019) and school (e.g., Duncan, Schmitt, Burke, & McClelland, 2018; Schmitt, McClelland, Tominey, & Acock, 2015) as contexts that bolster the development of executive function. Future work may consider examining this association moderated by more proximal contexts to substance use that could alter the longitudinal pathway.

Alternatively, it may be that earlier executive function deficits does not lead to later substance use, but instead the cross-sectional studies are tapping into an association from substance use to executive function deficits. There is some literature that suggests substance use precedes and predicts lower levels of executive functioning (Medina, Hanson, Schweinsburg, Cohen-Zion, Nagel, & Tapert, 2007; Schweinsburg, Brown, & Tapert, 2008). A limitation of these studies is that only the substance use to executive function direction was tested, and there was no control for between-person differences or stability in each phenotype over time. Thus, more work is needed to disentangle the executive function-substance use association, by examining whether executive function and substance use are a bidirectional association across development or if substance use leads to executive function deficits (as opposed to a developmental model of earlier executive function predicting later substance use severity).

**Sibling Relationships for the Development of Disruptive behavior and Substance Use**

Sibling relationships are a particularly unique context for the development of problem behaviors (e.g., both disruptive behavior and substance use; Fagan & Najman, 2005; Kothari, Sorenson, Bank, & Snyder, 2014). However, the potential moderating role of sibling relationships for the developmental pathways from executive function to disruptive behavior and transitions to substance use have not yet been examined. To my knowledge there is no literature on the role of sibling relationships for executive function development during adolescence, or associations of executive function and substance use. Thus, sibling relationships are a significant, but under-studied, influence that may affect the pathways between executive function, disruptive behavior, and substance use, as well as a point of prevention and intervention for family-based programs targeting adolescent problem behavior. Thus, one aim of the current dissertation was to investigate whether disruptive behavior mediated the executive function-substance use

association in adolescence, and whether sibling relationship quality and siblings' substance use moderated associations of executive function with disruptive behavior and the disruptive behavior-substance use association.

Sibling relationship quality (i.e., positive or negative) and sibling substance use did not predict disruptive behavior (with the exception of negative sibling relationship quality) or substance use, contradicting prior sibling literature (Modry-Mandell, Gamble & Taylor, 2006; Rende, Slomkowski, Lloyd-Richardson, & Niaura, 2005; Slomkowski, Rende, Novak, Lloyd-Richardson, & Niaura, 2005; Solmeyer, McHale & Crouter, 2014; Whiteman et al., 2017). Various aspects of the sibling relationship contribute to the magnitude of sibling influence on youth behavior. Sibling observation/modeling, reinforcement, and extensive opportunities for practice have been found to be an important context for youth behavior (Bank, Burraston, & Snyder, 2004; Criss & Shaw, 2005; Whiteman, Jensen, & McHale, 2017). However, sibling modeling increases when siblings are more similar, more socially connected, or have a more positive relationship (Rende et al., 2005; Slomkowski et al., 2005). Thus, specific circumstances can impact how strongly siblings influence youth problem behavior (e.g., disruptive behavior and substance use). This dissertation did not have the power to examine interactions between sibling characteristics along with key study concepts. However, future work should examine sibling relationship quality interacting with sibling substance use. An alternative analysis that would shed light on the interaction of sibling relationship characteristics as they relate to youth development of problem behavior is a latent profile analysis to classify sibling relationships (e.g., a subgroup with youth that have siblings who use substances and that also have a close, positive relationship).

The current study examined the sibling relationship quality in the context of "the sibling you are closest with", however, there is much research that suggests sibling relationship quality is differentially important for outcomes depending on other characteristics of the sibling relationship such as age difference (Whiteman, Jensen, Mustillo, & Maggs, 2016; Whiteman, Jensen, & Maggs, 2014). Further, for sibling substance use, I was unaware of which sibling was reporting the use. For example, it could have been a sibling close in age or a sibling that no longer lives in the home. These contexts are especially salient given research that suggests siblings are more likely to model their siblings substance use when they are more socially connected, or have are closer in age (e.g., Rende et al., 2005; Slomkowski et al., 2005).

Therefore, an important takeaway from this dissertation is that while sibling relationship quality or sibling substance use alone may not be an influential context alone, understanding these characteristics in a broader context of the sibling relationships may be key to understanding siblings' role in the development of youth disruptive behavior and substance use. In an attempt to better address this issue of co-occuring sibling contexts (e.g., sibling relationships that are more warm and a sibling who reports substance use), I attempted to run a latent profile analysis to characterize sibling relationships by both relationship quality and siblings' own substance use, to use as a moderator for the mediated model of executive function to substance use through disruptive behavior. However, the cell sizes were not large enough to conduct this type of analysis.

## Conclusions

In total, this dissertation challenges previous work that has found a link between exposure to smoking during pregnancy and both executive function and disruptive behavior. Further, these findings reinforce the need to utilize genetically-informed designs when examining potential effects of smoking during pregnancy, as there was no smoking during pregnancy-disruptive behavior association when controlling for genetic and environmental confounds. Further, this dissertation suggests an opportunity for future work to explore the hierarchical development of executive function as it relates to disruptive behaviors in late childhood and early adolescence, given the lack of findings for a developmental link from early executive function (i.e., inhibition) to preadolescent disruptive behavior, as well as the null result of inhibition predicting disruptive behavior during late childhood/preadolescence (both working memory and set-shifting did show effects). Finally, the current dissertation challenges the concept of a developmental link between early executive function and later substance use, finding that late childhood executive function was not implicated in the development of adolescent substance use.

Adolescence is a unique sensitive period in development and through a combination of genetic and environmental influences, as well as biological changes, youth experience increased risky behavior during this time (e.g., Blakemore & Choudhury, 2006; Gray & Squeglia, 2018; Marceau, Kirisci, & Tarter, in press; Mendle & Ferrero, 2012, Ullsperger & Nikolas, 2017). Importantly, at this stage of greater risk, adverse behavioral outcomes can set youth on a trajectory of life-persistent patterns of problem behaviors (Baggio et al., 2015; Blanco et al.,

2016; Gray & Squeglia, 2018). Thus, research intended to elucidate and generate knowledge about prevention and intervention efforts is critical in this period when implementation may be most impactful and offset life-persistent maladjustment. The current dissertation supports previous work that suggests disruptive behavior is a risk factor for developing substance use, and remains a target for prevention and intervention efforts. Further, this work begins to challenge previously found associations between smoking during pregnancy, executive function, disruptive behavior, and substance use that has implications for how we view the development of substance use in adolescence and suggests future avenues for research.

**Future Directions**

In the current dissertation, associations may be attributable to the way in which disruptive behavior was measured. I included measures of specific disruptive behaviors; however, these samples contain a variety of measures of externalizing-type behavior. Potentially, a broader composite measure of externalizing behavior would capture effects, opposed to focusing on disruptive behaviors specifically. There is work that suggests a variety of sources contribute unique perspectives on youths' behavior (e.g., Achenbach, McComaughy, & Howell, 1987; Verhulst & Van der Ende, 1992). One potential opportunity would be to create a composite score of externalizing behavior that includes multiple informants (e.g., self-report, parent-report and peer report; Sharp, Barr, Ross, Bhimany, Ha, & Vuchinich, 2012).

Additionally, previous papers using CEDAR data have utilized a neurobehavioral composite variable of disinhibition with not only parent and teach reports of disruptive behavior (conduct disorder symptoms, oppositional defiant disorder symptoms, and attention-deficit/hyperactivity disorder symptoms), but also cognitive measures (e.g., emotion regulation and behavioral control; Tarter et al., 2003). Tarter and colleagues (2003) found that this composite measure of externalizing-type behaviors predicted substance use. Thus, analyses from this dissertation may be re-run with earlier executive functions predicting a broader measure of disinhibition which may then be linked to later substance use. This not only applies to the third study, but also study one and two. In the data for EGDS there are additional measures of social and communication competence, alternative measures of disruptive behavior (Connors' Parent Rating Scale), and substance use (substance use data currently being collected). In the data for MOMATCH there are also alternative measures of disruptive behavior (e.g., MAGIC, Connors,

and attention-deficit/hyperactivity disorder) and measures of substance use. Thus, in study one and two I could rerun analyses with a composite outcome variable that includes broader measures of externalizing behavior, such as conduct disorder symptoms, oppositional defiant disorder symptoms, and attention-deficit disorder symptoms, as well as substance use.

The current dissertation examined the sibling relationship as a context for the development of substance use. In particular, I examined, separately, whether sibling relationship quality or siblings' own substance use moderated the executive function-disruptive behavior and disruptive behavior-substance use associations. Inconsistent with the literature, aspects of the sibling relationship (i.e., positive and negative sibling relationship quality, as well as siblings' own substance use) did not predict disruptive behavior or substance use and did not interact with either executive function or disruptive behavior. Notably, the information regarding sibling characteristics (e.g., age, sex, disruptive behavior, executive functioning) were not available. To build from this work, it will be necessary to replicate these analyses while considering more specific sibling attributes.

In order to tap into the dyadic aspect of the sibling relationship, I must consider what the sibling is contributing. Following social learning theory, the behavior of a sibling (e.g., decreased executive function or increased disruptive behavior) would influence the behaviors they are modeling. Across development, youth may be more at risk for substance use, if across development siblings were not bolstering executive function skills (e.g., via interactions) while also modeling increased disruptive behaviors. For example, having a sibling with lower executive function and increased rates of disruptive behavior may further compound the developmental risk for modeling poorer behaviors across development that would then lead to increased severity of substance use (as opposed to only having data on siblings' substance use). Importantly, the average age of sibling in this study is unknown; it may be that siblings participating in the study are not old enough themselves to have reached the age of peak substance use in adolescence, or the risk behaviors associated in adolescence. Ideally, to examine siblings as a context for the development of executive function to substance use through disruptive behavior, data would be gathered about siblings who live at home and are closest in age to the target youth. Further, gathering information about the siblings' own development of executive function and disruptive behavior, to better capture the dyadic aspect of siblings influences across development.

This dissertation challenges the concept of a developmental link between executive function, disruptive behavior, and later substance use. Importantly, associations found in cross-sectional studies were not found here. This suggests that larger contextualized models may not be the correct avenue for future research based on cross-sectional studies. Instead, future work needs to better establish directionality and the processes through which these associations occur across development. Hamaker and colleagues (2015) proposed a random intercept cross-lagged panel model (RI-CLPM) that would address these questions. None of the studies used in the current dissertation had measurement strategies that are well-suited to RI-CLPM, and so this is an important future direction. Notably, this type of model is not only able to examine associations across time as a regular cross-lag panel model would but is also able to decompose between and within-person stability. Given the lack of within-person findings in the current dissertation, this model would allow me to best examine between family influences to examine whether there are developmentally lagged effects. The current dissertation suggests that this model would best capture links between executive function and delinquent behavior if these items were measured starting in late childhood through early and late adolescence. Further, the literature suggests that an at-risk sample would better show associations with both disruptive behavior and substance use (Hummer et al., 2011; Clark, Prior, & Kinsella, 2000). Finally, a genetically informed sample would be important to tease apart genetic liability for psychopathology and familial confounding.

# APPENDIX A: STUDY 1 METHODS

***Data preparation/measurement model*.** Prior to estimating models, the data were evaluated. Variables were normally distributed. I examined correlations to make sure they were all in expected directions and to examine the association of covariates (i.e., age, gender, socioeconomic status, openness of adoption, adoptive/birth parents' knowledge of each other, the percent of trials correct in the biological mothers' Go-No-Go executive function task, and a composite score of birth parent reports of disruptive behaviors) with key study concepts.

**Preliminary Tests**

***Power analysis***. A series of Monte Carlo simulation studies in Mplus was used to determine the power to detect hypothesized effects in the EGDS data. A limitation of simulation studies of complex models is the number of assumptions made during the analysis. Previous literature showed effects of .37 for associations of executive function and disruptive behavior (Giancola et al., 1996), and -0.08 for smoking during pregnancy and executive function (Micalizzi et al., 2018). To be conservative moderate effects were used, (.15) of executive function on disruptive behavior, (-.08) of smoking during pregnancy on executive function and (.08) for the direct effect of smoking during pregnancy on disruptive behavior. Under these conditions and with missing data on smoking during pregnancy (10%), executive function (20%) and disruptive behavior (30%), the study is powered to detect main effects of executive function (.63), but underpowered to detect effects of smoking during pregnancy (.25) and the indirect effect (.25). Further simulations suggested that the study is underpowered if all effects are small (e.g., .05, power=.12-.13 for direct and indirect effects). The study is adequately powered (.75) to detect the hypothesized indirect effect if the effect of smoking during pregnancy on executive function is medium (.15) and the effect of executive function on disruptive behavior is also medium (.15), and attrition is limited to 10% for executive function and disruptive behavior. *Aim 2.* A series of Monte Carlo simulation studies in Mplus was used to determine the power to detect hypothesized effects in the EGDS data. A limitation of simulation studies of complex models is the number of assumptions made during the analysis. Previous literature showed effects of .37 for associations of executive function and disruptive behavior (Giancola et al.,

1996), and -0.08 for smoking during pregnancy and executive function (Micalizzi et al., 2018). To be conservative moderate effects were used, (.15) of executive function on disruptive behavior, (-.08) of smoking during pregnancy on executive function and (.08) for the direct effect of smoking during pregnancy on disruptive behavior, and (.10) for the interaction of executive function*smoking during pregnancy. Under these conditions and with missing data on smoking during pregnancy (10%), executive function (20%) and disruptive behavior (30%), the study is powered to detect main effects of executive function (.64), but underpowered to detect effects of smoking during pregnancy (.22) on executive function and disruptive behavior and the interaction of executive function*smoking during pregnancy (.38). Further, simulations suggested that the study is underpowered if all effects are small (e.g., .05, power=.13-.15 for direct and interaction effects). The study is adequately powered (.63-.67) to detect the effect of smoking during pregnancy on executive function and disruptive behavior, as well as the interaction of smoking during pregnancy and executive function, if the effect of smoking during pregnancy on executive function is medium (.15) and the effect on disruptive behavior is also medium (.15), and the interaction effect is medium to large (.15). Further, the study is well powered (.76-.78) when all effects are medium to large (.15) and attrition is limited to 10% for executive function and disruptive behavior.

**Table A1**. Descriptive statistics of alternative measures of smoking during pregnancy

| **Measure of Exposure to Smoking During Pregnancy** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Severity Score (N=145)** | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
| | 2 | 0 | 0 | 20 | 0 | 0 | 123 |
| **Discrete Indicator (N=145)** | **No (0)** | **Yes (1)** | | | | | |
| | 2 | 143 | | | | | |
| **Maximum Quantity (N=145)** | **M(SD)** | **min** | **max** | | | | |
| | 906.34(698.43) | 0 | 3665.78 | | | | |
| **Sum Quantity (N=145)** | 2070.2(1717.28) | 0 | 8962.85 | | | | |
| **Number of Trimesters (N=148)** | **0** | **1** | **2** | | | | |
| | 4 | 30 | 114 | | | | |

Note. For the severity score of exposure 1: did not smoke during pregnancy; 2: smoked during first trimester only, 1–10 cigarettes per day 3: smoked during first trimester only, 11–19 cigarettes per day; 4: smoked during first trimester only, 20+ cigarettes per day 5: smoked beyond first trimester, 1–10 cigarettes per day (max of all trimesters); 6: smoked beyond first trimester, 11–19 cigarettes per day; (max of all trimesters); 7: smoked beyond first trimester, 20+ cigarettes per day (max of all trimesters).

Table A2. Results of missingness tests.

| | Age | Openness | Knowledge | AP Maternal EF | AP Paternal EF | AP Maternal AS | AP Paternal AS |
|---|---|---|---|---|---|---|---|
| SDP | 0(1) | 6.43(525.44)*** | 9.14(641.56)*** | 3.21(1) | 0.81(1) | 120.91(362.04)*** | 114.12(341.85)*** |
| Executive Function | 11.85(1) | 13.96(472.64)*** | 19.33(572.63)*** | 16.42(1) | 17.91(1) | 118.72(353.98)*** | 111.98(335.14)*** |
| Disruptive Behavior | 3.92(1) | 11.01(516.36)*** | 15.05(631.25)*** | 1.09(1) | 9.76(1) | 119.19(360.58)*** | 112.49(340.64)*** |

Table A2. Results of missingness chi-square tests continued

| | BP Risk Score | Secondhand Smoke | Disruptive Behavior (age 7) | BP Maternal EF | BP Paternal EF |
|---|---|---|---|---|---|
| SDP | 1.53(399.05) | 0.53(348.13) | 177.46(216.01)*** | 134.35(325.06)*** | 83.23(107.13)*** |
| Executive Function | 5.49(383.34)*** | 1.38(347.44) | 176.39(215.04)*** | 133.77(324.72)*** | 82.85(107.09)*** |
| Disruptive Behavior | 4.04(396.22)*** | 1.08(348.01) | 176.68(215.84)*** | 133.96(325)*** | 82.98(107.13)*** |



Note. SDP = smoking during pregnancy; AP = adoptive parent; AS = anti-social behavior; BP = birth parent; EF = executive function. Youth were more likely to have missing scores of smoking during pregnancy when they have on average: more openness and knowledge, lower adoptive parent anti-social behavior, lower disruptive behavior at age 7, increased birth parent executive function. Youth were more likely to have missing scores of executive function when they have on average: lower levels of openness and knowledge, decreased adoptive parent anti-social behavior, increased birth parent composite genetic risk, greater rates of disruptive behavior at age 7, and higher birth parent executive function. Youth were more likely to have missing scores of disruptive behavior when they have on average: decreased openness and knowledge, decreased adoptive parent anti-social behavior, increased birth parent composite genetic risk, lower disruptive behavior at age 7, and higher birth parent executive function. *p < .05, **p<.01, ***p<.001.

