Exploring the Underlying Mechanisms of Comorbid ADHD and Eating Disorders

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Exploring the Underlying Mechanisms of Comorbid ADHD and Eating Disorders

by

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A dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy
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DEDICATION

I dedicate this dissertation to everyone who helped me to get where I am today. First and foremost, to my parents, Denise and Larry, for everything you do to help me on a daily basis. You are the main reason I have been able to be successful in all of my endeavors. To my siblings, Scott, Adam, and Vicki for all of your love and support.

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Evidence suggests comorbidity of ADHD and eating disorders (EDs) among females. Capitalizing on the comorbidity of ADHD and EDs and subsequent obesity could lead to improved prevention and treatment of all three conditions. However, additional information regarding the comorbidity is necessary to develop such interventions, as little is known about how or why this co-occurrence exists. A comprehensive model of the underlying mechanisms associated with comorbid ADHD and EDs is needed to improve understanding of the development of the comorbidity. Moreover, while there are gender differences within each disorder, literature is limited regarding to the comorbidity among males, leading to a call for further investigation.

Based on the literature, this study investigated three hypotheses of the underlying mechanisms of the ADHD/ED comorbidity, including: 1) ADHD and EDs are the expression of a common genetic or neurobiological dysfunction that manifests itself as binge eating and ADHD, 2) psychosocial factors common to both EDs and ADHD mediate the association between the two conditions, and 3) a third underlying mental health condition mediates the relationship between the two conditions. Underlying factors proposed within these three hypotheses include dopamine, serotonin, and monoamine oxidase A genes, family support, social support, neuroticism, conscientiousness, cognitive control, working memory, major depression, anxiety disorder, alcohol use and substance use disorders, and childhood abuse.

In order to simultaneously investigate the three hypotheses, this study utilized secondary data analysis from 6,289 females and 5,248 males as part of the National Longitudinal Study of Adolescent Health. This data was used to test a model constructed via a combination of five
theories, specifically, the Biopsychosocial Model, the Life Course Approach, the Risk Regulator Framework, the Research Domain Criteria Matrix, and the Person-Environment Transaction Theory.

Findings of this study suggest that cognitive control, family support, and additional comorbid mental health illnesses such as depression, anxiety, and substance abuse disorder all mediate the relationship between ADHD and EDs. However, rather than leading to the comorbidity, ADHD led to other mental health issues which were then subsequently correlated to EDs; suggesting a comorbidity between these additional disorders and EDs with ADHD being a possible predictor of that comorbidity. In regards to genetics, the factors investigated in this study were not found to be directly associated with the comorbidity. Rather, these factors were connected to the psychosocial and psychiatric mediators, suggesting an indirect relationship between genetics and the comorbidity. With regards to males, differences were found between males with the comorbidity, ADHD alone, EDs alone, and neither disorder in regards to education attainment, BMI and obesity, delinquent behavior, and sexual behaviors were all observed. However, very few of the proposed underlying mechanisms among females were significantly associated with the comorbidity among males.

Results provide initial support for continued research on the underlying mechanisms of the ADHD/ ED comorbidity. This research has potential implications in many areas including primary and secondary prevention of EDs, improved treatment plans, prevention of psychostimulant medication abuse, and prevention and treatment of obesity. Next steps include the use of advanced statistical techniques in order to explore multiple combinations of underlying factors to the comorbidity and direct interactions between factors, including gene x environment interactions. Additional study replications are also needed with the incorporation of additional genetic components.
CHAPTER ONE: INTRODUCTION

The main goals of public health include preventing disease, promoting health, and prolonging the lifespan for the population at large (American Public Health Association [APHA], n.d.; World Health Organization, n.d.). Public health professionals aim to prevent health problems through health education and promotion, political action, and research (Centers for Disease Control and Prevention [CDC], n.d.). While traditional perspectives of public health may focus on physical conditions, such as vaccinations and environmental safety (CDC, n.d.), there is a growing recognition that complex public health issues are heavily influenced by behavioral health (Mabry, Olster, Morgan, & Abrams, 2008). The single-cause, single-disciplinary approach to health is no longer sufficient for handling complex, chronic diseases (Mabry et al., 2008).

Components of behavioral health, including substance abuse, tobacco use, and mental illness are among the leading predictors for the top chronic diseases in the United States (CDC, 2005, 2011). In general, people with serious mental illness die earlier than the general population (Nardone, Snyder, & Paradise, 2014). Subsequently, it is crucial to incorporate behavioral health into any public health intervention. Similarly, prevention and management of behavioral health conditions could be improved by the addition of aspects of the public health system including surveillance, monitoring, and health promotion. This type of integrated and holistic approach is especially beneficial for addressing issues related to co-occurring mental and physical health disorders.

While there are fundamental differences between public and behavioral health, each has a significant impact on the other. Despite the interplay of the two, behavioral health and public health systems are typically segregated, leading to a fragmented healthcare system (Nardone et
The fragmentation leads to inappropriate, redundant, and increased healthcare expenditures (Nardone et al., 2014). For example, just one-third of all Americans with mental health problems receive mental health treatment (Cunningham, 2009), leading to additional physical health issues, poor functioning, and increased healthcare spending among patients with complex comorbid conditions (Kathol, Butler, McAlpine, & Kane, 2010). Reducing the burden of, and ultimately preventing the most complex and chronic health problems, will require an understanding of the full range of determinants including biological, environmental, social, and behavioral mechanisms (Mabry et al., 2008).

This need for integration holds especially true for children with co-occurring conditions. Children with mental health disorders are at high risk for many preventable physical health diseases (Bazelon, n.d.). These co-occurring disorders have significant financial and emotional implications for the entire family (Busch & Barry, 2007). While it is generally accepted that physical and mental health disorders interact, rather than integrated with physical health care, mental health services are typically viewed as additional or secondary services (Kathol et al., 2010). Access to mental health care including screenings and treatment is crucial for children, as half of all serious mental illnesses begin by age fourteen (National Alliance on Mental Illness, 2013). Despite the need for mental health services, half of children with a mental health condition go without care (National Alliance on Mental Illness, 2013) and less than 10% of those receiving mental health care continue treatment for more than three months (Behrens, Lear, & Price, 2013). In general, getting treatment for a child’s physical health condition is easier than for a psychological condition (Behrens et al., 2013).

The Role of Behavioral Health in Public Health

Among the main tasks of public health is the prevention of death, disease, and disability (APHA, n.d.; World Health Organization, n.d.). Addressing issues associated with mental health is a key component for preventing disease as mental disorders are a leading cause of
premature death and account for approximately 25% of all disability (CDC, 2005; Nardone et al., 2014). For example, depression is a key risk factor for many physical health conditions including cardiovascular disease and diabetes (CDC, 2005, 2011), and positive mental health is associated with better endocrine functioning and immune response (CDC, 2011). Behavioral health is also a predictor of overall wellbeing as many of the risk factors of the most common causes of death and disease are behavioral, including substance abuse, tobacco use, and alcohol consumption (Glanz & Bishop, 2010). Moreover, behavioral health influences many risk behaviors associated with chronic diseases including nutrition and physical inactivity (CDC, 2005). Although the burden of mental illness as well as the connection between physical and mental health is widely recognized, mental health is not often included in public health campaigns and interventions (Bazelon Center for Mental Health Law, n.d.).

Among children and adolescents, the integration of public and mental health could allow for early detection and treatment of chronic and debilitating conditions. As it is well recognized that behavioral health factors can lead to physical health issues, behavioral healthcare settings can be used as a delivery mechanism for physical health screenings. This could be extremely beneficial for the long-term trajectory of children with co-occurring physical and mental health conditions. As previously stated, the majority of mental illness begins in childhood and adolescence (National Alliance on Mental Illness, 2013), and is associated with subsequent physical health issues (CDC, 2005, 2011). Early intervention among this subset of children would address the main goals of public health by reducing chronic disease burden and disability. Subsequently, integrated public health and mental health prevention could have significant impacts on healthcare spending. Healthcare cost is a major concern for public health and as behavioral health related issues lead to significant healthcare costs, targeting behavioral health for prevention and improved treatment efforts can help reduce the financial burden on the overall healthcare system.
The Role of Public Health in Behavioral Health

Excluding the costs of research, mental health issues costs the United States an estimated $150 billion annually (CDC, 2005). Public health can play a key role in behavioral health by reducing this financial burden though surveillance, screening, and prevention. The public health approach could include monitoring, assessment, prevention research, community education, health promotion, policy development, and systems change (CDC, 2011). Public health can provide support to behavioral health through community education, as public health has a long track record of success with community education and raising awareness (Bazelon Center for Mental Health Law, n.d.). Providing education and information related to accessing services could have significant impacts on prevention and treatment in behavioral health. As an example, a recent initiative from the Centers for Disease Control and Prevention has been successful at raising recognition of attention deficit disorder, a common childhood disorder with implications for several life domains (Bazelon Center for Mental Health Law, n.d.).

Secondary prevention, or early detection, can help reduce the consequences of both physical and mental health conditions. For example, early detection of eating disorders can increase the likelihood of long-term recovery, as delays in treatment are associated with prolonged illness, poor prognosis, and relapse (Agras, 2001; Cavanaugh & Lemberg, 1999; Mitchell, 1995; National Eating Disorder Association, n.d.; Thompson & Smolak, 2001; Thompson & Smolak, 2001). While public health agencies have been working with pediatricians and primary care providers to develop behavioral health screening tools for at-risk children (Bazelon Center for Mental Health Law, n.d.), there are many barriers to referrals for mental health providers (Kathol et al., 2010). These barriers lead to a need for improved referral systems and integration of care.

Between a half and two-thirds of Americans with mental health conditions are treated in primary care settings (CDC, 2011; Kathol et al., 2010). While access to mental health services is often considered a barrier to quality care (Cunningham, 2009), the shortage of mental health
providers has led to issues of access (Cunningham, 2009). Primary care providers (PCPs) are often used as referral mechanisms for other specialties; however, PCPs report that referrals to mental health specialists are twice as difficult to accomplish than any other specialty (Cunningham, 2009; Kathol et al., 2010). Moreover, even when a mental health specialist is available for a referral, long waits for an appointment, ranging from weeks to months, leads to poor outcomes for both physical and mental health conditions and increases service use and cost (Kathol et al., 2010). Without improvements in available mental health care services, an estimated $130 to $350 billion will be spent annually for additional service use among patients with co-occurring physical and mental health disorders (Kathol et al., 2010).

The lack of available mental health treatment options is exacerbated in the children’s healthcare system. As opposed to physical health services, mental health care for children is underdeveloped and less cohesive (Behrens et al., 2013). Pediatricians are more likely than any other PCPs to report issues related to mental health referrals (Cunningham, 2009). Specifically, pediatricians are 15% more likely to cite a shortage of providers as a barrier to referrals for outpatient mental health services (Cunningham, 2009). The integration of behavioral and public health could help to address this barrier.

**Integration of Behavioral and Public Health**

There is recent widespread recognition of potential positive implications of integrating public and behavioral health (CDC, 2011). This integration could be essential to overall health during a time of limited resources as system integration could be more effective than individual stakeholder efforts (CDC, 2011). Integrated care and research focuses on a holistic approach to health through the recognition of the complex and interacting components of the body and mind as a whole (Nardone et al., 2014).

In 1999, the Surgeon General released a report calling for the full integration of mental health into the nation’s public health system (CDC, 2011). Despite previous legislation aimed at
parity between physical and mental healthcare insurance coverage, including the Mental Health Parity Act of 1996 and the Mental Health Parity and Addiction Equity Act of 2008 (Centers for Medicare and Medicaid Services, n.d.), barriers to integration still persist. Integration would require increased coordination and cooperation among local, state, and federal agencies (Bazelon Center for Mental Health Law, n.d.), as well as significant effort from healthcare providers to adopt a holistic approach (Nardone et al., 2014). This adoption may be difficult as healthcare professions may view integrated approaches as overwhelming due to the additional time and follow-up needed for screening and referrals (Nardone et al., 2014).

Application of Integration to Comorbid ADHD/ ED

The benefits of integrated public and behavioral health could apply to many physical and mental health comorbidities. One such example is the co-occurrence of ADHD, eating disorders (EDs), and subsequent obesity. Evidence has established a link between ADHD, EDs, and subsequent obesity (Cortese et al., 2008; Cortese, Bernardina, & Mouren, 2007; Davis, Levitan, Smith, Tweed, & Curtis, 2006). Beyond evidence related to the prevalence of this comorbidity, it has also been found that binge eating and loss of control eating mediate the relationship between ADHD and obesity (Reinblatt et al., 2015), and there may be a severity link between all three (Irving & Neumark-Sztainer, 2002). Integrating public and behavioral health could significantly improve the quality of life for children and adolescents with comorbid ADHD/ EDs. This can be achieved through the utilization of public health prevention techniques applied to mental illness as well as through the development of integrated mental and physical health care treatment teams.

While there have been some effective school based ED primary prevention efforts, in general there are still major gaps. Among the gaps are prevention to address the needs of both genders, early detection efforts, and programs that address a broad spectrum of weight-related problems (Ciao, Loth, & Neumark-Sztainer, 2014). Similarly, although EDs are mental health
conditions with physical health consequences, and obesity is a physical health condition with mental health consequences, the conceptual similarities, shared risk factors, high correlation, and diagnostic crossover rates have led to a call for the promotion of healthy weight related programs as opposed to separate obesity and ED preventions (Irving & Neumark-Sztainer, 2002). As the comorbidity exists for both genders and is associated with subsequent obesity, targeting children and adolescents with ADHD for primary prevention could allow for efforts to address current gaps in prevention.

Utilizing public health prevention techniques and integrating physical and mental health into singular ED and obesity programs targeted at children and adolescents with ADHD could reduce program development and management costs (Irving & Neumark-Sztainer, 2002). Additionally, dual benefits of media literacy education and the use of social cognitive theory for prevention of both disorders have been proposed as justification for integrated prevention (Irving & Neumark-Sztainer, 2002). However, it was also noted that there are many barriers to this integration in that professionals from the two fields might not agree on the types of messages or content of an integrated model. Significant collaboration and open communication between mental health and physical health care providers would be needed to overcome this barrier (Irving & Neumark-Sztainer, 2002).

In regards to secondary prevention, ADHD typically manifests in childhood (American Psychiatric Association [APA], 2013), while the average age of onset of EDs ranges from adolescents to early adulthood (Hudson, Hiripi, Pope Jr, & Kessler, 2007; Swanson, Crow, Le Grange, Swendsen, & Merikangas, 2011). Based on this trajectory, secondary prevention aspects of public health, including screening, behavior monitoring, and early referral can be utilized among children with ADHD to prevent EDs and subsequent obesity. Although evidence of comorbidity, due to limited training, the majority of pediatric healthcare providers (90%) report low levels of self-competence with regard to assessment and treatment of EDs in children and adolescents (Girz, Robinson, & Tessier, 2014; Robinson, Boachie, & Lafrance, 2013).
Improvements to medical curriculum regarding this comorbidity, behavioral health screening, and public health secondary prevention tools could provide the necessary conditions for appropriate monitoring and prevention of the development of the comorbidity.

For treatment or tertiary prevention, it is important to note that EDs are most commonly treated by mental health professionals (Hay, 2013; Smolak & Thompson, 2009; Stein, Latzer, & Merick, 2009), while ADHD is primarily assessed and treated by PCPs (Rader, McCauley, & Callen, 2009). This fragmentation may contribute to the burden of the comorbidity and lead to increased health care utilization and spending. The promotion of care integration through team-based models (i.e., health homes, accountable care organizations) in which patient specific treatment plans are developed in collaboration between the PCP and mental health care provider could significantly improve treatment success for the subset of patients with both disorders. These holistic approaches could allow for children and adolescents with comorbid ADHD and ED to receive the proper treatment needed for both disorders.

**Problem Statement**

The burden associated with the comorbidity of ADHD and EDs and subsequent obesity could be significantly improved through the integration of primary and mental healthcare as well as public and behavioral health. Through coordinated care and improved training, this comorbidity allows for improved screening, prevention, and treatment of all three conditions. However, additional information regarding this comorbidity is necessary to develop such interventions. While there is evidence related to the existence of the comorbidity, little is known about how or why this co-occurrence exists.

A comprehensive model of the underlying mechanisms associated with comorbid ADHD and EDs is needed to improve understanding of the development of the comorbidity. This model could then lead to the development of screening tools to help identify the subset of patients at-risk for developing the comorbidity. Once identified as at-risk, this subset could be targeted for
prevention efforts and patient-specific treatment plans; ultimately preventing the comorbidity, associated obesity, and other physical health consequences.

The improvement of secondary prevention via education and monitoring of adolescents at-risk for comorbid ADHD and EDs could also help address the Healthy People 2020 objective of reducing the prevalence of disordered eating behaviors in adolescents (U.S. Department of Health and Human Services, 2012). Concomitantly, a better understanding of the development of the comorbidity can be used to improve training and continued education among physicians who treat ADHD. In order to establish the evidence needed for future integrated prevention and care efforts, the current study aims to increase understanding of the underlying mechanisms of the ADHD/ED comorbidity.
CHAPTER TWO: LITERATURE REVIEW

“Comorbidity between psychological disorders is often the rule rather than the exception”

(Bobadilla, Vaske, & Asberg, 2013, p. 2555)

Attention-deficit/hyperactivity disorder (ADHD) and eating disorders (EDs) are both significant public health concerns due to their prevalence, impact on physical and mental health, and associated academic and social impairment (Hudson et al., 2007; Ingram, Hechtman, & Morgenstern, 1999; National Institute of Mental Health, 2008; Polanczyk & Rohde, 2007; Swanson et al., 2011; Wade, Keski-Rahkonen, & Hudson, 2011; Wilfley, Wilson, & Agras, 2003; Willcutt, 2012). While each is separately associated with consequences for overall well being, evidence suggests that these two disorders co-occur (Cortese et al., 2007; Nazar et al., 2008), potentially leading to increased risk for negative outcomes throughout the life course.

Epidemiology of ADHD

ADHD is a neurobiological disorder categorized by inattention, hyperactivity, and impulsivity (APA, 2000, 2013; Rohde, Verin, & Polanczyk, 2012); however, it has not always been known as ADHD (Lange, Reichl, Lange, Tucha, & Tucha, 2010). In 1968, hyperkinetic reaction of childhood, described by overactivity, restlessness, distractibility, and short attention span, was added to the second edition of the diagnostic and statistical manual of mental disorders (DSM)(Lange et al., 2010). In the 1970s, focus shifted from hyperactivity to inattention and ultimately DSM III (1980) renamed the disorder attention deficit disorder (ADD) with or without hyperactivity (Lange et al., 2010). DSM III also established age of onset and duration
requirements as well as the minimum symptom cut-off needed for a diagnosis (APA, 1978; Lange et al., 2010).

Based on the lack of information in regards to the sub-types of the disorder (i.e., with or without hyperactivity), the DSM-III-R (1987) renamed the disorder attention deficit-hyperactivity disorder and listed all symptoms in one category (Lange et al., 2010). Increasing evidence in the early 1990s suggested differences in symptomology, impairment, and outcomes between children with inattentive symptoms compared to children with hyperactive symptoms (Barkley, 2005; Lange et al., 2010). This evidence led to the reinstatement of sub-types in the DSM IV (1994), specifically inattentive, hyperactive/impulsive, and combined sub-types (APA, 2000; Lange et al., 2010).

The release of the 2013 DSM V made several additional changes to the diagnostic criteria of ADHD based on the most current data on the disorder. To account for the fact that impairing symptoms persist in adulthood in up to 65% of cases, DSM V added information and criteria related to adult ADHD (APA, 2013; Faraone, Biederman, & Mick, 2006). Moreover, the age of onset criteria was changed from a required symptom onset prior to age seven (APA, 2000) to the increased age twelve (APA, 2013). Lastly, sub-types were replaced with predominant presentations based on evidence suggesting that children often shift between the sub-types over time, with most childhood hyperactive/impulsive cases being re-diagnosed as combined by school age (APA, 2000, 2013; Lahey, Applegate, McBurnett, & Biederman, 1994). Current criteria state that a diagnosis of ADHD requires the presence of six or more symptoms from either or both the inattentive or hyperactive/impulsive symptom categories occurring often for at least six months (APA, 2013). These symptoms must cause impairment in at least two settings, such as work, school, or home, and have clear evidence of interference with appropriate social, academic, or occupational functioning (APA, 2013).

ADHD is one of the most common childhood disorders in the United States, and prevalence has steadily increased over the past decade (Visser et al., 2014). Based on data
from the 2011 National Survey of Children’s Health, the prevalence of parent-reported ADHD diagnoses among children four to seventeen years old has continuously increased from 7.8% in 2003, to 9.5% in 2007, and most recently to 11% in 2011 (Visser et al., 2014). Diagnostic rates are higher in males than females (15.1% vs. 6.7% in 2011) (Visser et al., 2014). However, prevalence of ADHD among females has been observed at higher rates in community samples as opposed to clinical samples, potentially suggesting gender-based diagnostic and treatment disparities (Polanczyk & Rohde, 2007; Rohde et al., 2012).

Prevalence of diagnosed ADHD also differs by race and socioeconomic status. Specifically, prevalence is higher among African American and Caucasian children (twice as high compared to Hispanic children), children living in English speaking households (four times increased likelihood), and children from higher educated households (Visser et al., 2014). However, children living in households 200% below the federal poverty line have higher rates of diagnosed ADHD compared to children from high-income families (Visser et al., 2014). These differences may not be true socio-demographic differences but rather the result of disparities in healthcare insurance coverage, as children with health insurance have higher rates of diagnosed ADHD (Visser et al., 2014). Moreover rates are higher among those with public health insurance compared to private coverage. In 2011, 14.4% of children with public healthcare coverage had ever been diagnosed with ADHD (Visser et al., 2014).

Prevalence of diagnosed ADHD may be heavily influenced by health care coverage (Visser et al., 2014), diagnostic methodology (i.e. parent, teacher, and/ or child reported symptomology) (Polanczyk & Rohde, 2007), and the vagueness in diagnostic criteria. Since DSM III, diagnostic criteria required symptoms to be often and impairing, but the DSM does not define either term (APA, 1978, 2000, 2013). As attention span naturally varies in children, determining frequency and severity may be highly subjective (Buitelaar & Rothenberger, 2004; Polanczyk & Rohde, 2007).
Associated academic and social impairment has been observed in both children with and without formal ADHD diagnoses (Ingram et al., 1999; Loe & Feldman, 2007), thus it is necessary to investigate prevalence of ADHD symptoms or behaviors (i.e., sub-clinical) as well as diagnoses. A 2012 meta-analysis reported that using parent ratings only, 6.1% of children and adolescents met full criteria, while 8.8% met symptom only criteria. Similarly, with teacher ratings 7.1% met full criteria and 13.3% met symptoms only criteria. Lastly, based on self-report, 8.5% of children and adolescents met symptom criteria (Willcutt, 2012). Investigations of socio-demographic differences in symptomology have been inconsistent with some studies finding significant differences by race, socioeconomic status, and urbanicity, and others finding no differences (Angold et al., 2002; Kessler et al., 2005; Polanczyk & Rohde, 2007).

At both the clinical and sub-clinical level, ADHD is associated with decreased self-esteem, lack of financial independence, and academic and interpersonal impairment (Ingram et al., 1999; Loe & Feldman, 2007; Rohde et al., 2012). Impairment persists into adulthood, resulting in reduced quality of life, increased healthcare need, and associated healthcare costs (Eaton et al., 2010). The economic impact of ADHD in the United States is estimated at an annual incremental cost of $143 to $266 billion per year (Doshi et al., 2012). ADHD is rarely observed alone and is highly comorbid with other mental illnesses (Hill, 2012). Common psychiatric comorbidities include oppositional-defiant disorder, conduct disorder, antisocial personality disorder, developmental disorders, autism spectrum disorders, Tourette syndrome, bipolar disorder, depression, anxiety, substance abuse, and addictions (Biederman et al., 2006; Hill, 2012; Polanczyk & Rohde, 2007).

**Epidemiology of Eating Disorders**

Eating disorder is an umbrella term for a group of disorders described by persistent disturbances in eating or weight related behaviors; these disorders including Anorexia Nervosa
AN, Bulimia Nervosa (BN), Binge Eating Disorder (BED), and Eating Disorder Not Otherwise Specified (EDNOS) (APA, 2013).

AN is characterized by distorted body image, excessive dieting, severe weight loss, and a fear of weight gain (APA, 2013). Prior DSM IV criteria requiring amenorrhea, or the absence of at least three menstrual cycles, was removed from the recent DSM V to account for people that this criteria could not apply to such as males, pre-menarche females, and females taking oral contraceptives (APA, 2000, 2013). BN is characterized by episodes of binge eating, which entails eating a larger than normal amount of food in a discrete period of time and a sense of lack of control over eating, followed by inappropriate compensatory behaviors such as self-induced vomiting, fasting, excessive exercise, or misuse of laxatives, diuretics, or other medications (APA, 2013). For a DSM V diagnosis, these behaviors must occur on average once a week for three months (APA, 2013; Wilfley, Bishop, Wilson, & Agras, 2007); a decrease from the twice weekly required in DSM IV (APA, 2000, 2013).