# APPENDIX B: STUDY 2 METHODS

***Data preparation/measurement model***. Before testing hypotheses, I evaluated the data for violated assumptions. Importantly, variable scale, shape, and the presence of outliers were initially examined to avoid any incorrect inferences. Further, I used scatterplots to confirm that all variables were linearly (as opposed to non-linearly) related. Lastly, I examined correlations to make sure they were all in expected directions and to examine the association of covariates with key study concepts. Further, I tested formal assumptions of multi-level models by examining that error terms were normally distributed, the level 1 predictors were independent of the residual values, the residual values were not correlated with the level 1 predictors, and to test that level 1 and level 2 were independent.

**Preliminary Tests**

Maternal executive function was not normally distributed, indicated by the skewness statistic and was square root transformed. Further, mothers' measures of both attention deficit-hyperactivity disorder and conduct disorder were non-normally distributed. There was evidence of outliers (+/- 3 SD) and were winsorized as well as log transformed. I tested formal assumptions of multi-level models. First, I examined that error terms were normally distributed by outputting individuals' residual values and seeing whether they were skewed (+/-1). The scores for disruptive behavior were square root transformed due to being non-normally distributed, indicated by the skewness statistic (+/- 1). Second, I confirmed that the level 1 predictors were independent of the residual values. Using the outputted residual values, I examined the correlation with my level 1 independent variables. The residual values were not correlated with my level 1 predictors. To examine assumptions at level 2, I outputted the Bayes Empirical Estimates to test the residuals and confirmed that the level 2 predictors were independent of all μ's (defined below). Finally, to test whether errors at level 1 and level 2 were independent I confirmed there were not correlations of predictors at each level and random effects at other levels.

***Power analysis***. Based on power analyses, there is sufficient power to detect within-family effects (e.g., the interaction of smoking during pregnancy and executive function). Based

on previous literature, intra-class correlations (ICC) for adolescent disruptive behavior may be as low as .185 or as high as .71-.90 (Knopik et al., 2016; Marceau et al., 2017). Thus, power was calculated based on MO-MATCH's known sample size of 346 siblings clustered in 173 families and using estimated effective sample sizes with a range of design effect sizes, using SAS proc power (Snijder, 2005). Assuming ICC=.1085, the study is underpowered to detect small partial correlations < 0.1 (power < 0.33). However, for moderate and large effects (e.g., partial correlations > 0.2), the study is well powered (power > 0.92). Assuming ICC=.7-.983 (Knopik et al., 2016; Marceau et al., 2017), the study is underpowered to detect very small effects (partial correlations < 0.05; power < 0.69), however, there will be sufficient power to detect partial correlations > 0.10 (power > 0.99).

Table B1. Descriptive statistics of measures of smoking during pregnancy discussed in study two

| **Measure of Exposure to Smoking During Pregnancy** | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Severity Score** | **1** | **2** | **3** | **4** | **5** | **6** | **7** |
| | 142 | 48 | 8 | 14 | 81 | 15 | 29 |
| **Discrete Indicator** | **No (0)** | **Yes (1)** | | | | | |
| | 142 | 195 | | | | | |
| **Maximum Quantity** | **M(SD)** | **min** | **max** | | | | |
| | 6.38(9.07) | 0 | 98 | | | | |

Note. For the severity score of exposure 1: did not smoke during pregnancy; 2: smoked during first trimester only, 1–10 cigarettes per day 3: smoked during first trimester only, 11–19 cigarettes per day; 4: smoked during first trimester only, 20+ cigarettes per day 5: smoked beyond first trimester, 1–10 cigarettes per day (max of all trimesters); 6: smoked beyond first trimester, 11–19 cigarettes per day; (max of all trimesters); 7: smoked beyond first trimester, 20+ cigarettes per day (max of all trimesters)

Table B2. Results of missingness tests.

| | Age | Sex | Food Stamps | Maternal Executive Function | Maternal education | Maternal age |
|---|---|---|---|---|---|---|
| SDP | 249.45(14)*** | 1.25(1) | 1.54(2) | 17.49(363.73)*** | 4.06(10) | 94.92(16)*** |
| Executive Function | 21.97(14) | 0.01(1) | 10.51(2)* | 17.80(356.36)*** | 1.72(10) | 19.68(16) |
| Disruptive Behavior | 12.22(14) | 0.67(1) | 1.17(2) | 14.93(420.38)*** | 6.50(10) | 16.68(16) |

Table B2. Results of missingness tests continued.

| | Secondhand Smoke | Birth Order | Maternal ADHD | Maternal Conduct Disorder |
|---|---|---|---|---|
| SDP | 3.82(6) | 0(1) | 0.82(3) | 0(1) |
| Executive Function | 3.19(6) | 0(1) | 1.99(3) | 0(1) |
| Disruptive Behavior | 9.36(6) | 0(1) | 0.52(3) | 0.13(1) |

Note. SDP = smoking during pregnancy; ADHD = attention-deficit/hyperactivity disorder. Youth were more likely to be missing on smoking during pregnancy if they on average were younger, had lower maternal executive function and mothers were older. Youth were more likely to be missing on executive function if they on average had no food stamps and lower maternal executive function. Youth were more likely to be missing on disruptive behavior if they on average had lower maternal executive function. *p < .05, **p<.01, ***p<.001.

# APPENDIX C: STUDY 3 METHODS

***Data preparation/measurement model*.** To avoid questionable inferences, the variables being used in analyses were examined for scale, shape, and outliers. In the instance that a variable was non-normally distributed, indicated by an abnormal histogram and skewness statistics (greater than +/- 1), data was transformed accordingly. Notably, bootstrapping used in analyses (discussed in hypothesis testing) also addressed issues of non-normal data (Hayes, 2013). Additionally, in the instances of influential outliers, examined via bivariate plots, the data was winsorized for +/- 3 standard deviations above or below the mean. Further, using scatterplots, we confirmed the independent variables and dependent variable were linearly (as opposed to non-linearly) related. Lastly, we examined correlations to make sure they were all in expected directions and to examine the association of covariates with key study concepts.

**Preliminary Tests**

When evaluating the data, both substance use and disruptive behavior were skewed (skewness statistics greater than +/- 1). Disruptive behavior was square root transformed. Further, scatterplots suggested key study variables were linearly related.

***Power analysis*.** A Monte Carlo simulation study in Mplus was used to determine the power to detect hypothesized effects in the CEDAR data. A limitation of simulation studies of complex models is the number of assumptions made during the analysis. Simulations included 10% to 25% missing for each variable based on study attrition statistics. Previous literature showed effects of .37 for associations of executive function and disruptive behavior (Giancola et al., 1996), .13 for executive function and substance use (Giancola et al., 2001), .38 for disruptive behavior and substance use (Kirisci et al., 2015), .29 for adolescent substance use and sibling substance use (Windle, 2000), and .46 for sibling warmth and substance use (East & Khoo, 2005). To be conservative moderate effects were used, (.15) of executive function on disruptive behavior and substance use as well as disruptive behavior on substance use, as well as for the main effects of siblings on substance use, and the interactions of siblings*disruptive behavior, and siblings*executive function for substance use. The study is well powered to detect main effects and interaction terms of medium size (e.g., .15; power > .93) and the indirect effect (.78),

but underpowered to detect small effects (e.g., .05, power=.21-.24 for direct and interaction effects and .11 for the indirect effect).

Table C1. Results of missingness tests.

| | Age | Sex | Group | SES |
|---|---|---|---|---|
| Executive Function | 316.65(841.9)*** | 0.24(1) | 0.00(1) | 65.02(458.51)*** |
| Disruptive Behavior | 312.18(913.41)*** | 10.13(1)** | 9.12(1)** | 65.23(458.71)*** |
| Positive/Negative | 315.81(853.41)*** | 0.26(1) | 3.72(1) | 65.05(458.54)*** |

| | P-C Rel-Qual | SU (age 10-12) | Sibling SU |
|---|---|---|---|
| Executive Function | 81.45(274.11)*** | 9.94(9) | 0(1) |
| Disruptive Behavior | 81.58(274.16)*** | 4.81(9) | 0(1) |
| Positive/Negative | 81.47(274.12)*** | 3.91(9) | 0(1) |

Note. Positive = positive sibling relationship quality; negative = negative sibling relationship quality; SES = socioeconomic status; P-C Rel-Qual = parent child relationship quality; SU = substance use. Tests suggest that executive function was more likely to be missing for older youth, those with lower socioeconomic status, and worse parent-child relationship quality. Further, disruptive behavior was more likely to be missing for the older youth, lower socioeconomic status, individuals with a father diagnosed with substance use disorder, and males, and worse parent-child relationship quality. Finally, sibling relationship quality was more likely to be missing for older youth and those with higher socioeconomic status, and better parent-child relationship quality.

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. | 11. | 12. | 13. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Race | -- | | | | | | | | | | | | |
| 2. Socioeconomic Status | **.33**** | -- | | | | | | | | | | | |
| 3. Age | -.04 | .02 | -- | | | | | | | | | | |
| 4. Sex | .09 | -.10 | -.06 | -- | | | | | | | | | |
| 5. Parent-Child Relationship Quality | -.09 | -.08 | -.15 | -.01 | -- | | | | | | | | |
| 6. Baseline Substance Use | .03 | **.13*** | .10 | .01 | .11 | -- | | | | | | | |
| 7. Baseline Disruptive Behavior | -.09 | -.03 | **-.12*** | **.20**** | **.24*** | -.02 | -- | | | | | | |
| 8. Positive Sibling Relationship | -.08 | -.02 | -.01 | **-.15**** | **-.33**** | -.04 | -.10 | -- | | | | | |
| 9. Negative Sibling Relationship | .03 | .07 | .01 | -.02 | .19 | -.04 | .08 | -.10 | -- | | | | |
| 10. Sibling Substance Use | .03 | .03 | -.01 | .02 | .01 | .07 | -.04 | -.11 | -.06 | -- | | | |
| 11. Executive Function (Age 10-12) | **-.26**** | **-.16*** | -.01 | .00 | .13 | -.09 | .07 | -.01 | .02 | -.05 | -- | | |
| 12. Disruptive Behavior (T2) | -.11 | -.10 | -.10 | **.20**** | **.27**** | .03 | **.70**** | -.05 | .09 | .04 | .10 | -- | |
| 13.Substance Use (Age 16) | .08 | .02 | .07 | .09 | .13 | **.18**** | **.13*** | -.07 | -.01 | -.01 | -.01 | **.16*** | -- |

Note. *p < .05, **p<.01, ***p<.001. Correlations are for those in the no risk group (i.e., father with no substance use or psychiatric disorder).

| | 1. | 2. | 3. | 4. | 5. | 6. | 7. | 8. | 9. | 10. | 11. | 12. | 13. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1. Race | -- | | | | | | | | | | | | |
| 2. Socioeconomic Status | **.34**** | -- | | | | | | | | | | | |
| 3. Age | -.02 | .02 | -- | | | | | | | | | | |
| 4. Sex | **.24**** | **.15*** | **-.17**** | -- | | | | | | | | | |
| 5. Parent-Child Relationship Quality | -.11 | -.18 | **.22**** | -.08 | -- | | | | | | | | |
| 6. Baseline Substance Use | .10 | -.01 | .08 | .10 | .13 | -- | | | | | | | |
| 7. Baseline Disruptive Behavior | .08 | -.11 | -.04 | **.14*** | **.28**** | **.17**** | -- | | | | | | |
| 8. Positive Sibling Relationship | **-.14*** | -.10 | -.04 | **-.20**** | **-.24**** | .02 | **-.15*** | -- | | | | | |
| 9. Negative Sibling Relationship | .06 | .14 | .11 | -.04 | .12 | .09 | -.03 | -.06 | -- | | | | |
| 10. Sibling Substance Use | .01 | .12 | .02 | -.08 | .24 | -.04 | -.03 | -.08 | .08 | -- | | | |
| 11. Executive Function (Age 10-12) | -.11 | -.10 | -.05 | -.04 | -.07 | -.02 | .04 | .03 | .02 | -.11 | -- | | |
| 12. Disruptive Behavior (T2) | -.00 | -.13 | -.05 | **.19**** | **.30**** | **.24**** | **.68**** | **-.15*** | **.13*** | .03 | .09 | -- | |
| 13.Substance Use (Age 16) | **.17*** | -.10 | **.12*** | .07 | .14 | **.31**** | .09 | **-.14*** | .07 | .04 | **-.14*** | **.13*** | -- |

Note. *p < .05, **p<.01, ***p<.001. Correlations are for those in the risk group (i.e., father with substance use or psychiatric disorder).

# REFERENCES


Achenbach TM. (1991). *Manual for the Child Behavior Checklist*. Burlington, VT: University of Vermont, Department of Psychiatry.

Achenbach TM. (1991). *Manual of the Teacher's Report Form and 1991 profile.* Burlington, VT: University of Vermont, Department of Psychiatry.

Achenbach, T. M., McConaughy, S. H., & Howell, C. T. (1987). Child/adolescent behavioral and emotional problems: Implications of cross-informant correlations for situational specificity. *Psychological Bulletin, 101*(2), 213–232. doi:10.1037/0033-2909.101.2.213

Acock, A. C. (2005). Working with missing values. *Journal of Marriage and Family, 67*(4), 1012–1028. doi:10.1111/j.1741-3737.2005.00191.x

American Psychiatric Association (2013) *Diagnostic and statistical manual of mental disorders: DSM-5*, 5th edn. Arlington: American Psychiatric Publishing, Inc.

Anderson, P. (2002). Assessment and development of executive function (EF) during childhood. *Child Neuropsychology, 8(2),* 71–82. doi:10.1076/chin.8.2.71.8724

Andersen, S. L. (2016). Commentary on the special issue on the adolescent brain: Adolescence, trajectories, and the importance of prevention. *Neuroscience & Biobehavioral Reviews, 70*, 329–333. doi:10.1016/j.neubiorev.2016.07.012

Ando, J., Ono, Y., & Wright, M. J. (2001). Genetic structure of spatial and verbal working memory. *Behavior Genetics, 31*(6), 615-624. doi.org/10.1023/A:1013353613591

Anokhin, A. P., Heath, A. C., & Ralano, A. (2003). Genetic influences on frontal brain function: WCST performance in twins. *Neuroreport, 14*(15), 1975-1978. doi:10.1097/00001756-200310270-00019

Anthony, J. C., & Helzer, J. E. (1991). Syndromes of drug abuse and dependence. In L. N. Robins & D. A. Regier (Eds.), *Psychiatric disorders in America: The epidemiologic catchment area study* (pp. 116–154). New York, NY: Free Press.

Arnett, J. J. (2002). Adolescents in western countries in the 21st century: Vast opportunities – for all? *The World's Youth*, 307–343. doi:10.1017/cbo9780511613814.011

Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Sciences, 8*(4), 170–177. doi:10.1016/j.tics.2004.02.010

Avenevoli, S., & Merikangas, K. R. (2003). Familial influences on adolescent smoking. *Addiction, 98*, 1–20. doi:10.1046/j.1360-0443.98.s1.2.x

Aytaclar, S., Tarter, R. E., Kirisci, L., & Lu, S. (1999). Association between hyperactivity and executive cognitive functioning in childhood and substance use in early adolescence. *Journal of the American Academy of Child & Adolescent Psychiatry, 38(2),* 172–178. doi:10.1097/00004583-199902000-00016

Bank, L., Burraston, B., & Snyder, J. (2004). Sibling conflict and ineffective parenting as predictors of adolescent boys' antisocial behavior and peer difficulties: Additive and interactional effects. *Journal of Research on Adolescence, 14*(1), 99-125. https://doi.org/10.1111/j.1532-7795.2004.01401005.x

Baggio, S., Iglesias, K., Deline, S., Studer, J., Henchoz, Y., Mohler-Kuo, M., & Gmel, G. (2015). Not in education, employment, or training status among young Swiss men. Longitudinal associations with mental health and substance use. *Journal of Adolescent Health*, *56*(2), 238-243. doi: 10.1016/j.jadohealth.2014.09.006.