BED was added to the appendix of the DSM IV and listed as a disorder requiring further study (APA, 2013). It was subsequently added as an ED sub-type in DSM V (APA, 2013). Thus until the DSM V, anyone with BED would have been diagnosed with the EDNOS, as BED was not officially diagnosable. BED is characterized as binge eating without compensatory behaviors on average at least once a week over three months (APA, 2013; Wilfley et al., 2007). BED is often associated with obesity, however level of psychopathology, weight and shape concerns, and quality of life differ between obese individuals with BED and obese individuals without BED (Wonderlich, Gordon, Mitchell, Crosby, & Engel, 2009). Lastly, EDNOS is a catch-all term of any cases that do not meet full criteria for a specific ED (APA, 2013), for example someone who does not meet frequency criteria for BN or BED, or low weight criteria for AN. Based on DSM IV criteria, 60% of cases were considered EDNOS (Fairburn & Bohn, 2005). The changes in the DSM V, especially the addition of BED to the ED category, were made specifically to minimize the use of EDNOS (APA, 2013).
Although recent diagnostic changes help decrease the overuse of EDNOS, there are still several concerns with the diagnostic criteria. While EDs are diagnostically mutually exclusive disorders (APA, 2013), the core symptoms of all EDs are similar, including preoccupation with food and weight, and body dissatisfaction (Polivy & Herman, 2002). Moreover, despite the mutual exclusiveness, similar to ADHD sub-types, ED diagnoses are generally not stable over time (Fairburn & Cooper, 2011). People often change between restrictive, binging, and purging behaviors throughout the course of their disorder (Fairburn & Cooper, 2011). As a result, diagnoses are often considered “snapshots” of current behaviors as opposed to an indicator of a specific disorder (Fairburn & Cooper, 2011). For example, one study found that over a 30-month period, only a third of 192 women with an ED retained diagnostic criteria for the same ED (Milos, Spindler, Schnyder, & Fairburn, 2005). Similarly, a group of 216 women diagnosed with either AN or BN were followed via weekly ED symptom assessments over seven years. Nearly 75% of women with diagnosed AN experienced diagnostic crossover towards BN, with crossover most commonly occurring during a progression towards recovery. However, women with a BN diagnosis were unlikely to experience crossover to AN (Eddy et al., 2008).

Prevalence of EDs has generally increased over the past four decades (Hudson et al., 2007; Striegel-Moore & Franko, 2003; Tenore, 2001; Wade et al., 2011). Specifically, incidence rates of BN in women age ten to thirty-nine tripled between 1988 and 1993 (Hoek & van Hoeken, 2003), and AN incidence in women age fifteen to nineteen has continually increased in every decade since 1930 (Hoek & van Hoeken, 2003). Estimates suggest that the lifetime prevalence ranges from 0.5% to 1.0% for AN, 0.5% to 3.0% for BN, and 1.6% to 5.3% for BED (Striegel-Moore & Franko, 2003; Swanson et al., 2011). AN and BN rates are typically higher among females, while BED has been observed to be more prevalence among males (Hudson et al., 2007; Striegel-Moore & Franko, 2003; Swanson et al., 2011). Among adolescent boys, 6% report regular binge eating and 8.3% report regular episodes of loss of control eating (Mond et al., 2014).
Estimates from the 2001-2003 National Comorbidity Survey Replication suggest that the median age of onset of each type of ED ranges from eighteen to twenty-one years old, with onset of 18.9 years old for AN, 19.7 years old for BN, and 25.4 years old for BED (Hudson et al., 2007). However, estimates from the 2001-2004 adolescent supplement of the National Comorbidity Study Replication suggests much younger onset, with estimates of 12.3 years old for AN, 12.4 years old for BN, and 12.6 years old for BED (Swanson et al., 2011). Comparatively, results from a longitudinal investigation of a large community sample reported peak onset for BN and BED between seventeen and eighteen years old (Stice, Marti, Shaw, & Jaconis, 2009).

EDs are chronic and persistent. Years of disorder duration is much longer for disorders associated with binge eating with average disorder durations of 1.7 years for AN, 8.3 years for BN, and 8.1 years for BED (Hudson et al., 2007). Similarly, just slightly over half of all ED cases fully recover after 10-years and approximately one third of all patients relapse after recovery (Agras, 2001; Herzog et al., 1999; Steinhausen, 2009). Results from a longitudinal investigation with a community sample reported relapse rates of 41% for BN and 33% for BED (Stice et al., 2009).

EDs have the highest mortality rate of all mental illnesses (Arcelus, Mitchell, Wales, & Nielsen, 2011; Sullivan, 1995). Using random-effects meta-analysis, a recent study reported a 5.86 deaths per 1,000 person-years standardized mortality ratio (SMR) for AN (Arcelus et al., 2011). The SMR for BN was 1.93 deaths per 1,000 person-years, and 1.92 deaths per 1,000 person-years for EDNOS (Arcelus et al., 2011). A large portion of these deaths was due to suicide, with one in five deaths among AN patients due to suicide (Arcelus et al., 2011). Based on the studies reviewed, it was determined that factors that influenced mortality included older age and low body mass index at first presentation, alcohol misuse, and comorbid mental illnesses (Arcelus et al., 2011). More than half of all cases present with at least one comorbid condition, which most commonly were mood, anxiety, impulsive control, substance abuse, or
bipolar disorders (Hudson et al., 2007; McElroy, Kotwal, Keck Jr, & Akiskal, 2005). Comorbid psychiatric conditions are associated with a threefold increase in the risk of death among AN patients (Papadopoulos, Ekblom, Brandt, & Ekselius, 2009).

Beyond increased mortality, EDs are associated with long-term physical and mental health consequences (Haines & Neumark-Sztainer, 2006; National Eating Disorder Association (n.d.); Neumark-Sztainer et al., 2006; Neumark-Sztainer et al., 2007). Some of these consequences include cardiovascular damage, osteoporosis, kidney failure, ulcers, anxiety, depression, and alcohol and substance abuse (Fairburn & Harrison, 2003; Haines & Neumark-Sztainer, 2006; National Eating Disorder Association (n.d.); Neumark-Sztainer & Hannan, 2000; Neumark-Sztainer et al., 2006; Neumark-Sztainer et al., 2007). EDs are also associated with social and familial impairment. Additionally, AN is associated with severe social impairment, and BN and BED are associated with both social and family impairment (Swanson et al., 2011).

Disordered eating behaviors, including EDNOS, are cases of ED behaviors that do not meet full diagnostic criteria. However, these behaviors are still associated with severe health consequences, evident by the similar SMR rates between patients with BN and EDNOS (Arcelus et al., 2011). Cases of EDNOS or sub-clinical EDs often progress to clinical EDs, and patients with EDNOS have similar physical health consequences as patients with full diagnostic criteria (Neumark-Sztainer, 2003; Peebles, Hardy, Wilson, & Lock, 2010). EDNOS patients typically have similar psychological profiles to those who meet full criteria for AN and BN as well as the same outcomes in terms of heart rate, blood pressure, temperature, and QTc interval (Peebles et al., 2010).

Current estimates suggest that up to ten million males and twenty million females in the United States present with some form of disordered eating behavior (National Association of Anorexia Nervosa and Associated Disorders, n.d.). More specifically, 14% of all adolescents and 31% adult females engage in disordered eating behaviors (Reba-Harrelson et al., 2009; U.S. Department of Health and Human Services, 2012). One study conducted diagnostic
interviews among a large community sample of adolescent girls over eight years. Lifetime prevalence rates by age twenty were 0.6% for AN for both diagnosable cases and sub-clinical level behaviors; however, while 1.6% and 1.0% of the sample met criteria for BN and BED respectively, 6.1% and 4.6% had subthreshold behaviors of each disorder. A total of 12% of the sample had some form of ED behavior (Stice et al., 2009). While many sub-clinical cases progressed to diagnosable disorders, sub-clinical BN and BED are associated with significant impairment and distress (Stice et al., 2009). The prevalence and potential health consequences of EDNOS, or sub-clinical EDs, has resulted in the addition of a new *Healthy People 2020* objective, which aims to reduce the proportion of adolescents who engage in disordered eating behaviors in an attempt to control their weight (U.S. Department of Health and Human Services, 2012).

**Epidemiology of Comorbid ADHD/ED**

Evidence demonstrates comorbidity between ADHD and EDs with the majority of studies focusing on females. It was reported that worldwide an estimated 5.7% and 9.3% of people with ADHD have lifetime BN and BED respectively. Conversely, among people with BN and BED, 14.8% and 10.2% have lifetime histories of ADHD respectively (Kessler et al., 2013). Studies have found increased rates of ADHD among ED patients, increased rates of EDs among ADHD patients, increased rates of both among obesity patients, and correlations between the prevalence of both disorders in community based samples. Evidence has also recently been extended to young pediatric samples. All relevant studies identified to date are displayed in table 1 and 2. Table 1 displays all studies among ADHD or ED patients and table 2 displays all studies among obesity patients and non-patient samples.

In regards to ADHD among ED patients (see table 1), all of the eight studies have focused on female, adult patients. Although only two utilized comparison groups, across all there is a trend of increased prevalence of ADHD among ED patients. For example, one study
reported that 21.2% of 189 females at an inpatient ED facility displayed six or more current ADHD symptoms (Yates, Lund, Johnson, Mitchell, & McKee, 2009). A similar investigation of females receiving either inpatient or outpatient ED treatment found that 21% had childhood ADHD compared to a 2.5% of comparison controls. Moreover, a third of the ED sample reported sub-threshold childhood ADHD symptoms (Seitz et al., 2013). Additionally, a large outpatient ED clinic reported a significant positive association between ADHD symptoms and the frequency of binge eating episodes among female patients (Fernández-Aranda et al., 2013).

In regards to the twelve studies identified among ADHD patients (see table 1), a large portion utilized gender-mixed samples. Results varied in that significant rates of comorbid ADHD/EDs was found among gender-mixed samples; however, the few studies that stratified by gender found evidence of the relationship only among females (see table 1). One investigation of a gender mixed pediatric sample found that ADHD patients had significantly more parent-reported BN symptoms compared to controls at an eight year follow up with medium effect sizes (Mikami et al., 2010). A case-control, longitudinal, family study of girls found that those with ADHD were 3.6 times more likely to develop an ED, and 5.6 times more likely to develop BN than age-matched controls (Biederman et al., 2007). A similar investigation of a large, longitudinal birth cohort found a 5.7 times increased risk for EDs among boys and girls with ADHD compared to those without ADHD (Yoshimasu et al., 2012).

Four studies have evaluated both ADHD and binge eating among patients seeking treatment for obesity (see table 2). Three studies that used obese adolescent or adult samples noted significant associations between ADHD and binge eating (Cortese et al., 2006; Nazar et al., 2012; Nazar et al., 2014). These studies also found that ADHD is correlated with more severe BED and BN behaviors among weight loss seeking patients (Nazar et al., 2012; Nazar et al., 2014). However, the fourth was among a pediatric, gender-mixed sample and found no association between ADHD and disordered eating behaviors (Pauli-Pott, Becker, Albayrak, Hebebrand, & Pott, 2013).
Table 1. Comorbid ADHD/ED Studies with ADHD and ED Patient Samples

<table>
<thead>
<tr>
<th>1st Author, Year</th>
<th>Sample</th>
<th>Patient Status</th>
<th>Cases</th>
<th>Controls</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sokol, 1999</td>
<td>Adult</td>
<td>Not Reported</td>
<td>6 BN</td>
<td>7 HC</td>
<td>Higher ADHD symptom scale scores among BN v. HC</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wentz, 2005</td>
<td>Adult</td>
<td>Inpatient &amp;</td>
<td>9 BN,</td>
<td>NC</td>
<td>17% had childhood ADHD</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>Female</td>
<td>Outpatient</td>
<td>8 ANR,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blinder, 2006</td>
<td>Adult</td>
<td>Inpatient</td>
<td>882 BN,</td>
<td>NC</td>
<td>Rates of ADHD by subtype: BN (9%); AN (3%); EDNOS (6%);</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td>520 ANR,</td>
<td></td>
<td>No different in ADHD by ED subtype</td>
</tr>
<tr>
<td>Fischer, 2007</td>
<td>Adult</td>
<td>Outpatient</td>
<td>80 BN</td>
<td>NC</td>
<td>2.9% had ADHD</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yates, 2009</td>
<td>Adult</td>
<td>Inpatient</td>
<td>37 BN,</td>
<td>NC</td>
<td>5.3% met full criteria for ADHD; 21.2% had at least six current symptoms</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td>55 ANR,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fernández-Aranda, 2013</td>
<td>Adult</td>
<td>Outpatient</td>
<td>95 BN, 29 EDNOS,</td>
<td>NC</td>
<td>Positive correlation of ADHD symptoms and binge eating episodes</td>
</tr>
<tr>
<td>Spain</td>
<td>Female</td>
<td></td>
<td>24 BED</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seitz, 2013</td>
<td>Adult</td>
<td>Inpatient</td>
<td>57 BN</td>
<td>40 HC</td>
<td>BN v. HC: childhood ADHD (21% v. 2.5%); adult ADHD (10% v. 2.5%); 1/3 of BN had childhood symptoms</td>
</tr>
<tr>
<td>Germany</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stulz, 2013</td>
<td>Adult</td>
<td>Inpatient</td>
<td>6 BN, 5 ANB,</td>
<td>NC</td>
<td>29% of cases had ADHD symptoms; No correlation of severity of each</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Female</td>
<td></td>
<td>14 EDNOS</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biederman, 1994</td>
<td>Adult</td>
<td>Outpatient</td>
<td>101 ADHD</td>
<td>207 HC</td>
<td>Higher rate of BD in ADHD v. HC among females; no BN among any males</td>
</tr>
<tr>
<td>United States</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mattos, 2004</td>
<td>Adult</td>
<td>Outpatient</td>
<td>86 ADHD</td>
<td>NC</td>
<td>9 had BED; 1 had EDNOS</td>
</tr>
<tr>
<td>Brazil</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Kooij, 2004</td>
<td>Adult</td>
<td>Outpatient</td>
<td>45 ADHD</td>
<td>NC</td>
<td>9% (3 cases) had BN; 1 with past BN and 2 with current BN</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biederman, 2004</td>
<td>Adult</td>
<td>Outpatient</td>
<td>219 ADHD</td>
<td>215 HC</td>
<td>Higher rate of BD in ADHD vs. HC among females; no BN among any males</td>
</tr>
<tr>
<td>United States</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Surman, 2006</td>
<td>1 Pediatric Adult</td>
<td>Outpatient</td>
<td>Pediatric: 280 Adult: 101 219 ADHD</td>
<td>Pediatric: 242 Adult: 207 215 HC</td>
<td>Rate of BD in ADHD vs. HC: Pediatric: 1% of males; females (0% v. 0%); Adult 1: 12% of males (3% v. 0%); Adult 2: females (11% v. 0%); males (0% v. 0%)</td>
</tr>
<tr>
<td>United States</td>
<td>2 Adult Male &amp; Female</td>
<td></td>
<td>Adult 1: 101 Adult 2: 219 ADHD</td>
<td>Adult 1: 207 Adult 2: 215 HC</td>
<td></td>
</tr>
<tr>
<td>Sobanski, 2007</td>
<td>Adult</td>
<td>Outpatient</td>
<td>70 ADHD</td>
<td>70 HC</td>
<td>Higher rate of BED in ADHD vs. HC (11.4% v 1.4%)</td>
</tr>
<tr>
<td>Germany</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Mikami, 2008</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>127 ADHD</td>
<td>82 HC</td>
<td>Rate of BD symptoms: 5-10% in ADHD combined and 0-1% in ADHD inattentive and control groups; no diagnosable BD</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biederman, 2009</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>140 ADHD</td>
<td>120 HC</td>
<td>No BD found in either ADHD or HC</td>
</tr>
<tr>
<td>United States</td>
<td>Male</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mikami, 2010</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>432 ADHD</td>
<td>264 HC</td>
<td>Higher rate of BD symptoms in ADHD v. HC; no diagnosable BD</td>
</tr>
<tr>
<td>United States</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biederman, 1999, 2006, 2007, 2010</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>140 ADHD</td>
<td>120 HC</td>
<td>Longitudinal Sample Follow-Ups: Intake: ADHD: 1% had AN, 2% had BN, HC: 0% had AN or BN; Year 5: Past year ED (HR=4.4, p=.06); ADHD 3.6x and 5.6x more likely to have lifetime ED and lifetime BN; Year 11: Lifetime ED (HR=3.5); Rate of past year ED in ADHD v. HC (7% v. 3%)</td>
</tr>
<tr>
<td>United States</td>
<td>Female</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Yoshimasa, 2012</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>379 ADHD</td>
<td>758 HC</td>
<td>Risk of ED in ADHD v. HC (HR: 5.68)</td>
</tr>
<tr>
<td>United States</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinblatt, 2014</td>
<td>Pediatric</td>
<td>Outpatient</td>
<td>109 ADHD</td>
<td>143 HC</td>
<td>Children with ADHD 16x more likely to binge eat; ADHD was positively associated with BMI and the relationship was partially mediated by binge eating</td>
</tr>
<tr>
<td>United States</td>
<td>Male &amp; Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Notes: ED=eating disorder; AN=Anorexia Nervosa; ANR=Anorexia Nervosa Restricting Subtype; ANB=Anorexia Nervosa Binge/Purge Subtype; BN=Bulimia Nervosa; BED=Binge Eating Disorder; EDNOS=Eating Disorder Not Otherwise Specified; HR=hazard ratio; HC=healthy control; NC=no controls

1 two were male; 2 age range 15-35; 3 avg. age of 10.8; 4 psychiatric patients without ADHD
Seven studies have investigated the comorbidity among non-patient populations (see table 2). All reported evidence of the comorbidity, with the exception of one Canadian study that found a significant difference in the number of ADHD symptoms between normal weight participants and participants that were obese. However, a lack of a significant difference in the number of ADHD symptoms between the two obese samples suggests an association between ADHD with obesity and not BED (Davis et al., 2009). Conversely, among a young sample, after adjusting for body mass index, children with ADHD were 12 times more likely to have loss of control eating syndrome (LOS-ES) (Reinblatt et al., 2015). Moreover, a large U.S. nationally representative survey study reported that the relationship only existed with BED and BN behaviors and not restrictive behaviors. Specifically, participants with self-reported sub-clinical childhood ADHD symptoms with no official diagnosis were twice as likely to report sub-clinical BN or BED behaviors (Bleck, Debate, & Olivardia, 2014).

Associations between ADHD and binge eating have also been observed in young pediatric samples. With regards to current behaviors in younger samples, a retrospective chart review at two pediatric mental health clinics with participants that had an average age of 10.8 years old found a significant association between ADHD and binge eating. Moreover, ADHD was also associated with being overweight or obese, and the relationship of ADHD with weight was partially, but not completely, mediated by binge eating (Reinblatt et al., 2014). A second study investigated the relationship between ADHD and loss of control eating among a community-recruited sample of children with an average age of eleven years old. Loss of control eating is sometimes used to describe BED in children as it is considered difficult to determine what would constitute an objectively large binge among growing children. Instead loss of control eating represents subjective binge eating (Reinblatt et al., 2015). After adjusting for body mass index, children with ADHD were twelve times more likely to have loss of control eating (Reinblatt et al., 2015).
Regardless of the presence of an ED, ADHD has separately been associated with subsequent obesity (Cortese et al., 2008). High rates of ADHD have been noted among patients seeking weight loss treatment. One investigation of adult females at a nonsurgical obesity treatment center reported a 28.3% rate of diagnosable ADHD (Nazar et al., 2012). Similarly, estimated rates of ADHD among patients seeking bariatric surgery range from 26% to 61% (Nazar et al., 2014; Nicolau et al., 2013). ADHD symptoms may be a risk factor for less success of weight loss and weight maintenance and difficulties with compliance in bariatric surgery follow-up (Nicolau et al., 2013). Although studies have investigated the comorbidity of ADHD and obesity separate from that of ADHD and EDs, one that explored mediating factors related to

<table>
<thead>
<tr>
<th>Author, Year</th>
<th>Country</th>
<th>Sample</th>
<th>Patient Status</th>
<th>Cases</th>
<th>Controls</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortese, 2006</td>
<td>France</td>
<td>Adolescent Male &amp; Female</td>
<td>Inpatient</td>
<td>106 obese</td>
<td>NC</td>
<td>BN and ADHD symptoms significantly correlated even after controlling for depressive and anxiety symptoms</td>
</tr>
<tr>
<td>Nazar, 2012</td>
<td>Brazil</td>
<td>Adult Female</td>
<td>Outpatient</td>
<td>155 obese</td>
<td>NC</td>
<td>28.3% had ADHD; ADHD was correlated with more severe BED and BN symptoms</td>
</tr>
<tr>
<td>Pauli-Pott, 2013</td>
<td>Germany</td>
<td>Pediatric Male &amp; Female</td>
<td>Outpatient</td>
<td>128 obese</td>
<td>NC</td>
<td>ADHD symptoms were not associated with any ED behavior</td>
</tr>
<tr>
<td>Nazar, 2014</td>
<td>Brazil</td>
<td>Adult Female</td>
<td>Outpatient</td>
<td>171 obese</td>
<td>NC</td>
<td>ADHD symptoms significantly predicted binge eating behavior</td>
</tr>
</tbody>
</table>

**Table 2. Comorbid ADHD/ED Studies with Obese and Non-Patient Samples**

<table>
<thead>
<tr>
<th>1st Author, Year</th>
<th>Country</th>
<th>Sample</th>
<th>Patient Status</th>
<th>Cases</th>
<th>Controls</th>
<th>Key Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neumark-Sztainer, 1995</td>
<td>United States</td>
<td>Adolescents Male &amp; Female</td>
<td>Non-Patient</td>
<td>689 ADD: school survey recruited</td>
<td>1,371 HC</td>
<td>Higher rate of BED in ADD v. HC for both males and females</td>
</tr>
<tr>
<td>Davis, 2006</td>
<td>Canada</td>
<td>Adult Female</td>
<td>Non-Patient</td>
<td>110: community recruited</td>
<td>-</td>
<td>ADHD was associated with overeating (i.e., binge, emotional, and external, and depressed overeating); overeating was associated with increased BMI</td>
</tr>
<tr>
<td>Davis, 2009</td>
<td>Canada</td>
<td>Adult Male &amp; Female</td>
<td>Non-Patient</td>
<td>60: community recruited, obese with BED</td>
<td>61 HC; 60 No-BED OC</td>
<td>Higher rate of ADHD symptoms in obese v. normal weight; no difference between obese with BED and obese without BED</td>
</tr>
<tr>
<td>Kessler, 2013</td>
<td>Worldwide</td>
<td>Adult Male &amp; Female</td>
<td>Non-Patient</td>
<td>12,413: WHO World Mental Health Survey Initiative</td>
<td>-</td>
<td>Among adults with lifetime ADHD: 5.7% had a history of BN and 9.3% had a history of BED; Among adults with lifetime BN and BED: 14.8% (OR=5.8) and 10.2% (OR=3.9) had lifetime ADHD</td>
</tr>
<tr>
<td>Bleck, 2014</td>
<td>United States</td>
<td>Adult Male &amp; Female</td>
<td>Non-Patient</td>
<td>4,862: Add Health¹</td>
<td>-</td>
<td>ADHD was associated with clinical ED and sub-clinical BN and BED but not AN behaviors among females; No ADHD/ED association among males</td>
</tr>
<tr>
<td>Bleck, 2014</td>
<td>United States</td>
<td>Adult Male &amp; Female</td>
<td>Non-Patient</td>
<td>11,458: Add Health¹</td>
<td>-</td>
<td>Childhood ADHD symptoms were associated with adult BN symptoms but not associated with AN symptoms</td>
</tr>
<tr>
<td>Reinblatt, 2015</td>
<td>United States</td>
<td>Pediatric Male &amp; Female</td>
<td>Outpatient</td>
<td>79: community recruited, over 5th weight percentile</td>
<td>-</td>
<td>Children with ADHD were 12x more likely to have loss of control eating syndrome after controlling for BMI</td>
</tr>
</tbody>
</table>

**Notes:** ED=eating disorder; BN=Bulimia Nervosa; BED=Binge Eating Disorder; BMI=body mass index; OR=odds ratio; HC=healthy control; NC=no controls; OC=obese controls; ¹National Longitudinal Study of Adolescent to Adult Health; *avg. age is 11
ADHD and obesity found that binge eating but not depression mediated the ADHD/obesity relationship (Pagoto et al., 2009).