Bayer, S.A., Altman, J., Russo, R.J., Zhang, X. (1993). Timetables of neurogenesis in the human brain based on experimentally determined patterns in the rat. *Neurotoxicology 14*(1), 83-144

Bechara, A., Damasio, A. R., Damasio, H., & Anderson, S. W. (1994). Insensitivity to future consequences following damage to human prefrontal cortex. *Cognition, 50*(1-3), 7–15. doi:10.1016/0010-0277(94)90018-3

Becker, K., El-Faddagh, M., Schmidt, M. H., Esser, G., & Laucht, M. (2008). Interaction of dopamine transporter genotype with prenatal smoke exposure on ADHD symptoms. *The Journal of Pediatrics*, *152*(2), 263–269.e1. doi:10.1016/j.jpeds.2007.07.004

Bell, M. A., & Deater-Deckard, K. (2007). Biological systems and the development of self-regulation: integrating behavior, genetics, and psychophysiology. *Journal of Developmental & Behavioral Pediatrics, 28*(5), 409–420. doi:10.1097/dbp.0b013e3181131fc7

Belsky, J., Steinberg, L. D., Houts, R. M., Friedman, S. L., DeHart, G., Cauffman, E., et al (2007). Family rearing antecedents of pubertal timing. *Child Development, 78*, 1302–1321.

Berger, A., Tzur, G., & Posner, M. I. (2006). Infant brains detect arithmetic errors. *Proceedings of the National Academy of Sciences, 103*(33), 12649–12653. doi:10.1073/pnas.0605350103

Bernier, A., Carlson, S. M., & Whipple, N. (2010). From external regulation to self-regulation: Early parenting precursors of young children's executive functioning. *Child Development, 81*(1), 326–339. doi:10.1111/j.1467-8624.2009.01397.x

Bernier, A., Carlson, S. M., Deschênes, M., & Matte-Gagné, C. (2011). Social factors in the development of early executive functioning: a closer look at the caregiving environment. *Developmental Science, 15*(1), 12–24. doi:10.1111/j.1467-7687.2011.01093.x

Best, J. R., & Miller, P. H. (2010). A developmental perspective on executive function. *Child Development, 81*(6), 1641–1660. doi:10.1111/j.1467-8624.2010.01499.x

Bidwell, L. C., Marceau, K., Brick, L. A., Karoly, H. C., Todorov, A. A., Palmer, R. H., … Knopik, V. S. (2017). Prenatal exposure effects on early adolescent substance use: Preliminary evidence from a genetically informed bayesian approach. *Journal of Studies on Alcohol and Drugs, 78*(5), 789–794. doi:10.15288/jsad.2017.78.789

Bidwell, L. C., Palmer, R. H. C., Brick, L., Madden, P. A. F., Heath, A. C., & Knopik, V. S. (2016). A propensity scoring approach to characterizing the effects of maternal smoking during pregnancy on offspring's initial responses to cigarettes and alcohol. *Behavior Genetics, 46*(3), 416–430. doi:10.1007/s10519-016-9791-5

Biederman, J. (2005). Attention-deficit/hyperactivity disorder: A selective overview. *Biological Psychiatry, 57*(11), 1215–1220. doi:10.1016/j.biopsych.2004.10.020

Blackson, T. C., Butler, T., Belsky, J., Ammerman, R. T., Shaw, D. S., & Tarter, R. E. (1999). Individual traits and family contexts predict sons' externalizing behavior and preliminary relative risk ratios for conduct disorder and substance use disorder outcomes. *Drug and Alcohol Dependence, 56*(2), 115-131.

Blair, C., & Razza, R. P. (2007). Relating effortful control, executive function, and false belief understanding to emerging math and literacy ability in kindergarten. *Child Development, 78*(2), 647–663. doi:10.1111/j.1467-8624.2007.01019.x

Blakemore, S. J., & Choudhury, S. (2006). Development of the adolescent brain: implications for executive function and social cognition. *Journal of Child Psychology and Psychiatry, 47*(3-4), 296-312. doi: 10.1111/j.1469-7610.2006.01611.x.

Blanco, C., Hasin, D. S., Wall, M. M., Flórez-Salamanca, L., Hoertel, N., Wang, S., ... & Olfson, M. (2016). Cannabis use and risk of psychiatric disorders: prospective evidence from a US national longitudinal study. *JAMA Psychiatry*, *73*(4), 388-395. doi:10.1001/jamapsychiatry.2015.3229.

Blozis, S. A., Ge, X., Xu, S., Natsuaki, M. N., Shaw, D. S., Neiderhiser, J. M., … Reiss, D. (2013). Sensitivity analysis of multiple informant models when data are not missing at random. Structural equation modeling. *A Multidisciplinary Journal*, *20*(2), 283–298. doi:10.1080/10705511.2013.769393

Bornstein, M. H., Hahn, C.-S., & Haynes, O. M. (2010). Social competence, externalizing, and internalizing behavioral adjustment from early childhood through early adolescence: Developmental cascades. *Development and Psychopathology*, 22(4), 717–735. doi:10.1017/s0954579410000416

Boutwell, B., & Beaver, K. (2010). Maternal cigarette smoking during pregnancy and offspring externalizing behavioral problems: A propensity score matching analysis. *International Journal of Environmental Research and Public Health*, *7*(1), 146–163. doi:10.3390/ijerph7010146

Boylan, K., Vaillancourt, T., Boyle, M., & Szatmari, P. (2007). Comorbidity of internalizing disorders in children with oppositional defiant disorder. *European Child and Adolescent Psychiatry*, *16*(8), 484–494. doi: 10.1007/s00787-007-0624-1.

Bradley, R. H., McKelvey, L. M., & Whiteside-Mansell, L. (2011). Does the quality of stimulation and support in the home environment moderate the effect of early education programs? *Child Development*, *82*(6), 2110–2122. doi:10.1111/j.1467-8624.2011.01659.x

Branje, S. J., Van Lieshout, C. F., Van Aken, M. A., & Haselager, G. J. (2004). Perceived support in sibling relationships and adolescent adjustment. *Journal of Child Psychology and Psychiatry*, *45*(8), 1385-1396. doi:10.1111/j.1469-7610.2004.00332.x

Braza, P., Carreras, R., Muñoz, J. M., Braza, F., Azurmendi, A., Pascual-Sagastizábal, E., … Sánchez-Martín, J. R. (2013). Negative maternal and paternal parenting styles as predictors of children's behavioral problems: Moderating effects of the child's sex. *Journal of Child and Family Studies*, 24(4), 847–856. doi:10.1007/s10826-013-9893-0

Brennan, P. A., Hammen, C., Sylvers, P., Bor, W., Najman, J., Lind, P., … Smith, A. K. (2011). Interactions between the COMT Val108/158Met polymorphism and maternal prenatal smoking predict aggressive behavior outcomes. *Biological Psychology, 87*(1), 99–105. doi:10.1016/j.biopsycho.2011.02.013

Brocki, K. C., & Bohlin, G. (2006). Developmental change in the relation between executive functions and symptoms of ADHD and co-occurring behaviour problems. *Infant and Child Development, 15*(1), 19–40. doi:10.1002/icd.413

Brody, G. H., Stoneman, Z., & Burke, M. (1987). Child temperaments, maternal differential behavior, and sibling relationships. *Developmental Psychology,* 23(3), 354–362. doi:10.1037/0012-1649.23.3.354

Brody, G. H., Stoneman, Z., & McCoy, J. K. (1992). Parental differential treatment of siblings and sibling differences in negative emotionality. *Journal of Marriage and the Family, 54*(3), 643. doi:10.2307/353250

Bublitz, M. H., & Stroud, L. R. (2011). Maternal smoking during pregnancy and offspring brain structure and function: Review and agenda for future research. *Nicotine & Tobacco Research, 14*(4), 388–397. doi:10.1093/ntr/ntr191

Buist, K. L., Deković, M., & Prinzie, P. (2013). Sibling relationship quality and psychopathology of children and adolescents: A meta-analysis. *Clinical Psychology Review, 33*(1), 97–106. doi:10.1016/j.cpr.2012.10.007

Bunge, S. A., & Crone, E. A. (2009). Neural correlates of the development of cognitive control. In J. Rumsey & M. Ernst (Eds.), *Neuroimaging in developmental clinical neuroscience* (pp. 22–37). Cambridge, UK: Cambridge University Press.

Burt, S. A. (2009). Are there meaningful etiological differences within antisocial behavior? Results of a meta-analysis. *Clinical Psychology Review*, 29(2), 163–178. doi:10.1016/j.cpr.2008.12.004

Burt, S. A., McGue, M., Krueger, R. F., & Iacono, W. G. (2005). How are parent–child conflict and childhood externalizing symptoms related over time? Results from a genetically informative cross-lagged study. *Development and Psychopathology,* 17(01), 145-165. doi:10.1017/s095457940505008x

Buschgens, C. J. M., Swinkels, S. H. N., van Aken, M. A. G., Ormel, J., Verhulst, F. C., & Buitelaar, J. K. (2009). Externalizing behaviors in preadolescents: familial risk to externalizing behaviors, prenatal and perinatal risks, and their interactions. *European Child & Adolescent Psychiatry*, *18*(2), 65–74. doi:10.1007/s00787-008-0704-x

Campbell, S. B. (1995). Behavior problems in preschool children: A review of recent research. *Journal of Child Psychology and Psychiatry*, *36*(1), 113–149. doi:10.1111/j.1469-7610.1995.tb01657.x

Campione-Barr, N., Bassett Greer, K., Schwab, K., & Kruse, A. (2013). Differing domains of actual sibling conflict discussions and associations with conflict styles and relationship quality. *Social Development*, 666–683. doi:10.1111/sode.12059

Campione-Barr, N., & Smetana, J. G. (2010). "Who said you could wear my sweater?" adolescent siblings' conflicts and associations with relationship quality. *Child Development*, 81(2), 464–471. doi:10.1111/j.1467-8624.2009.01407.x

Carden, S. W., Holtzman, N. S., & Strube, M. J. (2017). CAHOST: An excel workbook for facilitating the Johnson-Neyman technique for two-way interactions in multiple regression. *Frontiers in Psychology, 8:* 1293. doi:10.3389/fpsyg.2017.01293

Carlson, N., & Birkett, M. (2017). *Physiology of Behavior* (12th ed.). Boston, MA: Pearson Education.

Casey, B. J., Trainor, R. J., Orendi, J. L., Schubert, A. B., Nystrom, L. E., Cohen, J. D., & Noll, D. C. (1996). A pediatric functional MRI study of prefrontal activation during performance of a Go-No-Go task. *NeuroImage, 3*(3), S593. doi:10.1016/s1053-8119(96)80595-7

Cassidy, A. R. (2015). Executive function and psychosocial adjustment in healthy children and adolescents: A latent variable modelling investigation. *Child Neuropsychology, 22*(3), 292–317. doi:10.1080/09297049.2014.994484

Castellanos-Ryan, N., Parent, S., Vitaro, F., Tremblay, R. E., & Seguin, J. R. (2013). Pubertal development, personality, and substance use: A 10-year longitudinal study from childhood to adolescence. *Journal of Abnormal Psychology, 122*, 782–796. https://doi.org/10.1037/a0033133

Caspi, A., Henry, B., McGee, R. O., Moffitt, T. E., & Silva, P. A. (1995). Temperamental origins of child and adolescent behavior problems: From age three to age fifteen. *Child Development, 66*(1), 55-68. doi:10.2307/1131190

Caspi, A., Moffitt, T.E., Thornton, A., Freedman, D., Amell, J.W., Harrington, H., Smeijers, J., & Silva, P.A. (1996). The life history calendar: A research and clinical assessment method for collecting retrospective event-history data. *International Journal of Methods in Psychiatric Research, 6*, 101-114.

CEDAR. (1989). *Drug use chart*. unpublished manuscript: University of Pittsburgh.

Census Bureau National Housing Demographics. (2017). Retrieved from https://www.census.gov/programssurveys/ahs/data/interactive/ahstablecreator.html#?s_areas=a00000&s_year=n2017&s_tableName=Table8a&s_byGroup1=a1&s_byGroup2=a1&s_filterGroup1=t1&s_filterGroup2=g1&s_show=S

Chatterton, Z., Hartley, B. J., Seok, M.-H., Mendelev, N., Chen, S., Milekic, M., … Haghighi, F. (2017). In utero exposure to maternal smoking is associated with DNA methylation alterations and reduced neuronal content in the developing fetal brain. *Epigenetics & Chromatin, 10*(1). doi:10.1186/s13072-017-0111-y

Chen, P., & Jacobson, K. C. (2012). Developmental trajectories of sub- stance use from early adolescence to young adulthood: Gender and racial/ethnic differences. *Journal of Adolescent Health, 50*, 154–163. http://dx.doi.org/10.1016/j.jadohealth.2011.05.013

Clark, D. A., Donnellan, M. B., Robins, R. W., & Conger, R. D. (2015). Early adolescent temperament, parental monitoring, and substance use in Mexican-origin adolescents. *Journal of adolescence, 41*, 121–130. doi:10.1016/j.adolescence.2015.02.010

Clark, C. A. C., Espy, K. A., & Wakschlag, L. (2016). Developmental pathways from prenatal tobacco and stress exposure to behavioral disinhibition. *Neurotoxicology and Teratology, 53*, 64–74. doi:10.1016/j.ntt.2015.11.009

Clark, D. B., Moss, H. B., Kirisci, L., Mezzich, A. C., Miles, R., & Ott, P. (1997). Psychopathology in preadolescent sons of fathers with substance use disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 36*(4), 495–502. doi:10.1097/00004583-199704000-00012

Clark, C., Prior, M., & Kinsella, G. J. (2000). Do executive function deficits differentiate between adolescents with ADHD and oppositional defiant/conduct disorder? A neuropsychological study using the Six Elements Test and Hayling Sentence Completion Test. *Journal of Abnormal Child Psychology, 28*(5), 403–414. doi:10.1023/A:1005176320912

Compton, K., Snyder, J., Schrepferman, L., Bank, L., & Shortt, J. W. (2003). The contribution of parents and siblings to antisocial and depressive behavior in adolescents: A double jeopardy coercion model. *Development and Psychopathology, 15*(01), 163–182. doi:10.1017/s0954579403000099

Conger, R. D., Conger, K. J., Elder, G. H., Lorenz, F. O., Simons, R. L., & Whitbeck, L. B. (1992). A family process model of economic hardship and adjustment of early adolescent boys. *Child Development, 63*(3), 526. doi:10.2307/1131344

Conger, R. D., Ge, X., Elder, G. H., Lorenz, F. O., & Simons, R. L. (1994). Economic stress, coercive family process, and developmental problems of adolescents. *Child Development, 65*(2), 541. doi:10.2307/1131401

Court, J. ., Lloyd, S., Johnson, M., Griffiths, M., Birdsall, N. J. ., Piggott, M. ., … Perry, R. . (1997). Nicotinic and muscarinic cholinergic receptor binding in the human hippocampal formation during development and aging. *Developmental Brain Research, 101*(1-2), 93–105. doi:10.1016/s0165-3806(97)00052-7

Court, J. A., Martin-Ruiz, C., Graham, A., & Perry, E. (2000). Nicotinic receptors in human brain: topography and pathology. *Journal of Chemical Neuroanatomy, 20*(3-4), 281–298. doi:10.1016/s0891-0618(00)00110-1

Criss, M. M., & Shaw, D. S. (2005). Sibling relationships as contexts for delinquency training in low-income families. *Journal of Family Psychology, 19*(4), 592–600. doi:10.1037/0893-3200.19.4.592

Crone, E. A., & Dahl, R. E. (2012). Understanding adolescence as a period of social–affective engagement and goal flexibility. *Nature Reviews Neuroscience, 13*(9), 636–650. doi:10.1038/nrn3313

Cronk, N. J., Slutske, W. S., Madden, P. A. F., Bucholz, K. K., Reich, W., & Heath, A. C. (2002). Emotional and behavioral problems among female twins: An evaluation of the equal environments assumption. *Journal of the American Academy of Child & Adolescent Psychiatry*, *41*(7), 829–837. doi:10.1097/00004583-200207000-00016

Daseking, M., Petermann, F., Tischler, T., & Waldmann, H.-C. (2015). Smoking during pregnancy is a risk factor for executive function deficits in preschool-aged children. *Geburtshilfe Und Frauenheilkunde*, *75*(01), 64–71. doi:10.1055/s-0034-1383419

Deater-Deckard, K., & Plomin, R. (1999). An adoption study of the etiology of teacher and parent reports of externalizing behavior problems in middle childhood. *Child Development*, 70(1), 144–154. doi:10.1111/1467-8624.00011

Defoe, I. N., Keijsers, L., Hawk, S. T., Branje, S., Dubas, J. S., Buist, K., … Meeus, W. (2013). Siblings versus parents and friends: longitudinal linkages to adolescent externalizing problems. *Journal of Child Psychology and Psychiatry*, 54(8), 881–889. doi:10.1111/jcpp.12049

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System*. PsycTESTS Dataset. doi:10.1037/t15082-000

D'Esposito, M., & Postle, B. R. (2015). The cognitive neuroscience of working memory. *Annual Review of Psychology*, *66*(1), 115–142. doi:10.1146/annurev-psych-010814-015031

Diagnostic criteria for Conduct Disorder. (n.d.). *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, Text Revision (DSM-IV-TR). doi:10.1176/appi.books.9780890423349.7856

Diamond, A. (2013). Executive functions. *Annual Review of Psychology*, *64*(1), 135–168. doi:10.1146/annurev-psych-113011-143750

Dick, D. M., Viken, R., Purcell, S., Kaprio, J., Pulkkinen, L., & Rose, R. J. (2007). Parental monitoring moderates the importance of genetic and environmental influences on adolescent smoking. *Journal of Abnormal Psychology*, 116(1), 213–218. doi:10.1037/0021-843x.116.1.213

Dobbing, J. (1971). Undernutrition and the developing brain: The use of animal models to elucidate the human problem. *Normal and Abnormal Development of Brain and Behaviour*, *74*(6), 433–442. doi:10.1007/978-94-010-2921-6_2

Dobbing, J., & Sands, J. (1979). Comparative aspects of the brain growth spurt. *Early Human Development, 3*(1), 79–83. doi:10.1016/0378-3782(79)90022-7

Dodge, K. A., Malone, P. S., Lansford, J. E., Miller, S., Pettit, G. S., & Bates, J. E. (2009). A dynamic cascade model of the development of substance-use onset. *Monographs of the Society for Research in Child Development, 74*(3), vii-119.