**Hypotheses of Comorbid ADHD/ED**

To date very little is known about the determinants of the comorbidity of ADHD and EDs. While there have been very few empirical investigations of either the determinants or underlying mechanisms to explain this comorbidity, several hypotheses have been suggested. Within a systematic review of the current evidence of the comorbidity, Cortese et al. (2007) suggested four potential hypotheses to explain the relationship: “1) inattention and/or impulsivity foster binge eating; 2) ADHD and binge eating share common neurobiological bases; 3) binge eating contributes to ADHD; and 4) psychopathological factors common to both binge eating and ADHD mediate the association” (Cortese et al., 2007, p.404). Similar hypotheses were recently suggested within the investigation of ADHD with loss of control eating among children. In order to explain the relationship, Reinblatt et al. (2015) proposed that the comorbidity of ADHD and loss of control eating could: “1) reflect the random base rates of [loss of control eating] and ADHD in the population; 2) result from an underlying common risk factor (such as impulsivity) leading to symptoms, or 3) reflect symptom overlap in these disorders, with ADHD presenting a behavioral form of impaired impulse control and LOC-ES presenting an eating based form of impaired impulse control” (Reinblatt et al., 2015, p.2).

Based on these initial hypotheses, justifications of the hypotheses, and findings from other studies, the current study proposed three hypotheses of the underlying mechanisms of the ADHD/ED comorbidity. Hypotheses include: hypothesis one [H1]) ADHD and binge eating are the expression of a common genetic or neurobiological dysfunction that manifests itself as binge eating and ADHD; hypothesis two [H2]) psychosocial factors common to both binge eating and ADHD mediate the association between the two conditions; and hypothesis three [H3]) a third underlying mental health condition mediates the relationship between the two conditions. These
hypotheses, suggested factors within each hypothesis, and the interaction between hypotheses all require further investigation.

Proposed Underlying Mechanisms of Comorbid ADHD/ED

The Reward Deficiency Syndrome (RDS) has been proposed to explain the potential common genetic or neurobiological dysfunction (H1) (Cortese et al., 2007). The RDS is characterized by a lack of dopamine based natural award (Comings & Blum, 2000). This dopamine deficiency then leads someone to seek reward through behaviors, typically impulsive or risky behaviors (Blum et al., 2000; Blum et al., 1996; Blum et al., 1995; Comings & Blum, 2000; Cortese et al., 2007). The RDS has been linked to ADHD, binge eating, and obesity; and in the case of the ADHD/ED comorbidity, someone with the RDS might present with impulsive behaviors that include both hyperactivity and binge eating (Blum & Noble, 2001; Comings & Blum, 2000; Noble, 2003; Wang, Volkow, & Fowler, 2002).

Several neurotransmitters and genes have been associated with the syndrome including serotonin, norepinephrine, GABA, opioid, and cannabinoid neurons, all of which modify dopamine metabolism and dopamine neurons (Comings & Blum, 2000). Defects in the genes associated with the production of these neurotransmitters results in the RDS. These genes include Dopamine Receptor D1, Dopamine Receptor D2, Dopamine Receptor D4, Dopamine Receptor D5, Dopamine Transporter DAT1, Dopamine B-Hydroxylase, adrenergic a2A and a2C Receptor, Monoamine Oxidase A and B, COMT val158, and Serotonin Transporter 5HTT (Comings & Blum, 2000).

Dopaminergic genes directly impact dopamine development, and thus are key genes associated with the RDS (Comings & Blum, 2000). The dopamine system genes are also the site for activation of the metabolism of ADHD psychostimulant medications (Li, Sham, Owen, & He, 2006). More specifically, the nine repeat and ten repeat genotypes of the dopamine transporter DAT1 have been associated with a range of risk taking behaviors including
delinquency, risky sex, risky drinking, and drug use (Guo, Cai, Guo, Wang, & Harris, 2010), as well as ADHD and EDs (Frieling et al., 2010; Swanson et al., 2000). The seven repeat genotype of the dopamine D4 receptor gene has been associated with mood disorders and substance use (Bobadilla et al., 2013), and has been observed at elevated rates in patients with ADHD (Bidwell et al., 2011; LaHoste et al., 1996; McClernon, Fuemmeler, Kollins, Kail, & Ashley-Koch, 2008; Swanson et al., 1998) and EDs (Bachner-Melman et al., 2007; Kaplan et al., 2008).

Genes associated with serotonin also play a key role in dopamine production and the RDS (Comings & Blum, 2000). The serotonin transporter 5-HTTLPR has been associated with both ADHD (Bidwell et al., 2011) and EDs (Frieling et al., 2006; Urwin & Nunn, 2004; Verkes, Pijl, Meinders, & Van Kempen, 1996). Lastly, monoamine oxidase A (MAOA) is associated with the RDS as it impacts the production of neurotransmitters including dopamine, serotonin, and norepinephrine (Comings et al., 2000). MAOA has been associated with ADHD (Bidwell et al., 2011; Kollins, McClernon, & Fuemmeler, 2005; McClernon et al., 2008), EDs (Urwin & Nunn, 2004; Verkes et al., 1996), and obesity (Camarena et al., 2004).

In regards to H2, potential psychosocial factors include social and familial support and personality traits. Both peer rejection and parent-child relationships have been associated with ADHD and EDs (Mikami, Hinshaw, Patterson, & Lee, 2008); similarly, personality traits such as novelty seeking, self-directedness, obsessive compulsiveness, and perfectionism have also been linked to the comorbidity (Fernández-Aranda et al., 2013). All three factors (i.e., family support, peer support, and personality) have been observed as mediating the association between ADHD with other mental illnesses. Specifically, personality factors including neuroticism and impulsiveness have been found to mediate the relationship between ADHD and addictions (Davis, Cohen, Davids, & Rabindranath, 2015), and parenting behaviors mediate the relationship between ADHD and depression (Ostrander & Herman, 2006). One study linking ADHD with addictions suggested that the substance abuse might result as a self-medicating or coping behavior in the absence of adequate social support (Davis et al., 2015). Based on the
high rates of co-occurrence of ADHD, EDs, substance abuse, and depression, described in detail below, and conceptual similarities in these disorders, the mediating influences of family support, social support, and personality might also apply to the relationship between ADHD and EDs.

Cognitive psychological factors may impact the connection between ADHD and EDs, specifically working memory and cognitive control (National Institute of Mental Health, n.d.) Cognitive control may be explained by deficient inhibitory control, which is an expression of impulsivity (Cortese et al., 2007). Impulsive symptoms like interrupting and intruding are part of the diagnostic criteria for ADHD (APA, 2013), and binge eating has been repeatedly conceptualized as a dysfunction in impulse control (Engel et al., 2005; Fahy & Eisler, 1993; Rosval et al., 2006; Wiederman & Pryor, 1996; Wonderlich, Connolly, & Stice, 2004). Evidence indicates 40% of patients with BN have been observed with impulse control problems in other life domains beyond eating (Gurze Books, 2013; Waxman, 2009). More specifically, deficient inhibitory control manifests as poor planning and difficulties in behavior monitoring, both of which may lead to binge eating and may appear in behaviors that contribute to the diagnoses of both EDs and ADHD (Davis et al., 2006).

Impulsivity, the stem of cognitive control issues, has been hypothesized as the mediating link between ADHD and EDs by multiple authors (Cortese et al., 2007; Reinblatt et al., 2014; Reinblatt et al., 2015; Steadman & Knouse, 2014); however, two investigations of this hypothesis found mixed results. Among a sample of 50 undergraduate students, impulsivity, both self reported via the Barratt Impulsiveness Scale and an executive functioning self-restraint scale, as well as measured with a computerized go/no-go task, could not explain the observed association of ADHD with BED symptoms (Steadman & Knouse, 2014). However, another study found significant associations between both parent reported lack of impulse control and results of a computer based neuropsychological assessment task of impulsive control with ADHD and loss of control eating in children (Reinblatt et al., 2015).
Lastly, a third underlying mental health condition may mediate the association between ADHD and EDs (H3). There are high levels of comorbidity across all mental illnesses with both ADHD and EDs having many noted comorbidities (Biederman et al., 2010; Blinder, Cumella, & Sanathara, 2006). The common comorbidities of depression, substance abuse, and anxiety disorders are all possible mediators between ADHD and EDs (Cortese et al., 2007). Psychiatric factors including depression, anxiety, and emotion regulation have been specifically hypothesized as potential mediators of the ADHD/ED relationship (Steadman & Knouse, 2014). Although not specifically proposed as an underlying mechanism, experiences of childhood abuse, both sexual and physical, may also mediate the relationship as childhood abuse and maltreatment has separately been linked to both ADHD (Erikson, 1968; Ouyang, Fang, Mercy, Perou, & Grosse, 2008) and EDs (Hall, Tice, Beresford, Wooley, & Hall, 1989; Wonderlich, Brewerton, Jocic, Dansky, & Abbott, 1997).

Although many have been proposed, to date only one potential underlying mechanism has been tested. The cognitive control, or impulsivity mediator has been explored but findings were mixed as described above. All other hypothesized factors have not yet been evaluated. Moreover, with the exception of the RDS and associated genetic factors, the majority of the predicted underlying factors were proposed independently of each other. An empirical evaluation is needed of the three hypotheses and associated factors in order to better understand how and why this comorbidity develops. A simultaneous investigation of the three hypotheses would allow for evaluation of each individual factor as well as the interaction of the factors. Results could help to develop a comprehensive model of the combined and interacting underlying mechanisms, which can then be used for improved prevention and treatment efforts.

**Comorbid ADHD/ ED among Males**

Current literature related to the ADHD/ED comorbidity has provided a theoretical background to guide the development of an understanding of this comorbidity among females.
However, there are significant gender differences in terms of manifestation and symptomology (Núñez-Navarro et al., 2012), risk factors (Strother, Lemberg, Stanford, & Turberville, 2012), and outcomes of ED (Stoving, Andries, Brixen, Bilenberg, & Horder, 2011) and based on the female focus, our knowledge of gender differences related to comorbid ADHD/ED is limited. While the majority of epidemiological studies have focused on females, the comorbidity has also been observed in gender mixed samples (Cortese et al., 2006; Davis et al., 2009; Fischer & Grange, 2007; Mattos et al., 2004; Mikami et al., 2010; Neumark-Sztainer, Story, Resnick, Garwick, & Blum, 1995; Sobanski et al., 2007). While there is evidence of its existence, understanding of the comorbidity in regards to underlying factors and characteristics associated with this subset of males is still underdeveloped.

While many of the proposed underlying mechanisms may hold true for both genders, some factors may be gender-specific. As one example, gender differences have been noted among the rates of comorbid mental illnesses among people with ADHD. Specifically, prevalence of major depression and generalized anxiety disorder were higher among females with ADHD, while comorbid substance use disorders were more common among males (Hesson & Fowler, 2015). While all three of these disorders have been proposed as potential mediators between ADHD and EDs, this finding suggests that female specific results of the underlying mechanism cannot be assumed among males. Moreover, females worldwide have been found to report higher levels of neuroticism and conscientiousness than males (Schmitt, Realo, Voracek, & Allik, 2008). In an investigation of the link between ADHD and addictions, it was reported that females with ADHD had higher scores in binge eating assessments while males had high scores for hypersexual behavior (Davis et al., 2015). These and other potential differences suggest that an independent investigation of the underlying mechanisms of the comorbidity among males is needed.

EDs among males are generally considered underdiagnosed and misunderstood (Smink, van Hoeken, & Hoek, 2012; Strother et al., 2012). While binge eating is the most
common ED amongst males (Hudson et al., 2007; Striegel-Moore & Franko, 2003; Swanson et al., 2011), to date the male ED literature has generally focused on exercise behavior (Nunez-Navarro et al., 2012; Stoving et al., 2011; Strother et al., 2012) and restriction among homosexual males (Fernandez-Aranda et al., 2004; Shiltz, n.d.). Men with ADHD and comorbid binge eating may constitute a different demographic category of males as compared to more studied groups in prior male ED research.

There are very few ED prevention options for males, with this gap particularly problematic for prevention of binge eating (Ciao et al., 2014). Targeting males at risk for comorbid ADHD/EDs for primary ED prevention may be an initial step to address this gap. However, in order to be able to target males at risk, information is needed to help identify those at risk. Determining any demographic, physical health, and behavioral health characteristics specific to this group of men could aid in the development of targeted prevention programming.

Some characteristics of interest may include intelligence, exercise behaviors, weight, delinquency behavior, and sexual behaviors. Both intelligence and personality might be important traits that could impact the ability to identify someone at risk for comorbid ADHD/ED. One study suggested that a female ED patient’s high intelligence and perfectionism might have contributed to the lack of diagnosis of her comorbid ADHD (Ioannidis, Serfontein, & Müller, 2014). Perceived intelligence may also impact academic success. This coupled with the impacts of ADHD on academic achievement may be the driving force for the low rates of academic success among adolescents with ADHD. Specifically, 25% of children with ADHD are held back a grade and 36% do not finish high school (Koch, 1999).

Based on the shared impulsive nature of ADHD and EDs, additional impulse related behaviors such as delinquent behavior and hypersexual behavior may be more common among males with both disorders. Increased sexual behavior has been noted among males with ADHD (Davis et al., 2015); and high rates of ADHD, up to 72% of males, have been noted within juvenile detention facilities (Koch, 1999). It has also been reported that 25% to 45% of
adolescents with untreated ADHD develop a conduct disorder or delinquent behaviors, 18% to 25% abuse illegal substances, and 25% are involved in a teen pregnancy (Koch, 1999).

Increased exercise behaviors as well as performance enhancing substance use are common ED behaviors in males (Blouin & Goldfield, 1995; Kanayama, Barry, Hudson, & Pope Jr, 2006; Pope, Kanayama, & Hudson, 2012; Pope, Katz, & Hudson, 1993). With links between ADHD and substance abuse (Disney, Elkins, McGue, & Iacono, 1999; Hesson & Fowler, 2015), as well as the noted potential for physical activity on ADHD treatment (Smith et al., 2013), these factors may be helpful in identifying males struggling with both disorders. Additionally, males with EDs are more likely to have a history of obesity (Fernández-Aranda et al., 2004; Núñez-Navarro et al., 2012), and as described above ADHD is also linked to obesity. EDs and ADHD medications are associated with heart health issues (McElroy et al., 2015; Striegel-Moore & Franko, 2003), subsequently obesity, obesity related, and heart related outcomes may be noteworthy and require close monitoring in males with comorbid ADHD/ED.
CHAPTER THREE: METHODS

Based on the current literature related to the ADHD/ED comorbidity, the goal of this study is to increase the understanding in regards to the underlying mechanisms of the ADHD/ED comorbidity. The study does so by addressing the following overall research question (RQ): what are the underlying mechanisms of the ADHD/ED comorbidity and how do these factors interact? In order to answer this question, the project consists of two aims with several accompanying sub-RQs.

Specific Aims

Aim One: Evaluate a Model of the Underlying Mechanisms of the ADHD/ED Comorbidity. Aim one focuses on simultaneously investigating the three hypotheses of the underlying mechanisms of the comorbidity among females. Guided by an innovative conceptual framework this aim addresses the following three sub-RQs: AIM1.RQ1) Which genetic risk factors are associated with the comorbidity? AIM1.RQ2) Which risk regulators (i.e., psychosocial and psychiatric factors) are associated with the comorbidity? AIM1.RQ3) How does the presence of the risk regulators impact the association (i.e., mediate) between the genetic factors and comorbid ADHD/EDs?

Aim Two: Explore the comorbidity and underlying mechanisms of ADHD/ED among males. Aim two focuses on the comorbidity among males, as evidence to date has overwhelmingly been focused on females, leaving a gap in our understanding of the comorbidity among males. This aim will explore the demographic, physical health, and behavioral health profile of males with the ADHD/ED comorbidity as well as the association of the proposed
Conceptual Framework

As previously stated, this dissertation project aims to simultaneously investigate the three proposed hypotheses and potential factors within each hypothesis. In order to do so, this study is guided by a conceptual framework that incorporates aspects of five models, including the Biopsychosocial Model (Engel, 1980), the Life Course Approach (Ben-Shlomo & Kuh, 2002), the Risk Regulator Framework (Glass & McAtee, 2006), the Research Domain Criteria Matrix (Morris & Cuthbert, 2012; National Institutes of Mental Health, n.d.), and the Person-Environment Transaction Theory (Caspi & Roberts, 2001). Components of each theory are incorporated into one collaborative framework to account for the combination of hypothesized underlying mechanisms that cannot be explained by one theory alone.

Biopsychosocial Model

The base of the conceptual framework is the Biopsychosocial Model. First described in 1980, the model proposed a new perspective that recognizes the connection between the body and mind as an alternative to the traditional biomedical model of clinical practice (Engel, 1980). The model incorporates a hierarchical system to explain health conditions. Levels of the system range from atoms and molecules through individual behavior and community and societal elements (Engel, 1980). One key aspect of the model is that nothing exists in isolation and that health is influenced by a complex interaction of biological, psychological and social factors (Engel, 1980). The Biopsychosocial Model serves as the base of the proposed conceptual
framework as it allows for the integration of all three proposed hypotheses of the underlying mechanisms of the ADHD/ED comorbidity (see figure 1). Specifically, the model accounts for the hypothesized genetic factors (H1), the psychosocial factors (H2), and the psychiatric factors (H3).

Figure 1: Hypothesized Underlying Mechanisms of Comorbid ADHD/ED in a Framework Combining the Biopsychosocial Model and Life Course Theory

Life Course Approach

While the Biopsychosocial Model allows for the simultaneous investigation of all three hypotheses, it fails to incorporate the temporal association between the factors. The genetic components of the underlying mechanism are developed prior to birth with the biological influence of these genetic polymorphisms manifesting over time. Moreover, while it is expected
that the psychosocial and psychological factors will be correlated, they are not expected to occur at the same point in time. Subsequently the Biopsychosocial Model is missing a needed life course or longitudinal component. The Life Course Approach, which is typically used in epidemiology, helps guide exploration of the long-term effects of physical and social exposures on chronic disease (Ben-Shlomo & Kuh, 2002). This approach includes the investigation of biological, behavioral, and psychosocial exposures or pathways over time in order to determine the impact of these pathways on associated health outcomes (Ben-Shlomo & Kuh, 2002; Elder, Johnson, & Crosnoe, 2003). It is hypothesized that the genetic factors are determined in gestation while psychosocial and psychiatric factors appear over time (Elder et al., 2003).

Risk Regulator Framework

While the integrated Biopsychosocial Model and Life Course Approach helps to explain the interaction of the three hypotheses, it does not account for hypothesized causal associations. H1 suggests that biological factors cause the appearance of the comorbidity, while H2 and H3 suggest that psychosocial and psychiatric factors do not necessarily cause the comorbidity but rather mediate the association between the two disorders (i.e., regulate risk but not causal mechanisms). The Risk Regulator Framework, developed by Glass and McAtee, helps incorporate the difference between risk factors and risk regulators, allowing for explorations of the hypothesized streams of causations (Glass & McAtee, 2006). The Risk Regulator Framework states that genetic and biological factors and biological systems are influenced by exposures overtime, which then influences the development of a behavior (Glass & McAtee, 2006).

Concomitantly, the built and social environments provide both opportunities for or restraints on the development and manifestation of a behavior (Glass & McAtee, 2006). A key component of the framework is the concept of a risk regulator, which was developed based on a perceived need for a new class of variables that influence behavior but do not fit the typical risk
factor definition in that a risk factor causes disease. Glass and McAtee provide poverty as an example of a risk regulator; while poverty is associated with many adverse health behaviors it does not directly cause any single disease (Glass & McAtee, 2006).

Figure 2: Integrated Conceptual Framework of the Three Hypotheses and Proposed Underlying Mechanisms of Comorbid ADHD/ED

The original definition of risk regulators was aimed at broad level factors such as the built environment, conditions of work, and laws and policies (Glass & McAtee, 2006); however, the proposed conceptual framework expands the concept of risk regulators to account for the
mediating effect of the psychosocial (H2) and psychiatric (H3) factors associated with ADHD/ED comorbidity. The proposed factors within H2 and H3 are not predicted to cause the comorbidity but rather are associated with the comorbidity and may influence the manifestation of the both disorders within the context of biological risk factors, suggesting that they regulate, or mediate, the risk of the genetic predictors. Figure 2 incorporates the Biopsychosocial Model and Life Course Approach with the Risk Regulator Framework. As can be seen in figure 2, the biological dimension of the Biopsychosocial Model is represented in the genetic substrate and both the psychological and social dimensions are represented in the risk regulators. The Life Course Approach is incorporated in that the “underwater” genetic substrate represents the gestational period and the risk regulators and development of the comorbidity occur over time after birth or “above water”.

Research Domain Criteria Matrix

Framing the conceptual framework through the Risk Regulator and Biopsychosocial Models also incorporates concepts from the Research Domain Criteria (RDoC) Matrix. The current mental health literature related to identification and diagnosis is split between the hard and social sciences; the goal of RDoC is to integrate these fields (Insel et al., 2010; Sanislow et al., 2010). The RDoC Matrix was conceptualized and developed by the National Institute of Mental Health as a new classification system to improve understanding of mental illness (Insel et al., 2010; National Institutes of Mental Health, n.d.). Previous criticism of the diagnostic criteria for many mental illnesses suggested that clinical diagnoses fail to align with emerging neuroscience and genetics research (Insel et al., 2010). RDoC proposed that theoretically, if we can identify specific genetic, neurobiological, and behavioral sequences that predict the development of a disorder or potential treatment impacts, then neurobiology based screening tests could be used to identify patients and improve outcomes (Insel et al., 2010; National
Institutes of Mental Health, n.d.) While this may be a distant future, the conceptual framework of this project can guide future research aiming towards this long-term goal.

RDoC comprises a matrix classifying brain disorders by domain or construct (e.g., cognitive systems, arousal) and unit of analysis (e.g., genes, cells, behavior) (Insel et al., 2010; Morris & Cuthbert, 2012). Reflecting the hierarchy of the Biopsychosocial Model, units of analysis range from genetics through the individual, family, and societal level, which each levels predicted to impact a mental illness (Insel et al., 2010). The proposed conceptual framework of the underlying mechanisms of the ADHD/ED comorbidity addresses the long-term goal of RDoC by incorporating genetic, psychosocial, cognitive, and psychiatric components within the model.

A second goal of RDoC is to identify fundamental behavioral components that may span multiple disorders and can be explored through neuroscience (Sanislow et al., 2010). The cognitive systems domain, specifically the cognitive control construct, cites both dopamine and serotonin at the genetic level and impulsive, unplanned, and reward-seeking behaviors at the behavior level (National Institutes of Mental Health, n.d.). Moreover, RDoC recognizes that many mental illnesses are neurodevelopmental disorders. Therefore addressing development issues across a variety of life span phases is a critical consideration for the RDoC matrix (National Institute of Mental Health, n.d.); providing further support for incorporating the Life Course Approach and RDoC constructs into the proposed conceptual framework. Another RDoC goal is to develop an improved understanding of cognitive control in relation to ADHD, juvenile bipolar disorder, and conduct disorders (National Institute of Mental Health, n.d.). Through the current investigation of cognitive control as a potential factor within the context of comorbid ADHD/ED, this study could provide some information towards addressing this goal.

**Person-Environment Transaction Theory**

Lastly, with the inclusion of personality traits in the psychosocial risk regulators, the conceptual framework also incorporates concepts from the person-environment transaction
theory. The theory was introduced within a description of the development of personality across the life course and specifically states that biological and social events often accentuate pre-existing personality differences between people (Caspi & Roberts, 1990, 2001). In other words, behavior is predicted by the interaction of personality traits and the environment. This theory is supported in the conceptual framework in that personality traits (i.e., risk regulators) interact with both the environment (i.e., social factors) and the environment of the individual (i.e., genetic factors), to impact behavior (i.e., ADHD/ED behaviors). This theory suggests that personality changes over time based on interactions with environmental factors; accordingly, the personality factors within the conceptual framework be assessed at multiple time points.

**Benefits of the Proposed Framework**

The conceptual framework combining the Biopsychosocial Model, the Life Course Approach, the Risk Regulator Framework, the RDoC Matrix, and the Person-Environment Transaction Theory allows for a complete understanding of the associations of the underlying mechanisms with the ADHD/ED comorbidity that could not be explained by one theory alone. The combination of construct from all of these theories helps provide the needed framework for an complex investigation of the ADHD/ED comorbidity. Based on extensive reviews, there are no other known theories that can incorporate all of the need constructs of this investigation.

The proposed model incorporates several aspects that can be compared to the widely used Socioecological Model (Glanz, Rimer, & Viswanath, 2008), which helps explore health behaviors and conditions through the interaction of factors at several levels ranging from micro to macro levels (Glanz et al., 2008). The SEM model is similar to the Biopsychosocial Model, however it excludes the needed life course approach to explore impacts of factors over time as well as factors developing in gestation. Moreover, while the visualization of the conceptual framework is heavily based on the Risk Regulator Framework, this framework alone cannot explain the full picture of underlying mechanisms, as it is not specific to mental or behavioral
health. The combination of these five theories provides an opportunity for a unique understanding that could not be explained otherwise.

**Application of the Conceptual Framework**

Figure 2 depicts the full conceptual framework along with pathways of interest. The theories described above are combined to provide a complete picture of the potential underlying mechanisms of the ADHD/ED comorbidity. The proposed model states that the observable factors serve as "risk regulators" that influence the risk of developing the health issue (i.e., comorbid ADHD/ED) over time by interacting with that person’s genetic and biological make-up. The framework also includes proposed pathways that independently illustrate the three proposed hypotheses, as well as how the risk regulators and genetic substrate are predicted to interact to influence the manifestation of the comorbidity.

The first three pathways were included based on the Risk Regulator Framework and Biopsychosocial Model. P1 denotes that risk factors within the genetic substrate are associated with the development of ADHD and EDs independently. P2 shows that the risk regulators may increase or decrease the risk of developing either ADHD or an ED. P2 is displayed as dotted lines as these risk regulators are not proposed to cause the development of either disorder but each in conjunction with other risk regulators, may impact the odds of developing the disorders. P3 was added to indicate the relationship between the genetic factors and risk regulators based on the Biopsychosocial Model, which suggests an interaction of the different domains.

The remaining pathways, P4-P6 investigates the three proposed hypotheses of the underling mechanism of the ADHD/ED comorbidity. More specifically, P4 investigates which genetic risk factors are associated with the comorbidity (H1). P5 investigates the relationship of the risk regulators with the comorbidity (H2 & H3). As with P2 this is displayed as a dotted line as the risk regulators are not predicted as direct risk factors to the comorbidity; instead they are proposed to mediate the connection between ADHD and EDs. Lastly, P6 investigates the
interaction of these three hypotheses by determining how the presence of the risk regulators impacts the association (i.e., mediate) between the genetic factors and comorbid ADHD/EDs. This last pathway allows for an investigation into how the three hypotheses interact.

This conceptual framework helps expand the current descriptive and theoretical ADHD/ED literature by developing a comprehensive model within which future research can be framed. No single underlying mechanism can alone predict the development of the ADHD/ED comorbidity; however, the entire model (i.e., a combination of multiple interacting factors), can be used to develop screening tools to identify individuals with the specific sequence of underlying mechanisms that might increase their odds for developing the comorbidity. This conceptual framework explore mental illness from a holistic approach, which may particularly benefit children and adolescents with comorbid ADHD and EDs as these disorders have many broad ranging implications for several life domains.

**Study Design**

This study's conceptual framework incorporates a large number of variables, which in combination with its complexity, requires a very large sample size. Based on available resources, collecting and processing genetics data, as well as variables across the life span would not be feasible. Based on these factors, this study utilized secondary data in order to obtain the large sample and wide range of variables needed to address the RQs. This method allows for simultaneous investigation of all proposed hypotheses related to the model as well as the use of variables measured across time. While there are many large secondary sources that collect information on ADHD and EDs, the National Longitudinal Study of Adolescent to Adult Health (Add Health) is the only secondary source that collected the psychosocial, psychiatric, and genetics variables needed to answer the proposed RQs. Moreover, its longitudinal design fits well with the conceptual framework.
Data Source

The Add Health study tracked a nationally representative sample of adolescents over many years. It began with wave I (1994) by interviewing a cohort of 20,745 students in seventh through twelfth grade. Students were interviewed at home with parental consent. There have been three subsequent follow-up home-based interviews; wave II (1995-1996), wave III (2001-2002), and wave IV (2007-2008) (Harris, 2011; Harris, Halpern, Whitsel, Hussey, & Tabor, 2009). The theoretical framework used for collection of the study’s data mirrors the proposed conceptual framework of the current study. Specifically, Add Health used an integrative life course theoretical framework to investigate the associations between context, behavior, and biology to determine how factors influence health and well being from childhood to adulthood (Carolina Population Center, 2014).

Although the data fit the needs of this study very well, there are several limitations to consider. First the data was not collected for the purposes of testing the specific RQs. Secondly, all variables, except for genetic genotypes, were self-reported and retrospective. In early waves these self-reports were provided by adolescents, which may bring additional bias. However, previous scale development of Add Health data, including scales of emotional distress, deviant behaviors, self-esteem, parent-family connectedness, and substance use have reported acceptable internal consistency, reliability, and moderate correlations between conceptually related constructs (Sieving et al., 2001). Lastly, the timing of each variable’s collection is a limitation as some are collected out of the hypothesized order. For example genetics data was collected at wave IV, after most of the risk regulating factors were collected, while the conceptual framework for the current project proposed that biological factors influence the development of the risk regulating factors. However, this is the only dataset that allows for an investigation of the large, complex framework of the underlying mechanism. Moreover, this will be the first investigation into the associations proposed in the framework, thus despite limitations, this descriptive study design will help provide initial information about the underlying
mechanisms of the comorbidity. Results of which can be used to reduce the complexity of the model and allow for more feasible primary data collection to further test the model with prospective data.

Participants

Add Health recruited 20,745 participants at wave I; specifically, 10,265 males and 10,480 females were initially interviewed. The current study used data from waves I, III, and IV. A total of 13,034 participants, 5,951 males and 7,083 females, completed interviews at each of these waves. Due to a complex sampling design, survey weights were applied to all analyses; thus 746 participants (345 male, 401 female) missing information for the longitudinal wave I, III, and IV grand sample weight were excluded from analysis.

Due to the importance of genetics to the research question, an additional 670 participants (320 males, 350 females) missing genetics data were excluded from analysis. Saliva samples were collected among a subset of participants at wave III and among the full sample at wave IV. Missing genetics data resulted from either refusal to consent to collection, issues related to saliva collection, or issues related to genotype extraction; however, significant efforts were made to minimize the amount of missing data.

Of the 15,140 participants interviewed at wave IV, 96% consented to providing a sample for genotyping. Samples were collected by trained and certified interviewers who were supplied with Blaise computer-assisted interview programs that provided step by step instructions and help screens as well as a hard-copy reference guides to help with the collection process (Smolen et al., 2013). With regards to analysis of the saliva samples, each sample was processed twice, on different days, and by different investigators. A third investigator then reviewed the results and in the case of any missing data or discrepant results, analysis was run a third time. Additionally, if genetic results were available from wave III but not wave IV, Add
Health combined the genotype data for the given participant from wave III into the wave IV dataset (Smolen et al., 2013).

Lastly, due to the central importance of ADHD and EDs, an additional 81 participants (38 males, 43 females) missing those variables were excluded. This resulted in a final sample size of 11,537 participants, with 6,289 females for aim one and 5,248 males for aim two. There were no statistically significant differences between those included and those excluded due to missing genetics, ADHD, or ED variables on all other hypothesized underlying mechanisms, or race, education, parent education, or family income.

**Measures**

The main constructs of this study are ADHD, EDs, and the comorbidity of the two disorders. In the development of the conceptual framework predicted underlying mechanisms were categorized into several groups including a genetic substrate, social factors, cognitive factors, personality factors, and psychiatric factors. All proposed scales were subjected to sample weighted confirmatory factor and reliability analyses. Based on the gender stratification of the two aims, each scale was evaluated separately by gender.

Confirmatory factor analyses (CFA) were performed in MPlus 7 using either weighted least squares means and variance adjusted (WLSMV) or maximum likelihood estimators with robust standard errors (MLR) estimators. WLSMV was used for the CFA models of ADHD and EDs to account for the binary nature of the items (Proitsi et al., 2011). MLR was used for all other CFA models with continuous factors to account for sample weighting. Several fit indices were used to evaluate model fit, including chi-square test of model fit, comparative fit index (CFI), root mean square error of approximation (RMSEA), weighted root mean square residual (WRMR), and standardized root mean square residual (SRMR).

The chi-square test of model fit compares the sample and fitted covariance matrices with a p-value greater than .05 indicating good model fit (Hu & Bentler, 1999; Schreiber, Nora,
Stage, Barlow, & King, 2006; Yu, 2002). However, sample size is used in the calculation of the chi-square value, and thus it is sensitive to sample sizes (Hu & Bentler, 1999). Due to the large sample size (females=6,289, males=5,248), although chi-square test values are reported, these results did not impact conclusions related to model fit. Indicators of good model fit were based on the following suggestions: CFI (> .95), RMSEA (< .06), SRMR (< .08), and WRMR (< 1.0) (Hu & Bentler, 1999; Schreiber et al., 2006; Yu, 2002). These cut-off criteria have been found acceptable with sample sizes over 250, and for both categorical and continuous outcomes, with the exception of SRMR with categorical data (Schreiber et al., 2006; Yu, 2002). Analyses of residuals was also performed to evaluate fit with a standardized residual over two indicating a lack of fit in the corresponding element of the model.

**ADHD and ED Indicators**

Separate indicator variables were constructed for ADHD and EDs. These indicators were then used to construct a comorbid ADHD/ ED indicator as well as a categorical variable of disorder status.

**ADHD Indicator.** Figure 3 depicts the construction of the ADHD indicator variable. Participants were considered to have reported ADHD if they reported clinical ADHD, sub-clinical ADHD, or both. Clinical ADHD (i.e., diagnosed) was assessed at wave IV. Participants were considered to have clinical ADHD if they responded yes to the yes/no question: “[have you] ever been told by a doctor, nurse, or other health care provider that [you] had attention problems or ADD or ADHD”. Sub-clinical ADHD (i.e., some symptoms or behaviors but not all criteria for a clinical diagnosis) was assessed at wave III, where participants were asked to retrospectively evaluate their behaviors between age five and twelve pertaining to seventeen DSM ADHD symptoms (see figure 3) (APA, 2000, 2013). Response choices were on a four-point Likert scale ranging from “never or rarely” to “very often”. Participants were considered to have sub-clinical
ADHD if they reported the presence of at least six ADHD symptoms “often” or “very often”; thus meeting the symptomology requirement for a diagnosis but not all criteria (e.g., duration, level of impairment) (APA, 2000, 2013). Questions assessing sub-clinical ADHD symptoms were developed with the ability of stratifying by ADHD DSM IV sub-type. However, based on recent changes to the DSM V in which sub-groups were replaced by predominant presentations due to the instability of the sub-types (APA, 2000, 2013), participants were considered to have reported six or more symptoms regardless of sub-type.
Previous analyses with this specific ADHD scale found adequate internal consistency with Cronbach’s alpha estimates ranging from 0.86 to 0.91, and a split half reliability of 0.86 (Beaver, Nedelec, Rowland, & Schwartz, 2012; Kollins, McClernon, & Fuemmeler, 2005). Moreover, childhood learning and behavioral problems are highly comorbid with ADHD (Boutros, 2013; Mayes, Calhoun, & Crowell, 2000), and previous investigations found that respondents that reported six or more ADHD symptoms in childhood were more likely to also report a learning or behavior problem at wave I and ADHD medication use at wave III (Kollins et al., 2005).

CFA results demonstrated adequate fit with both the female (see appendix A, figure A1) and male (see appendix A, figure A2) samples. Among females, CFA of the seventeen symptoms items resulted in the following fit indices: $X^2$(df=119)=893.66, $p<.001$; RMSEA=.03; CFI=.96; and WRMR=2.03. Although the WRMR was above the cut-off of 1.00, examination of residuals confirmed fit. The scale also demonstrated adequate reliability with a Cronbach’s alpha of .85. Results were almost identical among the males with a Cronbach’s alpha of .86 and the following fit indices: $X^2$(df=119)=732.62, $p<.001$; RMSEA=.03; CFI=.97; WRMR=2.00, and as with females, an examination of residuals confirmed fit.

**Eating Disorder Indicator.** Figure 4 depicts the construction of the ED indicator variable. As with ADHD, participants were considered to have reported an ED if they reported either a clinical ED, sub-clinical disordered eating behaviors, or both. Both clinical and sub-clinical indicators were measured at wave III. The participant was considered to have a clinical ED if they responded yes to the yes/no question asking “[have you] ever been told by a doctor that [you] had an ED, such as Anorexia Nervosa or Bulimia”. 
Guided by previous methodology, participants were considered to have a sub-clinical ED if they responded yes to using any disordered eating behaviors within the past week, thus meeting symptomology but not all criteria needed for a diagnosis (e.g., duration or frequency) (Conley & Boardman, 2007; Fuemmeler, Dedert, McClernon, & Beckham, 2009). Disordered eating behaviors were grouped into disordered weight loss and maintenance behaviors and binge eating behaviors. For the disordered weight loss and maintenance behaviors, participants were first asked if they were currently trying to lose weight or stay the same weight. If so, they were then read a list of weight loss methods and asked which were used in the past seven days in order to lose or maintain weight. Disordered weight loss and maintenance methods included self-induced vomiting, laxative use, diuretic use, weight loss pill use, or food supplements used
to replace a meal or to reduce appetite. Binge eating behavior in the past seven days was assessed via the following indicators: “have you eating so much in a short period that you would have been embarrassed if others has seen you do it” or “have you been afraid to start eating because you thought you wouldn’t be able to stop or control your eating”. These disordered eating behavior indicators were assessed on a yes/no scale and have been used in past studies with other samples (Neumark-Sztainer et al., 2006).

Analysis of the two sub-clinical factors results demonstrated a very well fit and reliable scale for both females (see appendix B, figure B1) and males (see appendix B, figure B1). Results were similar between the genders with the following fit indices for females: $X^2(df=13)=16.52, p=.22; \text{RMSEA}=.01; \text{CFI}=.99; \text{WRMR}=.68$; and the following indices for males: $X^2(df=13)=21.08, p=.07; \text{RMSEA}=.01; \text{CFI}=.95; \text{WRMR}=.78$. Cronbach’s alpha values were .88 and .89 for females and males respectively.

**Comorbid ADHD/ED.** Participants were considered to have comorbid ADHD/ED if they reported both ADHD and ED based on the indicators described above. For comparisons, a disorder status variable was created in which participants were categorized as having neither disorder, ADHD alone (i.e., no ED), ED alone (i.e., no ADHD), or comorbid ADHD/ED.

**Genetic Substrate**

The genetic substrate is comprised of candidate genes proposed to be link to the ADHD/ED comorbidity via the Reward Deficiency Syndrome (RDS). Available genetic candidates included in this study are dopamine receptor DRD4, dopamine transporter DAT1, serotonin transporter HTTLPR, and monoamine oxidase A. Saliva samples collected at wave IV were packaged and shipped to a central lab for DNA extraction, genotyping, and archiving. Genotype data was reported as the number of repeat sequences of a given polymorphism on
each allele. Genetic variables were constructed as bivariate indicators of if the specific repeat sequence, described below, was found on either allele A, or allele B, or both.

_Dopaminergic Genes._ The dopamine D4 receptor gene contains a 48 bp VNTR polymorphism in the third exon, which is composed of ten alleles with two to eleven repeats. An indicator was constructed for the seven repeat pattern in that participants were considered to have any seven repeats if they had seven repeats on either allele or both alleles. The dopamine transporter DAT1 contains a 40 bp VNTR in the 3' untranslated region of the gene. Two indicator variables were constructed to identify any nine repeats and any ten repeats.

_Serotonin Gene._ The serotonin transporter 5-HTTLPR, contains a 44-bp insertion / deletion polymorphism in the promoter region of the serotonin transporter (SLC6A4) gene (Smolen et al., 2013). The 5-HTTLPR alleles are considered either short or long with the most common variant of the short allele consisting of fourteen repeat sequences and the most common long allele consisting of sixteen repeats (Smolen et al., 2013). A bivariate indicator was constructed to identify any short (fourteen) repeat polymorphisms.

_Monoamine Oxidase A Gene._ The monoamine oxidase A upstream VNTR gene is located on the X chromosome and contains a 30 bp VNTR in 5' regulatory region of the gene (Smolen et al., 2013). Allele repeats range from two to five and are typically dichotomized where two or three repeats are considered “low expressing” or “not active” and 3.5, four or five repeats are considered “high expressing” or “active” (Smolen et al., 2013). An indicator variable was created to indicate any active repeats. Based on the X chromosome location of the MAOA gene, this indicator represents any active MAOA repeats on either allele A or allele B or both for females, while for men this indicator represents active MAOA on allele A only.
Reliability of Genetic Sampling. Although genetic sample processing was done under reliable conditions, an assessment of quality has been previously conducted (Smolen et al., 2013). During collection a random sample of 58 participants provided two samples one to two weeks apart. The samples were used to establish test-retest reliability. Kappa values suggested good to excellent reliability with percent agreement ranging from 84% to 97% per candidate gene. All genetic candidates included in the proposed analysis had agreement of 88% or higher (Smolen et al., 2013).

Social Factors

Proposed social factors include social and family support. Prior Add Health studies have combined parent, adult, teacher, and peer support into one social support scales (Beaver, Boutwell, & Barnes, 2014; Kort-Butler, 2010; Rawana, 2013; Wight, Botticello, & Aneshensel, 2006). However, these two constructs were hypothesized separately, thus separate family support and social support scales were constructed.

A recent study used a subset of Add Health to the development of the Battery of Adolescent Measures. The study used several measurement techniques and 88 items to create 19 assessment scales. The scales cover topics related to families and parents, peers and sexuality, schools, and neighborhoods (Benson & Faas, 2014). Both the social and family support scales were based off of subscales of the Battery of Adolescent Measures.

Family Support. The Parent-Family Connectedness factor within the Battery of Adolescent Measures is comprised of three subscales; family understanding, maternal warmth, and paternal warmth. Items from these three subscales were used to create a two-factor family support scale (see table 3). The original family understanding subscale of the Battery of Adolescent Measures consisted of three items; however, only one item measures how much the individual feels that their family understands them while the other two items measure how much
the individual feels that they and their family have fun together and how much they feel their family pays attention to them. For the purpose of this study, the subscale was renamed from family understanding to family connectedness to better reflect the content of the three items. Each item was measured on a five-point Likert scale ranging from “not at all” to “very much”. The original study reported a Cronbach’s alpha of .80 and factor loadings of all .81 and higher for each gender separately as well as the combined sample (Benson & Faas, 2014).

Originally two sub-scales, items from the maternal warmth and paternal warmth scales were combined to create one parent warmth scale in order to account for single parent households. Both maternal and paternal warmth were assessed using five items that were asked separately for each parent (see table 3). The items were all measured on a five-point Likert scale with the first three items ranging from “strongly disagree” to “strongly agree” and the last two items ranging from “not at all” to “very much”. The highest score between mothers and fathers on each item was used to create one parent warmth scale.

**Social Support.** While the Battery of Adolescent Measures contains several peer related sub-scales, the majority where focused on sexual health and did not fit the proposed construct of social support. However, the participants were school aged at wave I, and thus school setting would be expected to be a large factor in their perceived social support. To incorporate the school setting, a social support scale was build using the Battery’s school connectedness scale with the addition of two items to assess friendship connections and perceived social acceptance (see table 3). The original school connectedness sub-scale consisted of five factors; however, “the teachers at your school treat students fairly” was removed both to conceptually focus on peers and social relationships, but also due to low factor loadings in the original scale assessment. Two items, “how much do you feel that your friends care about you” and “you feel socially accepted” was added as a second proposed factor titled friend connectedness. These were added to assess friends and social connections beyond the school atmosphere. These six
items were all measured on five-point Likert scales with most ranging from “strongly disagree” to “strongly agree”, with the exception of “how much do you feel that your friends care about you,” which ranged from “not at all” to “very much”.

Table 3. Support Scale Items

<table>
<thead>
<tr>
<th>Scale</th>
<th>Wave I Items</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Family Support</strong></td>
<td></td>
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<tr>
<td>Parent Warmth</td>
<td>1. Most of the time, your {mother or father} is warm and loving toward you.</td>
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<td></td>
<td>2. You are satisfied with the way your {mother or father} and you communicate with each other.</td>
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<td></td>
<td>3. Overall you are satisfied with your relationship with your {mother or father}.</td>
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<td></td>
<td>4. How close do you feel to your {mother or father}?</td>
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<td></td>
<td>5. How much do you think your {mother or father} cares about you?</td>
</tr>
<tr>
<td>Family Connectedness</td>
<td>6. How much do you feel that people in your family understand you?</td>
</tr>
<tr>
<td></td>
<td>7. How much do you feel that you and your family have fun together?</td>
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<tr>
<td></td>
<td>8. How much do you feel that your family pays attention to you?</td>
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<tr>
<td><strong>Social Support</strong></td>
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<tr>
<td>School Connectedness</td>
<td>1. You feel close to people at your school.</td>
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<td></td>
<td>2. You feel like you are a part of your school.</td>
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<td></td>
<td>3. You are happy to be at your school.</td>
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<tr>
<td></td>
<td>4. You feel safe in your school.</td>
</tr>
<tr>
<td>Friend Connectedness</td>
<td>5. How much do you feel that your friends care about you?</td>
</tr>
<tr>
<td></td>
<td>6. You feel socially accepted.</td>
</tr>
</tbody>
</table>

Both family and social support scales were found to have good fit and reliability with gender samples. CFA results of the family support scale are displayed in appendix C (figure C1 and figure C2) and the social support scale are displayed in appendix D (figure D1 and figure D2). Among females, evaluation of the family support scale resulted in a Cronbach’s alpha of .92 and the follow CFA fit indices: $X^2(df=19)=435.04$, $p<.001$; RMSEA=.06; CFI=.95; and SRMR=.04. Results were similar among the males with a Cronbach’s alpha of .90 and the
following fit indices: \( X^2(\text{df}=19)=583.46 \), \( p<.001 \); RMSEA=.08; CFI=.90; SRMR=.06. Results for the social support scale were almost identical between the genders with the following fit indices for females: \( X^2(\text{df}=8)=81.54 \), \( p<.001 \); RMSEA=.04; CFI=.98; SRMR=.02; and the following fit indices for males: \( X^2(\text{df}=8)=47.80 \), \( p<.001 \); RMSEA=.03; CFI=.99; SRMR=.02. Cronbach’s alpha values were .90 and .84 for females and males respectively.

**Personality Factors**

Based on the person-environment transaction theory, personality is predicted to change over time, thus personality was assessed at both wave I and wave IV. However, due to the available items these measure slightly vary and thus were treated as separate constructs.

At wave I, personality scales based on the Five Factor Model or the “Big Five” were previously been constructed and evaluated (Young & Beaujean, 2011). These scales were creating used a lexical method to identify twenty-one personality items. Factor analysis techniques were then used with the entire sample split in half; half was used for EFA purposes and the other half was used in CFA with maximum likelihood estimates (Young & Beaujean, 2011). After several rounds of item reduction a final thirteen-item, a three-factor solution was derived and found to have good fit via CFA fit indices (CFI=.97, RMSEA=.08, SRMR=.02) (Young & Beaujean, 2011). The three factors represented traits of conscientiousness, neuroticism, and extroversion. Personality traits previously linked to the ADHD/ED comorbidity included novelty seeking, self-directedness, obsessive compulsiveness, and perfectionism (Fernández-Aranda et al., 2013). Based on the conceptual similarities of these hypothesized traits with available scales, the conscientiousness and neuroticism scales were included as potential underlining mechanisms (see table 4). All wave I items were measured on a five-point Likert scale ranging from “strongly agree” to “strongly disagree”. For clarity, neuroticism and conscientiousness scales at wave I are referred to as adolescent neuroticism and adolescent conscientiousness.
Wave IV included items of a similar nature to measure the same personality constructs, however item wording varied. These scales are also based on the Five Factor or Big Five personality model (Harris, 2011; Harris et al., 2009). As with wave I, all items were scored on a five-point Likert scale ranging from “strongly agree” to “strongly disagree”. Previous predictive validity was found in that all the wave IV items had high pattern coefficients on their intended factors via CFA methods (Young & Beaujean, 2011). Specific items of the conscientiousness and neuroticism scales are listed in table 4. For clarity purposes, the wave IV neuroticism and conscientiousness scales are referred to as adult neuroticism and adult conscientiousness.

<table>
<thead>
<tr>
<th>Table 4. Personality Scale Items</th>
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<tbody>
<tr>
<td>Scale</td>
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<tr>
<td>Neuroticism</td>
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<tr>
<td>Conscientiousness</td>
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One CFA model was constructed for all personality scales. Results are displayed in see appendix E (figure E1 and figure E2). Good fit was demonstrated for both the female and male samples. Among females, CFA resulted in the following fit indices: $X^2(\text{df}=113)=733.66$, $p<.001$; RMSEA=.03; CFI=.95; and SRMR=.03. Results were similar among the males with the following fit indices: $X^2(\text{df}=113)=488.20$, $p<.001$; RMSEA=.03; CFI=.96; SRMR=.03. As expected, conscientiousness at wave I was positively correlated with conscientiousness at wave IV, neuroticism at wave I was positively correlated with neuroticism at wave IV, and each assessment of conscientiousness was negatively correlated with each assessment of neuroticism. After CFA, negatively worded items were reversed for scale sum scoring.