Donnelly, B. W., Conger, R. D., & Elder, G. H. (1994). Families in troubled times: Adapting to change in rural america. *Journal of Marriage and the Family, 56*(3), 780-781. doi:10.2307/352890

D'Onofrio, B. M., Hulle, C. A. van, Waldman, I. D., Rodgers, J. L., Harden, K. P., Rathouz, P. J., & Lahey, B. B. (2008). Smoking during pregnancy and offspring externalizing problems: An exploration of genetic and environmental confounds. *Development and Psychopathology, 20*(1), 139–164. doi:10.1017/s0954579408000072

D'Onofrio, B. M., Singh, A. L., Iliadou, A., Lambe, M., Hultman, C. M., Grann, M., … Lichtenstein, P. (2010). Familial confounding of the association between maternal smoking during pregnancy and offspring criminality. *Archives of General Psychiatry, 67*(5), 529. doi:10.1001/archgenpsychiatry.2010.33

D'Onofrio, B. M., Van Hulle, C. A., Goodnight, J. A., Rathouz, P. J., & Lahey, B. B. (2011). Is maternal smoking during pregnancy a causal environmental risk factor for adolescent antisocial behavior? Testing etiological theories and assumptions. *Psychological Medicine, 42*(07), 1535–1545. doi:10.1017/s0033291711002443

Drake P, Driscoll AK, Mathews TJ. Cigarette smoking during pregnancy: United States, 2016. NCHS Data Brief, no 305. Hyattsville, MD: National Center for Health Statistics. 2018.

Dumas, T. C. (2005). Late postnatal maturation of excitatory synaptic transmission permits adult-like expression of hippocampal-dependent behaviors. *Hippocampus, 15*(5), 562–578. doi:10.1002/hipo.20077

Duncan, R. J., Schmitt, S. A., Burke, M., & McClelland, M. M. (2018). Combining a kindergarten readiness summer program with a self-regulation intervention improves school readiness. *Early Childhood Research Quarterly, 42*, 291–300. doi:10.1016/j.ecresq.2017.10.012

Dunn, J. (1983). Sibling relationships in early childhood. *Child Development, 54*(4), 787–811. doi:10.1111/j.1467-8624.1983.tb00503.x

Dunn, J., Slomkowski, C., & Beardsall, L. (1994). Sibling relationships from the preschool period through middle childhood and early adolescence. *Developmental Psychology, 30*(3), 315–324. doi:10.1037/0012-1649.30.3.315

Dunn, J., Slomkowski, C., Donelan, N., & Herrera, C. (1995). Conflict, understanding, and relationships: Developments and differences in the preschool years. *Early Education & Development, 6*(4), 303–316. doi:10.1207/s15566935eed0604_2

Dwairy, M. A. (2008). Parental inconsistency versus parental authoritarianism: Associations with symptoms of psychological disorders. *Journal of Youth and Adolescence,* 37(5), 616–626. doi:10.1007/s10964-007-9169-3

Dwyer, J. B., McQuown, S. C., & Leslie, F. M. (2009). The dynamic effects of nicotine on the developing brain. *Pharmacology & Therapeutics, 122*(2), 125–139. doi:10.1016/j.pharmthera.2009.02.003

East, P. L., & Khoo, S. T. (2005). Longitudinal pathways linking family factors and sibling relationship qualities to adolescent substance use and sexual risk behaviors. *Journal of Family Psychology, 19*(4), 571–580. doi:10.1037/0893-3200.19.4.571

Edelbrock, C., Rende, R., Plomin, R., & Thompson, L. A. (1995). A twin study of competence and problem behavior in childhood and early adolescence. *Journal of Child Psychology and Psychiatry, 36*(5), 775–785. doi:10.1111/j.1469-7610.1995.tb01328.x

Eiden, R. D., Lessard, J., Colder, C. R., Livingston, J., Casey, M., & Leonard, K. E. (2016). Developmental cascade model for adolescent substance use from infancy to late adolescence. *Developmental Psychology*, 52(10), 1619–1633. doi:10.1037/dev0000199

Eisenberg, N., Fabes, R., Shepard, S., Murphy, B., Guthrie, I., Jones, S., . . . Maszk, P. (1997). Contemporaneous and longitudinal prediction of children's social functioning from regulation and emotionality. *Child Development, 68*(4), 642-664. doi:10.2307/1132116

Eisenberg, N., Valiente, C., Spinrad, T. L., Cumberland, A., Liew, J., Reiser, M., … Losoya, S. H. (2009). Longitudinal relations of children's effortful control, impulsivity, and negative emotionality to their externalizing, internalizing, and co-occurring behavior problems. *Developmental Psychology, 45*(4), 988–1008. doi:10.1037/a0016213

Eisenberg, N., Zhou, Q., Spinrad, T. L., Valiente, C., Fabes, R. A., & Liew, J. (2005). Relations among positive parenting, children's effortful control, and externalizing problems: A three-wave longitudinal study. *Child development, 76*(5), 1055-1071. doi: 10.1111/j.1467-8624.2005.00897.x

Ekblad, M., Gissler, M., Lehtonen, L., & Korkeila, J. (2010). Prenatal smoking exposure and the risk of psychiatric morbidity into young adulthood. *Archives of General Psychiatry, 67*(8), 841. doi:10.1001/archgenpsychiatry.2010.92

Ekblad, M., Korkeila, J., & Lehtonen, L. (2014). Smoking during pregnancy affects fetal brain development. *Acta Paediatrica, 104*(1), 12–18. doi:10.1111/apa.12791

Ekblad, M. O., Rolan, E., Marceau, K., Palmer, R., Todorov, A., Heath, A. C., & Knopik, V. S. (in press). Disruptive behavior in siblings discordant for exposure to maternal smoking during pregnancy: A multi-rater approach. *Nicotine & Tobacco Research.* doi:10.1093/ntr/ntz214 [Epub ahead of print]

Eley, T. C., Lichtenstein, P., & Moffitt, T. E. (2003). A longitudinal behavioral genetic analysis of the etiology of aggressive and nonaggressive antisocial behavior. *Development and Psychopathology,* 15(2), 383–402. doi:10.1017/s095457940300021x

Eley, T. C., Lichtenstein, P., & Stevenson, J. (1999). Sex differences in the etiology of aggressive and nonaggressive antisocial behavior: Results from two twin studies. *Child Development,* 70(1), 155–168. doi:10.1111/1467-8624.00012

Enders, C., & Bandalos, D. (2001). The relative performance of full information maximum likelihood estimation for missing data in structural equation models. *Structural Equation Modeling: A Multidisciplinary Journal, 8*(3), 430–457. doi:10.1207/s15328007sem0803_5

Engelhardt, L. E., Briley, D. A., Mann, F. D., Harden, K. P., & Tucker-Drob, E. M. (2015). Genes unite executive functions in childhood. *Psychological Science, 26*(8), 1151–1163. doi:10.1177/0956797615577209

Enoch, M.-A. (2012). The influence of gene–environment interactions on the development of alcoholism and drug dependence. *Current Psychiatry Reports, 14*(2), 150–158. doi:10.1007/s11920-011-0252-9

Ernst, M. (2014). The triadic model perspective for the study of adolescent motivated behavior. *Brain and Cognition, 89,* 104–111. doi:10.1016/j.bandc.2014.01.006

Ernst, M., Moolchan, E. T., & Robinson, M. L. (2001). Behavioral and neural consequences of prenatal exposure to nicotine. *Journal of the American Academy of Child & Adolescent Psychiatry, 40*(6), 630–641. doi:10.1097/00004583-200106000-00007

Eslinger, P. J., Flaherty-Craig, C. V., & Benton, A. L. (2004). Developmental outcomes after early prefrontal cortex damage. *Brain and Cognition, 55*(1), 84–103. doi:10.1016/s0278-2626(03)00281-1

Espy, K. A., Kaufmann, P. M., Glisky, M. L., & McDiarmid, M. D. (2001). New procedures to assess executive functions in preschool children. *The Clinical Neuropsychologist, 15*(1), 46–58. doi:10.1076/clin.15.1.46.1908

Fagan, A. A., & Najman, J. M. (2005). The relative contributions of parental and sibling substance use to adolescent tobacco, alcohol, and other drug use. *Journal of Drug Issues, 35*(4), 869–883. doi:10.1177/002204260503500410

Fairchild, G., van Goozen, S. H. M., Stollery, S. J., Aitken, M. R. F., Savage, J., Moore, S. C., & Goodyer, I. M. (2009). Decision making and executive function in male adolescents with early-onset or adolescence-onset conduct disorder and control subjects. *Biological Psychiatry, 66*(2), 162–168. doi:10.1016/j.biopsych.2009.02.024

Feinberg, M. E., Solmeyer, A. R., & McHale, S. M. (2011). The third rail of family systems: sibling relationships, mental and behavioral health, and preventive intervention in childhood and adolescence. *Clinical Child and Family Psychology Review, 15*(1), 43–57. doi:10.1007/s10567-011-0104-5

Fergusson, D. M., Horwood, L. J., & Lynskey, M. T. (1994). The comorbidities of adolescent problem behaviors: A latent class model. *Journal of Abnormal Child Psychology*, 22(3), 339–354. doi:10.1007/bf02168078

Forbes, E. E., & Dahl, R. E. (2010). Pubertal development and behavior: hormonal activation of social and motivational tendencies. *Brain and Cognition, 72*(1), 66-72. doi:10.1016/j.bandc.2009.10.007

Forbes, E. E., Phillips, M. L., Silk, J. S., Ryan, N. D., & Dahl, R. E. (2011). Neural systems of threat processing in adolescents: role of pubertal maturation and relation to measures of negative affect. *Developmental Neuropsychology, 36*(4), 429–452. doi:10.1080/87565641.2010.550178

Forbes, E. E., Ryan, N. D., Phillips, M. L., Manuck, S. B., Worthman, C. M., Moyles, D. L., ... & Dahl, R. E. (2010). Healthy adolescents' neural response to reward: associations with puberty, positive affect, and depressive symptoms. *Journal of the American Academy of Child & Adolescent Psychiatry*, *49*(2), 162-172. doi:10.1016/j.jaac.2009.11.006

Ford, T., Goodman, R., & Meltzer, H. (2004). The relative importance of child, family, school and neighbourhood correlates of childhood psychiatric disorder. *Social Psychiatry and Psychiatric Epidemiology*, 39(6). doi:10.1007/s00127-004-0782-0

Forster, J. (2003). Social exchange of cigarettes by youth. *Tobacco Control, 12*(2), 148–154. doi:10.1136/tc.12.2.148

Friedman, N. P., Miyake, A., Young, S. E., DeFries, J. C., Corley, R. P., & Hewitt, J. K. (2008). Individual differences in executive functions are almost entirely genetic in origin. *Journal of Experimental Psychology: General, 137*(2), 201–225. doi:10.1037/0096-3445.137.2.201

Frye, D., David Zelazo, P., & Burack, J. A. (1998). Cognitive complexity and control. *Current Directions in Psychological Science, 7*(4), 116–121. doi:10.1111/1467-8721.ep10774754

Furman, W., & Buhrmester, D. (1985). Children's perceptions of the personal relationships in their social networks. *Developmental Psychology*, *21*(6), 1016-1024. doi: 10.1037/0012-1649.21.6.1016

Fuster, J. M. (1997). Network memory. *Trends in Neurosciences, 20*(10), 451–459. doi:10.1016/s0166-2236(97)01128-4

Gardner, T. W., Dishion, T. J., & Connell, A. M. (2007). Adolescent self-regulation as resilience: Resistance to antisocial behavior within the deviant peer context. *Journal of Abnormal Child Psychology*, 36(2), 273–284. doi:10.1007/s10802-007-9176-6

Garon, N., Bryson, S. E., & Smith, I. M. (2008). Executive function in preschoolers: A review using an integrative framework. *Psychological Bulletin, 134*(1), 31–60. doi:10.1037/0033-2909.134.1.31

Gale, C. R., Deary, I. J., Boyle, S. H., Barefoot, J., Mortensen, L. H., & Batty, G. D. (2008). Cognitive ability in early adulthood and risk of 5 specific psychiatric disorders in middle age. *Archives of General Psychiatry, 65*(12), 1410. doi:10.1001/archpsyc.65.12.1410

Giancola, P. R., Shoal, G. D., & Mezzich, A. C. (2001). Constructive thinking, executive functioning, antisocial behavior, and drug use involvement in adolescent females with a substance use disorder. *Experimental and Clinical Psychopharmacology*, *9*(2), 215–227. doi:10.1037/1064-1297.9.2.215

Giancola, P. R., & Tarter, R. E. (1999). Executive cognitive functioning and risk for substance abuse. *Psychological Science*, *10*(3), 203–205. doi:10.1111/1467-9280.0013

Gluckman, P. D., Hanson, M. A., Cooper, C., & Thornburg, K. L. (2008). Effect of in utero and early-life conditions on adult health and disease. *New England Journal of Medicine*, *359*(1), 61–73. doi:10.1056/nejmra0708473

Goldman-Rakic, P. S. (1987). Development of cortical circuitry and cognitive function. *Child Development*, *58*(3), 601. doi:10.2307/1130201

Gonzalez, R. (2007). Acute and non-acute effects of cannabis on brain functioning and neuropsychological performance. *Neuropsychology Review*, *17*(3), 347–361. doi:10.1007/s11065-007-9036-8

Gorman-Smith, D., & Loeber, R. (2005). Are developmental pathways in disruptive behaviors the same for girls and boys? *Journal of Child and Family Studies*, *14*(1), 15–27. doi:10.1007/s10826-005-1109-9

Graham, J. W. (2003). Adding missing-data-relevant variables to FIML-based structural equation models. Structural equation modeling. *A Multidisciplinary Journal*, *10*(1), 80–100. doi:10.1207/s15328007sem1001_4

Grania Sheehan, Yvonne Darlington, Patricia Noller & Judith Feeney (2004) Children's perceptions of their sibling relationships during parental separation and divorce, *Journal of Divorce & Remarriage*, *41*:1-2, 69-94, doi: 10.1300/J087v41n01_05

Gray, K. M., & Squeglia, L. M. (2018). Research Review: What have we learned about adolescent substance use?. *Journal of Child Psychology and Psychiatry*, *59*(6), 618-627. doi: 10.1111/jcpp.12783.

Grunbaum, J. A., Kann, L., Kinchen, S. A., Williams, B., Ross, J. G., Lowry, R., & Kolbe, L. (2002). Youth risk behavior surveillance - United States, 2001. *Journal of School Health*, *72*(8), 313–328. doi:10.1111/j.1746-1561.2002.tb07917.x

Guerrini, I., Quadri, G., & Thomson, A. D. (2014). Genetic and environmental interplay in risky drinking in adolescents: A literature review. *Alcohol and Alcoholism, 49*(2), 138–142. doi:10.1093/alcalc/agu003

Guillem, F., Rougier, A., & Claverie, B. (1999). Short-and long-delay intracranial ERP repetition effects dissociate memory systems in the human brain. *Journal of Cognitive Neuroscience, 11*(4), 437–458. doi:10.1162/089892999563526

Hajal, N., Neiderhiser, J., Moore, G., Leve, L., Shaw, D., Harold, G., … Reiss, D. (2015). Angry responses to infant challenges: Parent, marital, and child genetic factors associated with harsh parenting. *Child Development, 86*(1), 80–93. doi:10.1111/cdev.12345

Hammond, S. I., Müller, U., Carpendale, J. I., Bibok, M. B., & Liebermann-Finestone, D. P. (2012). The effects of parental scaffolding on preschoolers' executive function. *Developmental Psychology, 48*(1), 271. doi: 10.1037/a0025519

Harris, P. L. (2005). Conversation, pretense, and theory of mind. In J. W. Astington & J. A. Baird (Eds.), *Why Language Matters for Theory of Mind* (pp. 70-83). New York: Oxford University Press.

Hayes, A. F. (2009). Beyond Baron and Kenny: Statistical mediation analysis in the new millennium. *Communication Monographs, 76*(4), 408–420. doi:10.1080/03637750903310360

Hayes, A. F. (2013). *Introduction to Mediation, Moderation, and Conditional Process Analysis: A Regression-Based Approach*. New York, NY: The Guilford Press. Journal of Educational Measurement, 51(3), 335–337. doi:10.1111/jedm.12050

Heath, A. C., & Martin, N. G. (1994). Genetic influences on alcohol consumption patterns and problem drinking: Results from the australian NH&MRC twin panel follow-up survey. *Annals of the New York Academy of Sciences*, *708*(1 Types of Alco), 72–85. doi:10.1111/j.1749-6632.1994.tb24699.x

Hebel, J. R., Fox, N. L., & Sexton, M. (1988). Dose-response of birth weight to various measures of maternal smoking during pregnancy. *Journal of Clinical Epidemiology*, *41*(5), 483–489. doi:10.1016/0895-4356(88)90050-9

Heutink, P., Verhuls, F. C., & Boomsma, D. I. (2006). A longitudinal twin study on IQ, executive functioning, and attention problems during childhood and early adolescence. *Acta Neurol. Belg*, *106*, 191-207.

Hicks, B. M., Iacono, W. G., & McGue, M. (2012). Index of the transmissible common liability to addiction: Heritability and prospective associations with substance abuse and related outcomes. *Drug and Alcohol Dependence*, *123*, S18–S23. doi:10.1016/j.drugalcdep.2011.12.017

Hill, S. Y., & Muka, D. (1996). Childhood psychopathology in children from families of alcoholic female probands. *Journal of the American Academy of Child & Adolescent Psychiatry*, *35*(6), 725–733. doi:10.1097/00004583-199606000-00012

Hohmann, S., Zohsel, K., Buchmann, A. F., Blomeyer, D., Holz, N., Boecker-Schlier, R., … Laucht, M. (2016). Interacting effect of MAOA genotype and maternal prenatal smoking on aggressive behavior in young adulthood. *Journal of Neural Transmission, 123*(8), 885–894. doi:10.1007/s00702-016-1582-x

Hollenstein, T., & Lougheed, J. P. (2013). Beyond storm and stress: Typicality, transactions, timing, and temperament to account for adolescent change. *American Psychologist, 68*(6), 444–454. doi:10.1037/a0033586

Holz, N. E., Zohsel, K., Laucht, M., Banaschewski, T., Hohmann, S., & Brandeis, D. (2018). Gene x environment interactions in conduct disorder: Implications for future treatments. Neuroscience & Biobehavioral Reviews, 91, 239–258. doi:10.1016/j.neubiorev.2016.08.017

Horwitz, A. V., Videon, T. M., Schmitz, M. F., & Davis, D. (2003). Rethinking twins and environments: Possible social sources for assumed genetic influences in twin research. *Journal of Health and Social Behavior*, *44*(2), 111. doi:10.2307/1519802

Huang-Pollock, C. L., Carr, T. H., & Nigg, J. T. (2002). Development of selective attention: Perceptual load influences early versus late attentional selection in children and adults. *Developmental Psychology, 38*(3), 363–375. doi:10.1037/0012-1649.38.3.363

Hudziak, J. J., van Beijsterveldt, C. E. M., Bartels, M., Rietveld, M. J. H., Rettew, D. C., Derks, E. M., & Boomsma, D. I. (2003). Individual differences in aggression: Genetic analyses by age, gender, and informant in 3-, 3-, and 10-year-old Dutch twins. *Behavior Genetics*, 33(5), 575–589. doi:10.1023/a:1025782918793

Hughes, C. (2011). Changes and challenges in 20 years of research into the development of executive functions. *Infant and Child Development, 20*(3), 251–271. doi:10.1002/icd.736

Hughes, C., & Devine, R. T. (2019). For better or for worse? Positive and negative parental influences on young children's executive function. *Child Development*, *90*(2), 593-609. doi: 10.1111/cdev.12915

Huizink, A. C., & Mulder, E. J. H. (2006). Maternal smoking, drinking or cannabis use during pregnancy and neurobehavioral and cognitive functioning in human offspring. *Neuroscience & Biobehavioral Reviews, 30*(1), 24–41. doi:10.1016/j.neubiorev.2005.04.005

Hummer, T. A., Kronenberger, W. G., Wang, Y., Dunn, D. W., Mosier, K. M., Kalnin, A. J., & Mathews, V. P. (2010). Executive functioning characteristics associated with adhd comorbidity in adolescents with disruptive behavior disorders. *Journal of Abnormal Child Psychology, 39*(1), 11–19. doi:10.1007/s10802-010-9449-3

Iacono, W. G., Carlson, S. R., Taylor, J., Elkins, I. J., & McGue, M. (1999). Behavioral disinhibition and the development of substance-use disorders: Findings from the Minnesota Twin Family Study. *Development and Psychopathology, 11*, 869-900. doi: 10.1017/s0954579499002369.

Jaddoe, V. W. V., Troe, E.-J. W. M., Hofman, A., Mackenbach, J. P., Moll, H. A., Steegers, E. P., & Witteman, J. C. M. (2008). Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. *Paediatric and Perinatal Epidemiology, 22*(2), 162–171. doi:10.1111/j.1365-3016.2007.00916.x

Jenkins, J., & Dunn, J. (2009). Siblings within families: Levels of analysis and patterns of influence. *New Directions for Child and Adolescent Development, 2009*(126), 79–93. doi:10.1002/cd.258

Johnson, P. O., and Neyman, J. (1936). Tests of certain linear hypotheses and their applications to some educational problems. *Stat. Res. Mem. 1*, 57–39.

Johnston, L.D., O'Malley, P.M., Miech, R.A., Bachman, J.G., & Schulenberg, J.E. (2017). *Monitoring the future national survey results on drug use, 1975-2016: Overview, key findings on adolescent drug use.* Ann Arbor: Institute for Social Research, The University of Michigan.

Johnston, L., Miech, R., O'Malley, P., Bachman, J., Schulenberg, J., & Patrick, M. (2019). Monitoring the Future national survey results on drug use, 1975-2018: Overview, key findings on adolescent drug use. doi:10.3998/2027.42/150621

Jokela, M., Ferrie, J., & Kivimäki, M. (2009). Childhood problem behaviors and death by midlife: The british national child development study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 48(1), 19–24. doi:10.1097/chi.0b013e31818b1c76

Kahn, R. S., Khoury, J., Nichols, W. C., & Lanphear, B. P. (2003). Role of dopamine transporter genotype and maternal prenatal smoking in childhood hyperactive-impulsive, inattentive, and oppositional behaviors. *The Journal of Pediatrics, 143*(1), 104–110. doi:10.1016/s0022-3476(03)00208-7

Kandel, D. B., Johnson, J. G., Bird, H. R., Weissman, M. M., Goodman, S. H., Lahey, B. B., … Schwab-Stone, M. E. (1999). Psychiatric comorbidity among adolescents with substance use disorders: findings from the meca study. *Journal of the American Academy of Child & Adolescent Psychiatry*, 38(6), 693–699. doi:10.1097/00004583-199906000-00016

Kane, V. B., Fu, Y., Matta, S. G., & Sharp, B. M. (2003). Gestational nicotine exposure attenuates nicotine-stimulated dopamine release in the nucleus accumbens shell of adolescent lewis rats. *Journal of Pharmacology and Experimental Therapeutics, 308*(2), 521–528. doi:10.1124/jpet.103.059899

Keenan, K., & Shaw, D. (1997). Developmental and social influences on young girls' early problem behavior. *Psychological bulletin, 121*(1), 95-113. doi: 10.1037/0033-2909.121.1.95

Kelly, A. B., Evans-Whipp, T. J., Smith, R., Chan, G. C. K., Toumbourou, J. W., Patton, G. C., … Catalano, R. F. (2015). A longitudinal study of the association of adolescent polydrug use, alcohol use and high school non-completion. *Addiction, 110*(4), 627–635. doi:10.1111/add.12829

Kendler, K. S., & Gardner, C. O. (1998). Twin studies of adult psychiatric and substance dependence disorders: are they biased by differences in the environmental experiences of monozygotic and dizygotic twins in childhood and adolescence? *Psychological Medicine, 28(*3), 625–633. doi:10.1017/s0033291798006643

Kendler, K. S., Prescott, C. A., Myers, J., & Neale, M. C. (2003). The structure of genetic and environmental risk factors for common psychiatric and substance use disorders in men and women. *Archives of General Psychiatry, 60*(9), 929. doi:10.1001/archpsyc.60.9.929

Kendler, K. S., Schmitt, E., Aggen, S. H., & Prescott, C. A. (2008). Genetic and environmental influences on alcohol, caffeine, cannabis, and nicotine use from early adolescence to middle adulthood. *Archives of General Psychiatry, 65*(6), 674-682. doi:10.1001/archpsyc.65.6.674

Kilford, E. J., Garrett, E., & Blakemore, S. J. (2016). The development of social cognition in adolescence: An integrated perspective. *Neuroscience & Biobehavioral Reviews*, *70*, 106-120. doi:10.1016/j.neubiorev.2016.08.016

Kim, J.-Y., McHale, S. M., Wayne Osgood, D., & Crouter, A. C. (2006). Longitudinal course and family correlates of sibling relationships from childhood through adolescence. *Child Development, 77*(6), 1746–1761. doi:10.1111/j.1467-8624.2006.00971.x

Kim, J.-Y., McHale, S. M., Crouter, A. C., & Osgood, D. W. (2007). Longitudinal linkages between sibling relationships and adjustment from middle childhood through adolescence. *Developmental Psychology, 43*(4), 960–973. doi:10.1037/0012-1649.43.4.960

King, S. M., Iacono, W. G., & McGue, M. (2004). Childhood externalizing and internalizing psychopathology in the prediction of early substance use. *Addiction,* 99(12), 1548–1559. doi:10.1111/j.1360-0443.2004.00893.x

Kirisci, L., Mezzich, A., & Tarter, R. (1995). Norms and sensitivity of the adolescent version of the drug use screening inventory. *Addictive Behaviors, 20*(2), 149–157. doi:10.1016/0306-4603(94)00058-1

Kirisci, L., Tarter, R. E., & Hsu, T.-C. (1994). Fitting a two-parameter logistic item response model to clarify the psychometric properties of the drug use screening inventory for adolescent alcohol and drug abusers. Alcoholism. *Clinical and Experimental Research, 18*(6), 1335–1341. doi:10.1111/j.1530-0277.1994.tb01433.x

Kirisci, L., Vanyukov, M., Dunn, M., & Tarter, R. (2002). Item response theory modeling of substance use: An index based on 10 drug categories. *Psychology of Addictive Behaviors, 16*(4), 290–298. doi:10.1037/0893-164x.16.4.290

Knickmeyer, R. C., Kang, C., Woolson, S., Smith, J. K., Hamer, R. M., Lin, W., … Gilmore, J. H. (2011). Twin-singleton differences in neonatal brain structure. *Twin Research and Human Genetics, 14*(3), 268–276. doi:10.1375/twin.14.3.268

Knopik, V. S., Neiderhiser, J. M., DeFries, J. C., & Plomin, R. (2017). *Behavioral Genetics*, Seventh Edition. New York, NY: Worth Publishers.

Knopik, V. S. (2009). Maternal smoking during pregnancy and child outcomes: Real or spurious effect? *Developmental Neuropsychology, 34*(1), 1–36. doi:10.1080/87565640802564366

Knopik, V. S., Heath, A. C., Bucholz, K. K., Madden, P. A. F., & Waldron, M. (2009). Genetic and environmental influences on externalizing behavior and alcohol problems in adolescence: A female twin study. *Pharmacology Biochemistry and Behavior, 93*(3), 313–321. doi:10.1016/j.pbb.2009.03.011

Knopik, V. S., Heath, A. C., Marceau, K., Palmer, R. H. C., McGeary, J. E., Todorov, A., & Evans, A. S. (2015). Missouri mothers and their children: A family study of the effects of genetics and the prenatal environment. *Twin Research and Human Genetics, 18*(05), 485–496. doi:10.1017/thg.2015.46

Knopik, V. S., Marceau, K., Bidwell, L. C., Palmer, R. H., Smith, T. F., Todorov, A., ... & Heath, A. C. (2016). Smoking during pregnancy and ADHD risk: A genetically informed, multiple-rater approach. *American Journal of Medical Genetics Part B: Neuropsychiatric Genetics*, *171*(7), 971-981. Doi: 10.1002/ajmg.b.32421.

Knopik, V. S., Marceau, K., Palmer, R. H. C., Smith, T. F., & Heath, A. C. (2015). Maternal smoking during pregnancy and offspring birth weight: A genetically-informed approach comparing multiple raters. *Behavior Genetics, 46*(3), 353–364. doi:10.1007/s10519-015-9750-6

Kochanska, G., & Knaack, A. (2003). Effortful control as a personality characteristic of young children: Antecedents, correlates, and consequences. *Journal of Personality*, *71*(6), 1087–1112. doi:10.1111/1467-6494.7106008

Kothari, B. H., Sorenson, P., Bank, L., & Snyder, J. (2014). Alcohol and substance use in adolescence and young adulthood: The role of siblings. *Journal of Family Social Work, 17*(4), 324–343. doi:10.1080/10522158.2014.924457

Kuczynski, L., & Mol, J. D. (2015). *Dialectical Models of Socialization.* Handbook of Child Psychology and Developmental Science, 1–46. doi:10.1002/9781118963418.childpsy109

Kuja-Halkola, R., D'Onofrio, B. M., Larsson, H., & Lichtenstein, P. (2014). Maternal smoking during pregnancy and adverse outcomes in offspring: Genetic and environmental sources of covariance. *Behavior Genetics, 44*(5), 456–467. doi:10.1007/s10519-014-9668-4

Lahey, B. B., & D'Onofrio, B. M. (2010). All in the family: Comparing siblings to test causal hypotheses regarding environmental influences on behavior. *Current Directions in Psychological Science, 19*(5), 319–323. doi:10.1177/0963721410383977

Langenecker, S. A., Zubieta, J.-K., Young, E. A., Akil, H., & Nielson, K. A. (2007). A task to manipulate attentional load, set-shifting, and inhibitory control: Convergent validity and test–retest reliability of the Parametric Go/No-Go Test. *Journal of Clinical and Experimental Neuropsychology, 29*(8), 842–853. doi:10.1080/13803390601147611

Langley, K., Heron, J., Smith, G. D., & Thapar, A. (2012). Maternal and paternal smoking during pregnancy and risk of adhd symptoms in offspring: Testing for intrauterine effects. *American Journal of Epidemiology, 176*(3), 261–268. doi:10.1093/aje/kwr510

Lansford, J. E., Laird, R. D., Pettit, G. S., Bates, J. E., & Dodge, K. A. (2014). Mothers' and fathers' autonomy-relevant parenting: longitudinal links with adolescents' externalizing and internalizing behavior. *Journal of Youth and Adolescence, 43*(11), 1877–1889. doi:10.1007/s10964-013-0079-2

Latimer, K., Wilson, P., Kemp, J., Thompson, L., Sim, F., Gillberg, C., … Minnis, H. (2012). Disruptive behaviour disorders: A systematic review of environmental antenatal and early years risk factors. *Child: Care, Health and Development, 38*(5), 611–628. doi:10.1111/j.1365-2214.2012.01366.x

Lehto, J. E., Juujärvi, P., Kooistra, L., & Pulkkinen, L. (2003). Dimensions of executive functioning: Evidence from children. *British Journal of Developmental Psychology, 21*(1), 59–80. doi:10.1348/026151003321164627

Lerner, R. M., Johnson, S. K., & Buckingham, M. H. (2015). Relational developmental systems-based theories and the study of children and families: Lerner and spanier (1978) Revisited. *Journal of Family Theory & Review, 7*(2), 83–104. doi:10.1111/jftr.12067

Lewis, C., & Carpendale, J. I. M. (2009). Introduction: Links between social interaction and executive function. *New Directions for Child and Adolescent Development, 2009*(123), 1–15. doi:10.1002/cd.232

Leve, L. D., Neiderhiser, J. M., Shaw, D. S., Ganiban, J., Natsuaki, M. N., & Reiss, D. (2013). The early growth and development study: A prospective adoption study from birth through middle childhood. *Twin Research and Human Genetics*, *16*(1), 412-423.