Cognitive Factors

Predicted cognitive underlying factors based on the Research Domain Criteria Matrix include both cognitive control and working memory.

Cognitive Control. Cognitive control is conceptualized as impulsivity, disinhibition, and externalization and is associated with various areas of the prefrontal cortex (National Institutes of Mental Health, n.d.). In order to measure this construct, an assessment of impulsivity was selected as a proxy to measure cognitive and motor control. Wave III items were selected to align with items of the Barratt Impulsiveness Scale (BIS), one of the most widely used assessments of impulsivity (Fossati, Di Ceglie, Acquarini, & Barratt, 2001; Stanford et al., 2009). The BIS has a three second-order factor structure consisting of cognitive impulsiveness (i.e., making quick decisions), motor impulsiveness (i.e., acting without thinking), and non-planning impulsiveness (i.e., a lack of future thinking) (Barratt, 1985; Stanford et al., 2009). Six first order factors are as follows: cognitive impulsiveness (attention and cognitive instability), motor impulsiveness (motor and perseverance), non-planning impulsiveness (self-control, cognitive complexity) (Stanford et al., 2009). Higher scores on the BIS have been correlated with
substance use disorders, mood disorders, bipolar disorder, suicidal ideation, and serotonin and MAO genetic polymorphisms (Stanford et al., 2009). However, BIS scores were not associated with attention in laboratory experiments (Stanford et al., 2009), suggesting a distinction between BIS measured impulsivity and attention as conceptualized as ADHD. Through extensive examinations the thirty-item BIS scale has been found to be both reliable and valid (Barratt, 1965; Fossati et al., 2001; Patton & Stanford, 1995; Reid, Cyders, Moghaddam, & Fong, 2014; Reise, Moore, Sabb, Brown, & London, 2013; Stanford et al., 2009). Based on the content of the original items and available Add Health items, the non-planning impulsiveness factor was not included in the constructed cognitive control measure. The original items for the cognitive impulsiveness and motor impulsiveness factors are listed in table 5.

Six items were selected from wave III to reflect the cognitive impulsiveness and motor impulsiveness higher order factors (see table 5). All items were measured on five-point Likert scales either ranging from “not true” to “very true” or “strongly agree” to “strongly disagree” with the exception of the following item, “you had trouble keeping your mind on what you were doing during the past seven days” which was assessed on a four-point scale ranging from “never/rarely” to “most of the time/all of the time”. The constructed scale was based on the two higher order factors, as opposed to the four first order factors, based on the limitations of available questions.

As with all other scale assessments, CFA results demonstrated good fit for both samples (see appendix F, figure F1 and figure F2.). Among females, CFA of the two-factor scale resulted in the following fit indices: $X^2(df=8)=72.01$, $p<.001$; RMSEA=.04; CFI=.97; and SRMR=.02. Almost identical results were obtained with the male sample: $X^2(df=8)=41.18$, $p<.001$; RMSEA=.03; CFI=.98; SRMR=.02. Cronbach’s alpha estimates of the six items were .68 and .78 for females and males respectively.
Table 5. Original BIS-11 Items and Cognitive Control Scale Items

<table>
<thead>
<tr>
<th>Scale</th>
<th>Original BIS-11 Items</th>
<th>Wave III Items</th>
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<tbody>
<tr>
<td><strong>Cognitive Impulsiveness</strong></td>
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<tr>
<td>Attention</td>
<td>1. I don’t “pay attention”</td>
<td>1. I change my interest a lot, because my attention often shifts to something else</td>
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<td></td>
<td>2. I concentrate easily</td>
<td>2. You had trouble keeping your mind on what you were doing, during the past seven days</td>
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<td>3. I “squirm” at plays or lectures</td>
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<td>4. I am a steady thinker</td>
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<td></td>
<td>5. I am restless at the theater or lectures</td>
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<tr>
<td>Cognitive Instability</td>
<td>6. I have “racing” thoughts</td>
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<tr>
<td></td>
<td>7. I change hobbies</td>
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<td></td>
<td>8. I often have extraneous thoughts when thinking</td>
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<tr>
<td><strong>Motor Impulsiveness</strong></td>
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<td></td>
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<tr>
<td>Motor</td>
<td>1. I do things without thinking</td>
<td>1. I sometimes get so excited that I lose control of myself</td>
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<td></td>
<td>2. I make-up my mind quickly</td>
<td>2. I often do things based on how I feel at the moment</td>
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<td></td>
<td>3. I am happy-go-lucky</td>
<td>3. Do you agree or disagree that when making a decision, you go with your “gut feeling” and don’t think much about the consequences of each alternative?</td>
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<td></td>
<td>4. I act “on impulse”</td>
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<td></td>
<td>5. I act on the spur of the moment</td>
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<td></td>
<td>6. I buy things on impulse</td>
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<td></td>
<td>7. I spend or charge more than I earn</td>
<td></td>
</tr>
<tr>
<td>Perseverance</td>
<td>8. I change jobs</td>
<td>4. Do you agree or disagree that in social situations, you tend not to follow the crowd, but instead behave in a way that suits your mood at the time?</td>
</tr>
<tr>
<td></td>
<td>9. I change residences</td>
<td></td>
</tr>
<tr>
<td></td>
<td>10. I can only think about one thing at a time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>11. I am future oriented</td>
<td></td>
</tr>
</tbody>
</table>

**Working Memory.** Working memory, a type of short-term memory, is responsible for temporarily storing and manipulating, or processing new information (Baddeley, 1992). This was measured via a memory assessment test at wave IV. Participants were asked to repeat a string of numbers backwards. The strings began with two numbers and grew in length, up to eight numbers. The interviewer reported a binary variable indicating whether the string was correctly
repeated backwards. The constructed memory variable indicates the total number of correct sequences repeated backwards.

Psychiatric Factors

Psychiatric factors were measured via items from wave IV. The wave IV psychiatric items assess lifetime diagnoses. Although there is bias in that a participant may have had an undiagnosed psychiatric illness, using lifetime diagnoses at the most recent wave helps minimizing bias related to diagnoses made later in time (i.e., in between wave III and wave IV).

Depression and Anxiety Disorders. Lifetime clinical depression was measured via a yes/no indicator variable based on the following question, “Has a doctor, nurse or other health care provider ever told you that you have or had depression?” Similarly clinical anxiety or panic disorder was measured via a yes/no indicator variable based on, “Has a doctor, nurse or other health care provider ever told you that you have or had an anxiety or panic disorder?”

Childhood Abuse. Experiences of childhood sexual and physical abuse were assessed at wave III. Childhood sexual abuse was assessed via the following question: “By the time you started 6th grade, how often had your parents or other adult caregivers touched you in a sexual way, forced you to touch him or her in a sexual way, or forced you to have sexual relations?” Physical abuse was assessed with the following questions: “By the time you started 6th grade, how often had your parents or other adult caregivers slapped, hit, or kicked you?” Participants were considered as having experienced childhood abuse if either of these events were reported as happening even once. These same questions were also asked at wave IV with the timeframe of before age eighteen as opposed to before sixth grade; however, only the wave III assessment was included in this study in order to better represent these experiences in childhood as opposed to adolescents when ADHD or an ED may have already developed.
There is an assessment of lifetime diagnosed PTSD at wave IV, however that indicator was excluded, as it does not differentiate sexual and physical abuse experiences from PTSD as a result of other, non-abuse situations.

_Alcohol and Substance Abuse Disorders_. Wave IV contains several pre-constructed variables, two of which include lifetime alcohol abuse/dependency based on DSM IV criteria and lifetime other drug abuse/dependency based on DSM IV criteria (APA, 2000). The alcohol abuse/dependency and drug abuse dependency variables identify individuals with no history of abuse/dependency, a history of abuse, a history of dependency with no physiological symptoms, a history of dependency with physiological symptoms, and a history of dependency with clustering of three dependency symptoms in a twelve-month period. Specific items that were used in the construction of these variables are listed in table 6. Each variable was dichotomized to indicate a history of any alcohol abuse/dependency and any drug abuse/dependency. As the measures assess both abuse and dependency, they are referred to as indicators of alcohol and substance use disorders. The substance use disorder classification does not include abuse or dependency related to marijuana.

Good internal consistency (Cronbach’s alpha=.88) and significant correlations were found among the items used in the construction of these pre-calculated variables (p<.001). In order to evaluate the validity of these variables, comparisons were made between the dichotomized alcohol and drug indicators with following wave III variables: 1) “In the past 12 months have you attended a drug-abuse or alcohol-abuse treatment program?”; 2) “In the past 12 months have you received psychological or emotional counseling?” Both alcohol use disorders and substance use disorders were significantly correlated with both wave III items (p<.001).
<table>
<thead>
<tr>
<th>Wave IV Items</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alcohol Use Disorder</strong></td>
</tr>
<tr>
<td><strong>Abuse</strong></td>
</tr>
<tr>
<td>• How often has your drinking interfered with your responsibilities at work or school?</td>
</tr>
<tr>
<td>• How often have you been under the influence of alcohol when you could have gotten yourself or others hurt, or put yourself or others at risk, including unprotected sex?</td>
</tr>
<tr>
<td>• How often have you had legal problems because of your drinking, like being arrested for disturbing the peace or driving under the influence of alcohol, or anything else?</td>
</tr>
<tr>
<td>• How often have you had problems with your family, friends, or people at work or school because of your drinking?</td>
</tr>
<tr>
<td>• Did you continue to drink after you realized drinking was causing you problems with family, friends, or people at work or school?</td>
</tr>
<tr>
<td><strong>Dependency</strong></td>
</tr>
<tr>
<td>• Have you ever found that you had to drink more than you used to in order to get the effect you wanted?</td>
</tr>
<tr>
<td>• Has there ever been a period when you spent a lot of time drinking, planning how you would get alcohol, or recovering from a hangover?</td>
</tr>
<tr>
<td>• Have you often had to drink or kept drinking for a longer period of time than you intended?</td>
</tr>
<tr>
<td>• Has there ever been a period of time when you wanted to quit or cut down on your drinking?</td>
</tr>
<tr>
<td>• When you decided to cut down or quit drinking, were you able to do so for at least one month?</td>
</tr>
<tr>
<td>• During the first few hours of not drinking, do you experience withdrawal symptoms such as the shakes, feeling anxious, trouble getting to sleep or staying asleep, nausea, vomiting, or rapid heartbeats?</td>
</tr>
<tr>
<td>• Have you ever continued to drink after you realized drinking was causing you any emotional problems (such as feeling irritable, depressed, or uninterested in things or having strange ideas) or causing you any health problems (such as ulcers, numbness in your hands/feet or memory problems)?</td>
</tr>
<tr>
<td>• Have you ever given up or cut down on important activities that would interfere with drinking like getting together with friends or relatives, going to work or school, participating in sports, or anything else?</td>
</tr>
<tr>
<td><strong>Substance Use Disorder</strong></td>
</tr>
<tr>
<td><strong>Abuse</strong></td>
</tr>
<tr>
<td>• How often has your {favorite drug*} use interfered with your responsibilities at work or school?</td>
</tr>
<tr>
<td>• How often have you been under the influence of your {favorite drug*} when you could have gotten yourself or others hurt, or put yourself or others at risk, including unprotected sex?</td>
</tr>
<tr>
<td>• How often have you had legal problems because of your {favorite drug*} use, like being arrested for disturbing the peace or anything else?</td>
</tr>
<tr>
<td>• How often have you had problems with your family, friends, or people at work or school because of your {favorite drug*} use?</td>
</tr>
<tr>
<td>• Did you continue to use your {favorite drug*} after you realized using it was causing you problems with family, friends, or people at work or school?</td>
</tr>
<tr>
<td><strong>Dependency</strong></td>
</tr>
<tr>
<td>• Have you ever found that you had to use more {favorite drug*} use than you used to in order to get the effect you wanted?</td>
</tr>
<tr>
<td>• Has there ever been a period when you spent a lot of time using {favorite drug*}, getting it, or getting over its effects?</td>
</tr>
<tr>
<td>• Have you often had to use more {favorite drug*} or used {favorite drug*} longer than you intended?</td>
</tr>
<tr>
<td>• Has there ever been a period of time when you wanted to quit or cut down on your use of {favorite drug*}?</td>
</tr>
<tr>
<td>• When you decided to cut down or quit using {favorite drug*}, were you able to do so for at least one month?</td>
</tr>
<tr>
<td>• During the first few hours of not using {favorite drug*}, do you experience one or more withdrawal symptoms such as craving {favorite drug*}, feeling depressed, anxious, restless or irritable, having trouble concentrating, feeling tired or weak, having trouble sleeping, or a change in appetite?</td>
</tr>
<tr>
<td>• Have you ever continued to use {favorite drug*} after you realized using {favorite drug*} was causing you any emotional problems (such as feeling depressed or empty, feeling irritable or aggressive, feeling paranoid or confused, feeling anxious or tense, being jumpy or easily startled) or causing you any health problems (such as heart pounding, headaches or dizziness, or sexual difficulties)?</td>
</tr>
<tr>
<td>• Have you ever given up or cut down on important activities that would interfere with your {favorite drug*} use like getting together with friends or relatives, going to work or school, participating in sports, or anything else?</td>
</tr>
</tbody>
</table>
Demographic Variables

Demographic variables included race, grade at wave I, parent education level, annual family income, age at wave III, education attainment by wave III, and individual income at wave III. Race and grade were both self-reported by the participant during the wave I interview. Race was categorized as White (Non-Hispanic), Black (Non-Hispanic), Hispanic, Asian, or another race, and grade continuously ranged from seventh grade through twelfth grade. Grade was unknown among a small portion of participants either because the participant did not know his or her grade or because his or her school did not use standard grade levels.

A subset of the participants' parents was interviewed at wave I. Parent education level and annual family income at wave I were reported by the parent. Education level of the interviewed parent was categorized as less than high school, high school graduate, some college, and college graduate or higher. Annual family income was categorized as less than $24,000, $24,000 to $44,999, and $45,000 or higher. Both parent education level and annual family income information is unknown for a portion of participants either because the parent was not interviewed, refused to respond, or did not know. There are major concerns to note with these two variables. Since not all parents were interviewed and some of those that were did not answer these questions, there are a high proportion of unknowns within each variable. Thus, while distributions and results of gender comparisons are reported, both must be considered within the context of a large portion of unknowns for these variables, and thus might not be accurate.

Age at wave III was calculated by the participants' interviewer and was categorized into ages eighteen through twenty, twenty-one through twenty-three, and twenty-four through twenty-eight. Educational attainment was dichotomized into having graduated high school by wave III or not. Lastly, individual income at wave III was self-reported by the participant and categorized as less than $4,800 a year, $4,800 to $12,999 a year, and $13,000 or higher. Individual income is unknown for a large portion of participants due to either refusal to answer or
the participant reporting that they did not know. There are also concerns regarding this variable to consider. The variable assessed the individual’s personal income and not household income. With ages ranging from eighteen to twenty-eight some participants may have significant financial support from a parent or guardian, or potentially a significant other. Moreover, some of the participants were still in some form of school, limiting their ability to have an income as high as other participants not in school.

**Participant Characteristic Profile**

Several additional variables were collected in order to address the sub-RQs of aim two. These variables were only constructed for males and include demographic factors, physical health factors, and behavioral health factors.

**Demographic Factors.** In addition to the other basic demographic variables described above, an indicator of perceived intelligence was included. The original item, “compared with other people your age, how intelligent are you” was measured on a six-point Likert scale ranging from “moderately below average” to “extremely above average”. The item was dichotomized as an indicator of perceiving oneself as having above average intelligence.

**Physical Health Factors.** Physical health factors included physical activity, performance enhancing substance or steroid use, high cholesterol, hypertension, body mass index, and obesity. Physical activity was measured as the number of times the participant reported being active in the past week. Specifically, at wave I, the participant was asked, “During the past week, how many times did you…go rollerblading, roller-skating, skate-boarding, or bicycling; play an active sport such as baseball, softball, basketball, soccer, swimming, or football; exercise such as jogging, walking, doing karate, jumping rope, doing gymnastics or dancing.” At wave III, the participants were asked the same question for the following activities: bicycle,
skateboard, dance, hike, hunt, or yard work; roller blade, roller skate, downhill ski, snow board, play racquet sports, or aerobics; participate in strenuous team sports such as football, soccer, basketball, lacrosse, rugby, field hockey, or ice hockey; participate in individual sports such as running, wrestling, swimming, cross-country skiing, cycle racing, or martial arts; participate in gymnastics, weight lifting, or strength training; or play golf, go fishing or bowling, or play softball or baseball. For each wave a sum variable was created as the number of times the participant reported being active.

There are several limitations to note with regards to these two variables. First, the measures only assess activity in the prior week, which may not be representative of an average week. Secondly, the measure is the sum of times active, as opposed to the number of active days or number of times active for a specific amount of time or intensity. This means that each occurrence of activity may not have been at an intensity level or duration long enough for physical health benefits.

Use of a legal performance-enhancing substance for athletics, such as Creatine, Monohydrate, or Andro, anabolic steroids or other illegal performance enhancing substances was measured as any use in the past year. High cholesterol and hypertension were assessed at wave IV. Indicators represent the participant having been told by a doctor or health care provider that he or she had either condition. Continuous measures of body mass index and obesity were constructed using height and weight. At wave I the participants were asked to self-report their height and weight. Self-reported wave I body mass index was age adjusted. At wave III, the interviewer measured height and weight. An Indicator of obesity at each wave was constructed as having a body mass index of thirty or higher.

**Behavioral Health Factors.** Behavioral health factors included mental health care utilization, delinquent behavior, and sexual behaviors. Mental health care utilization was
measured as having self-reported being in psychological counseling or in alcohol abuse or drug abuse treatment within the past twelve months at wave III.

With regards to delinquent behaviors, Add Health included a delinquency scale at wave I. Participants were asked how often in the past twelve months did they do any delinquent behaviors from a list of fifteen behaviors. The list included: 1) paint graffiti or signs on someone else’s property or in a public place, 2) deliberately damage property that didn’t belong to you, 3) lie to your parents or guardians about where you had been or whom you were with, 4) take something from a store without paying for it, 5) get into a serious physical fight, 6) hurt someone badly enough to need bandages or care from a doctor or nurse, 7) run away from home, 8) drive a car without its owner’s permission, 9) steal something worth more than $50, 10) go into a house or building to steal something, 11) use or threaten to use a weapon to get something from someone, 12) sell marijuana or other drugs, 13) steal something worth less than $50, 14) take part in a fight where a group of your friends was against another group, or 15) act loud, rowdy, or unruly in a public place. All items were measured on a four-point scale ranging from “zero times” to “five or more times” and a continuous delinquency sum score was constructed. Arrest history was also included within delinquent behavior, measured as having ever been arrested, regardless of the crime or outcome, by wave IV.

Lastly, sexual behaviors and orientation were assessed at wave IV. Sexual behavior variables included age at first sex (vaginal or anal) and number of lifetime sex partners for all types of sexual activity. A sexual orientation variable was also included indicating if the participant reported being “100% homosexual” or “mostly homosexual/somewhat attracted to opposite sex” versus any other form of sexual orientation.

**Analytical Plan**

Statistical techniques varied by aim and RQ but included chi-square tests, Fisher’s exact tests, independent sample t-tests, simple linear regressions, simple logistic regressions, and
structural equation modeling. While the data is longitudinal and variables were selected from multiple waves, cross sectional analytical methods were used. Proper sample weights were applied to all analyses and all procedures were run in either SAS 9.4 or MPlus 7.

First, descriptives was gathered as well as chi-square test comparisons by gender for each demographic variable. Several demographic categorical variables contained multiple categorical outcomes (i.e., more than two). In these cases, an initial chi-square was run for the entire categorical variable. If the initial test revealed significant differences at an alpha of 0.10, separate chi-square tests were then run for each category within the variable.

Next, descriptives were assessed as well as chi-square comparisons by gender for neither disorder, any ADHD, ADHD alone (i.e., no ED), any ED, ED alone (i.e., no ADHD), and comorbid ADHD/EDs. Simple logistic regressions were conducted for each gender with ADHD as a predictor of ED within gender. A regression was used for this step as opposed to a correlation analysis due to the inability to apply sample weight to correlations in SAS 9.4.

Then, comparisons by gender and disorder status for each genetic, psychosocial, and psychiatric factor was conducted with either chi-square tests for categorical factors or independent sample t-tests for continuous factors when comparing by gender. Within each gender, regression analysis was used to compare females with neither disorder, ADHD alone, and ED alone to a reference category of females with comorbid ADHD/ED.

Next, analyses were conducted for aim one among females. Based on the lack of previous investigations of the proposed underlying mechanism and the complexity of the proposed model, before testing the entire structural equation model (i.e., simultaneous investigation of the three hypotheses), each individual factor was tested separately via simple unadjusted logistic regressions to evaluate the relationship of that factor with the comorbidity. This technique addressed the first two RQs, which aimed to determine which risk regulator and genetic factors were independently associated with the comorbidity. The same regressions are also displayed for ADHD alone and ED alone outcomes as comparisons.
Only factors that were significantly associated with the comorbidity on its own were retained for the structural equation model, with the exception of genetic factors. Despite issues related to multiple comparisons, this step was used solely to simplify the model to only potentially significant factors, thus any factors significant at an alpha level of .05 were retained. Regardless of independent logistic regression results, all genetic factors were retained for the full model due to the third RQ, which aims to investigate how the risk regulators impact the association between the genetic factors and the comorbidity, as well as for the third pathway investigating the direct link between the genetic factors and risk regulators.

The structural equation model initially consisted of a partial mediation model where the psychosocial and psychiatric factors mediate the relationship between ADHD and EDs as well as mediate the relationship between the genetic factors and the comorbidity with genetic factors also being directly linked to the comorbidity. From the conceptual framework (see figure 2) the main paths of interest for this structural equation model are P4 through P6; specifically, the pathway from the genetic substrate directly to the comorbidity, the mediation pathway of the psychosocial and psychiatric risk regulators between ADHD and EDs, and the indirect pathway from the genetic substrate to the psychosocial and psychiatric risk regulators to the comorbidity. The mediation model meets the temporal criteria needed for mediation, where the mediator (psychosocial and psychiatric factors) occurs temporally after the predictor (genetic factors) and prior to the outcome (comorbid ADHD/ED) (MacKinnon & Fairchild, 2009; MacKinnon, Fairchild, & Fritz, 2007). Although some of the variables are measured in wave IV, after the measurements of ADHD and EDs, the constructs theoretically occur in the correct order or assess factors that are not expected to change over time, for example lifetime diagnoses.

In MPlus 7, weighted least squares means and variance adjusted (WLSMV) was used to estimate the model due to the binary nature of the outcome (Proitsi et al., 2011). The same fit indices used to evaluate the CFA models, specifically the chi-square test of model fit, CFI, RMSEA, and WRMR were used to evaluate fit of the full structural equation model. Results of
the fit of the initial model with all retained factors as well as analysis of residuals, modification indices, and theoretical considerations were used to guide several rounds of model re-specification.

Lastly, aim two analyses were conducted among males. Descriptive of additional demographic, physical health, and behavioral health factors were assessed and compared across disorder status. Regressions were used to compare men with neither disorder, ADHD alone, and ED alone to a reference category of men with comorbid ADHD/ED. In order to determine the association of the underlying mechanism, simple unadjusted logistic regression models were constructed with individual comparisons of the association of each proposed factors with comorbidity ADHD/ED.
CHAPTER FOUR: RESULTS

Participant Descriptive Statistics

Table 7 displays descriptive information regarding basic demographics for the female sample (n=6,289) and male sample (n=5,248). The racial distribution was similar for both genders with no significant differences. Racial distributions were as follows: among females, 66.3% of participants reported that they were White (Non-Hispanic), 16.3% were Black (Non-Hispanic), 11.2% were Hispanic, 3.5% were Asian, and 2.7% were of another race. In comparison, among males, 65.5% reported being White (Non-Hispanic), 15.5% were Black (Non-Hispanic), 11.9% were Hispanic, 3.8% were Asian, and 3.4% were of another race.

There were no differences by gender, with regards to grade at wave I with the grade distribution being relatively evenly split for both genders. However, there were significant differences between genders regarding age at wave III (p<.001). Specifically, there were a higher proportion of females in the eighteen to twenty year old group (30.5% vs. 27.3%, p<.05), and a higher proportion of males in the twenty-four to twenty-eight year old group (20.3% vs. 23.6%, p<.001).

There were no differences between genders with regards to parent reported annual family income at wave I. Among females, 22.4% had an annual family income of less than $24,000, 24.4% had a family income of $24,000 to $44,999, 30.8% had a family income of $45,000 or higher, and family income was unknown for 22.3% of females. Similarly among males, 23.4% had an annual family income of less than $24,000, 25.1% had a family income of $24,000 to $44,999, 31.3% had a family income of $45,000 or higher, and family income was unknown for 20.1% of males.
Table 7. Sample Descriptive Statistics by Gender

<table>
<thead>
<tr>
<th></th>
<th>Females (n=6,289)</th>
<th>Males (n=5,248)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (Non-Hispanic)</td>
<td>66.3 (3,368)</td>
<td>65.5 (2,851)</td>
<td></td>
</tr>
<tr>
<td>Black (Non-Hispanic)</td>
<td>16.3 (1,442)</td>
<td>15.5 (995)</td>
<td>.3872</td>
</tr>
<tr>
<td>Hispanic</td>
<td>11.2 (930)</td>
<td>11.9 (849)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>3.5 (384)</td>
<td>3.8 (394)</td>
<td></td>
</tr>
<tr>
<td>Another Race</td>
<td>2.7 (164)</td>
<td>3.4 (159)</td>
<td></td>
</tr>
<tr>
<td>Grade at Wave I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7th Grade</td>
<td>17.9 (896)</td>
<td>17.3 (689)</td>
<td></td>
</tr>
<tr>
<td>8th Grade</td>
<td>15.6 (872)</td>
<td>16.9 (691)</td>
<td></td>
</tr>
<tr>
<td>9th Grade</td>
<td>17.0 (1,105)</td>
<td>17.2 (948)</td>
<td>.3009</td>
</tr>
<tr>
<td>10th Grade</td>
<td>16.7 (1,188)</td>
<td>15.1 (1,000)</td>
<td></td>
</tr>
<tr>
<td>11th Grade</td>
<td>14.5 (1,127)</td>
<td>15.4 (1,024)</td>
<td></td>
</tr>
<tr>
<td>12th Grade</td>
<td>15.7 (972)</td>
<td>15.9 (796)</td>
<td></td>
</tr>
<tr>
<td>Unknown¹</td>
<td>2.5 (129)</td>
<td>2.3 (100)</td>
<td></td>
</tr>
<tr>
<td>Parent Education Level²</td>
<td></td>
<td></td>
<td>.0529</td>
</tr>
<tr>
<td>Less than High School</td>
<td>14.8 (975)</td>
<td>14.1 (686)</td>
<td>.4761</td>
</tr>
<tr>
<td>High School Graduate</td>
<td>28.8 (1,606)</td>
<td>27.3 (1,322)</td>
<td>.2122</td>
</tr>
<tr>
<td>Some College</td>
<td>15.9 (1,033)</td>
<td>16.4 (946)</td>
<td>.6149</td>
</tr>
<tr>
<td>College Graduate or Higher</td>
<td>27.4 (1,800)</td>
<td>30.7 (1,615)</td>
<td>.0088</td>
</tr>
<tr>
<td>Unknown³</td>
<td>13.0 (875)</td>
<td>11.5 (679)</td>
<td>.0920</td>
</tr>
<tr>
<td>Annual Family Income at Wave I²</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $24,000</td>
<td>22.4 (1,368)</td>
<td>23.4 (1,129)</td>
<td></td>
</tr>
<tr>
<td>$24,000 – $44,999</td>
<td>24.4 (1,497)</td>
<td>25.1 (1,291)</td>
<td>.2630</td>
</tr>
<tr>
<td>$45,000 or Higher</td>
<td>30.8 (1,885)</td>
<td>31.3 (1,668)</td>
<td></td>
</tr>
<tr>
<td>Unknown³</td>
<td>22.3 (1,539)</td>
<td>20.1 (1,160)</td>
<td></td>
</tr>
<tr>
<td>Age at Wave III</td>
<td></td>
<td></td>
<td>.0006</td>
</tr>
<tr>
<td>18 – 20 years old</td>
<td>30.5 (1,596)</td>
<td>27.3 (1,133)</td>
<td>.0111</td>
</tr>
<tr>
<td>21 – 23 years old</td>
<td>49.2 (3,435)</td>
<td>49.1 (2,880)</td>
<td>.9332</td>
</tr>
<tr>
<td>24 – 28 years old</td>
<td>20.3 (1,258)</td>
<td>23.6 (1,235)</td>
<td>.0001</td>
</tr>
<tr>
<td>High School Graduate by Wave III</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>No</td>
<td>43.8 (2,660)</td>
<td>51.2 (2,519)</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>56.2 (3,629)</td>
<td>48.8 (2,729)</td>
<td></td>
</tr>
<tr>
<td>Individual Income at Wave III</td>
<td></td>
<td></td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Less than $4,800</td>
<td>26.6 (1,665)</td>
<td>19.7 (1,040)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>$4,800 – $12,999</td>
<td>24.0 (1,437)</td>
<td>21.9 (1,095)</td>
<td>.0801</td>
</tr>
<tr>
<td>$13,000 or Higher</td>
<td>28.4 (1,869)</td>
<td>40.6 (2,180)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Unknown³</td>
<td>21.1 (1,318)</td>
<td>17.8 (933)</td>
<td>.0025</td>
</tr>
</tbody>
</table>

Notes: Weighted % (n)

¹Not in school at the time of the interview or no grade level reported

²Self-reported by a parent at Wave I

³Not reported or no parent interviewed
There was one significant difference in regards to the education level of the interviewed parent, with males having a higher portion of the parent having graduated from college or higher (30.7% vs. 27.4%, p<.01). However, these distributions, the non-significant result with annual income, and significant result with education level must be considered within the limitations related to these variables described above.

Significant gender differences were found in regards to the participants’ educational attainment by wave III and personal income at wave III. Females were significantly more likely to have reported having graduated from high school by wave III (56.2% vs 48.8%, p<.0001); however on average, females had lower personal incomes at wave III. A significantly higher proportion of females reported a personal income of less than $4,800 annually (26.6% vs. 19.7%, p<.0001), and a significantly higher proportion of males reported an income of $13,000 or higher (40.6% vs. 28.4%, p<.0001). There was also a significant difference in the proportion of unknown with 21.1% of female incomes and 17.8% of male incomes unknown (p<.01). As described above, these results must be considered within the context of the limitations of this variable.

Prevalence of ADHD, EDs, and Comorbid ADHD/ ED

Table 8 displays prevalence information stratified by disorder status. A total of 15.5% (n=921) of females and 27.5% (n=1,309) of males reported any ADHD. A total of 11.2% (n=656) of females and 23.4% (n=1,124) of males reported ADHD alone (i.e. no ED). As expected, the prevalence was significantly higher among males for both any ADHD and ADHD alone (p<.0001). The prevalence of any ED and ED alone (i.e., no ADHD) was 21.0% (n=1,298) and 16.8% (n=1,033) among females and 10.9% (n=602) and 6.8% (417) among males, respectively.
As expected the rates of both any ED and ED alone were significantly higher among females (p<.0001). Although there were differences in prevalence of each individual disorder, there was no difference in the rate of the comorbidity, with 4.2% (n=265) of the females reporting both ADHD and an ED compared with 4.1% (n=185) of males (p=.8104). Moreover, both females and males with ADHD were significantly more likely to also report an ED (females: OR: 1.53, 95% CI: 1.25-1.87; males: OR: 1.70, 95% CI: 1.28-2.26).

More specifically, among the 921 females who reported having ADHD, 27.4% also reported an ED; and among the 1,298 females that reported having an ED, 20.2% also reported ADHD. In regards to males, 14.9% of the 1,309 males with ADHD also reported an ED, and 37.7% of the males with an ED also reported ADHD.

Prevalence of Genetic Factors

Table 9 displays descriptive statistics for the genetic factors by gender and table 10 displays similar information by gender and disorder status (i.e., neither disorder, ADHD alone,
ED alone, or comorbid ADHD/ED). As can be seen in both tables, the rates of the specific 
repeat patterns of interest are displayed for each gene.

### Table 9. Genetic Genotype Descriptives by Gender

<table>
<thead>
<tr>
<th>Genotype &amp; Repeat Pattern</th>
<th>Females (n=6,289)</th>
<th>Males (n=5,248)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Monoamine Oxidase A (MAOA) Active</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero Active</td>
<td>14.4 (1,008)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>One Active</td>
<td>46.2 (2,942)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Two Active</td>
<td>39.5 (2,335)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Zero Active</td>
<td>-</td>
<td>39.3 (2,130)</td>
<td>-</td>
</tr>
<tr>
<td>One Active</td>
<td>-</td>
<td>60.7 (3,118)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Any Active</strong></td>
<td>85.6 (5,278)</td>
<td>60.7 (3,120)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td><strong>Dopamine Receptor 4 (DRD4) 7 Repeat</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero 7 Repeats</td>
<td>63.2 (4,000)</td>
<td>64.4 (3,461)</td>
<td>-</td>
</tr>
<tr>
<td>One 7 Repeat</td>
<td>32.6 (2,022)</td>
<td>31.5 (1,571)</td>
<td>-</td>
</tr>
<tr>
<td>Two 7 Repeats</td>
<td>4.2 (267)</td>
<td>4.1 (216)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Any 7 Repeats</strong></td>
<td>36.8 (2,289)</td>
<td>35.6 (1,787)</td>
<td>.2860</td>
</tr>
<tr>
<td><strong>Dopamine Transporter (DAT1) 9 Repeat</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero 9 Repeats</td>
<td>58.1 (3,814)</td>
<td>60.3 (3,241)</td>
<td>-</td>
</tr>
<tr>
<td>One 9 Repeat</td>
<td>36.5 (2,134)</td>
<td>33.7 (1,731)</td>
<td>-</td>
</tr>
<tr>
<td>Two 9 Repeats</td>
<td>5.4 (341)</td>
<td>6.0 (276)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Any 9 Repeats</strong></td>
<td>41.9 (2,475)</td>
<td>39.7 (2,007)</td>
<td>.0675</td>
</tr>
<tr>
<td><strong>Dopamine Transporter (DAT1) 10 Repeat</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero 10 Repeats</td>
<td>5.8 (379)</td>
<td>7.0 (329)</td>
<td>-</td>
</tr>
<tr>
<td>One 10 Repeat</td>
<td>38.1 (2,251)</td>
<td>35.1 (1,802)</td>
<td>-</td>
</tr>
<tr>
<td>Two 10 Repeats</td>
<td>56.0 (3,659)</td>
<td>57.9 (3,117)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Any 10 Repeats</strong></td>
<td>94.2 (5,910)</td>
<td>93.0 (4,919)</td>
<td>.0498</td>
</tr>
<tr>
<td><strong>Serotonin Transporter (5-HTTLPR) Short Repeats</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zero Short Repeats</td>
<td>34.4 (2,197)</td>
<td>32.2 (1,756)</td>
<td>-</td>
</tr>
<tr>
<td>One Short Repeat</td>
<td>46.5 (2,865)</td>
<td>49.2 (2,461)</td>
<td>-</td>
</tr>
<tr>
<td>Two Short Repeats</td>
<td>19.1 (1,224)</td>
<td>18.6 (1,026)</td>
<td>-</td>
</tr>
<tr>
<td><strong>Any Short Repeats</strong></td>
<td>65.5 (4,089)</td>
<td>67.7 (3,487)</td>
<td>.0873</td>
</tr>
</tbody>
</table>

**Notes:** Weighted % (n)
Table 9 displays the rates for the sequence being found on both alleles (two active/two repeats), one but not the other allele (one active/one repeat), or it was not found on either allele (zero active/zero repeats). As an example with the DRD4 gene and the seven repeat, two repeats would equate to a genotype of seven/seven, one repeat would equate to either seven/not seven or not seven/seven, and zero repeats would equate to a genotype of not seven/not seven. Rates of the sequences of interest are also displayed as having any of the specific sequence on either allele.

As can be seen in table 9, there was a significant difference between the prevalence of any active MAOA between females and males (85.6% vs. 60.7%, p<.0001). This is as to be expected based on the fact that females have two chromosomes with which MAOA could possibly be active on, versus just one chromosome among the males. There was no difference in the prevalence of any seven repeats on the DRD4 gene with a rate of 36.8% among females and 35.6% among males. Both the nine repeats and ten repeats on the DAT1 gene were borderline significantly different between genders. The difference for the nine repeat was above the significant level for DAT1 with a rate of 41.9% among females and 39.7% among males (p=.0675), while the difference with regards to the ten repeat was just at the significance with prevalence of 94.2% among females and 93.0% among males (p=.0498). Lastly there were no differences in the rate of any short repeats on the serotonin transporter with a rate of 65.5% among females and 67.7% among males (p=.0873).

Table 10 displays the prevalence of each genetic factor by gender and disorder status, and results of logistic regression models for each status compared to comorbid ADHD/ED. There were just a few very slight differences by disorder status. Among these slight differences is the rate of any short 5-HTTLPR repeats between females with neither disorder (64.9%) and females with ED alone (64.8%) compared to females with comorbid ADHD/ED (73.1%). Both females with neither disorder and females with ED alone were just barely significantly less likely
to have any short repeats (Neither: OR: 0.68, 95% CI: 0.48-0.98, p=.0375; ED alone: OR: 0.68, 95% CI: 0.47-0.99, p=.0467).

The rate of any DRD4 seven repeats was slightly different between males with ADHD alone (34.2%) compared to males with comorbid ADHD/ED (43.4%); specifically, males with ADHD alone were slightly less likely to have any seven repeats (OR: 0.68, 95% CI: 0.47-0.98, p=.0363). The rate of any DAT1 nine repeats were slightly different between males with neither disorder (38.4%) compared to males with comorbid ADHD/ED (50.0%); specifically, males with neither disorder were slightly less likely to have any nine repeats (OR: 0.63, 95% CI: 0.40-0.98, p=.0416). Lastly, although not significantly different, males with ADHD only seemed to have lower rates of the DAT1 nine repeat (37.7%) compared to males with comorbid ADHD/EDs (50.0%, p=.0554).

Table 10. Genetic Genotype Descriptives by Gender and Disorder Status

<table>
<thead>
<tr>
<th>Disorder Status (n)</th>
<th>Any MAOA Active</th>
<th>Any DRD4 7 repeats</th>
<th>Any DAT1 9 repeats</th>
<th>Any DAT1 10 repeats</th>
<th>Any 5-HTTLPR short repeats</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neither Disorder (n=4,335)</td>
<td>85.8 (0.8)</td>
<td>35.9 (1.0)</td>
<td>41.2 (1.1)</td>
<td>94.1 (0.5)</td>
<td>64.9* (1.2)</td>
</tr>
<tr>
<td>ADHD Alone (n=656)</td>
<td>86.2 (1.7)</td>
<td>39.4 (2.6)</td>
<td>41.7 (2.3)</td>
<td>94.9 (1.1)</td>
<td>67.6 (2.5)</td>
</tr>
<tr>
<td>ED Alone (n=1,033)</td>
<td>84.4 (1.5)</td>
<td>38.8 (1.9)</td>
<td>44.2 (2.1)</td>
<td>93.6 (0.9)</td>
<td>64.8* (1.7)</td>
</tr>
<tr>
<td>Comorbid ADHD/ED (n=265)</td>
<td>86.2 (2.8)</td>
<td>37.5 (3.9)</td>
<td>45.1 (3.9)</td>
<td>95.6 (1.4)</td>
<td>73.1 (3.4)</td>
</tr>
<tr>
<td></td>
<td>Males</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neither Disorder (n=3,522)</td>
<td>60.5 (1.1)</td>
<td>35.2 (1.0)</td>
<td>38.4* (1.3)</td>
<td>93.5 (0.7)</td>
<td>67.5 (1.2)</td>
</tr>
<tr>
<td>ADHD Alone (n=1,124)</td>
<td>61.5 (1.9)</td>
<td>34.2* (1.8)</td>
<td>42.2 (2.0)</td>
<td>91.6 (1.1)</td>
<td>68.1 (1.8)</td>
</tr>
<tr>
<td>ED Alone (n=417)</td>
<td>58.4 (3.4)</td>
<td>38.5 (3.4)</td>
<td>37.7 (3.4)</td>
<td>92.6 (2.0)</td>
<td>68.7 (3.9)</td>
</tr>
<tr>
<td>Comorbid ADHD/ED (n=185)</td>
<td>64.2 (5.1)</td>
<td>43.4 (4.4)</td>
<td>50.0 (5.5)</td>
<td>92.3 (2.5)</td>
<td>67.5 (5.5)</td>
</tr>
</tbody>
</table>

Notes: Weighted % (SE)
* p<.05 compared to Comorbid ADHD/ED
Prevalence of Psychosocial and Psychiatric Mechanisms

Table 11 displays descriptive statistics for all psychosocial and psychiatric factors. There were many gender differences found. Specifically, females had significantly higher scores on the adolescent neuroticism, adult neuroticism, adult conscientiousness, and cognitive control scales, as well as higher rates of major depression and anxiety disorders (p<.0001). Conversely, females had significantly lower scores on the family support scale as well as lower rates of both alcohol and substance use disorders (p<.0001). There were no gender differences in regards to social support, adolescent conscientiousness, results of the memory task, or rates of having experienced childhood abuse.

Table 11. Psychosocial and Psychiatric Risk Regulators Descriptives by Gender

<table>
<thead>
<tr>
<th></th>
<th>All Females (n=6,289)</th>
<th>All Males (n=5,248)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosocial [weighted mean (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Support (SR1: 10 – 14)</td>
<td>33.3 (0.1)</td>
<td>34.2 (0.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Social Support (SR1: 7 – 30)</td>
<td>23.3 (0.1)</td>
<td>23.4 (0.1)</td>
<td>.7333</td>
</tr>
<tr>
<td>Personality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescent Neuroticism (SR1: 5 – 25)</td>
<td>9.9 (0.1)</td>
<td>8.9 (0.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Adolescent Conscientiousness (SR1: 4 – 20)</td>
<td>15.1 (0.1)</td>
<td>15.2 (0.1)</td>
<td>.3067</td>
</tr>
<tr>
<td>Adult Neuroticism (SR1: 4 – 20)</td>
<td>11.0 (0.1)</td>
<td>9.9 (0.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Adult Conscientiousness (SR1: 4 – 20)</td>
<td>14.8 (0.1)</td>
<td>14.3 (0.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Control (SR1: 6 – 29)</td>
<td>19.7 (0.1)</td>
<td>18.5 (0.1)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Memory (SR1: 0 – 7)</td>
<td>4.1 (0.0)</td>
<td>4.2 (0.1)</td>
<td>.0607</td>
</tr>
<tr>
<td><strong>Psychiatric [weighted % (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Depression</td>
<td>22.7 (1.0)</td>
<td>10.3 (0.7)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
<td>18.0 (0.8)</td>
<td>8.1 (0.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Alcohol Use Disorder</td>
<td>22.5 (1.0)</td>
<td>32.3 (1.2)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>6.7 (0.5)</td>
<td>9.5 (0.6)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Childhood Abuse</td>
<td>37.6 (1.1)</td>
<td>37.5 (1.1)</td>
<td>.9655</td>
</tr>
</tbody>
</table>

Notes: 1 Possible Scale Scores
Table 12 displays differences in the underlying mechanism by disorder status among females. Females with comorbid ADHD/ED had significantly lower scores on both the family and social support scales as compared to females with neither disorder and females with ED alone. Compared to all other categories, females with the comorbidity had higher scores on the adolescent neuroticism scale, and there were no differences with regards to adolescent conscientiousness. At wave IV, compared to females with neither disorder and females with ED alone, females with the comorbidity had significantly higher adult neuroticism scores and lower adult conscientiousness scores. Females with comorbid ADHD/ED had significantly lower cognitive control scores and higher rates of all psychiatric factors as compared to all other groups, with the except of alcohol use disorders.

Table 12. Psychosocial and Psychiatric Risk Regulators Descriptives by Disorder Status among Females (n=6,289)

<table>
<thead>
<tr>
<th></th>
<th>Neither Disorder (n=4,335)</th>
<th>ADHD Alone (n=656)</th>
<th>ED Alone (n=1,033)</th>
<th>Comorbid ADHD/ED (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosocial [weighted mean (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Support</td>
<td>33.4 (0.1)**</td>
<td>32.6 (0.3)</td>
<td>32.9 (0.2)**</td>
<td>31.3 (0.5)</td>
</tr>
<tr>
<td>Social Support</td>
<td>23.6 (0.1)**</td>
<td>22.3 (0.2)</td>
<td>23.4 (0.2)**</td>
<td>22.1 (0.4)</td>
</tr>
<tr>
<td>Personality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescent Neuroticism</td>
<td>9.7 (0.1)**</td>
<td>10.4 (0.2)**</td>
<td>10.2 (0.1)**</td>
<td>11.1 (0.3)</td>
</tr>
<tr>
<td>Adolescent Conscientiousness</td>
<td>15.1 (0.1)</td>
<td>15.2 (0.1)</td>
<td>15.0 (0.1)</td>
<td>14.9 (0.2)</td>
</tr>
<tr>
<td>Adult Neuroticism</td>
<td>10.7 (0.1)**</td>
<td>11.7 (0.2)</td>
<td>11.3 (0.1)**</td>
<td>12.0 (0.3)</td>
</tr>
<tr>
<td>Adult Conscientiousness</td>
<td>15.0 (0.1)**</td>
<td>13.9 (0.2)</td>
<td>14.9 (0.1)**</td>
<td>13.6 (0.3)</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Control</td>
<td>20.4 (0.1)**</td>
<td>17.5 (0.2)**</td>
<td>19.5 (0.2)**</td>
<td>16.8 (0.4)</td>
</tr>
<tr>
<td>Memory</td>
<td>4.1 (0.0)</td>
<td>3.9 (0.1)</td>
<td>4.2 (0.1)</td>
<td>4.0 (0.1)</td>
</tr>
<tr>
<td><strong>Psychiatric [weighted % (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Depression</td>
<td>18.3 (0.9)**</td>
<td>32.9 (2.8)**</td>
<td>26.5 (2.1)**</td>
<td>49.5 (3.4)</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
<td>14.3* (0.8)**</td>
<td>25.0 (2.3)**</td>
<td>23.2 (1.7)**</td>
<td>37.0 (4.0)</td>
</tr>
<tr>
<td>Alcohol Use Disorder</td>
<td>20.1 (1.0)*</td>
<td>26.3 (2.2)</td>
<td>28.2 (2.2)</td>
<td>28.8 (3.4)</td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>5.2 (0.5)**</td>
<td>9.4 (1.3)**</td>
<td>8.4 (1.2)**</td>
<td>17.1 (2.9)</td>
</tr>
<tr>
<td>Childhood Abuse</td>
<td>34.7 (1.2)**</td>
<td>44.4 (2.8)**</td>
<td>38.6 (2.1)**</td>
<td>62.7 (3.6)</td>
</tr>
</tbody>
</table>

Notes: Compared to Comorbid ADHD/ED: *p<.05; **p<.01; ***p<.001
Table 13 displays these differences by disorder status among males. There were no differences by disorder status with regards to social factors, personality in adolescence, and memory. A few personality differences at wave IV were found; males with comorbid ADHD/ED had higher adult neuroticism scores than males with neither disorder, and lower adult conscientiousness scores than males with neither disorder and males with ED alone. Males with the comorbidity had lower cognitive control scores compared to all other groups. Lastly, there were several differences within the psychiatric factors. Males with the comorbidity had higher rates of depression compared to males with neither disorder and males with ED alone, and higher rates of anxiety disorder compared to all groups. Males with the comorbidity also had higher rates of childhood abuse as compared to males with neither disorder.