Levens, S. M., Larsen, J. T., Bruss, J., Tranel, D., Bechara, A., & Mellers, B. A. (2014). What might have been? The role of the ventromedial prefrontal cortex and lateral orbitofrontal cortex in counterfactual emotions and choice. *Neuropsychologia, 54*, 77–86. doi:10.1016/j.neuropsychologia.2013.10.026

Levenson, M. R., Kiehl, K. A., & Fitzpatrick, C. M. (1995). Assessing psychopathic attributes in a non-institutionalized population. *Journal of Personality and Social Psychology, 68*(1), 151-158.

Li, M. D., Cheng, R., Ma, J. Z., & Swan, G. E. (2003). A meta-analysis of estimated genetic and environmental effects on smoking behavior in male and female adult twins. *Addiction, 98*(1), 23–31. doi:10.1046/j.1360-0443.2003.00295.x

Lindell, A. K., & Campione-Barr, N. (2017). Relative power in sibling relationships across adolescence. *New Directions for Child and Adolescent Development, 2017*(156), 49–66. doi:10.1002/cad.20201

Little, T. D. (2000). Modeling Longitudinal and Multilevel Data. doi:10.4324/9781410601940

Loeber, R., Burke, J. D., Lahey, B. B., Winters, A., & Zera, M. (2000). Oppositional defiant and conduct disorder: A review of the past 10 years, part i. *Journal of the American Academy of Child & Adolescent Psychiatry, 39*(12), 1468–1484. doi:10.1097/00004583-200012000-00007

Loeber, R., Burke, J., & Pardini, D. A. (2009). Perspectives on oppositional defiant disorder, conduct disorder, and psychopathic features. *Journal of Child Psychology and Psychiatry, 50*(1-2), 133–142. doi:10.1111/j.1469-7610.2008.02011.x

Loeber, R., Green, S. M., Lahey, B. B., Christ, M. A. G., & Frick, P. J. (1992). Developmental sequences in the age of onset of disruptive child behaviors. *Journal of Child and Family Studies, 1*(1), 21–41. doi:10.1007/bf01321340

MacGillivray, I., Campbell, D. M. & Thompson, B. (1988). *Twinning and twins.* Chichester: John Wiley & Sons.

Marceau, K., Bidwell, C. L., Karoly, H. C., Evans, A. S., Todorov, A. A., Palmer, R. H., …

Knopik, V. S. (2017). Within-family effects of smoking during pregnancy on ADHD: the importance of phenotype. *Journal of Abnormal Child Psychology, 46*(4), 685–699. doi:10.1007/s10802-017-0320-7

Marceau, K., & Jackson, K. (2017). Deviant peers as a mediator of pubertal timing–substance use associations: The moderating role of parental knowledge. *Journal of Adolescent Health, 61*(1), 53–60. doi:10.1016/j.jadohealth.2016.12.020

Marceau, K., Kirisci, L., & Tarter, R. E. (in press). Correspondence of pubertal neuroendocrine and tanner stage changes in boys and associations with substance use. *Child Development*, 00, 1-20. doi: 10.1111/cdev.13101.

Marceau, K., Ram, N., Houts, R. M., Grimm, K. J., & Susman, E. J. (2011). Individual differences in boys' and girls' timing and tempo of puberty: Modeling development with nonlinear growth models. *Developmental Psychology, 47*(5), 1389. doi: 10.1037/a0023838

Marceau, K., Rolan, E., Leve, L. D., Ganiban, J. M., Reiss, D., Shaw, D. S., … Neiderhiser, J. M. (2019). Parenting and prenatal risk as moderators of genetic influences on conduct problems during middle childhood. *Developmental Psychology, 55*(6), 1164–1181. doi:10.1037/dev0000701

Mark, K. M., Pike, A., Latham, R. M., & Oliver, B. R. (2016). Using twins to better understand sibling relationships. *Behavior Genetics, 47*(2), 202–214. doi:10.1007/s10519-016-9825-z

Marcela Raffaelli , Lisa J. Crockett & Yuh-Ling Shen (2005) Developmental stability and change in self-regulation from childhood to adolescence. *The Journal of Genetic Psychology, 166*, 54-76. doi: 10.3200/GNTP.166.1.54-76

McAlister, A., & Peterson, C. C. (2006). Mental playmates: Siblings, executive functioning and theory of mind. *British Journal of Developmental Psychology, 24*(4), 733–751. doi:10.1348/026151005x70094

McAlister, A. R., & Peterson, C. C. (2013). Siblings, theory of mind, and executive functioning in children aged 3-6 years: New longitudinal evidence. *Child Development, 84*(4), 1442–1458. doi:10.1111/cdev.12043

McArdle, P., Wiegersma, A., Gilvarry, E., Kolte, B., McCarthy, S., Fitzgerald, M., … Quensel, S. (2002). European adolescent substance use: The roles of family structure, function and gender. *Addiction*, 97(3), 329–336. doi:10.1046/j.1360-0443.2002.00066.x

McClelland, M.M., Geldhof, G.J., Cameron, C.E., & Wanless, S.B. (2015). Development and self-regulation. In W.F. Overton & P.C. Molenaar (Eds.), *Handbook of child psychology and developmental science*. Vol. 1: Theory and method (pp. 523-565). Hoboken, NJ: Wiley.

McGivern, R. F., Andersen, J., Byrd, D., Mutter, K. L., & Reilly, J. (2002). Cognitive efficiency on a match to sample task decreases at the onset of puberty in children. *Brain and Cognition, 50*(1), 73–89. doi:10.1016/s0278-2626(02)00012-x

McGue, M., Iacono, W. G., Legrand, L., Malone, S. & Elkins, I. (2001) The origins of age at first drink. I. Associations with substance-use disorders, disinhibitory behavior and psychopathology, and P3 amplitude. *Alcoholism: Clinical and Experimental Research*, 25, 1156–1165. doi:10.1097/00000374-200108000-00010

McGue, M., Sharma, A., & Benson, P. (1996). The effect of common rearing on adolescent adjustment: Evidence from a U.S. adoption cohort. *Developmental Psychology, 32*(4), 604–613. doi:10.1037/0012-1649.32.4.604

McHale, S. M., Bissell, J., & Kim, J.-Y. (2009). Sibling relationship, family, and genetic factors in sibling similarity in sexual risk. *Journal of Family Psychology, 23*(4), 562–572. doi:10.1037/a0014982

McHale, S. M., & Crouter, A. C. (1996). The family contexts of children's sibling relationships. Ablex Publishing.

McHale SM, Crouter AC, McGuire SA, Updegraff KA (1995) Congruence between mothers' and fathers' differential treatment of siblings: Links with family relations and children's well-being. *Child Development*, 116–128. doi.org/10.1111/j.1467-8624.1995.tb00859.x

McHale, S. M., & Pawletko, T. M. (1992). Differential treatment of siblings in two family contexts. *Child Development*, 63(1), 68–81. doi:10.1111/j.1467-8624.1992.tb03596.x

McHale, S. M., Updegraff, K. A., & Whiteman, S. D. (2012). Sibling relationships and influences in childhood and adolescence. *Journal of Marriage and Family, 74*(5), 913–930. doi:10.1111/j.1741-3737.2012.01011.x

McHale, S. M., Updegraff, K. A., & Whiteman, S. D. (2012). Sibling relationships and influences in childhood and adolescence. *Journal of Marriage and Family, 74*(5), 913–930. doi:10.1111/j.1741-3737.2012.01011.x

McLeod, J. D., & Kaiser, K. (2004). Childhood emotional and behavioral problems and educational attainment. *American Sociological Review*, 69(5), 636–658. doi:10.1177/000312240406900502

McMillan, C., Felmlee, D., & Osgood, D. W. (2018). Peer influence, friend selection, and gender: How network processes shape adolescent smoking, drinking, and delinquency. *Social Networks, 55*, 86–96. doi: 10.1016/j.socnet.2018.05.008

Medina, K. L., Hanson, K. L., Schweinsburg, A. D., Cohen-Zion, M., Nagel, B. J., & Tapert, S. F. (2007). Neuropsychological functioning in adolescent marijuana users: Subtle deficits detectable after a month of abstinence. *Journal of the International Neuropsychological Society, 13*(05). doi:10.1017/s1355617707071032

Meier, M. H., Hill, M. L., Small, P. J., & Luthar, S. S. (2015). Associations of adolescent cannabis use with academic performance and mental health: A longitudinal study of upper middle class youth. *Drug and Alcohol Dependence*, 156, 207–212. doi:10.1016/j.drugalcdep.2015.09.010

Mendle, J., & Ferrero, J. (2012). Detrimental psychological outcomes associated with pubertal timing in adolescent boys. *Developmental Review, 32*(1), 49–66. https://doi.org/10.1016/j.dr.2011.11.001

Mendle, J., Ferrero, J., Moore, S. R., & Harden, K. P. (2013). Depression and adolescent sexual activity in romantic and nonromantic relational contexts: A genetically-informative sibling comparison. *Journal of Abnormal Psychology, 122*(1), 51–63. doi:10.1037/a0029816

Meyers, J. L., Salvatore, J. E., Vuoksimaa, E., Korhonen, T., Pulkkinen, L., Rose, R. J., … Dick, D. M. (2014). Genetic influences on alcohol use behaviors have diverging developmental trajectories: a prospective study among male and female twins. *Alcoholism: Clinical and Experimental Research*, 38(11), 2869–2877. doi:10.1111/acer.12560

Micalizzi, L., & Knopik, V. S. (2017). Maternal smoking during pregnancy and offspring executive function: What do we know and what are the next steps? *Development and Psychopathology, 30*(4), 1333–1354. doi:10.1017/s0954579417001687

Micalizzi, L., Marceau, K., Brick, L. A., Palmer, R. H., Todorov, A. A., Heath, A. C., … Knopik, V. S. (2018). Inhibitory control in siblings discordant for exposure to maternal smoking during pregnancy. *Developmental Psychology, 54*(2), 199–208. doi:10.1037/dev0000423

Michael, H. B., & David, R. O. (1991). Psychiatric disorder and substance use in adolescence. *The Canadian Journal of Psychiatry*, 36(10), 699-705.doi:10.1177/070674379103601001

Miles, D. R., & Carey, G. (1997). Genetic and environmental architecture on human aggression. *Journal of Personality and Social Psychology, 72*(1), 207–217. doi:10.1037/0022-3514.72.1.207

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*(1), 167–202. doi:10.1146/annurev.neuro.24.1.167

Mischel, W., Shoda, Y., & Rodriguez, M. (1989). Delay of gratification in children. *Science, 244*(4907), 933–938. doi:10.1126/science.2658056

Miyake, A., Friedman, N. P., Emerson, M. J., Witzki, A. H., Howerter, A., & Wager, T. D. (2000). The unity and diversity of executive functions and their contributions to complex "frontal lobe" tasks: A latent variable analysis. *Cognitive Psychology*, *41*(1), 49-100. doi:10.1006/cogp.1999.0734

Modry-Mandell, K. L., Gamble, W. C., & Taylor, A. R. (2006). Family emotional climate and sibling relationship quality: Influences on behavioral problems and adaptation in preschool-aged children. *Journal of Child and Family Studies, 16*(1), 59–71. doi:10.1007/s10826-006-9068-3

Moffitt, T. E. (2005). The new look of behavioral genetics in developmental psychopathology: Gene-environment interplay in antisocial behaviors. *Psychological Bulletins, 131(4),* 533-554. doi:10.1037/0033-2909.131.4.533

Moffitt, T. E., Arseneault, L., Belsky, D., Dickson, N., Hancox, R. J., Harrington, H., … Caspi, A. (2011). A gradient of childhood self-control predicts health, wealth, and public safety. *Proceedings of the National Academy of Sciences, 108*(7), 2693–2698. doi:10.1073/pnas.1010076108

Moffitt, T. E., & Henry, B. (1989). Neuropsychological assessment of executive functions in self-reported delinquents. *Developmental Psychopathology*, 1, 105–118. doi:10.1017/S0954579400000298.

Moilanen, K. L., Shaw, D. S., & Maxwell, K. L. (2010). Developmental cascades: Externalizing, internalizing, and academic competence from middle childhood to early adolescence. *Development and Psychopathology*, 22(3), 635–653. doi:10.1017/s0954579410000337

Monitoring the Future national survey results on drug use, 1975-2016: Volume I, secondary school students. (2017). doi:10.3998/2027.42/139711

Muthén, L. K., & Muthén, B. O. (1998). *Mplus: The comprehensive modeling program for applied researchers; user's guide;[Version 1.0]*. Muthén & Muthén.

Natsuaki, M. N., Neiderhiser, J. M., Harold, G. T., Shaw, D. S., Reiss, D., & Leve, L. D. (2019, February 28). Siblings reared apart: A sibling comparison study on rearing environment differences. *Developmental Psychology*. Advance online publication. http://dx.doi.org/10.1037/dev0000710

Natsuaki, M. N., Ge, X., Reiss, D., & Neiderhiser, J. M. (2009) Aggressive behavior between siblings and the development of externalizing problems: Evidence from a genetically sensitive study. *Developmental Psychology, 45*, 1009-1018. doi: 10.1037/a0015698.

Neiderhiser, J. M., Marceau, K., De Araujo-Greecher, M., Ganiban, J. M., Mayes, L. C., Shaw, D. S., … Leve, L. D. (2016). Estimating the roles of genetic risk, perinatal risk, and marital hostility on early childhood adjustment: Medical records and self-reports. *Behavior Genetics*, *46*(3), 334–352. doi:10.1007/s10519-016-9788-0

Neiderhiser, J. M., Marceau, K., & Reiss, D. (2013). Four factors for the initiation of substance use by young adulthood: A 10-year follow-up twin and sibling study of marital conflict, monitoring, siblings, and peers. *Development and Psychopathology*, *25*(1), 133–149. doi:10.1017/s0954579412000958

Nelson, S. K., Kushlev, K., & Lyubomirsky, S. (2014). The pains and pleasures of parenting: When, why, and how is parenthood associated with more or less well-being? *Psychological Bulletin, 140*, 846–895. http://dx.doi.org/10.1037/a0035444

Nichols, T. R., Graber, J. A., Brooks-Gunn, J., & Botvin, G. J. (2006). Sex differences in overt aggression and delinquency among urban minority middle school students. *Journal of Applied Developmental Psychology*, *27*(1), 78–91. doi:10.1016/j.appdev.2005.12.006

NIDA. (2017, April 24). Trends & Statistics. Retrieved from https://www.drugabuse.gov/related-topics/trends-statistics on 2019, January 14.