Table 13. Psychosocial and Psychiatric Risk Regulator Descriptives by Disorder Status among Males (n=5,248)

<table>
<thead>
<tr>
<th></th>
<th>Neither Disorder (n=4,335)</th>
<th>ADHD Alone (n=656)</th>
<th>ED Alone (n=1,033)</th>
<th>Comorbid ADHD/ED (n=265)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Psychosocial [weighted mean (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family Support</td>
<td>34.4 (0.1)</td>
<td>33.6 (0.2)</td>
<td>34.1 (0.3)</td>
<td>34.2 (0.4)</td>
</tr>
<tr>
<td>Social Support</td>
<td>23.7 (0.1)</td>
<td>22.5 (0.2)</td>
<td>23.7 (0.2)</td>
<td>23.3 (0.5)</td>
</tr>
<tr>
<td>Personality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adolescent Neuroticism</td>
<td>8.7 (0.1)</td>
<td>9.3 (0.1)</td>
<td>9.1 (0.2)</td>
<td>9.0 (0.3)</td>
</tr>
<tr>
<td>Adolescent Conscientiousness</td>
<td>15.2 (0.1)</td>
<td>14.9 (0.1)</td>
<td>15.3 (0.2)</td>
<td>15.1 (0.3)</td>
</tr>
<tr>
<td>Adult Neuroticism</td>
<td>9.7 (0.1)*</td>
<td>10.2 (0.1)</td>
<td>10.0 (0.2)</td>
<td>10.8 (0.3)</td>
</tr>
<tr>
<td>Adult Conscientiousness</td>
<td>14.6 (0.1)*</td>
<td>13.6 (0.1)</td>
<td>14.2 (0.2)*</td>
<td>13.5 (0.4)</td>
</tr>
<tr>
<td>Cognitive</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive Control</td>
<td>19.2 (0.1)**</td>
<td>17.2 (0.1)**</td>
<td>18.7 (0.3)**</td>
<td>15.7 (0.5)</td>
</tr>
<tr>
<td>Memory</td>
<td>4.2 (0.1)</td>
<td>4.2 (0.1)</td>
<td>4.1 (0.1)</td>
<td>3.9 (0.2)</td>
</tr>
<tr>
<td><strong>Psychiatric [weighted % (SE)]</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major Depression</td>
<td>7.8 (0.6)**</td>
<td>15.6 (1.7)</td>
<td>9.6 (2.0)**</td>
<td>21.1 (4.1)</td>
</tr>
<tr>
<td>Anxiety Disorder</td>
<td>7.0 (0.7)**</td>
<td>9.7 (1.1)*</td>
<td>7.6 (1.8)**</td>
<td>16.1 (3.5)</td>
</tr>
<tr>
<td>Alcohol Use Disorder</td>
<td>30.8 (1.3)</td>
<td>36.1 (2.2)</td>
<td>34.4 (3.0)</td>
<td>32.8 (4.9)</td>
</tr>
<tr>
<td>Substance Use Disorder</td>
<td>7.8 (0.6)</td>
<td>13.7 (1.3)</td>
<td>9.1 (2.1)</td>
<td>13.3 (3.3)</td>
</tr>
<tr>
<td>Childhood Abuse</td>
<td>34.9 (1.3)*</td>
<td>42.7 (1.8)</td>
<td>39.9 (3.9)</td>
<td>45.4 (5.0)</td>
</tr>
</tbody>
</table>

Notes: Compared to Comorbid ADHD/ED: *p<.05; **p<.01; ***p<.001
**Aim One Results**

Aim one is to evaluate a model of the underlying mechanisms of the ADHD/ED comorbidity. Individual, unadjusted logistic regressions were constructed for each hypothesized underlying mechanism among females. Figure 5 displays the results of the association between each mechanism with ADHD alone and ED alone. As can be seen in figure 5, none of the genetic factors were associated either ADHD or ED alone. However, several psychosocial factors were correlated with each disorder. Specifically with regards to ADHD alone, significant correlations included decreased family support (OR: 0.97, 95% CI: 0.96-0.99), social support (OR: 0.93, 95% CI: 0.91-0.96), adult conscientiousness (OR: 0.87, 95% CI: 0.84-0.91), cognitive control (OR: 0.85, 95% CI: 0.82-0.87), and memory (OR: 0.92, 95% CI: 0.86-0.99), and increased adolescent (OR: 1.05, 95% CI: 1.02-1.08), and adult neuroticism (OR: 1.11, 95% CI: 1.07-1.16). There were less correlates to ED alone. Significant associations included decreased family support (OR: 0.98, 95% CI: 0.97-0.99), and increased adolescent (OR: 1.03, 95% CI: 1.01-1.06), and adult neuroticism (OR: 1.06, 95% CI: 1.03-1.10).

Generally speaking, all psychiatric factors were significantly associated with both ADHD alone and ED alone with the exception of no association between substance use disorder and childhood abuse with ED alone. For ADHD alone, positive significant associations were as follows: major depression (OR: 1.80, 95% CI: 1.38-2.36), anxiety disorder (OR: 1.61, 95% CI: 1.25-2.08), alcohol use disorder (OR: 1.26, 95% CI: 1.01-1.58), substance use disorder (OR: 1.54, 95% CI: 1.08-2.18), and childhood abuse (OR: 1.37, 95% CI: 1.10-1.72). Positive significant associations with regards to ED alone were as follows: major depression (OR: 1.29, 95% CI: 1.04-1.59), anxiety disorder (OR: 1.49, 95% CI: 1.22-1.81), and alcohol use disorder (OR: 1.45, 95% CI: 1.16-1.81).
Figure 5: Individual Logistic Regressions of the Association of Each Hypothesized Underlying Factor with ADHD Alone and ED Alone Among Females (n=6,289)

Figure 6 displays the results of similar logistic regression models of each underlying mechanism as associated with comorbid ADHD/ED. Within the genetic substrate, any short 5-HTTLPR repeats were positively associated (OR: 1.45, 95% CI: 1.01-2.06). Among psychosocial factors, positive associations included adolescent (OR: 1.12, 95% CI: 1.07-1.17), and adult neuroticism (OR: 1.15, 95% CI: 1.07-1.22). Negative associations included family support (OR: 0.93, 95% CI: 0.91-0.96), social support (OR: 0.93, 95% CI: 0.89-0.96), adolescent conscientiousness (OR: 0.85, 95% CI: 0.80-0.91), and cognitive control (OR: 0.82, 95% CI: 0.79-0.86).

Psychiatric factors, with the exception of alcohol use disorder, were all positively associated with comorbid ADHD/ED. Generally speaking, females with each of the psychiatric factors were between approximately three to four times more likely to have comorbid ADHD/ED:
major depression (OR: 3.58, 95% CI: 2.74-4.69), anxiety disorder (OR: 2.85, 95% CI: 2.01-4.03), substance use disorder (OR: 3.09, 95% CI: 2.02-4.71), and childhood abuse (OR: 2.93, 95% CI: 2.14-4.00).

![Diagram showing odds ratios and 95% CIs for various factors.](image)

**Figure 6: Individual Logistic Regressions of the Association of Each Hypothesized Underlying Factor Comorbid ADHD/ ED Among Females (n=6,289)**

Based on the results of the logistic regression models displayed in figure 6, the following factors were retained for structural equation modeling: childhood abuse, substance use disorder, anxiety disorder, major depression, cognitive control, conscientiousness at wave IV, neuroticism at both wave I and wave IV, social support, family support, and all genetic factors. In order to investigate mediating factors, the model included any ADHD and any ED indicators as opposed to the ADHD alone and ED alone indicators.
The initial model, based on the conceptual framework (figure 2), resulted in poor model fit as none of the genetic factors were leading to either disorder or the comorbidity. Based on this finding, the model was re-constructed as a mediation model focusing on H2 (psychosocial factors) and H3 (psychiatric factors), with the genetic factors predicted to be associated with each of the H2 and H3 factors per pathway three of the conceptual framework. This re- construction dropped the comorbidity indicator from the model; as each H2 and H3 factor was predicted to mediate the relationship of the two disorders as opposed to directly lead to comorbidity.

Figure 7. Structural Equation Model of the Underlying Mechanisms of Comorbid ADHD/ EDs among Females (n=6,289)

Although fit improved, the re-constructed model still had inadequate fit, and several factors including the DAT1 ten repeat, DRD4 seven repeat, social support, conscientiousness, and childhood abuse were not significant within the model. Guided by analysis of standardized
residuals, modification indices, as well as theoretical considerations, several rounds of re-
specification resulted in the final model shown in figure 7. Figure 7 displays standardized
estimates with all one directional associations connected with solid lines and all bidirectional
relationships (i.e., correlations) connected with dotted lines.

This final model has great fit with the following indices: $X^2 (df=17)=37.93, p=.0025$;
RMSEA=.01; CFI=.95; WRMR=.89. Psychosocial and psychiatric factors retained as significant
in this final model included depression, anxiety, substance use disorder, cognitive control, and
family support. Results suggest that while ADHD is directly associated with ED (standardized
estimate: 0.05, $p<.05$), there are also several indirect pathways from ADHD to ED.

Both psychosocial factors partially mediated the relationship between the two disorders
in that ADHD was negatively associated with both cognitive control and family support, which
each subsequently were negatively associated with ED. H3 proposed that psychiatric factors
mediate the relationship just as the psychosocial factors; however, this was not consistent with
model findings. ADHD was positively associated with each psychiatric factor (major depression,
anxiety disorder, and substance use disorder). However, these factors did not lead to EDs in
one directional nature as predicted, rather bidirectional correlations were found. This suggests
that rather than mediating ADHD to ED, it appears that the other psychiatric illnesses, including
depression, anxiety, and substance use, were each correlated or comorbid with EDs on their
own. ADHD lead to both ED and the second comorbid illness in single directional relationships.

Several genetic factors predicted psychosocial and psychiatric factors, as proposed in
pathway three. Specifically, any active MAOA was associated with major depression, any DAT1
nine repeats was associated with anxiety disorder, and any short 5-HTTLPR repeats was linked
to cognitive control. Lastly, as predicted, all psychosocial and psychiatric factors were
significantly correlated. The accumulation of all pathways from ADHD to ED equated to a total
standardized effect of 0.09 ($p<.001$).
Aim Two Results

Aim two explored the comorbidity and underlying mechanisms among males. Table 14 displays descriptives and comparative associations of demographic, physical health, behavioral health factors by disorder status for men. There were few differences between each sub-group with regards to demographic factors. The only significant differences were related to education and perceived intelligence. Males with comorbid ADHD/ED had significantly lower high school graduation rates by wave III (39.2%), as compared to men with neither disorder (51.1%, p<.05), and males with ED alone (58.1%, p<.01). Similarly, a significantly lower proportion of males with the comorbidity perceived themselves to be of above average intelligence (52.7%) as compared to men with neither disorder (63.9%, p<.05), and males with ED alone (67.8%, p<.05).

There was no physical health differences observed between men with the comorbidity and men with ED alone. Compared to men with neither disorder, men with comorbid ADHD/ED had higher levels of physical activity at wave III (8.6 v. 6.8, p<.01), higher rates of performance enhancer or steroid use (24.1% v. 15.9%, p<.05), higher rates of hypertension (41.0% v. 31.4%, p<.01), higher average body mass index scores at both wave I (23.7 v. 22.6, p<.001), and wave III (28.4 v. 26.2, p<.001), and higher rates of obesity at wave III (34.3% v. 19.8%, p<.01). Similarly results were obtained when compared to the ADHD alone group in that men with the comorbidity had higher rates of performance enhancer or steroid use (24.1% v. 14.9%, p<.01), higher average body mass index scores at both wave I (23.7 vs. 22.5, p<.001), and wave III (28.4 v. 26.1, p<.001), and higher rates of obesity at wave III (34.3% v. 22.5%, p<.01).

There was no behavioral health differences observed between men with the comorbidity and men with ADHD alone. However, as compared to men with neither disorder, a higher proportion of men with comorbid ADHD/ED reported being in psychological counseling within the year prior to wave III (10.7% vs. 3.9%, p<.05). Men with the comorbidity also had higher delinquency scores (5.3 vs. 4.5, p<.01), higher rates of having ever been arrested (50.3% vs. 38.7%, p<.05), and higher average number of lifetime sex partners (24.4 vs. 15.9, p<.05) as
compared to men with neither disorder. Lastly, as compared to men with ED alone, males with comorbid ADHD/ED had higher rates of having ever been arrested (50.3% vs. 34.1%, p<.01), and lower average age of sexual initiation (15.4 vs. 16.4, p<.05).

There were several differences that did not hit a statistically significant level, but are still worth noting, as the lack of significance may be due to power related concerns. Men with ADHD alone were physically active 6.9 times in the past week at wave III as compared to the 8.6 times men with ED alone, and 8.6 times men with the comorbidity were active. Rates of high cholesterol and hypertension were both higher among men with comorbid ADHD/ED than the other three categories. Although not significant, the rate of obesity at wave I was almost double among men with the comorbidity (13%) compared to men with ADHD alone (6.9%), and men with neither disorder (7.7%). While body mass index and obesity seemed to be higher when compared to the other groups, there was no difference in regards to either indicator between men with the comorbidity and men with ED alone.

With regards to noteworthy non-significant findings among the behavioral health factors, a lower proportion of men with ED alone were in psychological counseling (4.5%), compared to men with the comorbidity (10.7%). The average number of lifetime sexual partners was significantly higher among males with the comorbidity as compared to males with neither disorder. Although not significantly, the average was also highest among males with the comorbidity (24.4), compared to men with ADHD alone (19.6) and ED alone (14.5). Lastly, there appears to be small differences in the proportion of men that identify as homosexual. The lowest rates were among males with neither disorder (1.6%), and ADHD alone (1.5%). It was somewhat higher among males with the comorbidity (3.3%) and highest among males with ED alone (4.8%).
Table 14. Associated Demographic, Physical Health, and Behavioral Health Characteristics of Males by Disorder Status

<table>
<thead>
<tr>
<th></th>
<th>Neither Disorder (n=3,522)</th>
<th>ADHD Alone (n=1,124)</th>
<th>ED Alone (n=417)</th>
<th>Comorbid ADHD/ED (n=185)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic Profile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race and Nationality</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White (Non-Hispanic)</td>
<td>63.5 (3.2)</td>
<td>72.5 (3.0)</td>
<td>60.5 (4.8)</td>
<td>65.2 (5.4)</td>
</tr>
<tr>
<td>Black (Non-Hispanic)</td>
<td>16.5 (2.3)</td>
<td>13.3 (2.3)</td>
<td>15.1 (2.9)</td>
<td>12.8 (4.3)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>12.7 (1.9)</td>
<td>8.4 (1.5)</td>
<td>15.4 (4.0)</td>
<td>13.8 (3.5)</td>
</tr>
<tr>
<td>Asian</td>
<td>3.8 (0.9)</td>
<td>3.1 (1.0)</td>
<td>5.7 (1.8)</td>
<td>3.1 (2.1)</td>
</tr>
<tr>
<td>Another Race</td>
<td>3.5 (0.5)</td>
<td>2.8 (0.7)</td>
<td>3.3 (1.3)</td>
<td>5.1 (2.1)</td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School Graduate</td>
<td>51.1 (2.4)*</td>
<td>41.1 (2.6)</td>
<td>58.1 (3.6)**</td>
<td>39.2 (5.8)</td>
</tr>
<tr>
<td>Self Perceived Above Average Intelligence</td>
<td>63.9 (1.3)*</td>
<td>59.5 (2.2)</td>
<td>67.8 (3.7)*</td>
<td>52.7 (6.0)</td>
</tr>
<tr>
<td><strong>Parent Education Level</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High School Graduate</td>
<td>83.3 (1.7)</td>
<td>85.5 (2.2)</td>
<td>86.0 (2.9)</td>
<td>83.6 (4.8)</td>
</tr>
<tr>
<td><strong>Annual Family Income at Wave I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than $24,000</td>
<td>23.3 (1.8)</td>
<td>25.3 (2.6)</td>
<td>18.1 (3.2)</td>
<td>23.3 (5.6)</td>
</tr>
<tr>
<td>$24,000 – $44,999</td>
<td>25.8 (1.2)</td>
<td>24.5 (1.8)</td>
<td>23.1 (3.3)</td>
<td>20.8 (3.9)</td>
</tr>
<tr>
<td>$45,000 or Higher</td>
<td>30.8 (2.0)</td>
<td>30.1 (2.2)</td>
<td>37.3 (3.6)</td>
<td>37.6 (5.1)</td>
</tr>
<tr>
<td>Unknown(^1)</td>
<td>20.1 (1.1)</td>
<td>20.0 (2.0)</td>
<td>21.5 (3.2)</td>
<td>18.3 (3.5)</td>
</tr>
<tr>
<td><strong>Physical Health Profile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physical Activity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Past Week Physical Activity at Wave I(^1)</td>
<td>4.1 (0.1)</td>
<td>4.2 (0.1)</td>
<td>4.3 (0.2)</td>
<td>4.2 (0.2)</td>
</tr>
<tr>
<td>Past Week Physical Activity at Wave III(^1)</td>
<td>6.8 (0.2)**</td>
<td>6.9 (0.3)</td>
<td>8.2 (0.5)</td>
<td>8.6 (7.2)</td>
</tr>
<tr>
<td>Performance Enhancer or Steroid Use</td>
<td>15.9 (1.0)*</td>
<td>14.9 (1.4)**</td>
<td>23.1 (3.5)</td>
<td>24.1 (3.9)</td>
</tr>
<tr>
<td><strong>Health Conditions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High Cholesterol by Wave IV</td>
<td>7.6 (0.6)</td>
<td>8.9 (1.2)</td>
<td>9.7 (2.1)</td>
<td>11.0 (2.7)</td>
</tr>
<tr>
<td>Hypertension by Wave IV</td>
<td>31.4 (1.1)*</td>
<td>35.3 (1.8)</td>
<td>34.7 (3.3)</td>
<td>41.0 (5.1)</td>
</tr>
<tr>
<td><strong>Weight Related Conditions</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Self-Report) BMI at Wave I(^1)</td>
<td>22.6 (0.1)**</td>
<td>22.5 (0.2)**</td>
<td>24.2 (0.3)</td>
<td>23.7 (0.5)</td>
</tr>
<tr>
<td>(Self-Report) Obesity at Wave I</td>
<td>7.7 (0.7)</td>
<td>6.9 (1.1)</td>
<td>14.8 (2.9)</td>
<td>13.0 (5.1)</td>
</tr>
<tr>
<td>(Measured) BMI at Wave III(^1)</td>
<td>26.2 (0.1)**</td>
<td>26.1 (0.2)**</td>
<td>28.1 (0.4)</td>
<td>28.4 (0.8)</td>
</tr>
<tr>
<td>(Measured) Obesity at Wave III</td>
<td>19.8 (1.1)**</td>
<td>22.5 (1.9)*</td>
<td>31.1 (3.1)</td>
<td>34.3 (5.3)</td>
</tr>
<tr>
<td><strong>Behavioral Health Profile</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Mental Health Care Utilization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological Counseling at Wave III</td>
<td>3.9 (0.5)*</td>
<td>10.2 (1.3)</td>
<td>4.5 (1.6)</td>
<td>10.7 (3.5)</td>
</tr>
<tr>
<td>Drug or Alcohol Abuse Treatment at Wave III</td>
<td>3.5 (0.4)</td>
<td>5.5 (0.8)</td>
<td>2.8 (1.2)</td>
<td>4.8 (1.9)</td>
</tr>
<tr>
<td><strong>Delinquent Behavior</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Delinquency Scale at Wave I(^1)</td>
<td>4.5 (0.2)**</td>
<td>5.6 (0.3)</td>
<td>4.9 (0.4)</td>
<td>5.3 (0.6)</td>
</tr>
<tr>
<td>Ever Arrested by Wave IV</td>
<td>38.7 (1.4)*</td>
<td>49.6 (2.2)</td>
<td>34.1 (2.9)**</td>
<td>50.3 (4.8)</td>
</tr>
<tr>
<td><strong>Sexual Behaviors</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at First Sex(^1)</td>
<td>16.0 (0.1)</td>
<td>15.3 (0.2)</td>
<td>16.4 (0.3)*</td>
<td>15.4 (0.4)</td>
</tr>
<tr>
<td>Number of Lifetime Sex Partners at Wave IV(^1)</td>
<td>15.9 (0.8)*</td>
<td>19.6 (1.4)</td>
<td>14.5 (1.3)</td>
<td>24.4 (4.3)</td>
</tr>
<tr>
<td><strong>Sexual Orientation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100% or Mostly Homosexual</td>
<td>1.6 (0.3)</td>
<td>1.5 (0.5)</td>
<td>4.8 (1.6)</td>
<td>3.3 (1.6)</td>
</tr>
</tbody>
</table>

Notes: Weighted % (SE)
\(^1\)Weighted Mean (SE)
*p<.05, **p<.01, ***p<.001
As had been done in aim one, individual, unadjusted logistic regressions were constructed for each hypothesized underlying mechanism among males in order to investigate the association of each with comorbid ADHD/ED (see figure 8). Descriptive statistics and comparison tests described above resulted in very few significant differences between males with comorbid ADHD/ED and males in the other subgroups. Accordingly, there were few significantly associations of proposed underlying mechanisms with comorbid ADHD/ED among males.

Figure 8. Individual Logistic Regressions of the Association of Each Hypothesized Underlying Factor with Comorbid ADHD/ ED Among Males (n=5,248)

Results of logistic models (see figure 8) found that men with higher adult conscientiousness and cognitive control scores were less likely to have comorbid ADHD/ED
(conscientiousness: OR: 0.90, 95% CI: 0.82-0.99; cognitive control: OR: 0.83, 95% CI: 0.78-0.88). Conversely, males with higher adult neuroticism scores were more likely to have comorbid ADHD/ED (OR: 1.13, 95% CI: 1.04-1.23). Most noteworthy, men with major depression and men with anxiety disorders were both more than twice as likely to have comorbid ADHD/ED (depression: OR: 2.46, 95% CI: 1.49-4.06; anxiety: OR: 2.29, 95% CI: 1.35-3.88).
CHAPTER FIVE: DISCUSSION

Findings of this study provide support for several hypothesized underlying mechanisms of the ADHD/ED comorbidity. Specifically, among females, factors including cognitive control, family support, and additional comorbid mental health illnesses such as depression, anxiety, and substance disorder all mediate the relationship between ADHD and EDs. However, rather than leading to the comorbidity, ADHD led to other mental health issues which were then subsequently correlated to EDs; suggesting a comorbidity between these additional disorders and EDs with ADHD being a possible predictor of that comorbidity. This finding requires additional research with primary data collection to be confirmed. Moreover, other potential co-occurring mental disorders, such as bipolar disorder and OCD still require examination.

While a model of the underlying mechanisms is described in this study, this may be one of many potential models. Several factors that were significantly associated with ADHD alone, EDs alone, and the comorbidity via unadjusted analyses were dropped from the final model. These factors may still be underlying mechanisms, however they may be part of a separate combination of factors. Additional exploration is needed in regards to other potential combinations of underlying mechanisms.

In regards to genetics, the factors investigated in this study were not found to be directly associated with the comorbidity. Rather, these factors were connected to the psychosocial and psychiatric mediators, suggesting an indirect relationship between genetics and the comorbidity. Most importantly, while the model attenuated the relationship between ADHD and EDs, there was still a slightly significant pathway directly from ADHD to EDs. This suggests that the factors included in the model are still not completely explaining the connection between the two
disorders. Additional unexplored factors may help to fully account for the connection between ADHD and EDs.

With regards to males, comparisons of men with ADHD alone, EDs alone, and neither disorder suggest that there may be some noticeable differences compared to men with the comorbidity. Differences in regards to education attainment, BMI and obesity, delinquent behavior, and sexual behaviors were all observed. However, these differences alone may not be enough to identify the subset of males with ADHD or EDs that are at risk for the comorbidity. Replications of these results are needed with primary data collection to confirm, as well as to identify other potential differences. Moreover, very few of the proposed underlying mechanisms among females were significantly associated with the comorbidity among males. Continued research related to the development of the comorbidity in this population is needed to better understand potential male-specific determinants of comorbid ADHD/EDs.

Genetic Conclusions

There are several potential explanations for the lack of significant findings related to the genetic substrate. One is that this study explored the specific repeat patterns in isolation from accompanying genotypes. For example, both any nine repeats and any ten repeats of the DAT1 gene were investigated; however, these repeats were explored independently by comparing any nines and any tens on either allele separately to all other repeat options as opposed to each other. Yet it may not be the singular repeat patterns of nines or tens that lead to the comorbidity but combinations including these repeats. For example studies have compared the nine/nine genotype with the ten/ten and also ten/nine genotype (Guo et al., 2010). The unexplored ten/nine combination may play a role.

Additionally, this study compared any of the specified repeat patterns as opposed to comparing specific two chromosome genotypes. For example, the key genetic component may not be any nines but specifically one nine repeat or two nines (nine/nine). With two
chromosomes and two repeat sequences for each gene candidate, the combination repeats may have a role. For example, one study found differences in high calorie food intake between females with a ten/ten genotype on the SLC6A3 gene as compared to any nine repeats (Agurs-Collins & Fuemmeler, 2011).

Similarly, the identified repeat patterns of interest might not be the true component leading to the comorbidity. For example the two/two repeat of the DRD4 gene has been associated with increased depression levels (Guo & Tillman, 2009), and repeats greater than seven, as opposed to exactly seven has been linked to comorbid depression and marijuana use (Bobadilla et al., 2013). These and other repeats could potentially lead to comorbid ADHD/EDs. Specific genotypes of both alleles and additional repeat patterns warrant additional research.