Nigg, J. T., Wong, M. M., Martel, M. M., Jester, J. M., Puttler, L. I., Glass, J. M., … Zucker, R. (2006). Poor response inhibition as a predictor of problem drinking and illicit drug use in adolescents at risk for alcoholism and other substance use disorders. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(4), 468–475. doi:10.1097/01.chi.0000199028.76452.a9

Noble, K. G., Tottenham, N., & Casey, B. J. (2005). Neuroscience perspectives on disparities in school readiness and cognitive achievement. *The Future of Children, 15*(1), 71–89. doi:10.1353/foc.2005.0006

Nock, M. K., Kazdin, A. E., Hiripi, E., & Kessler, R. C. (2007). Lifetime prevalence, correlates, and persistence of oppositional defiant disorder: Results from the National Comorbidity Survey Replication. *Journal of Child Psychology and Psychiatry, 48*(7), 703–713. doi:10.1111/j.1469-7610.2007.01733.x

Noller, P., Feeney, J. A., Sheehan, G., Darlington, Y., & Rogers, C. (2008). Conflict in divorcing and continuously married families: A study of marital, parent–child and sibling relationships. *Journal of Divorce & Remarriage, 49*(1-2), 1–24. doi:10.1080/10502550801971223

Nosek, B. A., & Banaji, M. R. (2001). The go/no-go association task. *Social Cognition, 19*(6), 625–666. doi:10.1521/soco.19.6.625.20886

Odgers, C. L., Moffitt, T. E., Broadbent, J. M., Dickson, N., Hancox, R. J., Harrington, H., … Caspi, A. (2008). Female and male antisocial trajectories: From childhood origins to adult outcomes. *Development and Psychopathology*, 20(2), 673–716. doi:10.1017/s0954579408000333

Padmanabhan, A., & Luna, B. (2014). Developmental imaging genetics: Linking dopamine function to adolescent behavior. *Brain and Cognition, 89*, 27–38. doi:10.1016/j.bandc.2013.09.011

Paiva, F. S., Bastos, R. R., & Ronzani, T. M. (2012). Parenting styles and alcohol consumption among Brazilian adolescents. *Journal of Health Psychology*, 17(7), 1011–1021. doi:10.1177/1359105311428535

Parker, A. (1998). Development of the prefrontal cortex. *Journal of Developmental & Behavioral Pediatrics, 19*(4), 311. doi:10.1097/00004703-199808000-00013

Patterson, G. R. (1984). Siblings: Fellow travelers in the coercive family process. In R. J. Blanchard & D. C. Blanchard (Eds.), *Advances in the study of aggression* (pp. 235–264). New York: Academic Press.

Patterson, G. R., Dishion, T. J., & Bank, L. (1984). Family interaction: A process model of deviancy training. *Aggressive Behavior, 10*(3), 253–267.

Paus, T., Keshavan, M., & Giedd, J. N. (2008). Why do many psychiatric disorders emerge during adolescence*? Nature Reviews Neuroscience, 9*(12), 947–957. doi:10.1038/nrn2513

Pennington, B. F., & Ozonoff, S. (1996). Executive functions and developmental psychopathology. *Journal of Child Psychology and Psychiatry, 37*(1), 51–87. doi:10.1111/j.1469-7610.1996.tb01380.x.

Perrin, J. S., Herve, P.-Y., Leonard, G., Perron, M., Pike, G. B., Pitiot, A., … Paus, T. (2008). Growth of white matter in the adolescent brain: role of testosterone and androgen receptor. *Journal of Neuroscience, 28*(38), 9519–9524. doi:10.1523/jneurosci.1212-08.2008

Perry, N. B., Calkins, S. D., Dollar, J. M., Keane, S. P., & Shanahan, L. (2017). Self-regulation as a predictor of patterns of change in externalizing behaviors from infancy to adolescence. *Development and Psychopathology, 30*(2), 497–510. doi:10.1017/s0954579417000992

Peterson, B. S., Anderson, A. W., Ehrenkranz, R., Staib, L. H., Tageldin, M., Colson, E., … Ment, L. R. (2003). Regional brain volumes and their later neurodevelopmental correlates in term and preterm infants. *Pediatrics, 111*(5), 939–948. doi:10.1542/peds.111.5.939

Pettit, G. S., Laird, R. D., Dodge, K. A., Bates, J. E., & Criss, M. M. (2001). Antecedents and behavior-problem outcomes of parental monitoring and psychological control in early adolescence. *Child Development,* 72(2), 583–598. doi:10.1111/1467-8624.00298

Phillips, D. I. . (1993). Twin studies in medical research: can they tell us whether diseases are genetically determined? *The Lancet, 341*(8851), 1008–1009. doi:10.1016/0140-6736(93)91086-2

Piehler, T. F., Véronneau, M.-H., & Dishion, T. J. (2012). Substance use progression from adolescence to early adulthood: Effortful control in the context of friendship influence and early-onset use. *Journal of Abnormal Child Psychology, 40*(7), 1045–1058. doi:10.1007/s10802-012-9626-7

Pinquart, M. (2017). Associations of parenting dimensions and styles with externalizing problems of children and adolescents: An updated meta-analysis. *Developmental Psychology, 53*(5), 873-932. http://dx.doi.org/10.1037/dev0000295

Piper, B. J., & Corbett, S. M. (2011). Executive function profile in the offspring of women that smoked during pregnancy. *Nicotine & Tobacco Research, 14*(2), 191–199. doi:10.1093/ntr/ntr181

Poortman, A.-R., & Voorpostel, M. (2008). Parental divorce and sibling relationships. *Journal of Family Issues, 30*(1), 74–91. doi:10.1177/0192513x08322782

Prencipe, A., Kesek, A., Cohen, J., Lamm, C., Lewis, M. D., & Zelazo, P. D. (2011). Development of hot and cool executive function during the transition to adolescence. *Journal of Experimental Child Psychology, 108*(3), 621–637. doi:10.1016/j.jecp.2010.09.008

Raaijmakers, M. A. J., Smidts, D. P., Sergeant, J. A., Maassen, G. H., Posthumus, J. A., van Engeland, H., & Matthys, W. (2008). Executive functions in preschool children with aggressive behavior: impairments in inhibitory control. *Journal of Abnormal Child Psychology, 36*(7), 1097–1107. doi:10.1007/s10802-008-9235-7

Rakic, P., Bourgeois, J.-P., & Goldman-Rakic, P. S. (1994). Synaptic development of the cerebral cortex: implications for learning, memory, and mental illness. *The Self-Organizing Brain: From Growth Cones to Functional Networks*, 227–243. doi:10.1016/s0079-6123(08)60543-9

Ramsay, M. C. and Reynolds, C. R. 2000. Does smoking by pregnant women influence IQ, birth weight, and developmental disabilities in their infants? A methodological review and multivariate analysis.. Neuropsychology Review, 10: 1–40. doi:10.1023/a:1009065713389

Recchia, H. E., & Howe, N. (2009). Associations between social understanding, sibling relationship quality, and siblings' conflict strategies and outcomes. *Child Development, 80*(5), 1564–1578. doi:10.1111/j.1467-8624.2009.01351.x

Reef, J., Diamantopoulou, S., van Meurs, I., Verhulst, F. C., & van der Ende, J. (2010). Developmental trajectories of child to adolescent externalizing behavior and adult DSM-IV disorder: results of a 24-year longitudinal study. *Social Psychiatry and Psychiatric Epidemiology*, 46(12), 1233–1241. doi:10.1007/s00127-010-0297-9

Rende, R., Slomkowski, C., Lloyd-Richardson, E., & Niaura, R. (2005). Sibling effects on substance use in adolescence: social contagion and genetic relatedness. *Journal of Family Psychology, 19*(4), 611–618. doi:10.1037/0893-3200.19.4.611

Rende, R. D., Slomkowski, C. L., Stocker, C., Fulker, D. W., & et al. (1992). Genetic and environmental influences on maternal and sibling interaction in middle childhood: A sibling adoption study. *Developmental Psychology, 28*(3), 484–490. doi:10.1037/0012-1649.28.3.484

Reuben, J. D., Shaw, D. S., Neiderhiser, J. M., Natsuaki, M. N., Reiss, D., & Leve, L. D. (2015). Warm parenting and effortful control in toddlerhood: Independent and interactive predictors of school-age externalizing behavior. *Journal of Abnormal Child Psychology*, 44(6), 1083–1096. doi:10.1007/s10802-015-0096-6

Rey, J. M., Bashir, M. R., Schwarz, M., Richards, I. N., Plapp, J. M., & Stewart, G. W. (1988). Oppositional disorder: Fact or fiction? J*ournal of the American Academy of Child & Adolescent Psychiatry, 27*(2), 157–162. doi:10.1097/00004583-198803000-00004

Rhee, S. H., & Waldman, I. D. (2002). Genetic and environmental influences on antisocial behavior: A meta-analysis of twin and adoption studies. *Psychological Bulletin, 128*(3), 490–529. doi:10.1037/0033-2909.128.3.490

Riggio, H. R. (2001). Relations between parental divorce and the quality of adult sibling relationships. *Journal of Divorce & Remarriage, 36*(1-2), 67–82. doi:10.1300/j087v36n01_04

Riggs, N. R., Blair, C. B., & Greenberg, M. T. (2004). Concurrent and 2-year longitudinal relations between executive function and the behavior of 1st and 2nd grade children. *Child Neuropsychology, 9*(4), 267–276. doi:10.1076/chin.9.4.267.23513

Robbins, T. W., & Arnsten, A. F. T. (2009). The neuropsychopharmacology of fronto-executive function: Monoaminergic modulation. *Annual Review of Neuroscience, 32*, 267–287. doi:10. 1146/annurev.neuro.051508.135535

Rolan, E., & Marceau, K. (2018). Individual and sibling characteristics: parental differential treatment and adolescent externalizing behaviors. *Journal of Youth and Adolescence, 47*(12), 2535–2553. doi:10.1007/s10964-018-0892-8

Rolan, E. P., Schmitt, S. A., Purpura, D. J., & Nichols, D. L. (2018). Sibling presence, executive function, and the role of parenting. *Infant and Child Development, 27*(4), e2091. doi:10.1002/icd.2091

Romer, D., Betancourt, L., Giannetta, J. M., Brodsky, N. L., Farah, M., & Hurt, H. (2009). Executive cognitive functions and impulsivity as correlates of risk taking and problem behavior in preadolescents. *Neuropsychologia*, *47*(13), 2916–2926. doi:10.1016/j.neuropsychologia.2009.06.019

Rose, R. J., Dick, D. M., Viken, R. J., Pulkkinen, L., & Kaprio, J. (2004). Genetic and environmental effects on conduct disorder and alcohol dependence symptoms and their covariation at age 14. *Alcoholism: Clinical & Experimental Research, 28*(10), 1541–1548. doi:10.1097/01.alc.0000141822.36776.55

Rose-Jacobs, R., Soenksen, S., Appugliese, D. P., Cabral, H. J., Richardson, M. A., Beeghly, M., … Frank, D. A. (2011). Early adolescent executive functioning, intrauterine exposures and own drug use. *Neurotoxicology and Teratology*, *33*(3), 379–392. doi:10.1016/j.ntt.2011.02.013

Rothbart, M. K., Derryberry, D., & Posner, M. I. (n.d.). A psychobiological approach to the development of temperament. Temperament: Individual Differences at the Interface of Biology and Behavior. *Washington DC: American Psychological Association*, 83–116. doi:10.1037/10149-003

Rowe, R., Costello, E. J., Angold, A., Copeland, W. E., & Maughan, B. (2010). Developmental pathways in oppositional defiant disorder and conduct disorder. *Journal of Abnormal Psychology*, *119*(4), 726–738. doi:10.1037/a0020798

Rowe, R., Maughan, B., Pickles, A., Costello, E. J., & Angold, A. (2002). The relationship between DSM-IV oppositional defiant disorder and conduct disorder: findings from the Great Smoky Mountains Study. *Journal of Child Psychology and Psychiatry, 43*(3), 365–373. doi:10.1111/1469-7610.00027

Rowe, R., Maugham, B., Worthman, C. M., Costello, E. J., & Angold, A. (2004). Testosterone, antisocial behavior, and social dominance in boys: Pubertal development and biosocial interaction. *Biological Psychiatry, 55,* 546–552.

Rubia, K., Russell, T., Overmeyer, S., Brammer, M. J., Bullmore, E. T., Sharma, T., … Taylor, E. (2001). Mapping motor inhibition: Conjunctive brain activations across different versions of go/no-go and stop tasks. *NeuroImage, 13*(2), 250–261. doi:10.1006/nimg.2000.0685

Rubia, K., Smith, A. B., Brammer, M. J., & Taylor, E. (2003). Right inferior prefrontal cortex mediates response inhibition while mesial prefrontal cortex is responsible for error detection. *NeuroImage, 20*(1), 351–358. doi:10.1016/s1053-8119(03)00275-1

Rusby, J. C., Light, J. M., Crowley, R., & Westling, E. (2018). Influence of parent–youth relationship, parental monitoring, and parent substance use on adolescent substance use onset. *Journal of Family Psychology*, 32(3), 310–320. doi:10.1037/fam0000350

Rydell, M., Granath, F., Cnattingius, S., Magnusson, C., & Galanti, M. R. (2014). In-utero exposure to maternal smoking is not linked to tobacco use in adulthood after controlling for genetic and family influences: a Swedish sibling study. *European Journal of Epidemiology, 29*(7), 499–506. doi:10.1007/s10654-014-9912-5

Salatino-Oliveira, A., Murray, J., Kieling, C., Genro, J. P., Polanczyk, G., Anselmi, L., … Hutz, M. H. (2016). COMT and prenatal maternal smoking in associations with conduct problems and crime: the Pelotas 1993 birth cohort study. *Scientific Reports, 6*(1)m 29900. doi:10.1038/srep29900

Samek, D. R., McGue, M., Keyes, M., & Iacono, W. G. (2014). Sibling facilitation mediates the association between older and younger sibling alcohol use in late adolescence. *Journal of Research on Adolescence, 25*(4), 638–651. doi:10.1111/jora.12154

Samek, D. R., & Rueter, M. A. (2011). Considerations of elder sibling closeness in predicting younger sibling substance use: Social learning versus social bonding explanations. *Journal of Family Psychology, 25*(6), 931–941. doi:10.1037/a0025857

Samek, D. R., Ruester, M. A., Keyes, M. A., McGue,, M., & Iancono, W. G. (2015). Parent involvement, sibling companionship, and adolescent substance use: A Longitudinal, genetically informed design. *Journal of Family Psychology, 29*, 614-623. doi: 10.1037/fam0000097.

Sameroff, A. (2010). A unified theory of development: A dialectic integration of nature and nurture. *Child Development, 81*(1), 6–22. doi:10.1111/j.1467-8624.2009.01378.x

Scalco, M. D., Colder, C. R., Hawk, L. W., Read, J. P., Wieczorek, W. F., & Lengua, L. J. (2014). Internalizing and externalizing problem behavior and early adolescent substance use: A test of a latent variable interaction and conditional indirect effects. *Psychology of Addictive Behaviors, 28*(3), 828–840. doi:10.1037/a0035805

Schafer, J. L., & Olsen, M. K. (1998). Multiple imputation for multivariate missing-data problems: A data analyst's perspective. *Multivariate behavioral research, 33*(4), 545-571.

Scherrer, J. F., Xian, H., Pan, H., Pergadia, M. L., Madden, P. A. F., Grant, J. D., … Bucholz, K. K. (2012). Parent, sibling and peer influences on smoking initiation, regular smoking and nicotine dependence. Results from a genetically informative design. *Addictive Behaviors, 37*(3), 240–247. doi:10.1016/j.addbeh.2011.10.005

Schinke, S. P., Fang, L., & Cole, K. C. A. (2008). substance use among early adolescent girls: Risk and protective factors. *Journal of Adolescent Health*, 43(2), 191–194. doi:10.1016/j.jadohealth.2007.12.014

Schmitt, S. A., McClelland, M. M., Tominey, S. L., & Acock, A. C. (2015). Strengthening school readiness for Head Start children: Evaluation of a self-regulation intervention. *Early Childhood Research Quarterly, 30*, 20–31. doi:10.1016/j.ecresq.2014.08.001

Schoemaker, K., Mulder, H., Deković, M., & Matthys, W. (2012). Executive functions in preschool children with externalizing behavior problems: A meta-analysis. *Journal of Abnormal Child Psychology, 41*(3), 457–471. doi:10.1007/s10802-012-9684-x

Schuckit, M. A. (1996). An 8-year follow-up of 450 sons of alcoholic and control subjects. *Archives of General Psychiatry, 53*(3), 202. doi:10.1001/archpsyc.1996.01830030020005

Schultz, K. M., Molenda-Figueira, H. A., & Sisk, C. L. (2009). Back to the future: The organizational–activational hypothesis adapted to puberty and adolescence. *Hormones and Behavior, 55*, 597–604. doi:10.1016/j.yhbeh.2009.03.010

Sher, K. J., Walitzer, K. S., Wood, P. K., & Brent, E. E. (1991). Characteristics of children of alcoholics: Putative risk factors, substance use and abuse, and psychopathology. *Journal of Abnormal Psychology, 100*(4), 427–448. doi:10.1037/0021-843x.100.4.427

Slomkowski, C., Rende, R., Conger, K. J., Simons, R. L., & Conger, R. D. (2001). Sisters, brothers, and delinquency: Evaluating social influence during early and middle adolescence. *Child Development, 72*(1), 271–283. doi:10.1111/1467-8624.00278

Slomkowski, C., Rende, R., Novak, S., Lloyd-Richardson, E., & Niaura, R. (2005). Sibling effects on smoking in adolescence: Evidence for social influence from a genetically informative design. *Addiction, 100*(4), 430–438. doi:10.1111/j.1360-0443.2004.00965.x

Tapert, S., Schweinsburg, A., & Brown, S. (2008). The influence of marijuana use on neurocognitive functioning in adolescents. *Current Drug Abuse Reviews, 1*(1), 99–111. doi:10.2174/1874473710801010099

Tolan, P. H., & Leventhal, B. L. (Eds.). (2013). Disruptive Behavior Disorders. doi:10.1007/978-1-4614-7557-6

Sharp, C., Barr, G., Ross, D., Bhimani, R., Ha, C., & Vuchinich, R. (2011). Social discounting and externalizing behavior problems in boys. *Journal of Behavioral Decision Making, 25*(3), 239–247. doi:10.1002/bdm.719

Shea, A., & Steiner, M. (2008). Cigarette smoking during pregnancy. *Nicotine & Tobacco Research, 10*(2), 267–278. doi:10.1080/14622200701825908

Skoglund, C., Chen, Q., D′Onofrio, B. M., Lichtenstein, P., & Larsson, H. (2013). Familial confounding of the association between maternal smoking during pregnancy and ADHD in offspring. *Journal of Child Psychology and Psychiatry, 55*(1), 61–68. doi:10.1111/jcpp.12124

Slomkowski, C., Rende, R., Novak, S., Lloyd-Richardson, E., & Niaura, R. (2005). Sibling effects on moking in adolescence: Evidence for social influence from a genetically informative design. *Addiction, 100*(4), 430-438. doi: 10.1111/j.1360-0443.2004.00965.x.