Beyond additional genotype patterns and repeats sequences, it may be different genes that explain the comorbidity. There are several possible genes not included in this study that may be among the underlying mechanisms of comorbid ADHD/ED. These include DRD2, which has been linked to substance abuse, eating pathology, obesity, and ADHD (Agurs-Collins & Fuemmeler, 2011; Comings et al., 2000; Pagoto et al., 2009), in addition to DRD1, DRD3, and DRD5 (Comings et al., 2000; Davis et al., 2009). One study related to the RDS reported that noradrenergic genes such as DBH Taq I, ADRA2A, and ADRA2C were more important in ADHD than dopamine or serotonin genes (Comings & Blum, 2000; Comings et al., 2000). Alterations in the catecholamine-O-methyltransferase (COMT) enzyme, which affects memory and attention, have also been suggested as the common underlying biological mechanism of both disorders (Kapoor, 2008). High levels of COMT activity have been observed in ADHD patients (Eisenberg et al., 1999), and it increases the risk of developing binge eating (Frieling et al., 2006; Mikołajczyk, Śmiarowska, Grzywacz, & Samochowiec, 2006). As literature on the genetic influences of mental illness continue to expand in accordance with the new RDoC matrix, these additional genetic factors should be evaluated in conjunction with the additional repeat sequences, genotype patterns, as well as the genetic factors included within this study.
It is also important to note that the initial hypothesis of the RDS was that defects in dopamine, a neurotransmitter, leads to reward seeking behavior associated with ADHD and EDs. Genetic factors are important because they influence the development and regulation of dopamine. However, genes may be indirect to the true underlying mechanism of the neurobiology of the person.

With a limited number of options, the cited repeat sequences in this study are very common in the general populations. For example with the DRD4 gene, the two, three, four, and seven repeats account for 98% of the population (Lichter et al., 1993), yet not everyone develops ADHD, EDs, or other associated dopamine related mental illnesses. The existence of the repeat pattern might not be as important as the factors causing the gene to manifest as RDS and mental illness.

Similarly, many of the genes described in this study are associated with several other mental health and risk taking outcomes. MAOA is linked to alcoholism and drug abuse (Comings et al., 2000). The DAT1 gene has been linked to delinquency, increased number of sexual partners, binge drinking, smoking quantity and frequency, marijuana use, cocaine and other illegal drug use, and lack of seatbelt use (Guo et al., 2010). The serotonin transporter gene has been linked to marijuana use, neglect, criminal activity, antisocial behaviors, and overall life satisfaction (De Neve, 2011; Vaske, Newsome, & Wright, 2012). The factors that cause dopamine based genetic components to manifest as the RDS and ADHD and EDs as opposed to these other illnesses is not fully understood. Improved understanding in these factors might better explain the biological underlying mechanism and could guide neuroscience based screening tools.

Lastly, It has been suggested that investigations of genetic and environmental interactions that typically focus on one factor at a time may result in constrained views of the social world (Shanahan, Vaisey, Erickson, & Smolen, 2008). The independent analysis of each gene within the current study may be subject to this concern. Along with the constrained view,
the reward deficiency syndrome is polygenic, meaning that many genes and neurotransmitters play a role (Comings et al., 2000). It may not be any gene independently but the combination or interactions of many genes that result in comorbid ADHD/EDs.

Next Steps

As mentioned above, it has been said that investigating genetic and environmental interactions one factor at a time leads to constrained conclusions (Shanahan et al., 2008). This limitation was recognized within a study that aimed to explore the interactions of social capital, DRD2, and educational attainment. In order to overcome the limitation, the study utilized qualitative comparative analysis to determine the multiple combinations of factors leading to their predicted outcome (Shanahan et al., 2008). Based on the conclusion that the model described in this study may be just one of several potential combinations of underlying mechanisms, continued research in this area could benefit from further exploration using similar qualitative comparative analysis techniques. This form of analysis would help establish all possible groupings of factors that lead to comorbid ADHD/ED, which would help continue to improve the overall understanding of the mechanisms that foster the comorbidity in different people.

Although both genetics and the psychosocial and psychiatric factors were included within the model simultaneously, this study did not investigate the many possible direct interactions. Key interacting combinations might have been missed. For example, an interaction between the serotonin transporter gene with stress predicts ADHD severity (Meer et al., 2014). Similarly, gene x environment interactions of the serotonin transporter with home and neighborhood quality predicts self-esteem (Jonassaint et al., 2012). Future investigations should focus on improving our understanding of all mechanisms to the comorbidity as well as their interacting effects. Lastly, due to the limitations of this secondary data analysis and potential measurement concerns, next steps will include comparisons to other large national datasets.
and ultimately primary data collected. This will both allow for the addition of several other potential underlying mechanisms and will be used to verify this study’s findings.

**Implications**

Once the full picture of the underlying mechanisms of ADHD and EDs is understood, next steps include the development of prevention programs and improved treatment plans. This comorbidity has implications in many areas including primary and secondary prevention of EDs, improved treatment plans, prevention of psychostimulant medication abuse, and prevention and treatment of obesity.

**Implications for ED Prevention**

Historically, successful eating disorder prevention programs have been, female-focused, selective as opposed to universal, and targeted to older teens (over fifteen years old) (Stice, Shaw, & Marti, 2007). There has been a noted need for prevention at a universal level that address a broad spectrum of weight-related problems (Ciao et al., 2014). ADHD is most commonly associated with binge eating (Cortese et al., 2007), both of which are then associated with obesity (Cortese et al., 2008). Capitalizing on the comorbidity between ADHD and EDs via targeting children with ADHD for ED prevention efforts may address some of the gaps in the current prevention literature through the prevention of several weight-related problems including binge eating and obesity.

Additionally, secondary prevention is considered a promising area for early intervention of EDs (Ciao et al., 2014). Early detection, or secondary prevention is crucial in that it can increase the likelihood of long-term recovery as delays in treatment are associated with prolonged illness, poor prognosis, and relapse (Agras, 2001; Cavanaugh & Lemberg, 1999; Mitchell, 1995; National Eating Disorder Association, n.d.; Thompson & Smolak, 2001; Thompson & Smolak, 2001). However, less than a third of cases are detected by healthcare
professionals (Keski-Rahkonen et al., 2009). Potential influencing factors of the low rates of early detection may be the lack of effective training and integrated care. The majority of physicians report being dissatisfied with the quality of ED educations in training programs. These deficiencies in education are particularly prominent in the children’s health systems in regards to assessment and treatment among adolescents (Girz et al., 2014), resulting in as many as 90% of family physicians reporting low levels of self-competence with regard to assessment and treatment of EDs in children and adolescents (Girz et al., 2014; Robinson et al., 2013).

The ADHD/ED comorbidity has the potential to impact care integration. Mental health professionals typically treat EDs (Hay, 2013; Smolak & Thompson, 2009; Stein et al., 2009), while ADHD is primarily assessed and treated by primary care physicians (Rader et al., 2009). The lack of integrated care for children with ADHD may contribute to both the low levels of competence among primary care providers and the low rates of early detection. This allows for an opportunity to develop secondary prevention efforts via physicians treating adolescents with ADHD as well as the promotion of care integration through a medical health team (e.g., health homes, accountable care organizations).

The development of a comprehensive model of the underlying mechanisms associated with comorbid ADHD and EDs can help target the specific subset of patients that would most benefit from these prevention efforts as well as additional primary prevention. The understanding of the underlying factors could help develop screening tools to identify the at-risk subset of ADHD patients who then could be targeted for ED prevention.

Concomitantly, improved education of EDs and ED related consequences could be developed and delivered to both parents and adolescents with ADHD. Additional behavioral monitoring plans could be developed and enacted. In additional based on the impulse related eating as well as consequences of ADHD medications on night time eating, (described below), may result in the need for ADHD specific nutrition plans. Dieticians could work with families of
children with ADHD to establish plans specifically to help reduce the potential for binge eating. The improvement of primary and secondary prevention of EDs among children and adolescents with ADHD via identification, referral, education, and monitoring could help address the Healthy People 2020 objective of reducing the prevalence of disorder eating behaviors in adolescents (U.S. Department of Health and Human Services, 2012).

**Implications for Males with EDs**

Implications for ED prevention via children and adolescents with ADHD could also extend to males. It is generally accepted that male EDs are underdiagnosed and misunderstood (Smink et al., 2012; Strother et al., 2012). While binge eating is the most common ED amongst males, to date the literature has focused on exercise behavior (Núñez-Navarro et al., 2012; Stoving et al., 2011; Strother et al., 2012) and restriction among homosexual males (Fernández-Aranda et al., 2004; Shiltz). Despite this lack of information, previous studies have found a significant gender differences in terms of manifestation and symptomology (Núñez-Navarro et al., 2012), risk factors (Strother et al., 2012), and outcomes of EDs (Stoving et al., 2011). Additionally, females are more likely to receive treatment for an ED and also to receive treatment longer than males (Stuhldreher et al., 2012). While outcomes appear to be better among males in terms of time to remission (Stoving et al., 2011), the majority of effective ED prevention efforts and research have been female focused (Ciao et al., 2014).

Information about the male specific determinants and correlates of comorbid ADHD/EDs could help in the development of ED prevention efforts among this at-risk population that currently lack prevention efforts. Moreover, ADHD and binge eating are strongly associated with obesity (Cortese et al., 2008; Cortese et al., 2007; Davis et al., 2006; Nazar et al., 2008), and males with EDs more often have a history of obesity compared to females with EDs.
(Fernández-Aranda et al., 2004; Núñez-Navarro et al., 2012). Thus, the development of ED prevention among males with ADHD may also address the call for prevention of broad spectrum weight-related problems prevention (Ciao et al., 2014).

Implications for Integrated Treatment Plans

The first-line treatment for ADHD is psychostimulant medication (Farber, 2010; Krisanaprakornkit, Ngamjarus, Witoonchart, & Piyavhatkul, 2010; National Institutes of Mental Health, 2008; Rader et al., 2009). The rate of medication use is on the rise. In 2011, 69% of children with an ADHD diagnosis were using medication (Visser et al., 2014). In terms of the general population, in 2011, 6.1% of all children in the United States, or 3.5 million, were using prescribed ADHD medication, up from 4.8% in 2007 (Visser et al., 2014). While stimulants are often very effective in reducing the impairment of ADHD, common side effects of these medications include appetite suppression and weight loss (Farber, 2010; Krisanaprakornkit et al., 2010; National Institutes of Mental Health, 2008; Rader et al., 2009). Some of the issues resulting from psychostimulants might include nighttime binge eating resulting from appetite suppression and decreased daytime food intake followed by increased eating at night when the medications wear off (Racicka, Hanć, Giertuga, Bryńska, & Wolańczyk, 2015).

While psychostimulant medications are common, there are non-stimulant options for children with ADHD including norepinephrine-reuptake inhibitors and antidepressants (Rader et al., 2009). Several antidepressants target dopamine receptors (Rader et al., 2009). The potential dopamine imbalance underlying mechanism of the ADHD/ED comorbidity might suggest that these medications could be a better option for the subset of patients with both disorders. Clinical trials for these treatment options have shown effectiveness; however, these non-stimulant options are typically reserved as a second line option for children that do not respond to psychostimulants (Rader et al., 2009). The use of dopamine targeting
antidepressants would treat the underlying biological factors as opposed to the behavioral manifestations of the RDS. It would also eliminate potential harmful ED related side effects from the stimulants.

The reduced cognitive control underlying mechanism can also inform improved treatment plans. Rather than giving patients with comorbid ADHD/ED a cognitive enhancing medication, patients that are identified as at-risk might benefit from behavioral focused options such as cognitive behavioral therapy. Cognitive behavioral therapy is an effective treatment option for both ADHD and BED (Iacovino, Gredysa, Altman, & Wilfley, 2012; National Institute of Mental Health, 2008; Wilson, Wilfley, Agras, & Bryson, 2010). Additionally, several studies have noted positive outcomes from guided self-help based cognitive behavior therapy on reducing binge eating episodes (Lynch et al., 2010; Striegel-Moore et al., 2010; Wilson et al., 2010). ADHD/ED specific treatment options like cognitive behavioral therapy would allow for collaborative treatment plans in which a single method is used to address both disorders.

Although there are concerns related to the use of psychostimulants among patients with EDs (Farber, 2010; Keshen & Ivanova, 2013), there is also evidence that psychostimulants may be effective in treating BN and BED by reducing binge eating episodes (Dukarm, 2005; Kooij et al., 2004; Sokol, Gray, Goldstein, & Kaye, 1999). On January 30, 2015 the food and drug administration approved the use of Vyvanse, a psychostimulant developed for the treatment of ADHD, for treating BED among adults (U.S. Food and Drug Administration, 2015). This is the first approved medication for BED.

While there have been several published case studies demonstrating positive impacts of psychostimulants on binging (Keshen & Ivanova, 2013; Kooij et al., 2004; Schweickert, Strober, & Moskowitz, 1997; Sokol et al., 1999), FDA approval was based on the findings of three clinical trials including an eleven-week Phase II proof-of-concept, placebo-controlled study and two twelve-week Phase III placebo-controlled studies (Citrome, 2015; McElroy et al., 2015). Phase II tested doses of 30mg, 50mg, and 70mg per day and phase III compared doses of 50mg and
70mg per day with placebo controls. The trials found that both 50mg and 70mg but not 30mg per day resulted in reduced binge eating episodes per week. Phase III effect sizes ranged from 0.83 to 0.97 (Citrome, 2015; McElroy et al., 2015). Phase III reported that 42.2% within the 50mg per day group and 50% in the 70mg per day group achieved binge eating cessation, compared to 21.3% in the placebo group (McElroy et al., 2015). Conclusions stated that short-term treatment with Vyvanse could produce therapeutic effects for BED (Citrome, 2015).

While these medications may help alleviate binging episodes, the long-term impact of psychostimulant use among ED patients as well as the impact on diverse groups is unclear. The majority of trial participants were white and female. Moreover, anyone with comorbid illnesses was excluded (McElroy et al., 2015), which is a particularly noteworthy limitation given the high rates of comorbidities with EDs. The appetite-suppressing side effect was noted as requiring further consideration (Citrome, 2015). To date, the longest trial lasted twelve weeks. A longer fifty-two week open-label trial is underway, although results are not yet available (Citrome, 2015). Despite the lack of long-term data, and information related to diverse groups, as well as those with comorbidities, Vyvanse is now approved and available to patients with BED. In support of psychostimulant treatment options, a review of the available clinical trial data suggested that while cognitive behavioral and interpersonal therapy may be effective for BED, access to these options might be limited due to availability and cost (Citrome, 2015).

Increased understanding of the long-term consequences of using psychostimulants to treat EDs is crucial based on the potential for addiction and physical health consequences. First, psychostimulants are associated with heart issues such as increased blood pressure; this risk may already be elevated in these patients due to the comorbid obesity (McElroy et al., 2015; Striegel-Moore & Franko, 2003). Secondly, the medications are addictive (Farber, 2010). This is of increased concern in the subset of patients as both ADHD and EDs are associated with addiction (Biederman et al., 1999; Biederman et al., 2010; Hudson et al., 2007; Polanczyk & Rohde, 2007). However, it has also been noted that the side effect of decreased appetite may
diminish overtime, reducing risk of abuse for weight loss purposes (Keshen & Ivanova, 2013). Based on the potential for abuse for the purposes of weight loss (Farber, 2010), and the unclear long term effects, there is a need for further investigation of how these medications specifically impact patients with comorbid ADHD/ED (Keshen & Ivanova, 2013). At the very least, until longitudinal investigations have been conducted, increase caution, monitoring, and follow up may be important among patients using psychostimulants to treat BED.

**Implications for Prevention of Psychostimulant Abuse**

There is a concern for the potential of abuse of psychostimulants due to its addictive nature and its potential for cognitive enhancement and weight loss (Farber, 2010). The medications may also lead to subsequent substance abuse problems (Davis et al., 2015).

Evident suggest that psychostimulant abuse is a widespread and growing public health issue. Rates of psychostimulant abuse among grade school and high school students range from 5% to 9% and 5% to 35% among college students (Low & Gendaszek, 2002; Rabiner et al., 2009; Varga, 2012; Wilens et al., 2008). Ritalin is a common psychostimulant used to treat ADHD (National Institute of Mental Health, 2008). Over 90% of the all Ritalin worldwide is prescribed and consumed within the United Stated (Koch, 1999). Moreover, many adolescents lack the knowledge of the potential negative health consequences of psychostimulant abuse (White, Becker-Blease, & Grace-Bishop, 2006). Supporting this lack of awareness, the number of calls to poison control due to psychostimulant abuse among adolescents age thirteen to nineteen rose by 76% between 1998 and 2005 (Setlik, Bond, & Ho, 2009).

While the most common motivation for abuse is enhanced academic or cognitive performance, motives also include “getting high” and weight loss. Several studies that investigated motives for abuse found a small proportion of women who reported abuse for the purposes of weight loss (Rabiner et al., 2009; Varga, 2012). One study reported that 51.7% of psychostimulant abusers endorse weight loss as a motivation for the abuse (Tolleson-Rinehart,
The risk for abuse may be elevated in adolescents with comorbid ADHD/ED. An improved understanding of the impact of medication and long-term consequences of these medications is needed specifically among this subset of patients. Efforts to decrease psychostimulant abuse through alternate treatment plans and secondary prevention through monitoring medication use among children and adolescents with ADHD who are at-risk for co-occurring EDs may significantly impact the risk for prescription medication abuse.

Implications for Obesity Prevention and Treatment

ADHD and binge eating are linked to obesity (Cortese et al., 2007; Davis et al., 2006; Nazar et al., 2008). ADHD is positively correlated with overeating, depressive, and binge eating, which are subsequently positively associated with BMI (Davis et al., 2006). Specifically, individuals with ADHD might fail to plan meals and meal plans, skip meals due to distractions, or have difficulty maintaining intentions to moderate food intake (Pagoto et al., 2009). Most importantly, the presence of both disorders impacts the likelihood of weight loss success. Both ADHD and binge eating are associated with less weight loss success, poor weight loss maintenance, and difficulties with compliance in bariatric surgery follow-up (Alfonsson, Parling, & Ghaderi, 2012; Linde et al., 2004; Nicolau et al., 2013). With as many as 61% of patients seeking treatment for obesity having signs of ADHD, treating the ADHD first could lead to weight loss and decreased need for surgery (Levy, Fleming, & Klar, 2009; Nicolau et al., 2013).

One study of obese patients with newly diagnosed ADHD compared patients that began pharmacotherapy for the ADHD to those that did not accept ADHD treatment. After an average of 466 days of continuous ADHD treatment, patients being treated for ADHD lost an average of 12.36% of their initial weight while the control patients gained an average of 2.78% (Levy et al., 2009). A similar investigation was conducted in Canada and found that patients that accessed ADHD medication treatment lose an average of 10.35% of their initial weight and those that did
not accept treatment gained 7.03% (Gruss, Mueller, Horbach, Martin, & Zwaan, 2012). This suggests that obese patients should be screened for comorbid ADHD/binge eating and patient specific treatment plans focused on the ADHD/ED should be used to reduce the burden of obesity among this subset (Levy et al., 2009). Additionally, vomiting is common among patients post-surgery, however among a sample of post-surgery patients, 60% reported post-op vomiting with 12% admitting to vomiting with the goal of losing weight (de Zwaan et al., 2010). This suggests that issues related to ADHD and EDs among these patients needs to be monitored post-surgery as well as screened prior to surgery (de Zwaan et al., 2010). However, it has been found that the Eating Disorder Examination Questionnaire (EDEQ) does not work the same way among bariatric surgery patients (Hrabosky et al., 2008). Exploratory and confirmatory factor analysis among bariatric patients found a different factor pattern than the original EDEQ (Hrabosky et al., 2008). Additional research is needed to determine or develop the best screening tool for both EDs as well as comorbid ADHD/EDs among this population.

As obesity is associated with a wide range of physical health issues and excess medical costs (Hammond & Levine, 2010; Wilfley et al., 2003), reducing the burden of comorbid ADHD and EDs may indirectly help reduce the overall burden of obesity, which can have significant implications for all aspects of life. The prevention and treatment of obesity among children and adolescents with comorbid ADHD/ED could be focused specifically on the underlying mechanisms of the comorbidity. Specifically, inhibitory control could be a possible treatment target that would both prevent and treat obesity (Reinblatt et al., 2015).

**Support for Care Integration**

A better understanding of the ADHD/ED comorbidity has the potential to impact many fields including adolescent behavioral health, general pediatric practices, ED prevention, and obesity prevention and treatment. Beyond the implications described above, the ADHD/ED comorbidity could impact the integration of physical and mental healthcare. There has been
recent widespread recognition of potential positive implications of integrating care (CDC, 2011). This integration could be essential to overall health, as it would focus on a holistic approach to health (Nardone et al., 2014). A holistic approach to care might improve all aspects of treatment for children and adolescents with co-occurring ADHD, EDs, and obesity, due to the multiple, complex, and interacting underlying mechanisms. The integrated approach could also have implications for the entire family by decreasing the mental and financial burden commonly associated with caring for a child with a mental illness (Bazelon Center for Mental Health Law, n.d.). In general, getting treatment for a child’s physical health condition is easier than treatment for a psychological condition (Glanz & Bishop, 2010). This has led to many issues related to access and coverage in children’s mental health systems. However, due to the fact that ADHD is commonly treated in a primary care setting, training pediatric healthcare providers to identify, monitor, and treat EDs would promote care integration of ADHD, EDs, and obesity, ultimately providing improved holistic care, increased provider competence, and decreased burden for both the child or adolescent and the entire family.

**Conclusion**

The comorbidity of ADHD and EDs may have several negative consequences to overall health and wellbeing. A lack of understanding of the disorder and difficulties treating both disorders in fragmented healthcare systems may lead to continued difficulties for the subset of patients with this comorbidity. Nonetheless, there is a potential for many types of prevention and improved treatment that could greatly impact the quality of life and burden of mental illness related to the comorbidity. However, in order to capitalize on these opportunities, a significant amount of research is still needed. This research should include investigations of additional underlying mechanisms, confirmation through primary data collection, advanced statistical techniques to identify multiple combinations of factors, exploration of male-specific determinants, and direct gender comparisons. Ultimately, research could lead to the
development of improved prevention and treatment that would improve the quality of life for anyone with comorbid ADHD/EDs and decrease the prevalence of both EDs and obesity.
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Appendix A: Confirmatory Factor Analysis of ADHD Symptoms

Figure A1. Confirmatory Factor Analysis of ADHD Symptoms among Females

Notes:
WLSMV Estimator
All < .001
Standardized Estimates (Standard Error)
χ²(dfe=113)=333.66, p<.001; RMSEA=.03; CFI=.96; WRMR=2.03
Figure A2. Confirmatory Factor Analysis of ADHD Symptoms among Males
Appendix B: Confirmatory Factor Analysis of ED Symptoms

In the past 7 days, in order to lose weight or stay the same weight, you:

- Made yourself throw up
- Took weight-loss pills
- Took laxatives
- Used diuretics - that is, water pills
- Took food supplements (powders, herbal supplements, mineral pills, or vitamins to take the place of meals or to reduce appetite)

In the past 7 days, have you:

- Eaten so much in a short period that you would have been embarrassed if others had seen you do it?
- Been afraid to start eating because you thought you wouldn’t be able to stop or control your eating?

Figure B1. Confirmatory Factor Analysis of ED Symptoms among Females

Notes:
WLSMV Estimator
All < .001
Standardized Estimates (Standard Error)
$X^2$ (df=13) = 165.52, p = .001; RMSEA = .01; CFI = .99; WRMR = .68
Figure B2. Confirmatory Factor Analysis of ED Symptoms among Males
Appendix C: Confirmatory Factor Analysis of Family Support Scale

Figure C1. Confirmatory Factor Analysis of Family Support Scale among Females

Notes:
MLR Estimator
All < .001
Standardized Estimates (Standard Error)
X²(30) = 435.04, p < .001; RMSEA = .06; CFI = .95; SRMR = .04
Figure C2. Confirmatory Factor Analysis of Family Support Scale among Males

Notes:
MLR Estimator
All < .001
Standardized Estimates (Standard Error)
χ²(df=19) = 583.46, p < .001; RMSEA = .08; CFI = .90; SRMR = .06
Appendix D: Confirmatory Factor Analysis of Social Support Scale

Figure D1. Confirmatory Factor Analysis of Social Support Scale among Females

Notes:
MLR Estimator
All < .001
Standardized Estimates (Standard Error)
X^2(df=8)=81.54, p<.001; RMSEA=.04, CFI=.98, SRMR=.02
Figure D2. Confirmatory Factor Analysis of Social Support Scale among Males
Appendix E: Confirmatory Factor Analysis of Personality Scales

Figure E1. Confirmatory Factor Analysis of Personality Scales among Females
Figure E2. Confirmatory Factor Analysis of Personality Scales among Males
Appendix F: Confirmatory Factor Analysis of Cognitive Control Scale

Figure F1. Confirmatory Factor Analysis of Cognitive Control Scale among Females

Notes:
MLR Estimator
All <.001
Standardized Estimates (Standard Error)
χ²(df=8)=72.01, p<.001; RMSEA=.04; CFI=.97; SRMR=.02
Figure F2. Confirmatory Factor Analysis of Cognitive Control Scale among Males

Notes:
MLR Estimator
All < .001
Standardized Estimates (Standard Error)
X²(df=8) = 41.18, p < .001; RMSEA = .03; CFI = .98; SRMR = .02