Slomkowski, C., Rende, R., Conger, K. J., Simons, R. L., & Conger, R. D. (2001). Sisters, brothers, and delinquency: evaluating social influence during early and middle adolescence. *Child Development, 72*(1), 271–283. doi:10.1111/1467-8624.00278

Sobell, L. C., & Sobell, M. B. (1995). Alcohol consumption measures. *Assessing alcohol problems: A guide for clinicians and researchers, 2*, 75-99.

Solmeyer, A. R., McHale, S. M., & Crouter, A. C. (2014). Longitudinal associations between sibling relationship qualities and risky behavior across adolescence. *Developmental Psychology, 50*(2), 600–610. doi:10.1037/a0033207

Squeglia, L. M., Jacobus, J., Nguyen-Louie, T. T., & Tapert, S. F. (2014). Inhibition during early adolescence predicts alcohol and marijuana use by late adolescence. *Neuropsychology, 28*(5), 782–790. doi:10.1037/neu0000083

Stanger, C., & Lewis, M. (1993). Agreement among parents, teachers, and children on internalizing and externalizing behavior problems. *Journal of Clinical Child Psychology, 22*(1), 107–116. doi:10.1207/s15374424jccp2201_11

Steinbeis, N., & Crone, E. A. (2016). The link between cognitive control and decision-making across child and adolescent development. *Current Opinion in Behavioral Sciences, 10*, 28–32. doi:10.1016/j.cobeha.2016.04.009

Steinberg, L. (2005). Cognitive and affective development in adolescence. *Trends in Cognitive Sciences, 9*(2), 69–74. doi:10.1016/j.tics.2004.12.005

Steinberg, L., Albert, D., Cauffman, E., Banich, M., Graham, S., & Woolard, J. (2008). Age differences in sensation seeking and impulsivity as indexed by behavior and self-report: Evidence for a dual systems model. *Developmental Psychology, 44*(6), 1764–1778. doi:10.1037/a0012955

Stocker, C. M. (1994). Children's perceptions of relationships with siblings, friends, and mothers: Compensatory processes and links with adjustment. *Journal of Child Psychology and Psychiatry, 35*(8), 1447-1459.

Stocker, C. M., Burwell, R. A., & Briggs, M. L. (2002). Sibling conflict in middle childhood predicts children's adjustment in early adolescence. *Journal of Family Psychology*, 16, 50–57. doi: http://dx.doi.org/10.1037/0893-3200.16.1.50.

Stocker, C., & McHale, S. M. (1992). The nature and family correlates of preadolescents' perceptions of their sibling relationships. *Journal of Social and Personal Relationships, 9*, 179–195. https://doi.org/10.1177/0265407592092002\

Stocker, C. M., & Youngblade, L. (1999). Marital conflict and parental hostility: Links with children's sibling and peer relationships. *Journal of Family Psychology, 13*(4), 598-609. http://dx.doi.org/10.1037/0893-3200.13.4.598

Stormshak, E. A., Comeau, C. A., & Shepard, S. A. (2004). The relative contribution of sibling deviance and peer deviance in the prediction of substance use across middle childhood. *Journal of Abnormal Child Psychology, 32*(6), 635–649. doi:10.1023/b:jacp.0000047212.49463.c7

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18*(6), 643–662. doi:10.1037/h0054651

Susman, E., & Rogol, A. (2004). Puberty. In R. Lerner & L. Steinberg (Eds.), Handbook of adolescent psychology. New York: Wiley.

Sutin, A. R., Flynn, H. A., & Terracciano, A. (2017). Maternal cigarette smoking during pregnancy and the trajectory of externalizing and internalizing symptoms across childhood: Similarities and differences across parent, teacher, and self reports. *Journal of Psychiatric Research*, 91, 145–148. doi:10.1016/j.jpsychires.2017.03.003

Swendsen, J., Burstein, M., Case, B., Conway, K.P., Dierker, L., He, J., & Merikangas, K.R. (2012). Use and abuse of alcohol and illicit drugs in US adolescents: Results of the National Comorbidity Survey-Adolescence Supplement. *Archive of General Psychiatry, 69*, 390-398.

Tackett, J. L., Krueger, R. F., Iacono, W. G., & McGue, M. (2005). Symptom-based subfactors of DSM-defined conduct disorder: Evidence for etiologic distinctions. *Journal of Abnormal Psychology*, 114(3), 483–487. doi:10.1037/0021-843x.114.3.483

Tarter, R. E., Kirisci, L., Mezzich, A., Cornelius, J. R., Pajer, K., Vanyukov, M., … Clark, D. (2003). Neurobehavioral disinhibition in childhood predicts early age at onset of substance use disorder. *American Journal of Psychiatry, 160*(6), 1078–1085. doi:10.1176/appi.ajp.160.6.1078

Tarter, R. E., & Vanyukov, M. M. (2001). Introduction: Theoretical and operational framework for research into the etiology of substance use disorders. *Journal of Child & Adolescent Substance Abuse, 10*(4), 1–12. doi:10.1300/j029v10n04_01

Tarter, R., Vanyukov, M., Giancola, P., Dawes, M., Blackson, T., Mezzich, A., & Clark, D. B. (1999). Etiology of early age onset substance use disorder: A maturational perspective. *Development and Psychopathology, 11*(4), 657–683. doi:10.1017/s0954579499002266

Tarter, R., Vanyukov, M., Giancola, P., Dawes, M., Blackson, T., Mezzich, A., & Clark, D. B. (1999). Etiology of early age onset substance use disorder: A maturational perspective. *Development and Psychopathology, 11*(4), 657–683. doi:10.1017/s0954579499002266

Thompson, P. M., Giedd, J. N., Woods, R. P., MacDonald, D., Evans, A. C., & Toga, A. W. (2000). Growth patterns in the developing brain detected by using continuum mechanical tensor maps. *Nature, 404*(6774), 190–193. doi:10.1038/35004593

Thorell, L. B., & Wåhlstedt, C. (2006). Executive functioning deficits in relation to symptoms of ADHD and/or ODD in preschool children. *Infant and Child Development*, *15*(5), 503–518. doi:10.1002/icd.475

Tillman, C., Brocki, K. C., Sørensen, L., & Lundervold, A. J. (2013). A longitudinal examination of the developmental executive function hierarchy in children with externalizing behavior problems. *Journal of Attention Disorders*, *19*(6), 496–506. doi:10.1177/1087054713488439

Todd, R. D., Joyner, C. A., Heath, A. C., Neuman, R. J., & Reich, W. (2003). Reliability and stability of a semistructured dsm-iv interview designed for family studies. *Journal of the American Academy of Child & Adolescent Psychiatry*, *42*(12), 1460–1468. doi:10.1097/00004583-200312000-00013

Trucco, E. M., Hicks, B. M., Villafuerte, S., Nigg, J. T., Burmeister, M., & Zucker, R. A. (2016). Temperament and externalizing behavior as mediators of genetic risk on adolescent substance use. *Journal of Abnormal Psychology*, *125*(4), 565.

Ullsperger, J. M., & Nikolas, M. A. (2017). A meta-analytic review of the association between pubertal timing and psychopathology in adolescence: Are there sex differences? *Psychological Bulletin, 143*, 903–938. https://doi.org/10.1037/bul0000106

Updegraff, K. A., McHale, S. M., Whiteman, S. D., Thayer, S. M., & Delgado, M. Y. (2005). Adolescent sibling relationships in Mexican American families: Exploring the role of familism. *Journal of Family Psychology*, *19*(4), 512–522. doi:10.1037/0893-3200.19.4.512

Van der Valk, J. C., Verhulst, F. C., Neale, M. C., & Boomsma, D. I. (1998). Longitudinal genetic analysis of problem behaviors in biologically related and unrelated adoptees. *Behavior Genetics*, 28(5), 365–380. doi:10.1023/a:1021621719059

Vardavas, C. I., Hohmann, C., Patelarou, E., Martinez, D., Henderson, A. J., Granell, R., … Kogevinas, M. (2016). The independent role of prenatal and postnatal exposure to active and passive smoking on the development of early wheeze in children. *European Respiratory Journal, 48(*1), 115–124. doi:10.1183/13993003.01016-2015

Verhulst, F. C., & Van der Ende, J. (1992). Agreement between parents' reports and adolescents' self-reports of problem behavior. *Journal of Child Psychology and Psychiatry and Allied Disciplines*, *33*(6), 1011–1023. doi: 10.1111/j.1469-7610.1992.tb00922.

Verweij, K. J. H., Zietsch, B. P., Lynskey, M. T., Medland, S. E., Neale, M. C., Martin, N. G., … Vink, J. M. (2010). Genetic and environmental influences on cannabis use initiation and problematic use: a meta-analysis of twin studies. *Addiction, 105*(3), 417–430. doi:10.1111/j.1360-0443.2009.02831.x

Volling, B. L., & Belsky, J. (1992). The contribution of mother-child and father-child relationships to the quality of sibling interaction: A longitudinal study. *Child Development, 63*(5), 1209–1222. doi:10.1111/j.1467-8624.1992.tb01690.x

Volling, B. L., McElwain, N. L., & Miller, A. L. (2002). Emotion regulation in context: the jealousy complex between young siblings and its relations with child and family characteristics. *Child Development, 73*(2), 581–600. doi:10.1111/1467-8624.00425

Wakschlag, L. S., Kistner, E. O., Pine, D. S., Biesecker, G., Pickett, K. E., Skol, A. D., … Cook, E. H. (2010). Interaction of prenatal exposure to cigarettes and MAOA genotype in pathways to youth antisocial behavior. *Molecular Psychiatry, 15*(9), 928–937. doi:10.1038/mp.2009.22

Wakschlag, L. S., Pickett, K. E., Kasza, K. E., & Loeber, R. (2006). Is prenatal smoking associated with a developmental pattern of conduct problems in young boys?. *Journal of the American Academy of Child & Adolescent Psychiatry, 45*(4), 461-467.

Wang, L., & Preacher, K. J. (2013). Moderated mediation analysis using bayesian methods. *PsycEXTRA Dataset.* doi:10.1037/e607542013-001

Wechsler, D. (2003). Wechsler Intelligence Scale for Children, Fourth Edition. PsycTESTS Dataset. doi:10.1037/t15174-000

Wechsler Adult Intelligence Scale (All Versions). (1997). Springer Reference. doi:10.1007/springerreference_183817

Weeland, J., Overbeek, G., Orobio de Castro, B., & Matthys, W. (2015). Underlying mechanisms of gene–environment interactions in externalizing behavior: A systematic review and search for theoretical mechanisms. *Clinical Child and Family Psychology Review, 18*, 413–442. doi:10. 1007/s10567-015-0196-4

Wilens, T. E., Martelon, M., Fried, R., Petty, C., Bateman, C., & Biederman, J. (2011). Do executive function deficits predict later substance use disorders among adolescents and young adults? *Journal of the American Academy of Child & Adolescent Psychiatry, 50*(2), 141–149. doi:10.1016/j.jaac.2010.11.010

Windle, M. (2000). Parental, sibling, and peer influences on adolescent substance use and alcohol problems. *Applied Developmental Science, 4*(2), 98–110. doi:10.1207/s1532480xads0402_5

Whiteman, S. D., Jensen, A. C., & Maggs, J. L. (2014). Similarities and differences in adolescent siblings' alcohol-related attitudes, use, and delinquency: evidence for convergent and divergent influence processes. *Journal of Youth and Adolescence, 43*(5), 687–697. doi:10.1007/s10964-013-9971-z

Whiteman, S. D., Jensen, A. C., Mustillo, S. A., & Maggs, J. L. (2016). Understanding sibling influence on adolescents' alcohol use: Social and cognitive pathways. *Addictive Behaviors, 53*, 1–6. https://doi.org/10.1016/j.addbeh.2015.09.007

Whiteman, S. D., Jensen, A. C., & McHale, S. M. (2017). Sibling influences on risky behaviors from adolescence to young adulthood: Vertical socialization or bidirectional effects? *New Directions for Child and Adolescent Development, 2017*(156), 67–85. doi:10.1002/cad.20197

Wiebe, S. A., Clark, C. A. C., De Jong, D. M., Chevalier, N., Espy, K. A., & Wakschlag, L. (2015). Prenatal tobacco exposure and self-regulation in early childhood: Implications for developmental psychopathology. *Development and Psychopathology, 27*(02), 397–409. doi:10.1017/s095457941500005x

Windle, M. (2000). Parental, sibling, and peer influences on adolescent substance use and alcohol problems. *Applied Developmental Science, 4*(2), 98-110, doi: 10.1207/S1532480XADS0402_5

Yechiam, E., Goodnight, J., Bates, J. E., Busemeyer, J. R., Dodge, K. A., Pettit, G. S., & Newman, J. P. (2006). A formal cognitive model of the go/no-go discrimination task: Evaluation and implications. *Psychological Assessment, 18*(3), 239–249. doi:10.1037/1040-3590.18.3.239

Yoon, G., Westermeyer, J., Warwick, M., & Kuskowski, M. A. (2012). Substance use disorders and adoption: Findings from a national sample. *PloS One, 7*(11), e49655. https://doi.org/10.1371/journal.pone.0049655

Young, S. E., Friedman, N. P., Miyake, A., Willcutt, E. G., Corley, R. P., Haberstick, B. C., & Hewitt, J. K. (2009). Behavioral disinhibition: Liability for externalizing spectrum disorders and its genetic and environmental relation to response inhibition across adolescence. *Journal of Abnormal Psychology*, 118(1), 117–130. doi:10.1037/a0014657

Zecevic, N., & Rakic, P. (2001). Development of layer I neurons in the primate cerebral cortex. *The Journal of Neuroscience*, *21*(15), 5607–5619. doi:10.1523/jneurosci.21-15-05607.2001

Zelazo, P. D. (2013). Developmental psychology: A new synthesis. In P. D. Zelazo (Ed.), The Oxford handbook of developmental psychology: Vol. 1. Body and mind (pp. 3–12). New York, NY: Oxford University Press.

Zelazo, P. D., Blair, C. B., & Willoughby, M. T. (2016). Executive function: implications for education. NCER 2017-2000. *National Center for Education Research*.

Zelazo, P. D., & Carlson, S. M. (2012). Hot and Cool Executive Function in Childhood and Adolescence: Development and Plasticity. *Child Development Perspectives*, *6*(4), 354-360. doi:10.1111/j.1750-8606.2012.00246.x

Zelazo, P. D., Carter, A., Reznick, J. S., & Frye, D. (1997). Early development of executive function: A problem-solving framework. *Review of General Psychology*, *1*(2), 198–226. doi:10.1037/1089-2680.1.2.198

Zelazo, PD., Müller, U. Executive function in typical and atypical development. In: Goswami, U., editor. Handbook of Child Cognitive Development. Oxford: Blackwell; 2002. p. 445-469.

Zelazo, P. D., Qu, L., & Kesek, A. C. (2010). Hot executive function: Emotion and the development of cognitive control. In S. D. Calkins & M. A. Bell (Eds.), *Child development at the intersection of emotion and cognition* (pp. 97–111). Washington, DC: American Psychological Association.